Regular article

The mechanism of Huangqi Guizhi Decoction in improving pulmonary embolism based on network pharmacology and molecular docking technology

Yiting Wang, Bo Hong, Yanan Bao, Huan Cong, Jiawen Liu, Dan Zeng, Wenjing Li*

College of Pharmacy, Qiqihar Medical University, Qiqihar 161000, Heilongjiang, China

Abstract

This study explored the therapeutic targets and molecular mechanisms of Huangqi Guizhi Decoction (HGD) in alleviating pulmonary embolism (PE) by employing network pharmacology and molecular docking techniques. Firstly, the effective active components of the Chinese herbs in HGD were retrieved from the Traditional Chinese Medicine Systems Pharmacology Database (TCMSP), and their potential therapeutic targets were predicted using the Swiss Target Prediction platform. Subsequently, PE-related target genes were obtained from the Online Mendelian Inheritance in Man (OMIM) database and GeneCards database. Then, the Wei Sheng Xin tool was used to generate a Venn diagram for identifying the common targets between the herb-related targets and PE-related targets. After screening these common targets, a "drug-component-target network" and a protein-protein interaction (PPI) network were constructed. Furthermore, Gene Ontology (GO) enrichment analysis and Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analysis were conducted on the intersecting targets, and molecular docking verification was performed using AutoDockTools and PyMol software. Finally, 20 active components were screened from *Astragali Radix*, 7 from *Cinnamomi Ramulus*, 13 from *Paeoniae Radix Alba*, 5 from *Zingiberis Rhizoma Recens*, and 29 from *Jujubae Fructus*, with a total of 983 therapeutic targets. Among these targets, 134 were associated with PE, and protein kinase B1 (AKT1), mitogen-activated protein kinase 1 (MAPK1), and transformation-related protein 53 (TP53) served as the core targets. The results of GO and KEGG enrichment analyses indicated that the alleviation of PE by HGD is mainly related to pathways including immune response, regulation of gene expression, atherosclerosis, and tumorigenesis. Molecular docking results showed that the key active components in HGD could bind to the core targets spontaneously and stably. This study revealed that HGD may alleviate symptoms in PE patients by regulating signaling pathways, modulating platelet function to exert anticoagulant effects, and regulating the expression of anti-inflammatory genes, which provided a direction for subsequent experimental research.

Keywords: Huangqi Guizhi Decoction; pulmonary embolism; network pharmacology; molecular docking

1 Introduction

Pulmonary Embolism (PE) is a disease that causes pulmonary circulatory disorder due to embolism of the pulmonary artery or its branches, and it is associated with high incidence, misdiagnosis, disability, and mortality rates. Adequate treatment of PE can significantly reduce the mortality rate. but most patients still need to take anticoagulant drugs for a long time, thus increasing the risk of bleeding [1-4]. According to

These authors have no conflict of interest to declare.

* Author to whom correspondence should be addressed. Address: Pharmacy School, Qiqihar Medical University, 333 Bukui Street, Qiqihar 161000, China; Tel.: +86-452-2663159; E-mail: lwj022325@163.com.

Received: 2025-09-25 Accepted: 2026-01-14

the theory of Traditional Chinese Medicine (TCM), PE is caused by deficiency of lung yang-qi, with the superficial excess syndrome manifested as blood stasis obstructing the pulmonary vessels. Therefore, the main principle for the treatment of PE should be to replenish qi and unblock meridians [5].

Huangqi Guizhi Decoction (HGD), as recorded in the "Jin Kui Yao Lue" by Zhang Zhongjing of the Han Dynasty, has the functions of tonifying qi and blood, warming the meridians and relieving stiffness, and promoting blood circulation to unblock blockages [6]. This formula is composed of five medicinal materials: *Astragali Radix*, *Cinnamomi Ramulus*, *Paeoniae Radix Alba*, *Zingiberis Rhizoma Recens*, and *Jujubae Fructus*. Among them, *Astragali Radix* is the sovereign drug, which is sweet and slightly warm. It enters the lung and spleen meridians and has the functions of tonifying qi and consolidating the exterior, and greatly replenishing lung qi [5]. It contains various active components such as Astragalus Polysaccharides, Astragalus Flavonoids, and Astragalus Saponins, which can exert effects through multiple targets and multiple pathways [7]. *Cinnamomi Ramulus* is the assistant drug, which is pungent, sweet, and warm. It enters the lung, heart, and bladder meridians. It has the functions of inducing sweating and relieving the exterior, warming and unblocking the meridians, assisting yang and transforming qi, and calming the qi and suppressing the reflux [8]. *Paeoniae Radix Alba* nourishes yin and blood and harmonizes the meridians as the assistant drug. *Zingiberis Rhizoma Recens* warms the lung and dispels cold, and *Jujubae Fructus* replenishes the middle and benefits qi, and harmonizes the medicinal properties as the mediator [9]. This prescription features a concise herbal formulation with ingenious compatibility. *Astragali Radix* paired with *Cinnamomi Ramulus* has the effects of replenishing qi, consolidating the exterior, and dredging the meridians. *Cinnamomi Ramulus* paired with *Paeoniae Radix Alba* has the effects of regulating ying (nutrient) and wei (defensive) qi, dredging the meridians and collaterals, and relieving blood impediment. *Astragali Radix* paired with *Paeoniae Radix Alba* has the effects of replenishing both qi and blood, as well as promoting menstrual flow and activating blood circulation. *Cinnamomi Ramulus* paired with *Zingiberis Rhizoma Recens* has the effect of warming the middle jiao and assisting yang qi. *Paeoniae Radix Alba* paired with *Jujubae Fructus* has the effect of harmonizing the middle jiao and nourishing ying qi. *Zingiberis Rhizoma Recens* paired with *Jujubae Fructus* has the effects of regulating the spleen and stomach, and harmonizing ying and wei qi. Used together, these herbs exert a variety of effects such as dredging the vessels, relieving impediment, and regulating ying and wei qi [10].

In modern clinical practice, HGD is often used alone or in combination with other drugs for the treatment of cardiovascular and cerebrovascular diseases, orthopedic diseases, peripheral vascular diseases, peripheral nerve diseases, renal diseases, as well as conditions such as rheumatoid arthritis (RA) and nonalcoholic steatohepatitis (NASH) [11]. Zhao et al. used HGD for syndrome differentiation and treatment of lower extremity venous thromboembolism in lung cancer patients [12]. This approach not only significantly alleviated the patients' clinical symptoms but also greatly shortened the duration of the acute and subacute phases of deep vein thrombosis (DVT). Medically, both lower extremity venous thromboembolism and PE are classified as venous thromboembolism (VTE). Despite this commonality there is a scarcity of research focusing on the therapeutic effects of HGD on PE. Since PE is caused by conditions such as yang-qi deficiency and blood stasis, and HGD has the effect of strengthening yang and resolving blood stasis which can improve PE symptoms, this study explores the active components, action targets, and potential molecular mechanisms of HGD in

improving PE from the perspectives of network pharmacology and molecular docking, as shown in Fig. 1, aiming to provide a theoretical foundation and new insights for subsequent research.

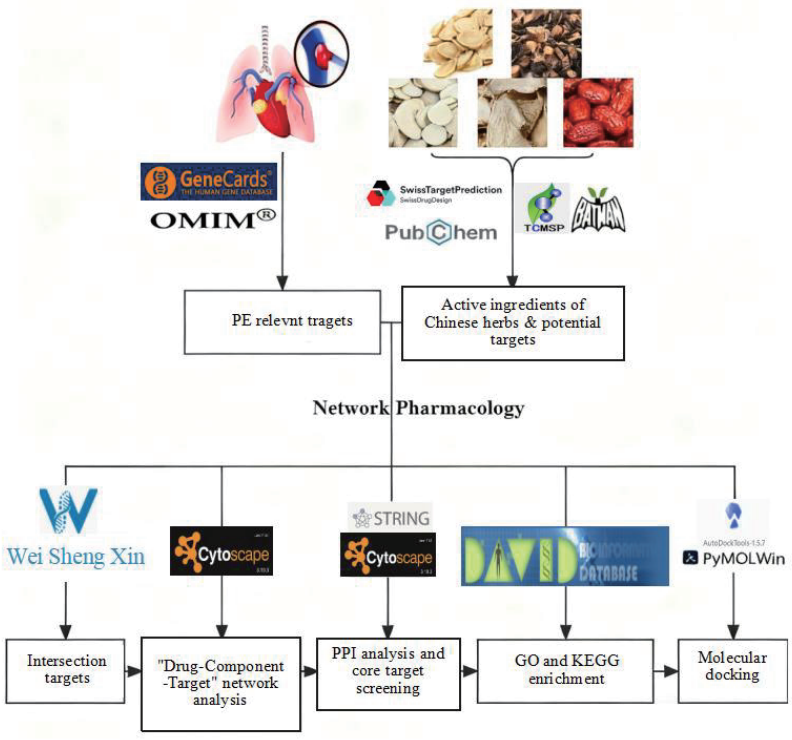


Fig. 1 Network pharmacology flowchart

2 Materials and methods

2.1 Screening of main active components and targets of HGD

The effective components, namely *Astragali Radix*, *Cinnamomi Ramulus*, *Paeoniae Radix Alba*, *Zingiberis Rhizoma Recens*, and *Jujubae Fructu*, were retrieved from the Traditional Chinese Medicine Systems Pharmacology Database and Analysis Platform (TCMSP, https://www.tcmsp-e.com/) with the screening criteria of oral bioavailability (OB) ≥ 30% and drug-likeness (DL) ≥ 0.18 and their canonical SMILES (Simplified Molecular-Input Line-Entry System) were acquired from the PubChem database (https://pubchem.ncbi.nlm.nih.gov/). Subsequently, the Swiss Target Prediction platform (http://www.swisstargetprediction.ch/) and BATMAN-TCM (http://bionet.ncpsb.org.cn/batman-tcm/) were used to predict the action targets of the active components, with the prediction score set to greater than 0 for inclusion and the UniProt database (https://www.uniprot.org) was employed to standardize protein names into corresponding gene names. Finally, duplicate targets were removed.

2.2 Prediction of targets related to PE

Using “pulmonary embolism” as the keyword, all disease-related targets were obtained from the OMIM database (https://www.omim.org/) and Genecards database (https://www.genecards.org/). After removing duplicate ones, the remaining targets were identified as the PE-related targets.

2.3 The common target of HGD and PE

The drug targets and disease targets were imported into the Wei sheng xin Platform (http://www.bioinformatics.com.cn/) to generate a Venn diagram, from which the common targets were obtained.

2.4 Construction of the "drug-component-target" network diagram

The effective components, target points and relevant target points of *Astragali Radix*, *Cinnamomi Ramulus*, *Paeoniae Radix Alba*, *Zingiberis Rhizoma Recens* and *Jujubae Fructus* were imported into Cytoscape 3.10.3, and a "drug-component-target" network was constructed. The nodes in the network represent the components and target points, while the edges between the nodes represent the interactions between them. Using the cytoNCA plugin, the degree of each node was calculated based on the number of its connecting edges. The higher the degree value, the more important the node.

2.5 PPI network and core target screening

Key targets were imported into the STRING database (https://cn.string-db.org/). The species was set to Homo sapiens, the confidence score was set to 0.900, and disconnected nodes were hidden. Subsequently, the PPI (Protein-Protein Interaction) data were downloaded and imported into Cytoscape 3.10.3 software to construct a visualized PPI network diagram. Core targets were identified as those with a degree value exceeding the median value across two rounds of screening.

2.6 Go and KEGG enrichment analysis

The common targets were imported into the DAVID database (https://davidbioinformatics.nih.gov/). With "OFFICIAL_GENE_SYMVOL" and "Homo sapiens" settings, the top 10 targets were selected for biological process (BP), cellular component (CC), and molecular function (MF), and the top 20 for KEGG signaling pathways. All results were visualized on the microinformatics platform based on the *P* value.

2.7 Molecular docking verification

The active components of HGD were subjected to molecular docking with the core targets. The 2D structures of the effective components of traditional Chinese medicine were downloaded from the PubChem database (https://pubchem.ncbi.nlm.nih.gov/), and Chem3D 23.1.1 was used to determine the minimum binding energy. The protein structure of the target protein was downloaded from the RCSB PDB database (http://www.rcsb.org/), and the water and ligand were removed using PyMOL 2.4.1 software. Subsequently, the protein molecules were hydrogenated and the active pocket was determined using AutoDockTools. The docking binding energy was calculated using Vina software, and the binding energy heatmap was generated using Origin. Finally, the docking results were visualized using PyMOL 2.4.1 software.

3 Results

3.1 The active components and potential targets of each traditional Chinese herb in HGD

20 active components of *Astragali Radix*, 7 active components of *Cinnamomi Ramulus*, 13 active components of *Paeoniae Radix Alba*, 5 active components of *Zingiberis Rhizoma Recens*, and 29 active components of *Jujubae Fructus* were screened, as shown in Table 1. The targets were standardized and processed in the TCMSP, PubChem, and Swiss TargetPrediction databases, and duplicates were excluded. A total of 983 potential targets for the effective components were obtained.

Table 1 Part of the active ingredients of HGD

Source	Mol ID	Molecule name	Molecular formula	PubChem cID
Astragali Radix	MOL000354	isorhamnetin	$C_{16}H_{12}O_7$	5281654
	MOL000392	formononetin	$C_{16}H_{12}O_4$	5280378
	MOL000398	isoflavanone	$C_{26}H_{22}O_9$	140571770
	MOL000417	Calycosin	$C_{16}H_{12}O_5$	5280448
	MOL000422	kaempferol	$C_{15}H_{10}O_6$	5280863
Cinnamomi Ramulus	MOL001736	(-)-taxifolin	$C_{15}H_{12}O_7$	712316
	MOL000358	beta-sitosterol	$C_{29}H_{50}O$	222284
	MOL000359	sitosterol	$C_{29}H_{52}O$	3084097
	MOL000492	(+)-catechin	$C_{15}H_{14}O_6$	9064
	MOL004576	taxifolin	$C_{15}H_{12}O_7$	439533
Paeoniae Radix Alba	MOL001921	Lactiflorin	$C_{23}H_{26}O_{10}$	5318917
	MOL001925	paeoniflorin	$C_{23}H_{28}O_{11}$	442534
	MOL000358	beta-sitosterol	$C_{29}H_{50}O$	222284
	MOL000359	sitosterol	$C_{29}H_{50}O$	222284
	MOL000422	kaempferol	$C_{15}H_{10}O_6$	5280863
Zingiberis Rhizoma Recens	MOL000358	beta-sitosterol	$C_{29}H_{50}O$	222284
	MOL006129	6-methylgingediacetate2	$C_{19}H_{32}O_4$	N/A
	MOL000449	Stigmasterol	$C_{29}H_{48}O$	5280794
	MOL001771	poriferast-5-en-3beta-ol	$C_{29}H_{50}O$	457801
	MOL008698	Dihydrocapsaicin	$C_{18}H_{29}NO_3$	107982
Jujubae Fructus	MOL000358	beta-sitosterol	$C_{29}H_{50}O$	222284
	MOL000492	(+)-catechin	$C_{15}H_{14}O_6$	9064
	MOL002773	beta-carotene	$C_{40}H_{56}$	5280489
	MOL000096	(-)-catechin	$C_{15}H_{14}O_6$	73160
	MOL000098	quercetin	$C_{15}H_{10}O_7$	5280343

3.2 Targets related to PE

Using “pulmonary embolism” as the keyword, a total of 1999 entries from GeneCards and 179 entries from OMIM were retrieved. All the relevant targets from these two databases were combined and duplicates were removed before being saved. A total of 2028 lung embolism-related targets were obtained.

3.3 Common targets of HGD and PE

After intersecting the potential targets of HGD and the targets related to PE, we obtained a total of 134 common targets, as shown in Fig. 2.

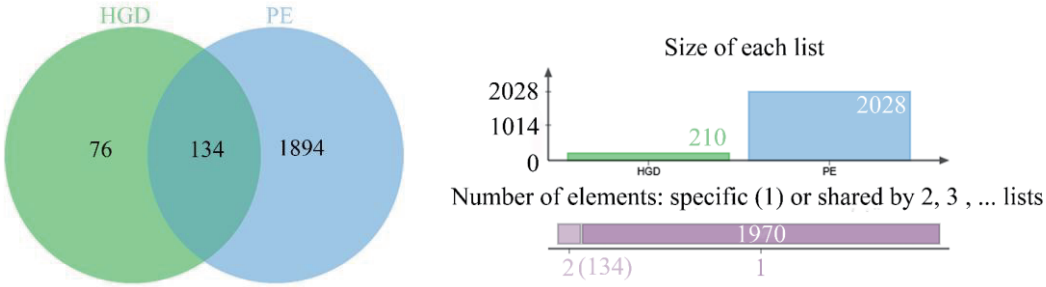


Fig. 2 Common target Venn diagram of HGD and PE

3.4 "Drug-Component-Target" network diagram

Using the Cytoscape 3.10.3 software, a "drug-component-target" network diagram was constructed, as shown in Fig. 3.

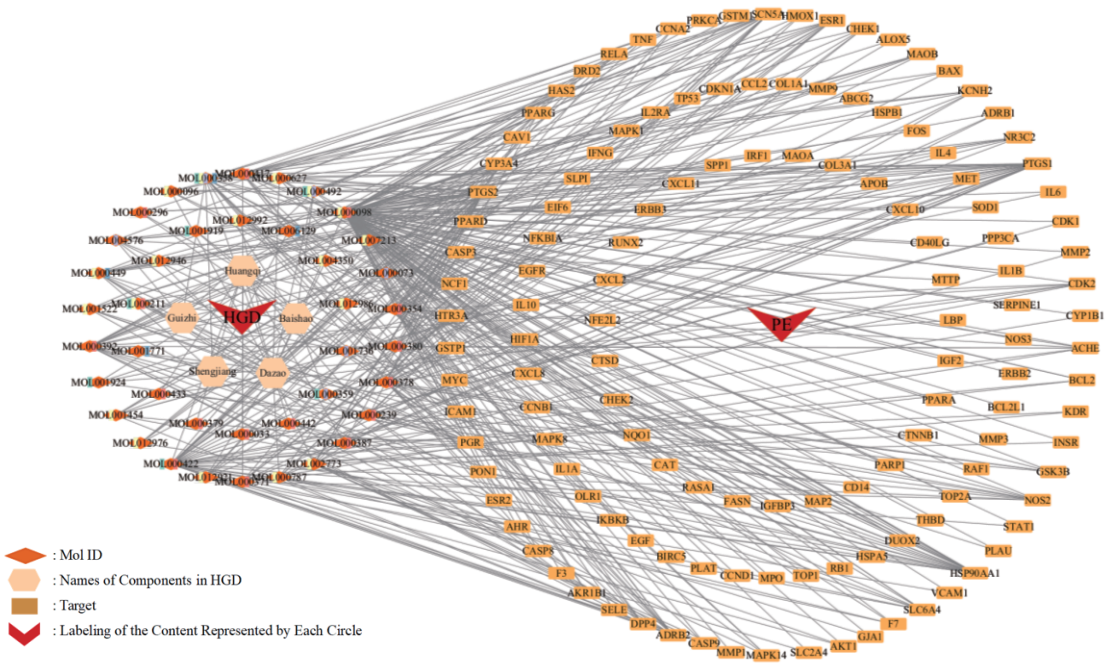


Fig. 3 "Drug-Component-Target" network diagram

3.5 Construction of the PPI network and screening of core genes

134 target genes were selected through the STRING database with a confidence level > 0.90. Unrelated targets were excluded to construct the PPI network, as shown in Fig. 4. Using the exported file, with the condition of "degree > median value" set twice, 10 core genes were obtained, as shown in Fig. 5.

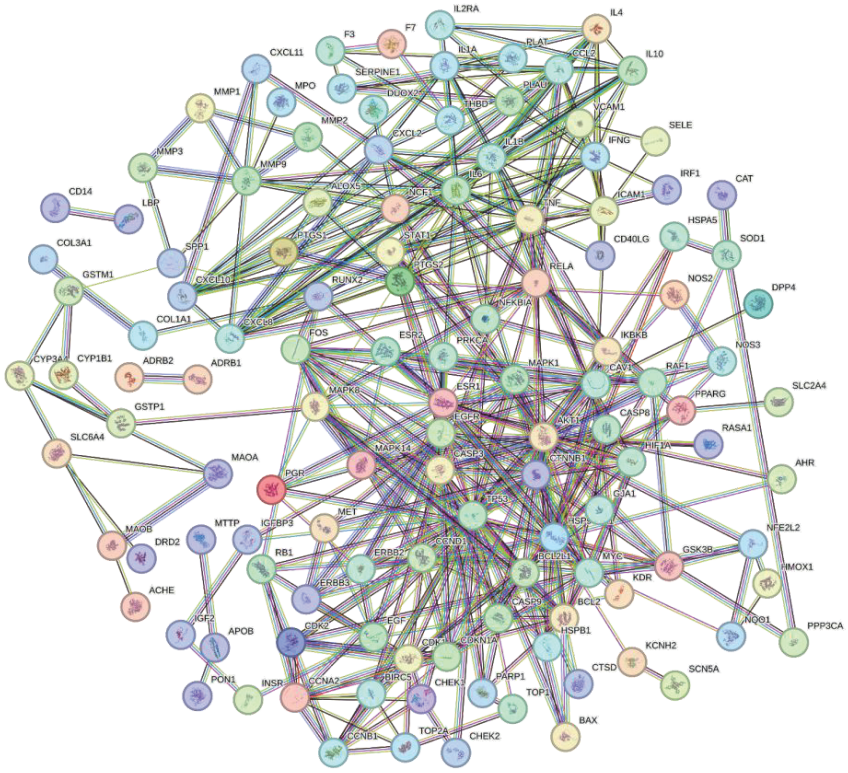
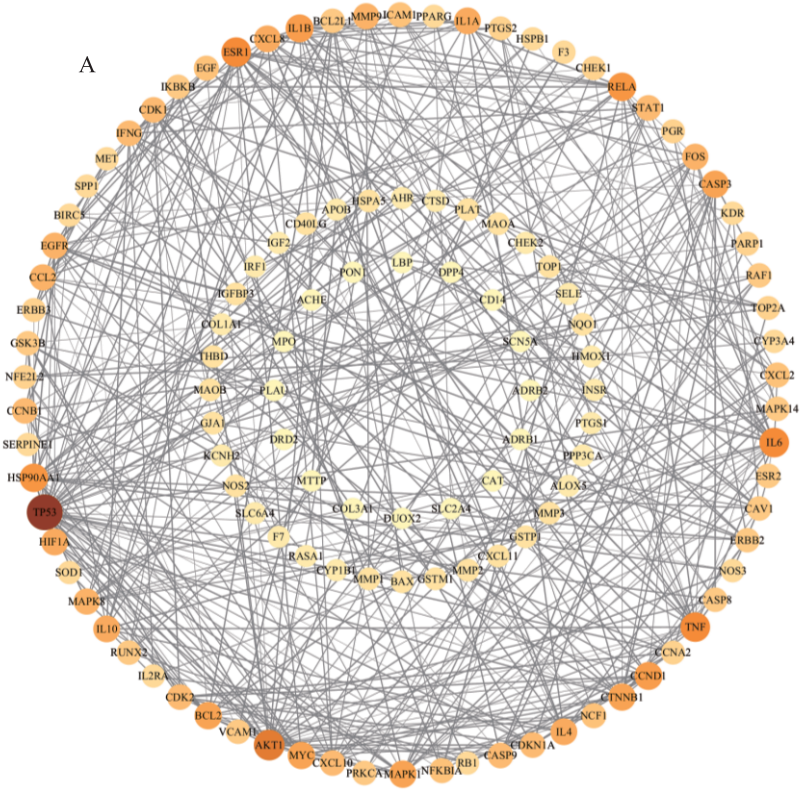
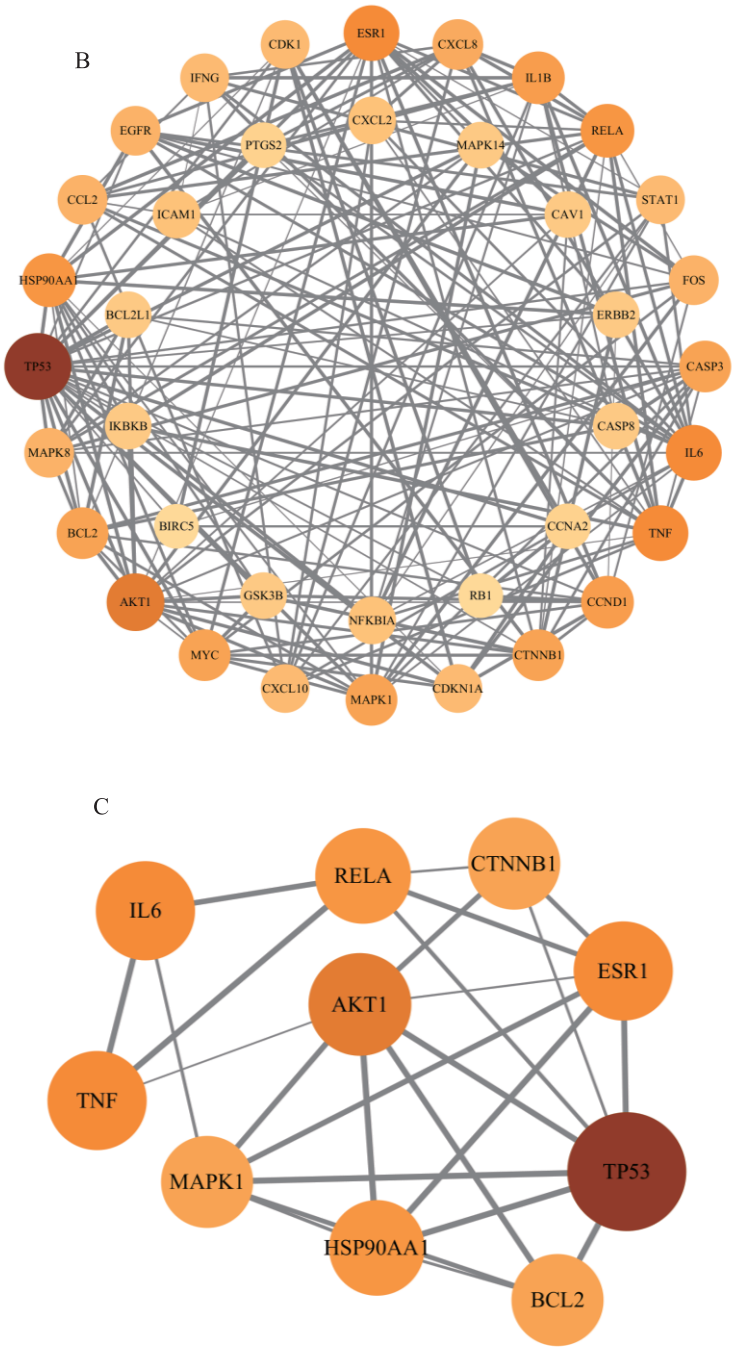


Fig. 4 PPI network diagram of interaction targets





A: Initial data; B: The first screening results; C: The result of the second screening

Fig. 5 Screening of core genes

Table 2 Protein interaction network parameters (TOP 10)

Gene name	Protein names	Betweenness	Closeness	Degree	Eigenvector	LAC	Network
TP53	Cellular tumor antigen p53	345.89	0.73	26	0.37	6.6	21.92
AKT1	RAC serine/threonine-protein kinase	110.38	0.65	17	0.28	6.0	11.18
IL6	Interleukin-6	86.72	0.56	15	0.17	5.6	10.52
TNF	Tumor necrosis factor	113.81	0.59	15	0.17	5.6	10.60
ESR1	Estrogen receptor	52.26	0.63	15	0.26	6.4	10.77
RELA	GTP pyrophosphokinase	116.46	0.61	13	0.19	4.8	7.07
HSP90AA1	Heat shock protein HSP 90-alpha	38.60	0.55	13	0.22	5.1	7.65
BCL2	Apoptosis regulator Bcl-2	19.38	0.54	11	0.20	5.1	6.60
CTNNB1	Catenin beta-1	27.27	0.57	11	0.20	4.9	6.60
MAPK1	Mitogen-activated protein kinase 1	35.10	0.59	11	0.20	4.9	6.03

3.6 GO and KEGG enrichment analysis

The 134 common targets were subjected to GO and KEGG enrichment analysis using the DAVID database. The GO enrichment analysis results showed the top ten items in terms of count, as shown in Fig. 6. Biological processes (BP) mainly include gene expression regulation, cell proliferation and apoptosis, and biological metabolism regulation; Cell composition (CC) mainly include cell membrane-related structures, extracellular plasma membrane, and receptor complexes; Molecular functions (MF) mainly include protein binding, protein kinase activity, and nuclear receptor activity. The KEGG analysis results showed the top 20 pathways, as shown in Fig. 7. The larger the bubble in the figure, the more genes enriched in that pathway. The darker the color, the smaller the *P* value. The main pathways include PI3K-Akt pathway, IL-17 signaling pathway, and tumor necrosis factor signaling pathway.

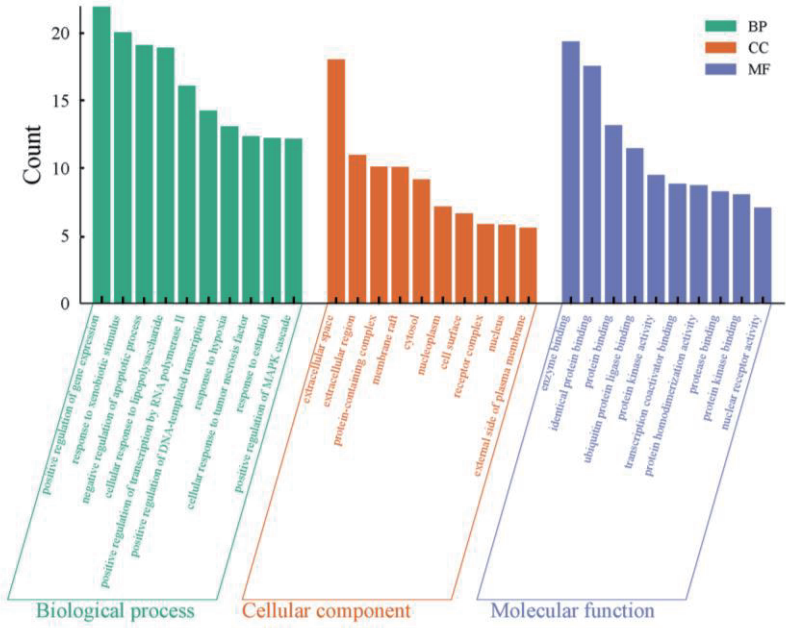


Fig. 6 GO functional enrichment analysis results

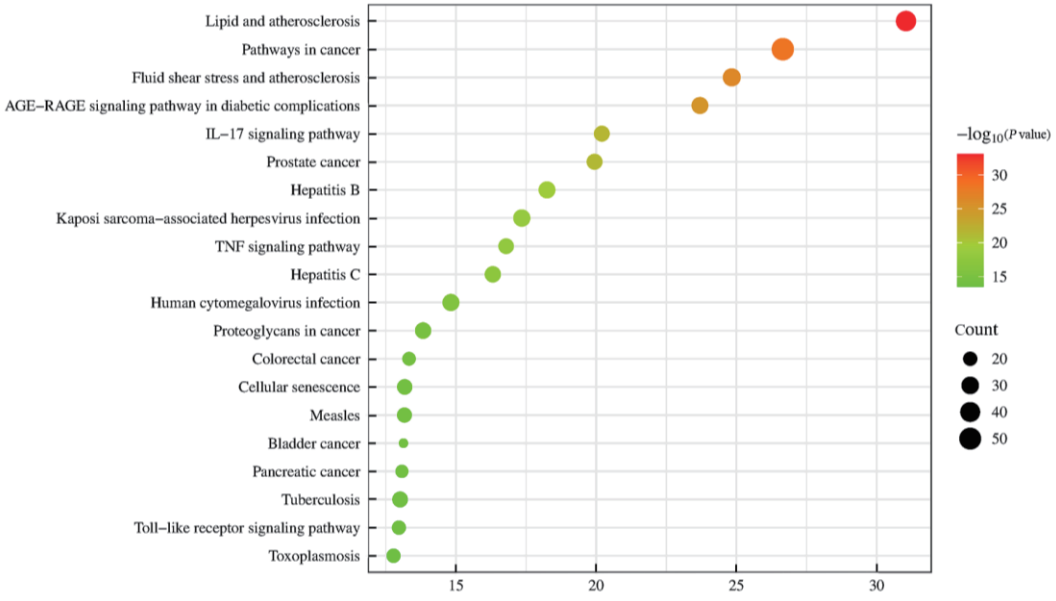


Fig. 7 KEGG enrichment pathway analysis results

3.7 The docking results of the core targets and the active ingredient molecules

Based on relevant literature and collated databases, molecular docking analysis was conducted between the main active components and the core targets. The docking binding energy reflects the affinity between ligands and active components. Generally speaking, a value less than -5.0 kcal/mol indicates that the active components have good affinity for the ligands. The results showed that both the core genes and the active components have good

binding ability, and the binding energy between the core targets and the active components is shown in Fig. 8. The docking results indicated that RELA, IL6, TNF, BCL2, TP53, CTNNB1, MAPK1, AKT1, HSP90AA1, and ESR1 could combine with multiple active components. Among them, astragaloside I, paeoniflorin, formononetin, calycosin, *β*-sitosterol, kaempferol, isorhamnetin, stigmasterol and quercetin were selected as key components for molecular docking to verify their affinity. Fig. 9 and Table 3 suggest that HGD may improve PE through the above components and targets.

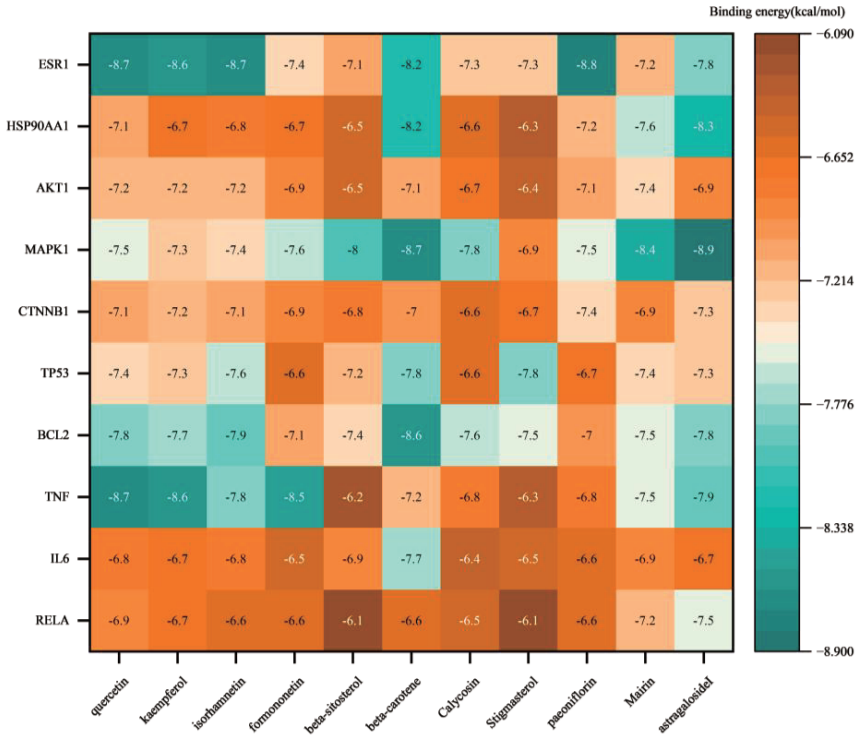


Fig. 8 Molecular docking binding energy

Table 3 Results of molecular docking binding energy

No.	Protein name	Active ingredients	Binding energy/(kcal/mol)
A	TNF	Quercetin	-8.7
B	ESR1	Quercetin	-8.7
C	HSP90AA1	AstragalosideI	-8.3
D	MAPK1	AstragalosideI	-8.9
E	ESR1	Stigmasterol	-7.3
F	TNF	Formononetin	-8.5
G	CTNNB1	Paeoniflorin	-7.3
H	ESR1	Paeoniflorin	-8.8
I	MAPK1	Calycosin	-7.8
J	TP53	*β*-sitosterol	-7.2
K	TNF	Kaempferol	-8.6
L	ESR1	Isorhamnetin	-8.7

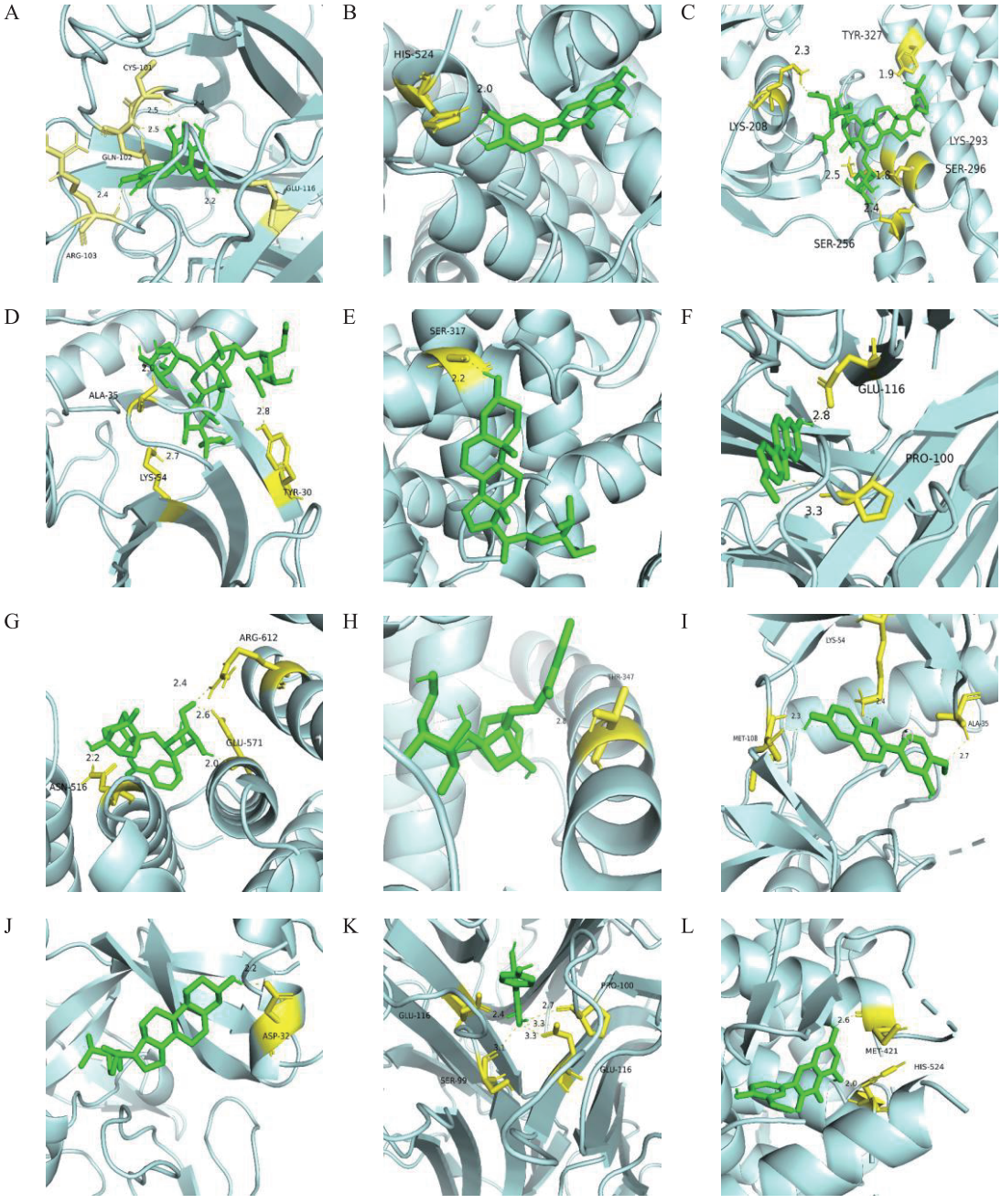


Fig. 9 Diagram of molecular docking

4 Discussion

PE is a condition where blood clots form and block the pulmonary arteries and their branches, thereby disrupting the pulmonary function and causing circulatory disorders, posing a significant threat to health. The inflammatory response and the coagulation process are crucial factors in the formation of the embolism [13]. Currently, numerous studies in both domestic and international Western medicine explore the pathogenesis of PE, mainly focusing on factors such

as endothelial damage in the venous system [14]. Traditional Chinese medicine has no records of PE in ancient texts. Modern medicine classifies it under syndromes such as "chest pain", "seizure disorders", "fluid retention", and "blood disorders". Western medical treatment mainly consists of anticoagulation and thrombolytic interventional therapies. Traditional Chinese medicine employs different therapeutic methods and prescriptions [15]. HGD is a classic Chinese medicine formula. Modern pharmacology indicates that HGD has various effects such as antioxidative stress, regulation of blood viscosity, anti-platelet aggregation, and improvement of microcirculation [16]. In this formula, Astragali Radix and Cinnamomi Ramulus can improve microcirculation [17]. Astragali Radix and Paeoniae Radix Alba inhibit inflammatory responses and antioxidation. Zingiberis Rhizoma Recens and Jujubae Fructus have antioxidative stress and anti-thrombosis effects. However, the mechanism remains unclear at present. This study employs network pharmacology and molecular docking technology to analyze the screened and collected active components (such as quercetin and kaempferol) and key targets (such as RELA and TNF), thereby interpreting the mechanism by which HGD alleviates PE through the TCM principle of "replenishing qi and dredging collaterals" at the molecular level. It aims to provide new insights for the subsequent treatment of PE.

The active components screened in this study, including quercetin, calycosin, β-sitosterol, paeoniflorin, and astragaloside I, play an important role in improving PE. Existing studies have shown that flavonoids are beneficial to cardiovascular function and immunity, which also possess properties such as antioxidant activity and lung function protection [18-19]. As a natural flavonoid, quercetin alleviates PE through a dual mechanism: on one hand, it inhibits PLCγ2-IP3 signaling in platelets, blocks calcium ion-mediated aggregation, and thereby reduces thrombus formation at the source [20-21]; on the other hand, it decreases the levels of pro-inflammatory factors (e.g., interleukin-6 (IL-6) and tumor necrosis factor-α [TNF-α]) via the NF-κB pathway, while increasing the activity of SOD and GSH, thus alleviating inflammatory damage to lung tissue [22]. Meanwhile, kaempferol upregulates the expression of G protein-coupled estrogen receptor (GPER), activates downstream SRC family kinases, promotes the release of heparin-binding epidermal growth factor (HB-EGF), and thereby reversely activates the epidermal growth factor receptor (EGFR) to facilitate the recovery of vascular endothelial cells [23]. Calycosin, an isoflavone compound, exhibits anti-tumor, antioxidant, and anti-abnormal lipid metabolism effects [24]. It inhibits pro-cancer signaling pathways such as PI3K/Akt to induce cancer cell apoptosis [25], and can also reduce the expression of vascular endothelial growth factor (VEGF) to inhibit tumor angiogenesis [26]. β-sitosterol, a plant sterol, prevents cardiovascular diseases through antioxidant, anti-inflammatory effects and improving endothelial function [27]. Paeoniflorin, a terpenoid compound, exerts an anti-thrombotic effect by reversing the significant imbalance in the expression levels of human 6-keto-prostaglandin F1α (6-k-PGF1α) and thromboxane B2 (TXB2); additionally, it alleviates the release of pro-inflammatory factors by inhibiting the MAPK/NF-κB pathway [28-29]. Astragaloside I can inhibit the occurrence of lung cancer by suppressing MAPK-related pathways; at the same time, it activates the AMPK/SIRT signaling pathway to inhibit inflammatory responses and reduce the release of pro-inflammatory factors [30].

In the PPI analysis network of targets through which HGD acts on PE, RELA, IL6, TNF, BCL2, TP53, CTNNB1, MAPK1, AKT1, HSP90AA1, and ESR1 were identified as core genes. Results of GO enrichment analysis showed that HGD alleviates PE mainly by exerting functions related

to pathways including receptor-mediated signaling pathways, immune response, regulation of gene expression, atherosclerosis, and tumorigenesis. According to the KEGG pathway analysis results, HGD can act through the PI3K-Akt pathway: it hyperphosphorylates anti-apoptotic proteins to reduce the apoptosis of hypoxic endothelial cells, and upregulates VEGF to promote pulmonary microvascular neovascularization [31-34].

Molecular docking results also indicated that the active components (such as quercetin, formononetin, astragaloside I, and paeoniflorin) exhibit significant binding activity with core targets. Among them, astragaloside I has a binding energy of -8.9 kcal/mol when combined with MAPK1, forming a stable complex. The efficacy of these active components has been widely recognized, and it is consistent with the results of the network pharmacology and molecular docking in this experiment.

Currently, studies on HGD for alleviating PE are relatively limited. This study applied network pharmacology and molecular docking technology and found that HGD has great potential in this regard. However, this study has certain limitations, and the results still require further experimental verification. Therefore, we will further verify its pathways and targets using methods such as animal experiments and *in vitro* experiments, thereby providing a more comprehensive and reliable basis for understanding the role of HGD in alleviating PE.

5 Conclusion

This study preliminarily revealed the potential molecular mechanism by which HGD alleviates PE using network pharmacology and molecular docking techniques. By identifying key components such as quercetin, eremophilin, astragalosideI, and Paeoniflorin, as well as key targets such as RELA, IL6, TNF, BCL2, TP53, CTNNB1, and MAPK1, it provided objective evidence and theoretical basis for further experimental verification of HGD's therapeutic effects on PE.

Acknowledgements

The work was supported by Research Project on Traditional Chinese Medicine in Heilongjiang Province in 2025 (Research on the pharmacological substance basis of Huangqi Guizhi decoction in improving acute pulmonary embolism and lung injury based on the theory of "Diaphoresis and expanding meridian" No. ZHY2025-043).

References

[1] He JG, Cheng XS. Advances in diagnosis and treatment of pulmonary embolism. Chin J Tuberc Respir Dis, 2000, 9: 50-52.

[2] Jonathan P, Adam SC. Management of acute pulmonary embolism. JAMA, 2020, 324: 597-598.

[3] Guo DJ, Hu DX, Zhou WR, et al. Clinical analysis and discussion on the diagnosis and treatment of acute pulmonary embolism. Chin J Cardiol, 2003, 1: 52-54.

[4] Liu HG, Wang F, Ma J. Observation on N-terminal pro-brain natriuretic peptide and long-term prognosis of middle and high-risk patients with acute pulmonary embolism treated with the Jiajian Xiaotao Tong prescription. Liaoning J Tradit Chin Med, 2025, 52: 126-129.

[5] Liu XL, Liu YJ, Bai J, et al. Analysis of the effect of the blood-activating and tumor-dissolving formula combined with conventional thrombolytic and anticoagulant therapy in the treatment of acute pulmonary embolism. Chin J Tradit Chin Med Pharm, 2019, 37: 2021-2024.

[6] Zhang YY, Cai JH, Zhao CY, et al. Research progress on chemical components, pharmacological effects and clinical applications of Huangqi Guizhi Wuwu decoction. J Guangdong Pharm Univ, 2025, 41: 172-180.

[7] Hu WY, Li H, Wang BS, et al. Research progress on the mechanism of astragalus and its active components in preventing and treating rheumatoid arthritis. Chin J Tradit Chin Med, 2025, 7: 1-6.

[8] Li X, Zhao JG, Wu WH, et al. Research progress on chemical components and pharmacological effects of Guizhi. J Tradit Chin Med, 2023, 51: 111-114.

[9] Zhang Y, Guan J, Liu SS, et al. Research progress on chemical components and pharmacological effects of Huangqi Guizhi Wuwu decoction. J Jilin Med Coll, 2018, 39: 295-298.

[10] Zhang HB, Ge TJ, Han DL. The Prescription combination and application of Huangqi Guizhi Wuwu decoction. J Shandong Univ Tradit Chin Med, 2003, 4: 256-257.

[11] Lu GY, Wang JY, Gao Z, et al. Research progress of the classic formula Huangqi Guizhi Wuwu decoction and prediction analysis of quality markers. Chin J Chin Med, 2023, 48: 5438-5449.

[12] Zhao ZL, Zhao YH, Chen MY, et al. One case of lung cancer lower limb venous thrombosis treated with Huangqi Guizhi Wuwu decoction by Zhao Yuanhong. Shanghai J Tradit Chin Med, 2018, 52: 29-30.

[13] Song JX, Yang Y, Chen R, et al. Research progress on prognosis evaluation of patients with acute pulmonary embolism. J Mol Imaging, 2025, 48: 905-910.

[14] Tahir T, Swetha K, Umesh S, et al. Acute pulmonary embolism: contemporary approach to diagnosis, risk-stratification, and management. Int J Angiol, 2019, 28: 100-111.

[15] Lu BQ, Zhu QC, Yang HQ. Advances in the treatment of pulmonary embolism with traditional chinese and western medicine. Xinjiang J Tradit Chin Med, 2023, 41: 82-86.

[16] Hu J, Tang GJ, Rao OY, et al. Exploring the mechanism of Huangqi Guizhi Wuwu decoction in anti-cerebral ischemia-reperfusion injury based on bioinformatics and experimental verification. Chin J Exp Tradit Med Formulae, 2025, 8: 1-20.

[17] Zhao MZ, Wang B, Zhao XM, et al. Study on the effects and mechanism of ephedra-galangal formula on respiratory function and airway inflammation in rats with asthma caused by cold-dampness accumulation in the lung. Chin Pharm J, 2025, 36: 1717-1721.

[18] Chen S, Wang XJ, Yu C, et al. A review of classification, biosynthesis, biological activities and potential applications of flavonoids. Molecules, 2023, 28: 25-51.

[19] Zhang DX. Research progress on the pharmacological effects of flavonoids in astragalus. Nei Mongol J Tradit Chin Med, 2021, 40: 148-149.

[20] Ding YY, Che DL, Li CM, et al. Quercetin inhibits Mrgprx2-induced pseudo-allergic reaction via PLCγ-IP3R related Ca^{2+} fluctuations. Int Immunopharmacol, 2019, 66: 185-197.

[21] Roger VK, Attila B, Marion AH, et al. Antithrombotic potential of blockers of store-operated calcium channels in platelets. Arterioscler Thromb Vasc Biol, 2012, 32: 1717-1723.

[22] Huang YL. Research progress on flavonoids in plants. China Fruit Veg, 2025, 45: 71-79.

[23] Hu WH, Wang HY, Xia YT, et al. Kaempferol, a major flavonoid in ginkgo folium, potentiates angiogenic functions in cultured endothelial cells by binding to vascular endothelial growth factor. Chin J Tradit Chin Med Mod Dist Educ, 2020, 11: 23-34.

[24] Zhang H, Tu HY, Xiong SL, et al. Research progress on chemical components of flavonoids in medicinal plants and their pharmacological effects. J Hunan Univ Chin Med, 2023, 43: 1925-1931.

[25] Cao YL, Li F, Zhao H, et al. Flavonoids from Melia azedarach inhibit androgen-independent LNCaP cells through the PI3K/AKT pathway. Acta Univ Med Anhui, 2018, 53: 1017-1021.

[26] Abeer MM, Yang WC, Maarten CB. Soy isoflavones and prostate cancer: a review of molecular mechanisms. J Steroid Biochem Mol Biol, 2014, 140: 116-132.

[27] Nasreddine EO, Saad B, Asaad K, et al. Unveiling the molecular mechanisms: dietary phytosterols as guardians against cardiovascular diseases. Nat Prod Bioprospect, 2024, 14: 1-29.

[28] Bai X, Wang X, Nan ML, et al. Research progress on natural pentacyclic triterpenoids and their derivatives in

anti-cerebrovascular and cardiovascular diseases. Chin Herb Med, 2019, 50: 745-752.

[29] Quan SH, Zhou ZJ, Peng QM, et al. Study on the effect of total glycosides of white peony on reducing dry eye disease through MAPK/NF-κB signaling pathway. Chin Mod Tradit Chin Med Remote Educ, 2025, 23: 116-119.

[30] Xiong R, Yang XH, Kun J, et al. The mechanism of astragaloside IV alleviating acute lung injury in septic rats through regulating the AMPK/SIRT1 signaling pathway. Chin J Geriatr, 2025, 45: 3677-3681.

[31] Li L, Wang JY, Ye JY, et al. Thrombopoietin protects neural cells and endothelial cells from apoptosis via PI3K/AKT pathway. Blood, 2020, 136: 8-9.

[32] Cheng SY, Zhang XX, Qian F, et al. Astragaloside IV exerts angiogenesis and cardioprotection after myocardial infarction via regulating PTEN/PI3K/Akt signaling pathway. Life Sci, 2019, 227: 82-93.

[33] Tzu SY, Tze HL, Jen FL, et al. Astragalus membranaceus enhances myotube hypertrophy through PI3K-mediated Akt/mTOR signaling phosphorylation. Nutrients, 2022, 14: 1670.

[34] Xu J, Zhang YH, Chen JJ, et al. Exploring the mechanism of modified astragalus and Guizhi Wuwu decoction in treating rheumatoid arthritis based on network pharmacology and cellular experiments. Henan Tradit Chin Med, 2024, 44: 542-548.