Scientific Research Publishing

Journal of Biosciences and Medicines, 2025, 13(8), 436-450
https://www.scirp.org/journal/jbm
ISSN Online: 2327-509X
ISSN Print: 2327-5081

Exploring the Medication Rules of Traditional Chinese Medicine in the Treatment of Coronary Heart Disease Complicated with Depression Based on Data Mining

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How to cite this paper: Zheng, C.C., Yang, L.Q. and Zeng, Q.Q. (2025) Exploring the Medication Rules of Traditional Chinese Medicine in the Treatment of Coronary Heart Disease Complicated with Depression Based on Data Mining. *Journal of Biosciences and Medicines*, **13**, 436-450.
https://doi.org/10.4236/jbm.2025.138034

Received: July 21, 2025
Accepted: August 23, 2025
Published: August 26, 2025

Abstract

Objective: To explore the medication and prescription rules of traditional Chinese medicine (TCM) compounds in the treatment of coronary heart disease complicated with depression, so as to provide data support for the treatment of coronary heart disease complicated with depression by the method of strengthening the spleen, soothing the liver, promoting blood circulation, and resolving phlegm, and to innovate ideas for clinical treatment. **Methods:** The data of TCM literature on the clinical treatment of coronary heart disease complicated with depression published publicly by April 30, 2025, were mined; a target database was constructed, and the TCM Inheritance Assistant System of the China Academy of Chinese Medical Sciences was used to conduct statistical analyses on syndromes, drug frequencies, properties and flavors, meridian tropisms, efficacies, association rules, cluster analysis, etc. of the literature data. **Results:** A total of 154 studies, 157 effective TCM compounds, and 161 TCM herbs were included in this study. The main TCM syndromes of the disease were liver depression, qi stagnation, blood stasis, phlegm-blood stasis, spleen deficiency, qi deficiency, phlegm turbidity, etc.; the corresponding treatment principles included soothing the liver and relieving depression, promoting blood circulation to remove blood stasis, resolving phlegm and removing turbidity, calming the mind and stabilizing the will, strengthening the spleen and replenishing qi, etc.; 14 herbs, such as *Bupleurum chinense*, were high-frequency herbs. The properties and flavors of the drugs were mainly

cold, warm, neutral, bitter, pungent, and sweet, and most of them entered the liver, spleen, lung, and heart meridians. The main efficacies of the drugs were tonifying deficiency, promoting blood circulation to remove blood stasis, and regulating qi. The results of the drug association rule analysis showed 21 pairs of drugs with high support and 27 drug associations with high confidence. The drug cluster analysis yielded 5 groups of clustered prescriptions. After removing duplicates and integrating the high-frequency clustered prescriptions (≥30 frequencies), the core prescription for the treatment of coronary heart disease complicated with depression was obtained (*Bupleurum chinense*, *Glycyrrhiza uralensis*, *Poria cocos*, *Ligusticum chuanxiong*, *Codonopsis pilosula*, *Atractylodes macrocephala*, *Salvia miltiorrhiza*, *Curcuma aromatica*, *Cyperus rotundus*, *Pinellia ternata*, *Trichosanthes kirilowii*). **Conclusion:** The core pathogenesis of coronary heart disease complicated with depression is deficiency of both the heart and spleen, liver depression and qi stagnation, and mutual binding of phlegm and blood stasis. The disease location mainly involves the heart, liver, and spleen. The treatment is mainly based on strengthening the spleen, soothing the liver, promoting blood circulation, and resolving phlegm.

Keywords

Coronary Heart Disease Complicated by Depression, Treatment with Traditional Chinese Medicine, Medication Rules, Data Mining

1. Introduction

Dual-heart disease refers to the coexistence of cardiovascular disease and mental illness, which interact to form complex pathophysiological changes. Coronary heart disease (CHD) complicated by depression is the most common clinical type [1]. Statistics show that the incidence of depression in CHD patients is approximately 15% - 30%, and it increases to 30% - 60% after acute myocardial infarction. Moreover, CHD patients with depression have a significantly higher incidence of cardiovascular accidents [2]. With population aging and changes in work and living pressures, the morbidity and mortality of CHD complicated by depression have increased annually, imposing growing economic and life burdens on society, especially in underdeveloped ethnic regions, and have become a major public health concern. Therefore, analyzing the medication and prescription rules for this disease can provide theoretical support for subsequent diagnosis, treatment, and medication.

2. Materials and Methods

2.1. Literature Sources

Data were retrieved from TCM digital libraries, CNKI, Wanfang Data, VIP Database, Web of Science, and PubMed, covering publicly published TCM clinical lit-

erature from database inception to April 30, 2025.

2.2. Search Strategy

The retrieval was conducted using keyword-based searches. For Chinese databases, advanced searches were performed by combining terms related to coronary heart disease (CHD), including "冠心病" (coronary heart disease), "心肌缺血性心脏病" (myocardial ischemic heart disease), "冠状动脉病" (coronary artery disease), "冠状动脉粥样硬化性心脏病" (coronary atherosclerotic heart disease), "心绞痛" (angina pectoris), "心肌梗死" (myocardial infarction), "胸痹" (chest impediment), "心痹" (heart impediment), "胸痛" (chest pain), and "真心痛" (true heart pain), with terms related to depression, such as "抑郁症" (depression), "抑郁综合征" (depressive syndrome), "心境障碍" (mood disorder), "情感障碍" (affective disorder), "郁证" (depressive syndrome in TCM), "百合病" (lily disease), and "脏躁" (hysteria). For foreign databases, the search term employed was "Coronary heart disease AND Depression".

2.3. Inclusion Criteria

Literature must meet all the following conditions: 1) Clear diagnosis of CHD complicated with/associated with depression by modern medicine; 2) Treatment based on TCM compound prescriptions; 3) TCM compounds with clinical efficacy; 4) Clear composition and dosage of TCM compounds; 5) Oral administration route.

2.4. Exclusion Criteria

Literature was excluded if it met any of the following: 1) Literature types, such as research progress, meta-analyses, conference papers, pure animal experiments, or pharmacological studies; 2) Literature with unclear composition or dosage of proprietary Chinese medicines or hospital preparations; 3) Literature on ethnic minority herbal compounds; 4) Literature with erroneous data.

2.5. Database Establishment and Standardization

2.5.1. Database Establishment

The retrieved literatures were used by two researchers to independently extract information such as traditional Chinese medicine prescriptions, syndrome types, and efficacy indicators from the literatures. The literatures were imported into artificial intelligence models (DeepSeek, Kimi) for review, and the objectivity of data extraction was ensured through a consistency test (Kappa = 0.85). Discrepancies were resolved through third-party review to reduce information bias. A database for traditional Chinese medicine treatment of coronary heart disease complicated with depression was established.

2.5.2. Database Standardization

Aliases and alternative names of TCM herbs in the literature were standardized according to the 2020 edition of *Pharmacopoeia of the People's Republic of China*

(e.g., "夜交藤" was standardized to "首乌藤"). Herb names with different processing methods were also standardized (e.g., "法半夏" was standardized to "半夏").

3. Results

3.1. Literature Inclusion

A total of 1320 Chinese literature sources were initially retrieved. After removing non-target and duplicate literature by two researchers with AI assistance, 154 target literature sources were included, involving 157 effective TCM compounds and 161 TCM herbs after deduplication and integration. The compound categories included qi-regulating, blood-regulating, phlegm-resolving, harmony-restoring, tonifying, and mind-calming formulas. Search procedures and results are shown in Figure 1.

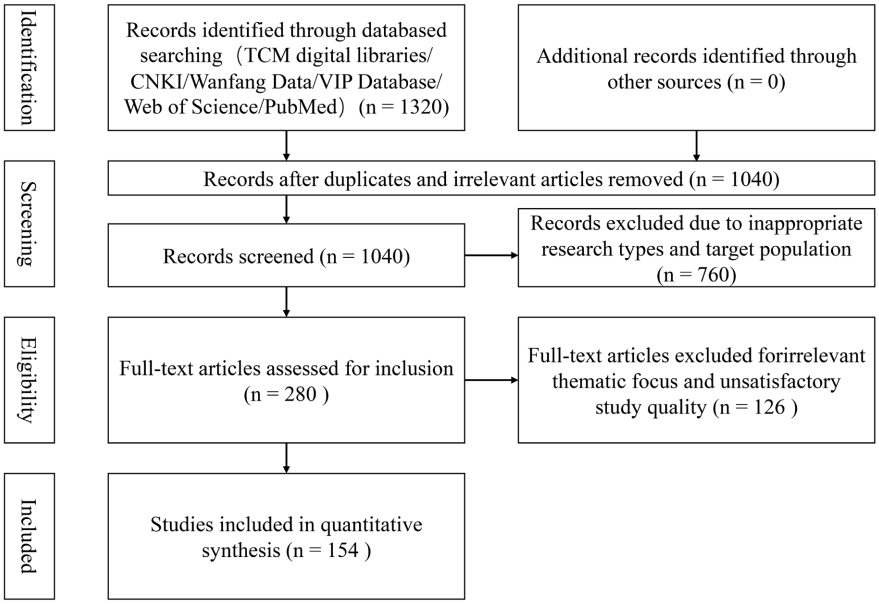

Figure 1. Search procedures and results.

3.2. Data Statistics

3.2.1. Disease Syndromes

Statistical analysis of syndromes in 154 publications showed that syndromes with frequencies ≥ 20 were: liver depression (72.08%), qi stagnation (48.70%), blood stasis (35.71%), phlegm-blood stasis (25.97%), spleen deficiency (19.48%), qi deficiency (14.29%), and phlegm turbidity (12.99%).

3.2.2. Treatment Principles

Statistical analysis of TCM treatment principles in 154 literatures showed that the principles with frequencies ≥ 30 were: soothing the liver (72.73%), promoting blood circulation (61.69%), resolving phlegm (36.36%), calming the mind (32.47%), relieving depression (27.92%), strengthening the spleen (20.13%), and replenishing qi (19.48%).

3.2.3. Herb Frequency Statistics

Herbs with frequencies ≥ 25 in the 157 compounds are shown in Table 1.

Table 1. Statistics of high-frequency herbs.

No.	Herb	Frequency	Frequency (%)	No.	Herb	Frequency	Frequency (%)
1	*Bupleurum chinense*	112	71.34	12	*Codonopsis pilosula*	38	24.20
2	*Glycyrrhiza uralensis*	95	60.51	13	*Atractylodes macrocephala*	37	23.57
3	*Ligusticum chuanxiong*	84	53.50	14	*Trichosanthes kirilowii*	35	22.29
4	*Salvia miltiorrhiza*	79	50.32	15	*Paeonia lactiflora* var. *rubra*	33	21.02
5	*Poria cocos*	72	45.86	16	*Albizia julibrissin*	31	19.75
6	*Paeonia lactiflora*	72	45.86	17	*Corydalis yanhusuo*	31	19.75
7	*Curcuma aromatica*	69	43.95	18	*Ziziphus jujuba* var. *spinosa*	30	19.11
8	*Angelica sinensis*	51	32.48	19	*Os draconis*	26	16.56
9	*Citrus aurantium*	50	31.85	20	*Citrus reticulata*	26	16.56
10	*Cyperus rotundus*	49	31.21	21	*Astragalus membranaceus*	25	15.92
11	*Pinellia ternata*	46	29.30	22	*Concha ostreae*	25	15.92

3.2.4. Statistics of Herb Nature, Flavor, and Meridian Tropism

For herb nature, cold herbs were most frequently used (630 times, 54.12%), followed by warm herbs (594 times, 51.03%) and neutral herbs (406 times, 34.88%); cool and hot herbs were less used (Figure 2). For flavors, bitter herbs were most common (935 times, 34.93%), followed by pungent herbs (738 times, 27.57%) and sweet herbs (731 times, 27.31%); sour and salty herbs were less used (Figure 3). For meridian tropism, herbs mainly entered the liver meridian (904 times, 19.59%), followed by the spleen meridian (835 times, 18.10%), the lung meridian (787 times, 17.06%), and the heart meridian (782 times, 16.95%) (Figure 4).

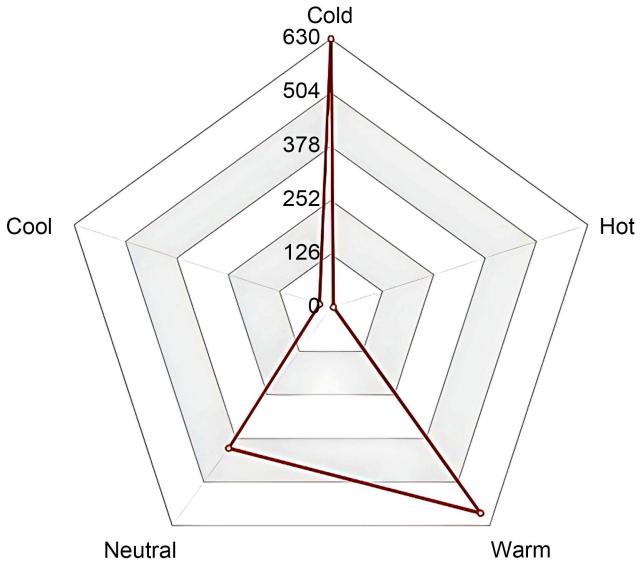

Figure 2. Distribution of herb natures.

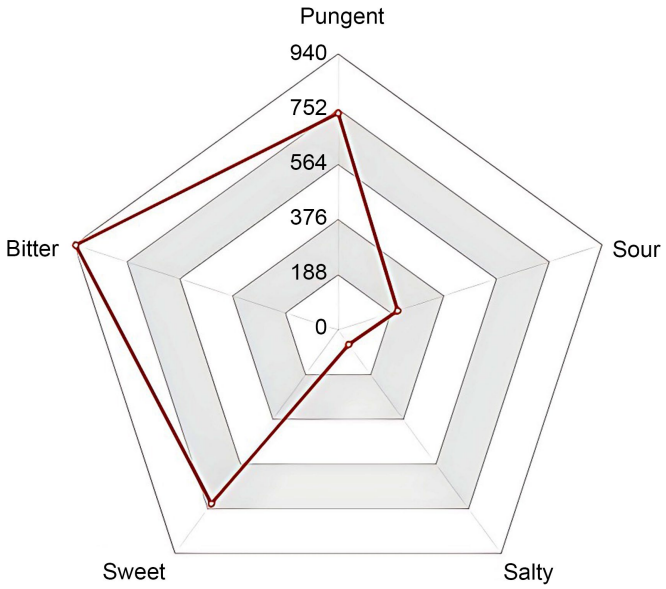

Figure 3. Distribution of herb flavors.

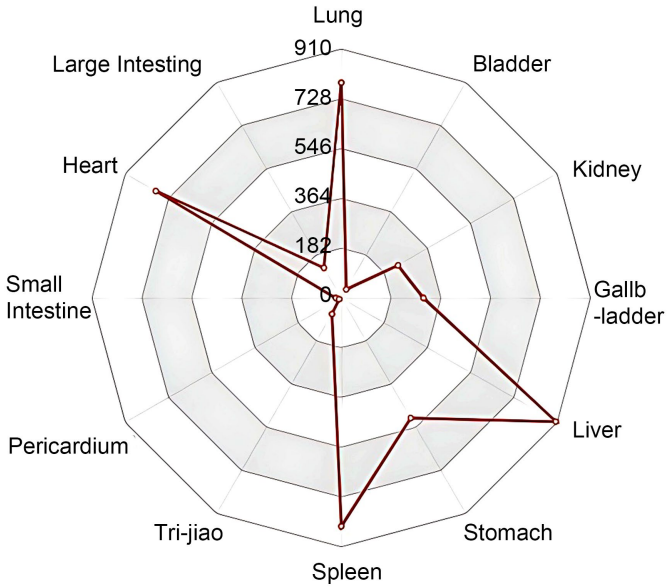

Figure 4. Distribution of herb meridian tropisms.

3.2.5. Efficacy Statistics

Herb efficacies with frequencies > 80 are shown in **Table 2**.

Table 2. Statistics of herb efficacies.

No.	Efficacy Category	Frequency	Frequency (%)	No.	Efficacy Category	Frequency	Frequency (%)
1	Tonifying deficiency	423	25.42	10	Astringent	27	1.62
2	Promoting blood circulation and removing stasis	323	19.41	11	Hemostatic	26	1.56

Continued

3	Regulating qi	210	12.62	12	Resuscitating	23	1.38
4	Relieving exterior syndrome	167	10.04	13	Resolving dampness	20	1.20
5	Clearing heat	105	6.31	14	Purgative	9	0.54
6	Calming the mind	96	5.77	15	Promoting digestion	8	0.48
7	Resolving phlegm, relieving cough and asthma	96	5.77	16	Warming interior	5	0.30
8	Promoting diuresis and draining dampness	82	4.93	17	Dispelling wind-dampness	1	0.06
9	Calming the liver and extinguishing wind	43	2.58	/	/	/	/

3.2.6. Association Rule Analysis

Association rule analysis of all herbs (support ≥ 40, confidence ≥ 0.60) identified 21 high-support herb pairs and 27 high-confidence herb associations. Core herbs included *Bupleurum chinense*, *Glycyrrhiza uralensis*, *Paeonia lactiflora*, *Ligusticum chuanxiong*, *Curcuma aromatica*, *Salvia miltiorrhiza*, *Poria cocos*, *Citrus aurantium*, and *Cyperus rotundus* (Table 3, Table 4, Figure 5).

Table 3. Statistics of Herb Pairs (Support ≥ 40).

No.	Herb Pair	Frequency	No.	Herb Pair	Frequency
1	*Bupleurum chinense*, *Glycyrrhiza uralensis*	71	12	*Bupleurum chinense*, *Glycyrrhiza uralensis*, *Paeonia lactiflora*	46
2	*Bupleurum chinense*, *Paeonia lactiflora*	66	13	*Bupleurum chinense*, *Citrus aurantium*	45
3	*Bupleurum chinense*, *Ligusticum chuanxiong*	65	14	*Glycyrrhiza uralensis*, *Salvia miltiorrhiza*	44
4	*Bupleurum chinense*, *Curcuma aromatica*	60	15	*Bupleurum chinense*, *Cyperus rotundus*	44
5	*Bupleurum chinense*, *Salvia miltiorrhiza*	54	16	*Glycyrrhiza uralensis*, *Poria cocos*	44
6	*Glycyrrhiza uralensis*, *Ligusticum chuanxiong*	51	17	*Ligusticum chuanxiong*, *Cyperus rotundus*	43
7	*Ligusticum chuanxiong*, *Paeonia lactiflora*	50	18	*Glycyrrhiza uralensis*, *Curcuma aromatica*	42
8	*Bupleurum chinense*, *Ligusticum chuanxiong*, *Paeonia lactiflora*	49	19	*Bupleurum chinense*, *Glycyrrhiza uralensis*, *Ligusticum chuanxiong*	41
9	*Ligusticum chuanxiong*, *Salvia miltiorrhiza*	49	20	*Bupleurum chinense*, *Paeonia lactiflora*, *Curcuma aromatica*	40
10	*Bupleurum chinense*, *Poria cocos*	48	21	*Paeonia lactiflora*, *Curcuma aromatica*	40
11	*Glycyrrhiza uralensis*, *Paeonia lactiflora*	48	/	/	/

Table 4. Analysis of herb association rules (Confidence ≥ 0.60).

No.	Association Rule	Confidence	No.	Association Rule	Confidence
1	*Paeonia lactiflora*, *Curcuma aromatica* → *Bupleurum chinense*	1.00	15	*Salvia miltiorrhiza* → *Bupleurum chinense*	0.69
2	*Ligusticum chuanxiong*, *Paeonia lactiflora* → *Bupleurum chinense*	0.98	16	*Paeonia lactiflora* → *Ligusticum chuanxiong*	0.69
3	*Glycyrrhiza uralensis*, *Paeonia lactiflora* → *Bupleurum chinense*	0.96	17	*Bupleurum chinense*, *Curcuma aromatica* → *Paeonia lactiflora*	0.67
4	*Paeonia lactiflora* → *Bupleurum chinense*	0.92	18	*Poria cocos* → *Bupleurum chinense*	0.67
5	*Cyperus rotundus* → *Bupleurum chinense*	0.90	19	*Paeonia lactiflora* → *Glycyrrhiza uralensis*	0.67
6	*Citrus aurantium* → *Bupleurum chinense*	0.90	20	*Bupleurum chinense*, *Glycyrrhiza uralensis* → *Paeonia lactiflora*	0.65
7	*Cyperus rotundus* → *Ligusticum chuanxiong*	0.88	21	*Salvia miltiorrhiza* → *Ligusticum chuanxiong*	0.63
8	*Curcuma aromatica* → *Bupleurum chinense*	0.87	22	*Bupleurum chinense* → *Glycyrrhiza uralensis*	0.63
9	*Glycyrrhiza uralensis*, *Ligusticum chuanxiong* → *Bupleurum chinense*	0.80	23	*Bupleurum chinense*, *Ligusticum chuanxiong* → *Glycyrrhiza uralensis*	0.63
10	*Ligusticum chuanxiong* → *Bupleurum chinense*	0.77	24	*Bupleurum chinense*, *Paeonia lactiflora* → *Curcuma aromatica*	0.61
11	*Glycyrrhiza uralensis* → *Bupleurum chinense*	0.75	25	*Ligusticum chuanxiong* → *Glycyrrhiza uralensis*	0.61
12	*Bupleurum chinense*, *Ligusticum chuanxiong* → *Paeonia lactiflora*	0.75	26	*Poria cocos* → *Glycyrrhiza uralensis*	0.61
13	*Bupleurum chinense*, *Paeonia lactiflora* → *Ligusticum chuanxiong*	0.74	27	*Curcuma aromatica* → *Glycyrrhiza uralensis*	0.61
14	*Bupleurum chinense*, *Paeonia lactiflora* → *Glycyrrhiza uralensis*	0.70	/	/	/

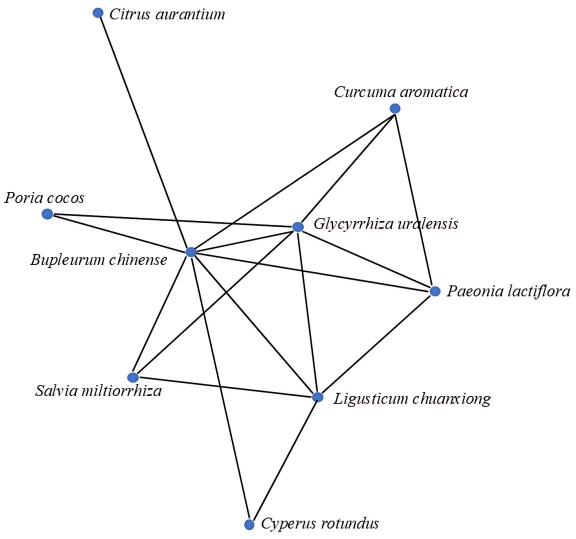

Figure 5. Network topology of core herbs.

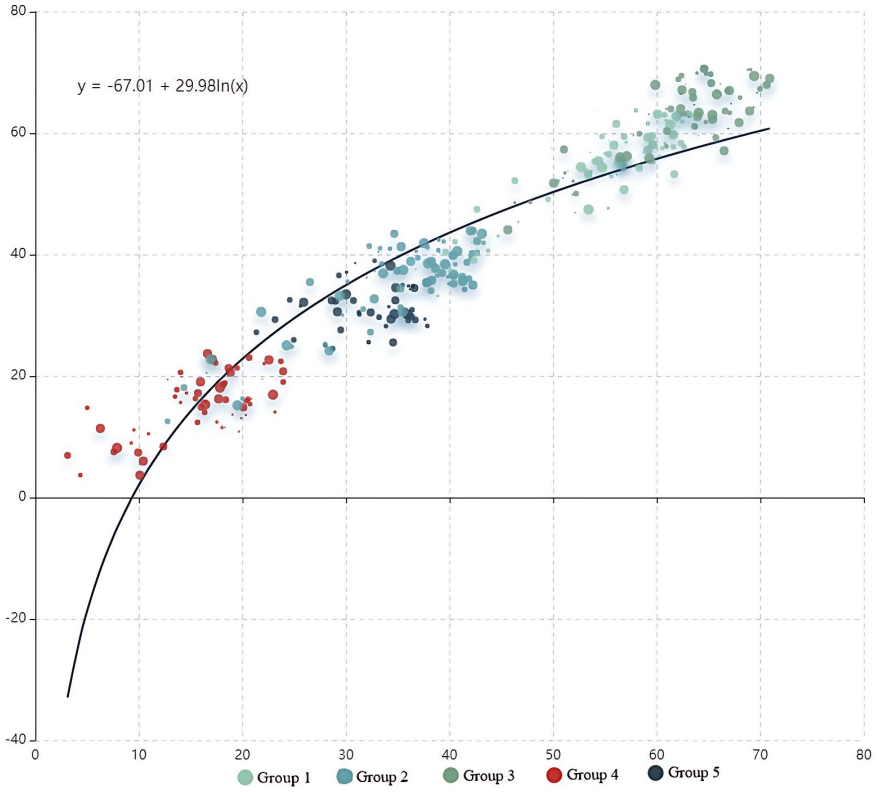

Figure 6. Cluster analysis of core herb combinations.

3.2.7. Cluster Analysis

Cluster analysis (K = 5, validated by the K-means algorithm and regression simulations) identified 5 core herb combinations, with 3 groups having frequencies > 30 (**Table 5**, **Figure 6**).

Table 5. Statistics of core herb combinations.

No.	Core Herb Combination	Prescriptions (n)
1	*Bupleurum chinense*, *Poria cocos*, *Glycyrrhiza uralensis*, *Ligusticum chuanxiong*, *Codonopsis pilosula*, *Atractylodes macrocephala*	42
2	*Bupleurum chinense*, *Salvia miltiorrhiza*, *Curcuma aromatica*, *Glycyrrhiza uralensis*, *Paeonia lactiflora*, *Cyperus rotundus*	41
3	*Pinellia ternata*, *Glycyrrhiza uralensis*, *Bupleurum chinense*, *Poria cocos*, *Trichosanthes kirilowii*, *Ligusticum chuanxiong.*	37
4	*Carthamus tinctorius*, *Paeonia lactiflora* var. *rubra*, *Glycyrrhiza uralensis*, *Angelica sinensis*, *Ligusticum chuanxiong*, *Bupleurum chinense.*	22
5	*Bupleurum chinense*, *Curcuma aromatica*, *Paeonia lactiflora*, *Ligusticum chuanxiong*, *Concha ostreae*, *Os draconis.*	15

4. Discussion

Traditional Chinese medicine (TCM) does not have a specific term for CHD complicated with depression, which falls under the categories of "心痛" (heart pain),

"胸痹" (chest impediment), "胸痛" (chest pain) combined with "郁证" (depression syndrome), "百合病" (lily disease), and "脏躁" (hysteria). Symptoms include chest pain, chest tightness, palpitations, shortness of breath, sighing, lethargy, poor appetite and sleep, fatigue, a dark tongue with a white greasy coating, and a thready, string-like, or deep pulse. TCM physicians have long recognized the interaction between zang-fu organs, qi movement, and emotions. *Su Wen·Ling Lan Mi Dian Lun* states, "The heart is the monarch organ, from which spirit brilliance emanates." *Ling Shu·Ben Shen* notes, "Grief, sorrow, worry, and anxiety disturb the heart; when the heart is disturbed, all zang-fu organs shake" and "Deficiency of heart qi leads to sadness, while excess leads to incessant laughter." *Su Wen·Ju Tong Lun* describes, "Anger causes qi to rise; joy causes qi to relax; sorrow causes qi to dissipate; fear causes qi to sink; shock causes qi to become chaotic; overthinking causes qi to stagnate." *Jin Kui Yao Lue·Xiong Bi Xin Tong Duan Qi Bing Mai Zheng Zhi Jiu* records, "Pulse examination should identify excess and deficiency; faint yang and tight yin pulses indicate chest impediment and pain, resulting from extreme deficiency. Yang deficiency in the upper jiao and tight yin pulses cause chest impediment and heart pain." *Lin Zheng Zhi Nan Yi An* states, "Depressive disorders always start with qi disease; when qi flows smoothly, there is no depression." *Dan Xi Xin Fa·Liu Yu* emphasizes, "Harmony of qi and blood prevents disease; depression gives rise to various illnesses." With social and economic development, changes in lifestyle, and work pressure, TCM physicians vary in clinical medication based on regional environment, constitution, and personal experience.

All included prescriptions in this study clearly specified disease names, formula names, herb names, and dosages, with no forbidden herb combinations or highly toxic herbs, and no reported adverse reactions. Prescription composition and dosages were appropriate, with reasonable monarch-minister-assistant-guide 配伍, reflecting the rationality and safety of TCM in disease treatment. Formula categories mainly included qi-regulating, blood-regulating, phlegm-resolving, harmony-restoring, tonifying, and mind-calming formulas, aligning with the pathogenesis of deficiency, depression, phlegm, and stasis in CHD complicated with depression [3]. For syndromes of CHD complicated with depression, liver depression, qi stagnation, blood stasis, and phlegm turbidity are predominant. *Za Bing Yuan Liu Xi Zhu·Xin Tong* states, "Heart pain may be caused by cold pathogen, phlegm-fluid retention, or blood stasis, treated by warming and unblocking cold, promoting blood circulation and removing stasis." *Zheng Yin Mai Zhi·Xiong Bi* notes, "Chest impediment presents with chest tightness, shortness of breath, wheezing, cough with saliva, chest and back pain, deep and slow pulse at cun position, and tight and rapid pulse at guan position, due to phlegm-fluid stagnation and failure of chest yang to circulate." Additionally, *Zheng Yin Mai Zhi·Yu Zheng* states, "Depressive syndrome results from emotional discomfort and qi stagnation, treated by soothing the liver, relieving depression, regulating qi, and harmonizing the middle jiao." *Ling Shu·Ben Shen* states, "Deficiency of heart qi leads to

sadness," indicating that insufficient qi and blood production or disordered qi and blood in the heart may cause spirit malnutrition and depression. Thus, spleen deficiency, qi stagnation, blood stasis, and phlegm turbidity are key pathogenic factors. The root cause of this disease lies in dysfunction of liver dispersion; liver depression impairs the spleen, and the spleen and stomach are the hub of qi movement. Qi disorder leads to zang-fu dysfunction: "Smooth liver qi ensures harmonious heart qi; stagnant liver qi causes heart qi deficiency." The heart is the monarch of zang-fu organs, and liver qi interacts with heart qi; liver qi stagnation gives rise to various symptoms. Therefore, treatment should focus on soothing the liver and relieving depression, combined with nourishing the heart and calming the spirit, strengthening the spleen and resolving dampness, and promoting blood circulation and unblocking collaterals for optimal efficacy.

In terms of herb nature, flavor, and meridian tropism, herbs for CHD complicated with depression are mainly cold, warm, or neutral, with bitter and pungent flavors, primarily entering the liver, spleen, and heart meridians. *Jing Yue Quan Shu·Za Zheng Mo·Yu Zheng* states: "For anger injuring the liver with unresolved rebellious qi causing distension or pain, Jie Gan Jian is appropriate. For anger injuring the liver leading to fire, heat, flank pain, distension, or bleeding, Hua Gan Jian is suitable. For unresolved anger depression with phlegm formation, Wen Dan Tang is used. For liver and spleen injury after anger with fatigue and poor appetite, Wu Wei Yi Gong San is indicated." CHD complicated with depression is a chronic disease; long-term stagnation generates internal heat, damaging yin and blood. Treatment follows "cooling heat syndromes" (for heat) and "tonifying deficiency syndromes" (for spleen and liver), using cold, warm, and neutral herbs. Bitter flavor drains and dries; pungent flavor circulates, disperses, opens orifices, and resolves dampness; sweet flavor tonifies, relieves pain, and harmonizes; sour flavor astringes, relieves pain, and softens the liver. Combined flavors achieve draining stagnant heat, pungent dispersion for blood circulation, sweet nourishment, and sour astringency for pain relief, reflecting TCM principles of combining tonification and draining, and balancing cold and heat. The liver is most closely related to this disease: "The liver is a hard organ needing free flow"; impaired dispersion affects the spleen ("Treating liver disease requires strengthening the spleen first"). Spleen deficiency reduces qi and blood production; the heart governs blood vessels and stores spirit, so insufficient vessel filling leads to spirit disturbance. The lung governs qi, disperses, descends, and regulates water passages, cooperating with liver dispersion to ensure smooth qi movement. Modern studies by Xu *et al.* [4] using data mining on medication rules for CHD complicated with depression identified *Bupleurum chinense*, *Curcuma aromatica*, *Cyperus rotundus*, *Salvia miltiorrhiza*, *Ligusticum chuanxiong*, *Paeonia lactiflora*, *Poria cocos*, and *Glycyrrhiza uralensis* as core herbs, with neutral, cold, and warm natures and sweet, bitter, and pungent flavors, entering the heart, liver, and spleen meridians, consistent with our findings.

Association rule analysis identified 21 high-support herb pairs (frequencies ≥

50: *Bupleurum chinense-Glycyrrhiza uralensis*, *Bupleurum chinense-Paeonia lactiflora*, *Bupleurum chinense-Ligusticum chuanxiong*, etc.) and 27 high-confidence associations (confidence ≥ 0.90: *Paeonia lactiflora-Curcuma aromatica→Bupleurum chinense*, *Ligusticum chuanxiong-Paeonia lactiflora→Bupleurum chinense*, etc.). Nine core herbs were identified: *Bupleurum chinense*, *Glycyrrhiza uralensis*, *Paeonia lactiflora*, *Ligusticum chuanxiong*, *Curcuma aromatica*, *Salvia miltiorrhiza*, *Poria cocos*, *Citrus aurantium*, and *Cyperus rotundus*, with combined effects of soothing the liver, relieving depression, promoting blood circulation, regulating qi, strengthening the spleen, and softening the liver. This formulation is derived from *Chai Hu Shu Gan San* (Bupleurum Liver-Soothing Powder) by removing *Citrus reticulata* and adding *Salvia miltiorrhiza*, *Poria cocos*, and *Citrus aurantium*, thereby enhancing the effects of strengthening the spleen, resolving phlegm, and promoting blood circulation.

Cluster analysis yielded 5 core formulas as basic combinations for treatment: 1) Group 1 (*Bupleurum chinense*, *Poria cocos*, *Glycyrrhiza uralensis*, *Ligusticum chuanxiong*, *Codonopsis pilosula*, *Atractylodes macrocephala*) is derived from *Xiao Yao San* minus *Angelica sinensis* and *Paeonia lactiflora*, plus *Ligusticum chuanxiong* and *Codonopsis pilosula* to enhance qi circulation, pain relief, spleen strengthening, and qi replenishment, focusing on soothing the liver, relieving depression, strengthening the spleen, and replenishing qi. Zong *et al.* [5] used *Xiao Yao San* for 8 weeks in 60 patients, achieving a 90% total effective rate in improving angina and depression with few adverse reactions ($P < 0.05$ vs. control). Lyu [6] observed 39 patients treated with *Xiao Yao San* plus fluoxetine, showing a significantly higher effective rate and lower recurrence than control ($P < 0.05$). 2) Group 2 (*Bupleurum chinense*, *Salvia miltiorrhiza*, *Curcuma aromatica*, *Glycyrrhiza uralensis*, *Paeonia lactiflora*, *Cyperus rotundus*) is modified from *Chai Hu Shu Gan San* minus *Citrus reticulata*, *Citrus aurantium*, and *Ligusticum chuanxiong*, adding *Salvia miltiorrhiza* and *Curcuma aromatica* to enhance qi and blood circulation and liver-soothing depression relief, suitable for liver qi stagnation, blood stasis with internal heat. Hu [7] used modified *Chai Hu Shu Gan San* in 31 patients, showing superior TCM syndrome scores, anxiety-depression scores, and angina scores vs. control ($P < 0.05$). 3) Group 3 (*Pinellia ternata*, *Glycyrrhiza uralensis*, *Bupleurum chinense*, *Poria cocos*, *Trichosanthes kirilowii*, *Ligusticum chuanxiong*) is derived from *Gua Lou Xie Bai Ban Xia Tang* minus *Allium macrostemon*, adding *Bupleurum chinense*, *Poria cocos*, and *Ligusticum chuanxiong* to enhance phlegm resolving, liver soothing, blood circulation, and pain relief, suitable for phlegm-stasis binding and qi stagnation-blood stasis. Wang *et al.* [8] observed 64 patients treated with modified *Gua Lou Xie Bai Ban Xia Tang* for 2 months, with a 93.65% total effective rate significantly higher than control and reduced levels of inflammatory factors (IL-1β, IL-6, TNF-α; $P < 0.01$). Zhai *et al.* [9] identified common herbs for chest impediment as *Allium macrostemon*, *Trichosanthes kirilowii*, *Poria cocos*, *Pinellia ternata*, and *Zingiber officinale* through textual research. Additionally, the 2017 *Expert Consensus on Inte-*

grative Chinese and Western Medicine Diagnosis and Treatment of Atherosclerosis [10] included modified *Gua Lou Xie Bai Ban Xia Tang* for phlegm-stasis syndrome of atherosclerosis. Group 3 formula adds *Bupleurum chinense*, *Ligusticum chuanxiong*, and *Poria cocos* to enhance liver-soothing depression relief and mind-calming, beneficial for CHD complicated with depression.

After deduplication and integration of core formulas with frequencies > 30, the core prescription for CHD complicated with depression was determined: *Bupleurum chinense*, *Poria cocos*, *Ligusticum chuanxiong*, *Codonopsis pilosula*, *Atractylodes macrocephala*, *Salvia miltiorrhiza*, *Curcuma aromatica*, *Cyperus rotundus*, *Pinellia ternata*, *Trichosanthes kirilowii*, and *Glycyrrhiza uralensis*. This prescription is modified from *Chai Hu Shu Gan San* as the base formula. Experimental studies [11] showed that modified *Chai Hu Shu Gan San* improved the depressive state and myocardial ischemia in CHD-complicated-depression rat models, and regulated serum lipid levels (TC, TG, LDL, HDL) and the contents of Apelin-13 and ERK1/2 ($P < 0.01$). Numerous clinical studies [12]-[14] confirmed that modified *Chai Hu Shu Gan San* combined with conventional Western medicine was more effective than the control in treating CHD complicated with depression ($P < 0.05$), demonstrating its solid clinical foundation. Targeted modification of classic formulas, based on modern constitution, symptoms, and signs, enhances efficacy.

Analysis of the core prescription's compatibility showed that *Bupleurum chinense* combined with *Cyperus rotundus* and *Curcuma aromatica* forms a key herb group for soothing the liver, regulating qi, and relieving depression, strengthening both depression relief and blood circulation for pain relief. *Poria cocos* combined with *Atractylodes macrocephala* and *Codonopsis pilosula* enhances spleen strengthening, qi replenishment, mind calming, and spirit stabilizing, reflecting the principle of "strengthening the spleen first when treating liver disease." *Salvia miltiorrhiza* combined with *Ligusticum chuanxiong* promotes blood circulation, removes stasis, and unblocks collaterals for pain relief. *Pinellia ternata* combined with *Trichosanthes kirilowii* resolves phlegm, dissipates masses, and regulates qi in the chest. *Glycyrrhiza uralensis* harmonizes all herbs and relieves spasm for pain relief. The entire prescription constructs a comprehensive treatment system of "co-regulating the liver, spleen, and heart; simultaneously treating deficiency, excess, phlegm, and stasis." Through synergistic compatibility of tonification with qi regulation and collateral unblocking, it achieves "soothing the liver and regulating qi without consuming healthy qi, promoting blood circulation and unblocking collaterals without leaving stasis, strengthening the spleen and replenishing qi to consolidate the root without causing stagnation or assisting pathogens," balancing regulation. Herb compatibility emphasizes both qi-blood co-regulation (nourishing blood to soften the liver, replenishing qi to promote blood circulation) and zang-fu synergy (soothing the liver and strengthening the spleen to calm the spirit, resolving phlegm and unblocking collaterals to stabilize the heart), forming a bidirectional regulation mechanism of "strengthening the root to consolidate the foundation"

and "eliminating pathogens to unblock collaterals." It ultimately integrates four-dimensional efficacies: "strengthening the spleen and nourishing blood, soothing the liver and relieving depression, promoting blood circulation and resolving phlegm, calming the mind and stabilizing the spirit," fully embodying TCM characteristics of "treating both the root and branch, combining attack and tonification."

5. Conclusion

This study analyzed TCM medications and prescription rules for CHD complicated with depression using literature data mining. The core treatment principles include soothing the liver and regulating qi, promoting blood circulation and unblocking collaterals, resolving phlegm and removing turbidity, relieving depression and stabilizing the mind, strengthening the spleen and replenishing qi, harmonizing the liver and spleen, and replenishing qi to stabilize the heart, emphasizing zang-fu function synergy and qi movement balance for treating both the root and branch. Herb compatibility coordinates "spleen strengthening, liver soothing, blood circulation promotion, and phlegm resolving." Additionally, artificial intelligence models were used to assist in literature review, key data extraction, and statistical analysis, significantly reducing researchers' workload in tedious data processing, improving efficiency, and providing new ideas for future literature data mining research.

Funding

Self-funded project of Guangxi Zhuang Autonomous Region Administration of Traditional Chinese Medicine (GXZYA20230181, GXZYA20230200); Scientific Research Project of Guangxi University of Chinese Medicine (General Fund) (2024MS017); Open Project of Guangxi Health Emergency Skills Training Center for the Year 2024 (HESTCG202403); Doctoral Research Start-up Fund of Guangxi University of Chinese Medicine.

Author Contributions

Zheng Chuncheng conceived and designed the study, analyzed the data, and drafted the manuscript. Yang Liqiang and Zeng Qingqing contributed to data collection and manuscript revision. All authors read and approved the final manuscript.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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