Review Article Efficacy and safety of Guanxin Danshen dropping pills for the treatment of angina pectoris: a meta-analysis

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Abstract: Objective: To evaluate the effect of Guanxin Danshen dropping pills (GDDP) for treating angina pectoris (AP) in patients with coronary heart disease (CHD). Methods: Randomized controlled trials (RCTs) evaluating GDDP for AP in CHD patients were systematically screened from PubMed, Cochrane Library, Web of Science, China Biology Medicine disc (CBM), China National Knowledge Infrastructure (CNKI), China Science and Technology Journal Database (VIP), and WanFang databases from database inception to March 2023. Bias assessment followed the Cochrane Manual 5.1 criteira, and data analysis was performed using RevMan 5.3. Results: Twenty articles were included in the meta-analysis. Compared to standard therapy, GDDP exhibited a superior efficacy in treating AP (P < 0.01), significantly improved electrocardiogram (ECG) outcomes in AP patients (P < 0.00001), reduced frequency of AP episodes (P < 0.01), lowered incidence of cardiovascular events in AP patients (P = 0.01) and significantly elevated hypersensitive C-reactive protein (hs-CRP) and interleukin-18 (IL-18) levels (all P < 0.01). However, it did not significantly affect the levels of interleukin-6 (IL-6), tumor necrosis factor- α (TNF- α), or matrix metalloproteinase-9 (MMP-9) (all P > 0.05). GDDP also reduced total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) levels (all P < 0.01) as well as whole blood viscosity (WBV), plasma viscosity, fibrinogen and hematocrit levels (all P < 0.01). Additionally, the combination of GDDP and conventional CHD treatment was found to be safe. Conclusion: Combining GDDP with conventional western medicine was more effective than either treatment alone in reducing cardiovascular events, alleviating angina symptoms, improving inflammation, and optimizing hemorheological parameters, without increasing side effects. These findings underscore GDDP's use as a complementary treatment for CHD.

Keywords: Guanxin Danshen dropping pill, angina pectoris (AP), coronary heart disease (CHD), systematic evaluation

Introduction

China is currently experiencing a continuous increase in the incidence of cardiovascular diseases, primarily driven by aging of the population [1]. Presently, approximately 11 million individuals in China are affected by coronary heart disease (CHD), making it a significant public health concern. CHD and angina pectoris (AP) are clinical syndromes characterized by inadequate blood supply to the coronary arteries, leading to sudden and temporary myocardial ischemia and hypoxia, with paroxysmal chest pain or discomfort as the predominant symptoms [2]. Importantly, these diseases are not only becoming more prevalent but also affecting individuals at a younger age, and the high morbidity and mortality rates associated with CHD and AP impose substantial economic and emotional burdens on society and affected families [3, 4].

Currently, western medicine, primarily through the use of nitroglycerin with Ca²⁺ channel blockers and β receptor blockers, remains the mainstay therapy for CHD to improve coronary blood flow and reduce myocardial oxygen consumption. Traditional Chinese medicine (TCM), with a history spanning millennia, plays a vital role in disease prevention and treatment. Natural TCM remedies are favored for their distinct advantages over synthetic chemicals, including low toxicity, minimal adverse reactions, and enhanced safety [5]. Over time, TCM has gained increasing acceptance in western societies [6, 7]. Epidemiological surveys have indicated that CHD presently accounts for 50% to 75% of all fatalities related to heart disease, making it the leading cause of cardiovascular-related mortality [8]. Patients suffering from AP often exhibit vulnerable plaques within their coronary arteries. To prevent plaque damage, therapeutic strategies emphasize coronary artery dilation, plaque adhesion inhibition, and reduction of myocardial oxygen consumption [9].

In TCM, CHD-associated AP is attributed to a combination of qi deficiency and blood stagnation, predominantly affecting cardiac function and classified as a syndrome involving both excess and deficiency factors. TCM therapeutic strategies for managing AP in CHD emphasize enhancing blood circulation to alleviate blood stasis while fortifying qi and nourishing the blood [10].

Guanxin Danshen dropping pills (GDDP) consist of a blend of three herbs: Radix Salviae Miltiorrhizae, Radix Notoginseng, and Borneolum Syntheticum. The primary active compound in Salvia Miltiorrhiza is salvianolic acid B [11]. GDDP are indicated for treating chest obstruction arising from gi stagnation and blood stasis, manifesting in symptoms such as chest distress, precordial pain and AP associated with CHD. Clinically used for cardiovascular conditions since its introduction in 1994, GDDP have demonstrated notable efficacy [12]. As a Chinese medicinal product, GDDP has undergone phase II clinical trials in China. Furthermore, the U.S. Food and Drug Administration (FDA) conducted clinical trials on GDDP, granting it entry into the FDA's approval process [13]. Experimental investigations have revealed that GDDP can enhance coronary blood flow and reduce myocardial oxygen consumption. It also increases activities of myocardial superoxide dismutase and plasmin, inhibits lipid peroxidation, and suppresses inflammatory responses around coronary atherosclerotic plaques, ultimately stabilizing these plaques [14]. While existing literature suggests that GDDP holds promise for CHD treatment, much of the evidence comes from studies with relatively small sample sizes, so large-scale, evidence-based research remains limited.

This study aims to evaluate comprehensively the efficacy and safety of GDDP for managing AP, providing evidence-based guidance for its clinical use.

Materials and methods

Literature search

A combination of computer-based and manual retrieval methods was employed to screen relevant studies on the treatment of CHD patients with compound GDDP. Searches were conducted across PubMed, Cochrane Library, Web of Science, CBM, CNKI, VIP, and WanFang databases, from inception to March 2023. This study has been registered in INPLASY (INPLASY2024110043). Chinese searching terms included "Guanxin Danshen Dropping Pills", "CHD", "AP", "meta-analysis", and "systematic review". English searching terms included "Compound Danshen Dropping Pills", "Dan Shen Pill", "Composite Salvia Dropping Pill", "Compound Salvia Droplet Pills", "CHD", "Angina", "meta-analysis", "system evaluation", "systematic review".

Chinese database retrieval formula (Example based on CNKI, adjusted as needed for other Chinese databases):

Serial number retrieval expression

#1 Danshen Dripping Pills

- #2 Compound Danshen Dripping Pills
- #3 Coronary heart disease
- #4 Coronary artery disease
- #5 Acute coronary syndrome
- #6 Angina pectoris
- #7 Unstable angina pectoris
- #8 #3 or #4 or #5 or #6 or #7
- #9 #1 and #9
- #10 #2 and #9

English database retrieval strategy (Example based on PubMed, adjusted as needed for other English databases):

Serial number retrieval expression

- #1 Compound Danshen Dripping Pills
- #2 Coronary heart disease
- #3 Acute coronary syndrome
- #4 Angina pectoris
- #5 Unstable angina
- #6 Unstable angina pectoris
- #7 #2 or #3 or #4 or #5 or #6
- #8 #1 and #7

Inclusion criteria and exclusion criteria

Inclusion criteria: 1) Randomized controlled clinical trials; 2) The intervention regimen involved Guanxin Danshen Dripping Pills in combination with conventional western medicine in the observation group and conventional western medicine alone in control group; 3) Patients with an AP onset age of 35-85 years and who were diagnosed with coronary heart disease (CHD) according to recognized diagnostic criteria.

Exclusion criteria: 1) Case studies, reviews, lectures, abstracts, or research on the same material; 2) Studies involving combined surgical treatments; or 3) Animal studies or cell experiments.

Literature retrieval and evaluation

Literature evaluation, data retrieval, and quality assessment were conducted independently by two reviewers, following the predefined criteria. Disagreements were resolved through discussion or consultation with a third reviewer if necessary. Bias analysis for the included RCTs was performed according to the criteria outlined in Cochrane Manual 5.1.

The quality of the included studies was assessed using the risk of bias evaluation method recommended by the Cochrane Collaboration. This assessment was carried out independently by two investigators, with discrepancies resolved through discussion. Bias assessment included random allocation scheme generation, blinding of participants and personnel, blinding of outcome assessors, data integrity, and selective reporting. Studies were categorized as "low", "unclear", or "high" risk of bias for each criterion.

Observational outcomes

The outcomes included clinical efficacy against angina pectoris, frequency of angina attacks, electrocardiogram efficacy, cardiovascular events, inflammatory response, blood lipid levels, and hemorheology.

Clinical efficacy in angina pectoris was judged by improvement in the severity of angina pain and reduction in the frequency of attacks. Clinical efficacy was evaluated based on the "Criteria for Evaluating the Efficacy of Coronary Heart Disease Angina Pectoris and Electrocardiogram" and the "Clinical Disease Diagnosis Criteria for Healing and Improvement".

Electrocardiogram (ECG) Efficacy: Significant effect: ECG returns to approximately normal or reaches normal levels; Effective: ST segment reduction with recovery > 0.05 mV, partial T wave normalization (e.g., changes from flat to upright), or improvement in atrioventricular/ intraventricular conduction block; Invalid: No significant changes compared to pre-treatment levels; Aggravation: Worsening of ST segment depression, deeper T wave, or T wave changes from flat to inverted.

Statistical analysis

Data were analyzed using RevMan 5.3 software. Funnel plots were used to evaluate potential publication bias for outcomes with ten or more included studies. Binary data were expressed as odds ratio (OR) or relative risk (RR) with 95% confidence intervals (CIs). Continuous outcomes were expressed as standardized mean difference (SMD) or weighted mean difference (WMD) with 95% CIs as the effect measures. When no significant heterogeneity was detected (P \ge 0.10 or I² \le 50%), a fixed-effects model (FEM) was applied. If significant heterogeneity was present (P < 0.10 or $I^2 >$ 50%), a random-effects model (REM) was used. In cases with significant heterogeneity, descriptive analyses were used when heterogeneity

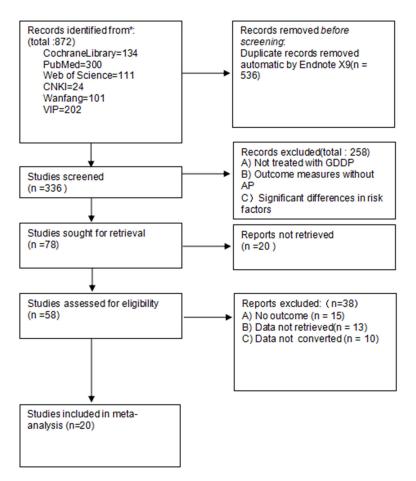


Figure 1. Literature screening process and results.

could not be addressed; sensitivity analysis was conducted by excluding studies contributing to notable statistical heterogeneity to identify sources of variability. If heterogeneity remained substantial after sensitivity analysis, only descriptive analyses were conducted. P < 0.05 signified statistical significance.

Results

Basic information of literature

A total of 872 papers were initially retrieved. After removing 536 duplicates, 336 papers remained for initial screening. After reviewing titles and abstracts, 258 papers were excluded. Subsequent evaluation using the inclusion and exclusion criteria resulted in the final inclusion of 20 papers [15-34], comprising a total of 25,326 patients. The selection process is detailed in **Figure 1**, and the characteristics of the included studies are summarized in **Table 1**. Results of bias risk assessment

All 20 included studies were RCTs with a high level of methodological quality. The bias risk assessment results are presented in **Figure 2** (risk of bias summary) and **Figure 3** (proportion of risk categories).

Meta-analysis results

Treatment efficacy in angina pectoris (AP): Nine RCTs evaluated the effects of GDDP on AP, and the heterogeneity among studies was low (P = 0.91, I² = 0%), supporting the adoption of a FEM. The results showed that the GDDP cohort had significantly higher overall effective rates for improving angina symptoms compared to the controls (OR = 3.95, 95% CI [2.60, 5.99], P < 0.00001; Figure 4).

Frequency of AP attacks: Eleven RCTs evaluated the effects of GDDP on frequency

of AP attacks, and the heterogeneity among studies was low (P = 0.50, I² = 0%), supporting the use of FEM in meta-analysis. The results revealed a reduction in frequency of AP attacks in the GDDP group compared to the controls (SMD = -0.97, 95% CI [-1.22, -0.73], P < 0.00001; **Figure 5**), indicating that additional GDDP treatment outperformed western medicine alone in reducing the frequency of AP attacks.

Electrocardiogram parameters: Eleven RCTs evaluated the effects of GDDP on ECG parameters, and the heterogeneity among studies was low (P = 0.94, $I^2 = 0\%$), supporting the use of FEM for meta-analysis. The results revealed higher effective rates on ECG for the GDDP group compared to the control group (OR = 2.61, 95% CI [1.91, 3.56], P < 0.00001; Figure 6).

Cardiovascular events: Three RCTs evaluated the effects of GDDP on cardiovascular events,

	T :	Types of	Experimental	Control	Intervention	measure	Treatment	Age (yea	irs)	Outcome
First author	CHD Group Group Experimental group		Control group	Course	Experimental group	Control group	Measures			
Xie L [27]	2014	Unstable AP	40	40	GDDP + Routine	Compound Danshen tablets	Eight weeks	62.6	60.9	124
Zhang HX [28]	2014	Stable AP	30	30	GDDP + Isosorbide Mononitrate	Compound Danshen tablets	Six months	35-69	36-70	15
Long YL [29]	2008	Unstable AP	42	38	GDDP + Routine	Routine	Four months	56.74	57.38	124
Li CL [30]	2012	AP of CHD	60	40	Guanxin Danshen dropping pills	Isosorbide mononitrate	Eight weeks	63.6	62.7	24
Li XX [31]	2013	AP of CHD	69	69	GDDP + Routine	Compound Danshen tablets	ompound Danshen tablets Eight weeks		52.9±3.7	234
Xie X [32]	2012	Unstable AP	61	61	Guanxin Danshen dropping pills	Compound Danshen tablets	Eight weeks	57.4	56.7	24
Gao HM [33]	2016	AP of CHD	84	82	GDDP + Routine	Routine	Eight we eks	55.89±10).15	2346
Zhang Q [34]	2012	AP of CHD	48	47	GDDP + Routine	Routine	Two weeks	55.6±7.	8	67
Tan J [35]	2010	Unstable AP	37	20	GDDP + Routine	Routine	Four weeks	51.01±7	.3	(4)(7)
Yang J [36]	2012	AP of CHD	50	50	GDDP + Routine	Routine	Four weeks	62.3±6	.4	467
E LS [37]	2018	AP of CHD	60	60	GDDP + Routine	Routine	Three months	30.58±4.27	40.24±4.79	567
Li L [38]	2013	AP of CHD	53	53	GDDP + Simvastatin	Simvastatin	Four weeks	58.6±7.5	57.3±7.2	67
Wang SK [39]	2019	Unstable AP	122	95	GDDP + Isosorbide Dinitrate	Isosorbide dinitrate	28 d	46-85	43-85	5
Zhang DD [40]	2018	Stable AP	36	36	GDDP + Routine	Routine	Four weeks	66.90	65.2	35
Huang YC [41]	2010	AP of CHD	60	60	Guanxin Danshen dropping pills	Compound Danshen tablets	30 d	60.3±7.	0	25
Qu HY [42]	2016	AP of CHD	32	32	GDDP + Routine	Routine	Four weeks	64.8	63.5	5
Xing CC [43]	2012	Unstable AP	22	21	GDDP + Clopidogrel	Clopidogrel	30 d	65.2±6	.2	47
Shi PX [44]	2014	AP of CHD	40	40	Guanxin Danshen dropping pills	Compound Danshen tablets	Four weeks	63.5±8	.9	24
Cai ZF [45]	2007	Unstable AP	59	60	Guanxin Danshen dropping pills	Routine	Four weeks	65.6	64.7	47
Zhang LL [46]	2013	AP of CHD	20	21	GDDP + Routine	Routine	Six weeks	58.4±9.2	59.3±8.9	25

Table 1. Basic information of included studies

① Cardiovascular events; ② Curative effect of angina pectoris; ③ Attack frequency of angina pectoris; ④ Electrocardiogram curative effect; ⑤ Inflammatory factor index; ⑥ Blood lipid improvement level; ⑦ Hemorheology. The studies included in this table are all from China. GDDP: Guanxin Danshen dropping pills, AP: angina pectoris, CHD: coronary heart disease.

Zhang Q 2012	Zhang LL 2013	Zhang HX 2014	Zhang DD 2018	Yang J 2012	Xing CC 20	Xie X 2012	Xie L2014	Wang SK 2019	Tan J 2010	Shi PX 2014	QU HY 2016	Long YL 2008	Li XX 2013	LI L 2013	Li CL 2012	Huang YC 2010	Gao HM 2016	E LS 2018	Cai ZF 2007	
•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	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)
•	•	•	•	•	~	•	•	•	•	~	•	~	•	•	•	~	•	••	•	Other bias

Figure 2. Risk of bias graph.

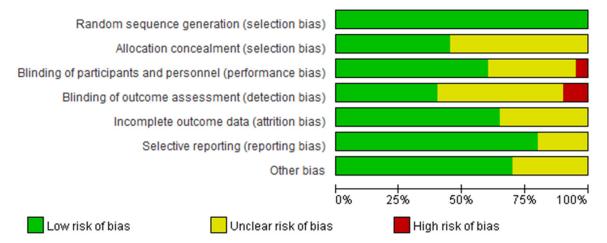


Figure 3. Risk of bias summary.

	Experimental		Contr	ol		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	M-H, Fixed, 95% Cl
Gao HM 2016	76	84	65	82	25.4%	2.48 [1.01, 6.13]	
Huang YC 2010	57	60	48	60	9.7%	4.75 [1.27, 17.82]	
Li CL 2012	56	60	31	40	10.1%	4.06 [1.16, 14.28]	
Li XX 2013	64	69	53	69	15.6%	3.86 [1.33, 11.24]	
Long YL 2008	38	42	28	38	11.4%	3.39 [0.96, 11.94]	
Shi PX 2014	38	40	27	40	5.5%	9.15 [1.91, 43.90]	
Xie L2014	38	40	36	40	7.3%	2.11 [0.36, 12.24]	
Xie X 2012	57	61	46	61	12.2%	4.65 [1.44, 14.96]	
Zhang LL 2013	19	20	14	20	2.8%	8.14 [0.88, 75.48]	· · · · · · · · · · · · · · · · · · ·
Total (95% CI)		476		450	100.0%	3.95 [2.60, 5.99]	•
Total events	443		348				
Heterogeneity: Chi ² = 3	3.21, df = 8	(P = 0.9)	92); I ² = 0	%			
Test for overall effect:	Z = 6.44 (P	< 0.000	0.01 0.1 1 10 100 Favours [experimental] Favours [control]				



and the heterogeneity among studies was low (P = 0.91, $I^2 = 0\%$), supporting the use of FEM in meta-analysis. The results showed a significantly lower rate of cardiovascular events in the experimental group as compared to the

control group (OR = 0.23, 95% CI [0.07, 0.73], P = 0.01; **Figure 7**).

Inflammatory reaction: Five RCTs evaluated the effects of GDDP on inflammatory reac-

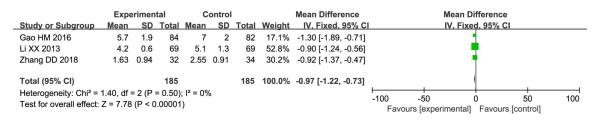


Figure 5. Forest chart of Guanxin Danshen Dripping Pills for improving angina pectoris attack frequency.

	Experime	ental	Contr	ol		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% C	M-H, Fixed, 95% Cl
Cai ZF 2007	14	20	8	18	5.0%	2.92 [0.77, 11.07]	
Gao HM 2016	74	84	62	82	14.8%	2.39 [1.04, 5.48]	
Li CL 2012	45	60	19	40	11.3%	3.32 [1.41, 7.78]	
Li XX 2013	58	69	46	69	14.5%	2.64 [1.17, 5.96]	
Long YL 2008	39	42	27	38	4.0%	5.30 [1.35, 20.79]	
Shi PX 2014	33	40	27	40	9.4%	2.27 [0.79, 6.49]	
Tang Z 2010	27	37	14	20	9.7%	1.16 [0.35, 3.84]	
Xie L2014	37	40	31	40	4.6%	3.58 [0.89, 14.39]	
Xie X 2012	51	61	41	61	13.3%	2.49 [1.05, 5.90]	
Xing CC 20	16	22	9	21	5.0%	3.56 [0.99, 12.73]	
Yang J 2012	45	50	42	50	8.3%	1.71 [0.52, 5.66]	
Total (95% CI)		525		479	100.0%	2.61 [1.91, 3.56]	•
Total events	439		326				
Heterogeneity: Chi ² = 4	4.15, df = 1	0 (P = 0	.94); I ² =	0%			
Test for overall effect:	Z = 6.06 (P	< 0.000	001)				0.01 0.1 1 10 100 Favours [experimental] Favours [control]

Figure 6. Forest diagram of Guanxin Danshen Dripping Pills for improving electrocardiogram parameters.

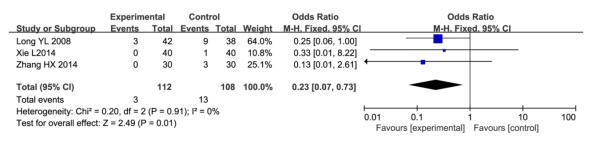


Figure 7. Forest plot of Guanxin Danshen Dropping Pills for reducing cardiovascular events.

tions, and the heterogeneity among studies was substantial (P < 0.00001, I² = 99%), necessitating the use of REM. Subgroup analysis showed markedly reduced hs-CRP levels in the GDDP group compared to controls (SMD = -1.43, 95% CI [-2.20, -0.65], P = 0.0003); however, IL-6 (SMD = -11.88, 95% CI [-27.72, 0.65], P = 0.14), TNF- α (SMD = -1.88, 95% CI [-27.72, -0.65], P = 0.14) and MMP-9 levels (SMD = -25.85, 95% CI [-96.63, 44.930], P = 0.47) were similar between the two groups. Moreover, a significant reduction in IL-18 levels was observed in the OGGD group compared to the controls (SMD =

-22.53, 95% Cl [-37.02, -8.03], P = 0.002; Figure 8).

Blood lipid levels: Five RCTs evaluated the effects of GDDP on blood lipid levels, and the heterogeneity among studies were significant (P < 0.00001, $I^2 = 96\%$), necessitating the use of REM. The results showed significantly greater reductions in TC levels (SMD = -1.18, 95% CI [-1.77, -0.59], P < 0.00001), TG levels (SMD = -1.20, 95% CI [-2.01, -0.05], P = 0.003) and LDL-C levels (SMD = -1.25, 95% CI [-1.89, -0.60], P = 0.002) in GDDP group compared to the control group; however, the reduction in

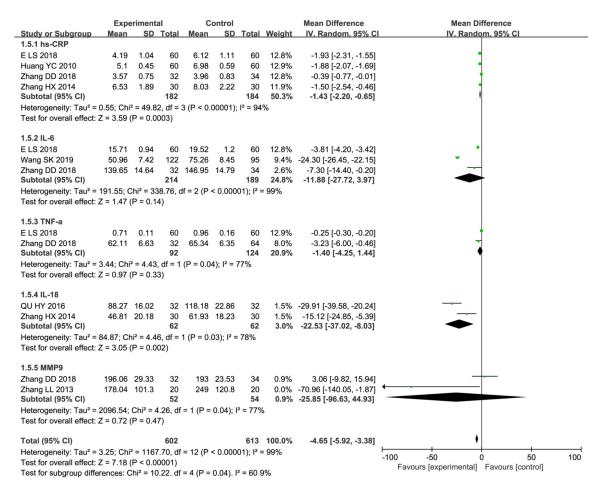


Figure 8. Forest diagram of Guanxin Danshen Dropping Pills for reducing inflammatory reaction.

HDL-C (SMD = 0.73, 95% CI [-0.05, 1.52], P = 0.07) was comparable between the two groups (Figure 9).

Hemorheology: Seven studies, comprising 1,800 patients, evaluated the effects of GDDP on hemorheology, and the heterogeneity among studies was substantial (P < 0.00001, I² = 88%), necessitating the use of REM. The results showed greater improvements were observed in the GDDP group compared to the control group. Specifically, the GDDP group demonstrated significant reductions in plasma viscosity (SMD = -1.11%, 95% CI [-1.30, -0.82], P < 0.00001), fibrinogen levels (SMD = -0.26, 95% CI [-0.30, -0.22], P < 0.00001), and hematocrit levels (SMD = -2.46, 95% CI [-3.11, -1.82], P < 0.00001) (Figure 10).

Adverse reactions: Adverse reactions were monitored in four of the 20 included studies. Most reported adverse reactions were mild gastrointestinal discomfort that required no treatment and did not affect the trials. These findings suggest that GDDP is well-tolerated by study participants.

Sensitivity analysis

For studies where ECG improvement was the primary efficacy indicator, a sensitivity analysis was conducted using data from more than 10 relevant papers. Exclusion of a randomly selected study did not alter the overall results, demonstrating the stability and robustness of the findings (**Figure 11**).

Publication bias evaluation

Publication bias is a recognized concern in systematic reviews, since studies with positive results are often more likely to be published, while studies with negative or neutral outcomes may face challenges in submission or publica-

	Experimental Control				ontrol			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% C	I IV. Random, 95% CI
1.6.1 TC									
E LS 2018	3.34	0.36	60	3.93	0.52	60	5.6%	-1.31 [-1.71, -0.92]	•
Gao HM 2016	4.89	1.15	84	6.74	2.01	82	5.7%	-1.13 [-1.46, -0.80]	4
LI L 2013	5.21	0.83	53	5.78	0.94	53	5.6%	-0.64 [-1.03, -0.25]	· · · · · · · · · · · · · · · · · · ·
Yang J 2012	5.05	0.18	50	5.17	0.36	50	5.6%	-0.42 [-0.81, -0.02]	
Zhang Q 2012	3.08	0.21	48	3.85	0.38	47	5.4%	-2.49 [-3.04, -1.95]	•
Subtotal (95% CI)			295			292	27.8%	-1.18 [-1.77, -0.59]	
Heterogeneity: Tau ² =	0.41; Cł	ni² = 43	3.23, df	= 4 (P <	< 0.000	001); l²	= 91%		
Test for overall effect:	Z = 3.92	! (P < (0.0001)						
1.6.2 TG									
E LS 2018	1.25	0.32	60	1.62	0.55	60	5.6%	-0.82 [-1.19, -0.44]	
Gao HM 2016	1.59	0.5	84	3.08	0.93	82	5.6%	-1.99 [-2.37, -1.62]	•
LI L 2013	1.51	0.76	53	1.72	0.83	53	5.6%	-0.26 [-0.64, 0.12]	
Yang J 2012	1.37	0.36	50	1.55	0.41	50	5.6%	-0.46 [-0.86, -0.07]	1
Zhang Q 2012	1	0.07	48	1.38	0.2	47	5.4%	-2.53 [-3.07, -1.98]	
Subtotal (95% CI)			295			292	27.8%	-1.20 [-2.01, -0.40]	
Heterogeneity: Tau ² =	0.80; Cł	ni² = 78	3.79, df	= 4 (P <	< 0.000	001); l²	= 95%		
Test for overall effect:	Z = 2.92	! (P = 0	0.003)						
1.6.3 LDL-C									
E LS 2018	1.91	0.31	60	2.59	0.55	60	5.6%	-1.51 [-1.92, -1.11]	•
Gao HM 2016	3.07	0.78	84	4.26	1.14	82	5.7%	-1.22 [-1.55, -0.88]	-
LI L 2013	2.75	0.47	53	3.15	0.87	53	5.6%	-0.57 [-0.96, -0.18]	•
Yang J 2012	2.73	0.35	50	2.9	0.43	50	5.6%	-0.43 [-0.83, -0.03]	•
Zhang Q 2012	2.1	0.07	48	2.58	0.25	47	5.4%	-2.61 [-3.16, -2.05]	•
Subtotal (95% CI)			295			292	27.7%	-1.25 [-1.89, -0.60]	
Heterogeneity: Tau ² =	0.50; Cł	ni² = 51	I.07, df	= 4 (P <	< 0.000	001); l²	= 92%		
Test for overall effect:	Z = 3.78	6 (P = 0	0.0002)						
1.6.4 HDL-C									
E LS 2018	1.36	0.3	60	1.23	0.33	60	5.6%	0.41 [0.05, 0.77]	•
LI L 2013	1.89	0.22	53		0.29	53	5.5%	1.58 [1.14, 2.02]	•
Yang J 2012		0.35	50		0.33	50	5.6%	0.23 [-0.16, 0.63]	•
Subtotal (95% CI)		0.00	163		0.00	163	16.7%	0.73 [-0.05, 1.52]	
Heterogeneity: Tau ² =	0.44: Ch	$ni^2 = 23$	3.34. df	= 2 (P <	< 0.000	001): l ²	= 91%		
Test for overall effect:				- (•			/ 0		
Total (95% CI)			1048			1039	100.0%	-0.89 [-1.34, -0.44]	
Heterogeneity: Tau ² =	0.90. Cł	ni² = 38		f = 17 (P < 0 (· · · · · · · · · · · · · · · · · · ·
Test for overall effect:					0.0	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	30 /6		-100 -50 0 50 100
Test for subgroup diffe			,		P = 0	1003) I	2 = 84 3%		Favours [experimental] Favours [control]
reaction subgroup diffe	ences:	- 110	19.12.	ui – 3 (i	- 0.0	5003). I	- 04.3%		

Figure 9. Forest diagram of Guanxin Danshen Dripping Pills for improving blood lipid levels.

tion. To evaluate publication bias, funnel plot analysis was performed for outcome measures related to ECG improvement, since the number of included trials exceeded 10. The funnel plot, based on data from 11 trials assessing the effectiveness rate of improving angina pectoris (AP) in coronary heart disease (CHD), showed that the points were predominantly concentrated in the central and upper regions of the plot and exhibited symmetry on both sides, suggesting an absence of publication bias.

Discussion

Coronary heart disease (CHD) remains a leading cause of global mortality, posing a substantial public health challenge [15]. Given its potential for preventing and treating CHD, Traditional Chinese Medicine (TCM) has garnered increasing research interest [16]. Among TCM formulations, Guanxin Danshen Dropping Pills (GDDP) represent an early form of traditional Chinese patent medicine specifically used for CHD treatment [17]. However, the effectiveness of GDDP in CHD treatment has not been extensively evaluated through largescale multicenter RCTs. Therefore, we conducted a comprehensive evaluation of GDDP's therapeutic benefits in CHD through a meta-analysis comprising 20 studies (n = 2,880 cases). The results revealed significant advantages of combining GDDP with standard treatment, particularly in terms of total effectiveness rate, ECG improvement, angina symptom relief, and improvements in hemorheology. Additionally, the risks of adverse reactions were similar.

CHD is a complex condition involving multiple systems, pathways, and processes, characterized by a coordinated interplay of various mechanisms. It is closely associated with heightened inflammatory responses, disruptions in the

	Expe	erimen	tal	С	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
1.7.1 Whole Blood Vis	scosity								
Cai ZF 2007	4.3	1.1	20	5.31	1.09	18	0.3%	-1.01 [-1.71, -0.31]	
LI L 2013	3.69	1.15	53	4.64	1.17	53	0.7%	-0.95 [-1.39, -0.51]	
Tan J 2010	3.72	1.14	37	4.67	1.16	20	0.4%	-0.95 [-1.58, -0.32]	
Xing CC 20	3.62	1.13	22	4.67	1.16	21	0.3%	-1.05 [-1.73, -0.37]	
Zhang Q 2012	3.58	1.01	48	4.81	1.12	47	0.8%	-1.23 [-1.66, -0.80]	
Subtotal (95% CI)			180			159	2.4%	-1.06 [-1.30, -0.82]	♦
Heterogeneity: Chi ² = I	0.98, df	= 4 (P :	= 0.91)	; I ² = 0%	6				
Test for overall effect:	Z = 8.62	? (P < 0	.00001)					
1.7.2 plasma viscosit	v								
Cai ZF 2007	-	0.16	20	2 1 1	0.32	18	5.2%	-0.55 [-0.71, -0.39]	+
E LS 2018		0.35	60		0.42	60		-0.34 [-0.48, -0.20]	-
LI L 2013		0.23	53		0.32	53		-0.36 [-0.47, -0.25]	•
Tan J 2010		0.21	37	1.93		20		-0.34 [-0.49, -0.19]	-
Xing CC 20	1.58	0.21	22	1.93		20		-0.35 [-0.51, -0.19]	-
Yang J 2012		0.18	50	1.72		50		-0.08 [-0.14, -0.02]	
Zhang Q 2012		0.27	48	1.95		47		-0.47 [-0.57, -0.37]	•
Subtotal (95% CI)	1.40	0.27	290	1.55	0.23	268		-0.26 [-0.30, -0.22]	
Heterogeneity: Chi ² =	7212 4	IF - 6 / F		10043-18	- 020		30.37	-0.20 [-0.30, -0.22]	
Test for overall effect:					- 327	,			
restion overall ellect.	2 - 12.3	13 (F ~	0.0000						
1.7.3 Fibrinogen									
Cai ZF 2007	3.11	0.88	20	3.6	0.72	18	0.5%	-0.49 [-1.00, 0.02]	
E LS 2018		0.41	60		0.49	60		-0.38 [-0.54, -0.22]	+
LI L 2013		5.35	53	3.99		53	0.0%	-0.35 [-2.37, 1.67]	
Tan J 2010		5.36	37		5.25	20	0.0%	-0.32 [-3.20, 2.56]	
Xing CC 20		2.46	22		3.99	21	0.0%	-0.99 [-2.98, 1.00]	
Yang J 2012	2.41	2.3	50		0.67	50		-0.89 [-1.55, -0.23]	
Zhang Q 2012		1.07	48		1.03	47		-0.90 [-1.32, -0.48]	
Subtotal (95% CI)			290			269		-0.47 [-0.61, -0.33]	♦
Heterogeneity: Chi ² =	7.00, df	= 6 (P :	= 0.32)	: I ² = 14	%				
Test for overall effect:	•			•					
				,					
1.7.4 Hematocrit									
Cai ZF 2007		2.16	20		2.12	18		-2.00 [-3.36, -0.64]	
LI L 2013	47.48	3.01	53	48.03	3.12	53	0.1%	-0.55 [-1.72, 0.62]	
Tan J 2010	44.33	2.36	37	48.38	2.12	20	0.1%	-4.05 [-5.25, -2.85]	
Xing CC 20	45.33	4.36		49.38		21	0.0%	-4.05 [-6.09, -2.01]	
Yang J 2012	40.96	6.6		44.24	4.26	50		-3.28 [-5.46, -1.10]	
Subtotal (95% CI)			182			162	0.3%	-2.46 [-3.11, -1.82]	◆
Heterogeneity: Chi ² =					= 80%				
Test for overall effect:	Z = 7.51	(P < 0	.00001)					
Total (95% CI)			942			858	100.0%	-0.30 [-0.34, -0.26]	
Heterogeneity: Chi ² =	192.15.	df = 23) (P < 0	.000011); ² = 8				
Test for overall effect:									-4 -2 0 2 4
Test for subgroup diffe					(P < 0.	00001)	. I² = 96.7	%	Favours [experimental] Favours [control]
= 1									

Figure 10. Forest diagram of Guanxin Danshen Dripping Pills for improving hemorheology.

coagulation and fibrinolytic systems, and hemodynamic alterations. The primary pathologic processes in CHD encompass an increased release of inflammatory mediators such as IL-6, hs-CRP, and IL-18, along with hemodynamic changes [18]. Elevated levels of TC, TG, and LDL-C can contribute to the formation of arterial plaques, while HDL-C aids in transporting cholesterol from peripheral tissues back to the liver for metabolism, exerting a protective effect [19, 20]. Abnormal hemorheology, including increased blood viscosity, is known to escalate the risk of cardiovascular diseases [21]. Research [22] has shown that atherosclerosis represents a chronic inflammatory process characterized by progressive thickening of arterial walls. Increased levels of inflammatory factors such as hs-CRP, IL-6, TNF-α, MMP-9, and SVCAM-1 can accelerate the development of atherosclerosis, rendering these inflammatory markers as risk factors for CHD [23]. Although interventional therapy, antiplatelet therapy, and lipid-lowering interventions have demonstrated efficacy in reducing cardiovascular events, patients with CHD still face a substantial risk. Our study reveals that CHD patients benefit from significant improvements in blood lipid profiles and hemorheology, along with a reduction in inflammatory marker levels, thereby mitigating CHD risk. These findings suggest that adding GDDP to conventional therapy can enhance overall clinical efficacy.

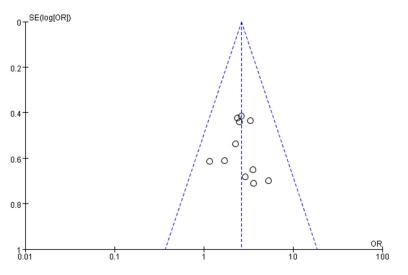


Figure 11. Funnel diagram.

Adverse reaction reports from the included studies indicated that only a small number of patients experienced mild gastrointestinal reactions. These effects were alleviated by adjusting the administration timing to after meals, indicating that GDDP are generally welltolerated and safe. However, it is essential to ensure the rational use of GDDP in clinical practice by adhering to prescribed instructions and applying TCM syndrome differentiation principles [24]. This approach is crucial to reduce side effects and optimize treatment safety.

In recent years, GDDP [14] has increasingly gained recognition as a widely used TCM medicine and an effective therapeutic option for managing CHD-associated AP. Its popularity is attributed to several advantages, including ease of administration, precise efficacy, high safety profile, minimal adverse reactions and enhanced therapeutic outcomes when used in conjunction with western medicine. Additionally, a randomized trial [25] highlighted an additional benefit of GDDP in significantly reducing patients' anxiety levels, offering dual benefits for both the heart and mental well-being. Overall, these findings offer strong evidence supporting the clinical application of GDDP.

This study comprehensively evaluated GDDP, focusing on its efficacy, safety, and other relevant indicators. The results indicate that GDDP exhibits notable therapeutic effectiveness in managing AP in patients with CHD. Key benefits include the improvement in ischemic electrocardiogram patterns, reductions in cholesterol and triglyceride levels, and enhancements in heart rate variability with minimal side effects. The observed differences in efficacy between GDDP and control interventions may be influenced by the relatively low methodological quality of the analyzed trials. Notably, the absence of multicenter, large-scale randomized trials is a limitation. Furthermore, some scholars have pointed out the potential for biased interpretations in countries with exceptionally high rates of positive outcomes [26].

Consequently, the possibility that negative test results for GDDP have not been published cannot be ruled out. Therefore, for a more robust understanding of GDDP's efficacy in CHD treatment, rigorously designed large-sample double-blind randomized placebo-controlled trials are essential.

This study has certain limitations that should be acknowledged: (1) Some studies did not report cases of dropout or exclusion, possibly introducing selectivity and measurement bias, which could impact the reliability of research findings; (2) Most of the papers are derived from research conducted by Chinese scholars, which may restrict the generalizability of the findings and this underscores the need to broaden the sample size. For future clinical trials, we recommend implementing randomization with concealed allocation, employing blind methods, and incorporating placebo controls whenever feasible. Detailed records and reporting of cases withdrawn from the trial and those lost to follow-up are essential. Additionally, long-term follow-up after treatment and reporting of crucial clinical outcomes should be conducted, and the use of internationally recognized rating scales and objective indices for evaluating treatment efficacy is advisable.

Conclusion

GDDP combined with conventional western medicine can reduce cardiovascular event risks among patients with CHD. It effectively improves clinical symptoms, lowers inflammatory responses, and does not increase the incidence of adverse reactions. These findings support the viability of GDDP as a therapeutic adjunct for managing CHD.

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Disclosure of conflict of interest

None.

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