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Study on the Pharmacological Material Basis and Mechanism of Action of Yangwei Qingre Huayu Decoction in the Treatment of Chronic Atrophic Gastritis Based on LC-MS and Network Pharmacology

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Keywords: Yangwei Qingre Huayu Decoction (YQHD); Chronic Atrophic Gastritis (CAG); UHPLC-Q Exactive Focus MS/MS; Network Pharmacology

Abstract: In order to investigate the bioactive substances and potential mechanisms of action of Yangwei Qingre Huayu Decoction (YQHD) in the treatment of chronic atrophic gastritis (CAG) using ultra-high-performance liquid chromatography coupled with quadrupole high-resolution mass spectrometry (UHPLC-Q-Exactive-MS/MS) combined with network pharmacology methods. UHPLC-Q-Exactive-MS/MS was used to obtain total ion chromatograms of the YQHD aqueous extract under different ion modes. The chemical constituents of the extract were rapidly identified, and potential active components were determined through literature review and database searches. Based on network pharmacology, a network of key components and critical targets was constructed. Gene ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) analyses were performed to identify key signaling pathways and targets. Resultly, a total of 162 active components were identified in YQHD, including salvianolic acids, ursolic acid, and tetrahydropalmatine. GO and KEGG analyses revealed core targets such as tumor protein P53 (TP53), heat shock protein HSP90AA1, and signal transducer and activator of transcription 3 (STAT3). Key pathways included the TNF signaling pathway and proteoglycans in cancer. In conclusion, the results suggest that YQHD may exert therapeutic effects on CAG through multi-component, multi-target, and multi-pathway mechanisms, providing scientific support for its further clinical application.

1. Introduction

Chronic Atrophic Gastritis (CAG) is a type of chronic gastritis characterized by the reduction of gastric mucosal glands due to repeated epithelial damage, which may be accompanied by or without intestinal metaplasia and/or pseudopyloric metaplasia. Clinically, it mainly manifests as nonspecific dyspeptic symptoms such as discomfort, fullness, and pain in the upper abdomen, often accompanied by digestive symptoms like loss of appetite, belching, acid reflux, nausea, and bitter taste in the mouth [1]. From the perspective of Traditional Chinese Medicine (TCM), CAG should be categorized under

conditions such as 'epigastric pain', 'hiccup', 'noisy stomach', and 'fullness'. Studies suggest that approximately 10% of CAG cases may progress to gastric cancer, with the widely recognized Correa model of gastric carcinogenesis describing the sequential transition from non-atrophic gastritis to atrophic gastritis, followed by intestinal metaplasia, dysplasia, and ultimately early gastric cancer [2]. Therefore, timely and proactive treatment of CAG is of paramount importance in preventing precancerous lesions of the stomach. Currently, Western medicine lacks specific drugs for the treatment of CAG, and mainly adopts symptomatic treatments such as mucosal protectants, prokinetic agents, and acid-suppressing medications [3]. Although these treatments may alleviate symptoms to some extent, recurrence is common among patients. In contrast, TCM offers advantages in the treatment of CAG and precancerous gastric lesions, with its emphasis on holistic regulation, treatment of both symptoms and root causes, individualized care, and syndrome differentiation. Clinical practice has shown that TCM may slow down or even reverse the progression of CAG [4].

Director Wen Xinli, of the Second Department of Gastroenterology at Shaanxi Provincial Hospital of Traditional Chinese Medicine, believes that the onset and progression of CAG is a long-term process that evolves from Qi stagnation to blood stasis, transitioning from a functional disorder to organic damage. During the course of CAG, blood stasis plays a constant role, not only as a pathological outcome but also as a pathogenic factor. Thus, treatment of CAG should prioritize the use of blood-activating and stasis-resolving drugs. Based on this theory, Director Wen formulated the Yangwei Qingre Huayu Decoction, which has shown promising clinical efficacy in the treatment of CAG, as demonstrated by Kou Yuan et al.'s clinical study [7]. This decoction effectively improves pathological features such as gastric mucosal atrophy, intestinal metaplasia, and dysplasia. However, there is currently a lack of research on the chemical composition and pharmacological mechanisms underlying Yangwei Qingre Huayu Decoction in the treatment of CAG. Therefore, this study employs ultra-high-performance liquid chromatography coupled with quadrupole high-resolution mass spectrometry (UHPLC-Q-Exactive-MS/MS) in combination with network pharmacology to analyze the potential mechanisms of action of Yangwei Qingre Huayu Decoction in the treatment of CAG.

2. Materials and Methods

2.1. Materials

2.1.1. Drugs and Sample Preparation

The following herbs were obtained from the pharmacy of Shaanxi Provincial Hospital of Traditional Chinese Medicine: Salvia miltiorrhiza,Hedyotis diffusa, vinegar-processed Corydalis yanhusuo, Scutellaria barbata, Dendrobium, Atractylodes macrocephala, Amomum villosum, sandalwood, licorice, Panax notoginseng, and lily bulbs. According to the prescription, the following herbs were weighed: Salvia miltiorrhiza, Oldenlandia diffusa, vinegar-processed Corydalis yanhusuo, Scutellaria barbata, Dendrobium, Atractylodes macrocephala, Amomum villosum, sandalwood, licorice slices, Panax notoginseng powder, and Lilii Bulbus. Nine herbs, excluding Amomum villosum and sandalwood, were soaked in 10 times their volume of water for 30 minutes in a decoction pot. The mixture was brought to a boil on high heat, followed by simmering for 55 minutes on low heat. Subsequently, the previously soaked Amomum villosum and sandalwood were added and decocted for an additional 5 minutes. The decoction was then filtered. For the second extraction, the filtered residue was added to 8 times its volume of water, boiled on high heat, and then simmered for 45 minutes on low heat. The two water extractions were combined to obtain the Yangwei Qingre Huayu Decoction. The decoction was stored in a refrigerator at 4 ℃ for future use. A 1 mL sample of this decoction was transferred to a 10 mL volumetric flask and diluted to the mark with methanol. After shaking, the solution was filtered through a 0.22 μm microporous membrane, and the filtrate

was collected for further analysis.

2.1.2. Instruments and Reagents

An Ultimate 3000 ultra-high-performance liquid chromatography (UHPLC) system coupled with a Q Exactive Focus mass spectrometer (Thermo Fisher Scientific, USA) was used. A Mill-Q ultrapure water purification system (Millipore, USA) and a Sartorius SQP electronic analytical balance (Sartorius Scientific Instruments, Beijing, China) were employed. Methanol was of chromatographic grade, formic acid was of mass spectrometric grade (Thermo Fisher Scientific, USA), and water was ultrapure. All other reagents were of analytical grade.

2.2. Methods

2.2.1. Chromatographic Conditions

A Thermo Accucore aQ C18 column (150 mm × 2.1 mm, 2.6 μm) was used. The mobile phase consisted of methanol (A) and 0.1% formic acid in water (B), and gradient elution was performed as follows: 0–13 minutes, 5%–60% A; 13–27 minutes, 60%–95% A; 27–30 minutes, 95% A. The flow rate was 0.3 $mL \cdot min^{-1}$, the injection volume was 2 μL, and the column temperature was maintained at 30 ℃.

2.2.2. Mass Spectrometry Conditions

The ion source was a heated electrospray ionization (H-ESI) source with a spray voltage of 3.5 kV. The sheath gas (N_2) flow rate was 40 arb, and the auxiliary gas flow rate was 10 arb. The auxiliary gas heater was set at 350 ℃, and the capillary temperature was 320 ℃. The S-lens RF level was set to 50, and automatic gain control (AGC) was 10^6. The scanning mode employed was positive and negative ion Full MS/dd-MS ² The Full MS resolution was set to 70,000, and the dd-MS ²resolution was 35,000. The scan range was m/z 120–1,800, with collision energies of 30 eV, 50 eV, and 70 eV.

2.2.3. Establishment of the Yangwei Qingre Huayu Decoction Chemical Composition Database

The chemical constituents of the 11 herbs in Yangwei Qingre Huayu Decoction (Salvia miltiorrhiza, Oldenlandia diffusa, vinegar-processed Corydalis yanhusuo, Scutellaria barbata, Dendrobium, Atractylodes macrocephala, Amomum villosum, sandalwood, licorice slices, Panax notoginseng powder, and Lilii Bulbus) were retrieved from the Traditional Chinese Medicine Systems Pharmacology Database and Analysis Platform (TCMSP, https://tcmsp-e.com) and HERB (http://herb.ac.cn). Additional data were supplemented by reviewing relevant literature. The compiled data were used to establish the chemical composition database of Yangwei Qingre Huayu Decoction.

2.2.4. Data Processing

Based on the exact relative molecular mass information obtained from mass spectrometry, the molecular ions with a mass-to-charge ratio (m/z) difference of less than 5 ppm between the measured and theoretical values were matched with the self-established Yangwei Qingre Huayu Decoction chemical composition database to preliminarily identify the compounds. Xcalibur 2.0 software was used to further extract chromatographic peaks and secondary fragment ion information of target compounds. The data were then combined with chemical composition databases and relevant literature to identify and confirm the predicted chemical constituents of Yangwei Qingre Huayu Decoction.

2.3. Network Pharmacology Analysis

2.3.1. Prediction of Targets for the Chemical Components of Yangwei Qingre Huayu Decoction

The chemical components of Yangwei Qingre Huayu Decoction were entered into the PubChem database (https://pubchem.ncbi.nlm.nih.gov/). After obtaining the SMILES format of the relevant compounds, the information was imported into the Swiss Target Prediction database (http://www.swisstargetprediction.ch/) to predict potential targets for the compounds [5].

2.3.2. Target Screening for Chronic Atrophic Gastritis

We used "Chronic Atrophic Gastritis" as the keyword, related disease targets were searched through the OMIM database (https://omim.org/) and GeneCards database (https://www.genecards.org/). The results from both databases were combined, and duplicate entries were removed to obtain potential targets related to Chronic Atrophic Gastritis (CAG). The identified disease targets were then intersected with the predicted targets of the active compounds of Yangwei Qingre Huayu Decoction using the Venny online tool (https://bioinfogp.cnb.csic.es/tools/venny/index.html). A Venn diagram was generated to visualize the potential therapeutic targets of Yangwei Qingre Huayu Decoction for CAG.

2.3.3. Construction of Protein-Protein Interaction Networks

The potential targets of Yangwei Qingre Huayu Decoction for the treatment of CAG were imported into the STRING database to obtain the protein-protein interaction (PPI) network. The network was saved in TSV format and imported into Cytoscape 3.7.2 for further organization. The targets were ranked according to betweenness centrality to identify key targets.

2.3.4. Construction of the "Drug-Component-Target" Network

The herbs, chemical compounds, and common target genes of Yangwei Qingre Huayu Decoction were imported into Cytoscape 3.7.2 to construct the "herb-compound-target" network for the treatment of CAG. The Network Analyzer tool in the software was used to calculate topological parameters of the network, and the core chemical components interacting with the disease targets were screened based on betweenness centrality, in descending order.

2.3.5. GO Functional and KEGG Pathway Enrichment Analysis

With $P < 0.05$ as the selection criterion, GO functional enrichment and KEGG pathway enrichment analyses were performed on the identified targets. The top ten pathways were selected and visualized for further interpretation.

3. Results

3.1. UHPLC-Q Exactive Focus MS/MS Analysis

We used UHPLC-Q Exactive Focus MS/MS, the total ion chromatograms (TICs) of the test samples were obtained under different ionization modes. The Yangwei Qingre Huayu Decoction exhibited good responses in both positive and negative ion modes, with dense response signals appearing within the 0–40 min range. A total of 925 chemical components were detected in the decoction. By analyzing the primary and secondary mass spectrometry data and cross-referencing the literature, 162 chemical components were identified. These components mainly included salvianolic

acids, ursolic acid, tetrahydropalmatine, apigenin, atractylenolide, quercetin, isoglycyrrhizin, and ginsenoside Rg3.

3.2. Network Pharmacology Analysis of Yangwei Qingre Huayu Decoction

3.2.1. Target Prediction of Yangwei Qingre Huayu Decoction for Treating Chronic Atrophic Gastritis

We followed the methods outlined above, mass spectrometry analysis and literature review yielded 162 chemical components of Yangwei Qingre Huayu Decoction, resulting in the identification of 1,319 potential therapeutic targets. We used "Chronic Atrophic Gastritis" as the keyword, 898 disease-related targets were retrieved from the databases after removing duplicates. By intersecting the therapeutic targets of the active components of Yangwei Qingre Huayu Decoction with the disease targets of CAG, 201 potential targets for treating CAG were identified. A Venn diagram was generated to visualize these targets, as shown in Figure 1.

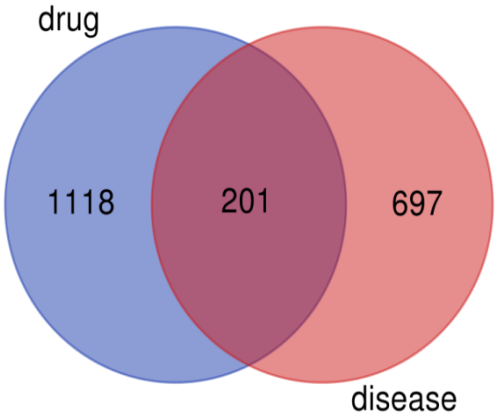

Figure 1: Venn diagram of the intersecting targets of YQHD and CAG

3.2.2. Construction of Protein-Protein Interaction Network

The 201 potential therapeutic targets of Yangwei Qingre Huayu Decoction for treating CAG were imported into the STRING database. Due to the large number of targets, a “highest confidence (0.900)” filter was applied to obtain the protein-protein interaction (PPI) network. The resulting PPI data were exported in TSV format and imported into Cytoscape 3.7.2 for further organization, generating a clearer PPI diagram (Figure 2). The diagram contained 201 nodes and 639 edges; the denser the connections, the stronger the interactions. Based on betweenness centrality ranking, the top ten key targets identified were: tumor protein P53 (TP53), heat shock protein HSP90AA1, signal transducer and activator of transcription 3 (STAT3), serine/threonine kinase (AKT1), fibronectin 1 (FN1), tumor necrosis factor (TNF), proto-oncogene tyrosine-protein kinase SRC, heat shock protein 70 (HSPA5), intercellular adhesion molecule-1 (ICAM1), and chemokine receptor CXCR4.

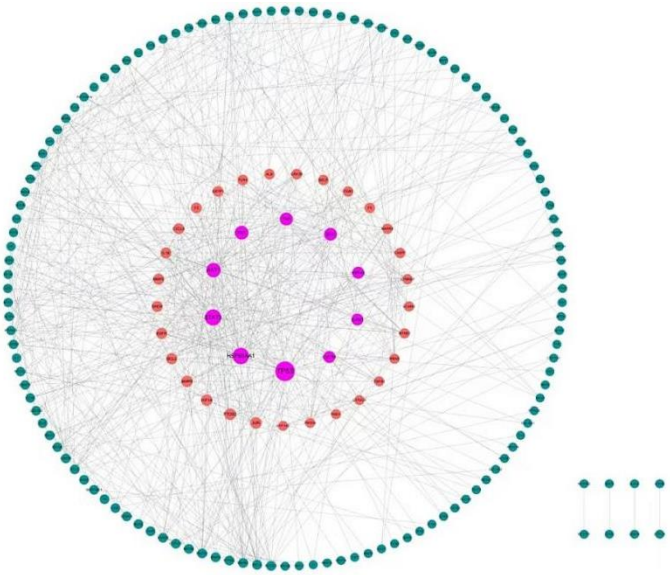

Figure 2: PPI Diagram

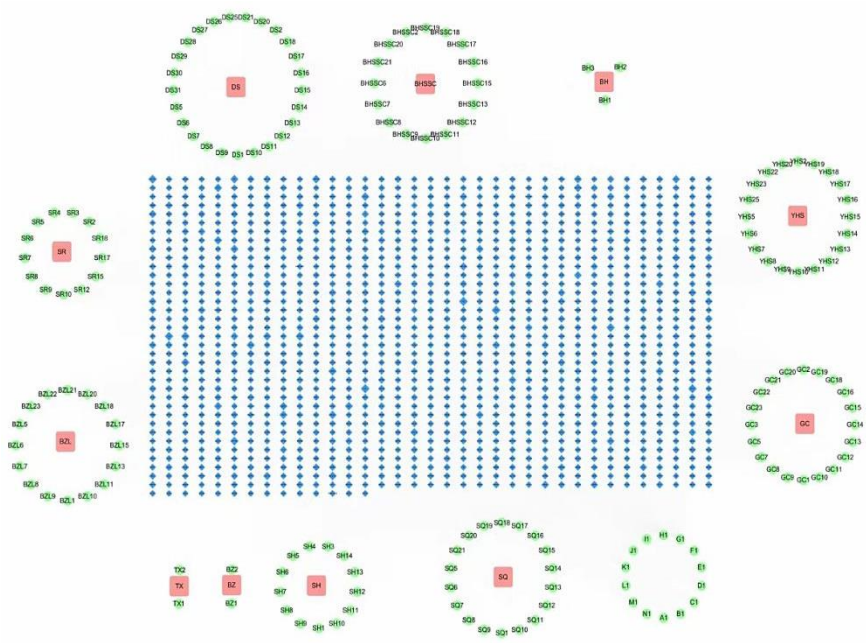

Figure 3: Drug-Component-Target Network

3.2.3. Construction of "Drug-Component-Target" Network

The herbal components and their corresponding targets for Yangwei Qingre Huayu Decoction were imported into Cytoscape 3.7.2 to construct the “Drug-Component-Target” network for treating CAG (Figure 3). The network consisted of 1,447 nodes and 18,730 edges, illustrating that the therapeutic effect of Yangwei Qingre Huayu Decoction on CAG is the result of multi-component, multi-target interactions. Using the Network Analyzer tool, the network topology parameters were calculated, and the top 20 core chemical components interacting with the disease targets were identified based on betweenness centrality. Details on these components, including retention times, mass spectrometry data, and identification results, are provided in Table 1.

Table 1: Mass spectrometry data and identification results of the core components of YQHD

NO.	Name	Molecular Formula	Retention Time (min)	Ion Mode	Secondary Ion Fragments	Source Medicinal Herb
1	quercetin	C15H10O7	16.69	[M+H]+	303.0497, 68.9971, 153.0182, 81.0333	Oldenlandia diffusa, Scutellaria barbata, licorice, Panax notoginseng, Amomum villosum, yanhusuo
2	salvianolic acid A	C26H22O10	19.93	[M-H]-	295.0613, 109.0295, 185.0244, 135.0453, 493.1203	Salvia miltiorrhiza
3	tetrahydropalmatine	C30H48O3	28.14	[M+H]+	455.3522, 107.0854, 119.0854, 93.0698, 437.3414	Salvia miltiorrhiza
4	L-Tetrahydropalmatine	C21H25NO4	16.91	[M+H]+	356.1852, 192.1019, 148.0757, 131.0732, 79.0543	yanhusuo
5	Apigenin	C15H10O5	27.17	[M-H]-	269.0456, 117.0347, 65.0034, 89.0397, 151.0038	Scutellaria barbata, Salvia miltiorrhiza
6	Atractylenolide II	C15H20O2	32.25	[M+H]+	91.0541, 115.0542, 187.1474, 151.0757, 215.1431	Atractylodes macrocephala
7	Isoliquiritigenin	C15H12O4	16.03	[M+H]+	137.0233, 81.0334, 65.0386, 147.0440, 257.0800	licorice
8	Ginsenoside	C36H62O9	30.95	[M+Na]+	661.4286, 64.9771, 203.0529, 143.0066	Panax notoginseng
9	Vanillic Acid	C8H8O4	8.8	[M+H]+	55.9346, 68.9971, 90.9476, 141.0546, 126.0310	Oldenlandia diffusa, Scutellaria barbata, yanhusuo
10	Palmitic Acid	C16H32O2	39.15	[M-H]-	255.2329, 61.9883, 242.0677, 78.9590, 128.0143	Salvia miltiorrhiza, yanhusuo, Scutellaria barbata
11	Ferulic Acid	C10H10O4	19.68	[M+H]+	55.9346, 72.9370, 90.9476, 123.9453, 163.0389	Oldenlandia diffusa, Salvia miltiorrhiza
12	Trifolioside	C21H20O11	21.66	[M-H]-	447.0935, 285.0406, 110.0010,	Panax notoginseng, Oldenlandia diffusa

					165.9908, 211.0397	
13	Luteolin	C16H12O6	26.58	[M-H]-	284.0328, 65.0033, 117.0346, 299.0200, 183.0449	Scutellaria barbata, licorice
14	Sigmoidin-B	C20H20O6	29.13	[M-H]-	125.0244, 57.0346, 229.0870, 83.0139, 146.0375, 309.8751	licorice
15	Isoferulic Acid	C10H10O4	19.68	[M+H]+	63.0230, 89.0385, 163.0389, 135.0440, 117.0336	Salvia miltiorrhiza
16	Yuanhunine	C21H25NO4	16.57	[M+H]+	356.1851, 192.1018, 176.0705, 148.0756, 131.0730	yanhusuo
17	uralsaponin C	C42H64O16	35.21	[M+Na]+	847.4077, 199.0211, 375。0529, 495.3434, 671.3726	licorice
18	fimbriol B	C15H12O4	16.74	[M+H]+	137.0233, 81.0334, 91.0540, 65.0386, 257.0800	Dendrobium
19	Bulbocapnine	C21H25NO4	17.63	[M+H]+	294.1247, 310.1196, 208.0879, 191.0853, 249.0903	yanhusuo
20	Baicalein	C15H10O5	27.17	[M-H]-	269.0456, 117.0346, 65.0033, 89.0395, 149.0242	Scutellaria barbata

3.2.4. GO Functional Analysis and KEGG Pathway Enrichment

GO and KEGG pathway enrichment analyses were conducted on the core targets. Using a threshold of $P<0.05$, the intersecting targets were analyzed for GO functions and KEGG pathway enrichment. GO functional analysis included biological processes (BP), cellular components (CC), and molecular functions (MF). The top 10 ranked pathways by ascending P-value are shown in Figure 4. The GO analysis results indicated that the primary biological processes involved were response to lipopolysaccharides, reactive oxygen species metabolic process, response to molecules of bacterial origin, and cellular response to chemical stress. The main cellular components involved were membrane rafts, membrane microdomains, external side of the plasma membrane, focal adhesion, and platelet alpha granules. The primary molecular functions included protease binding, phosphatase binding, and heme binding. The KEGG pathway enrichment analysis results are displayed in Figure 5. These results show that the chemical components of Yangwei Qingre Huayu Decoction mainly participate in pathways such as lipid and atherosclerosis, AGE-RAGE signaling pathway in diabetic

complications, prostate cancer, TNF signaling pathway, and proteoglycans in cancer, contributing to its therapeutic effect on CAG.

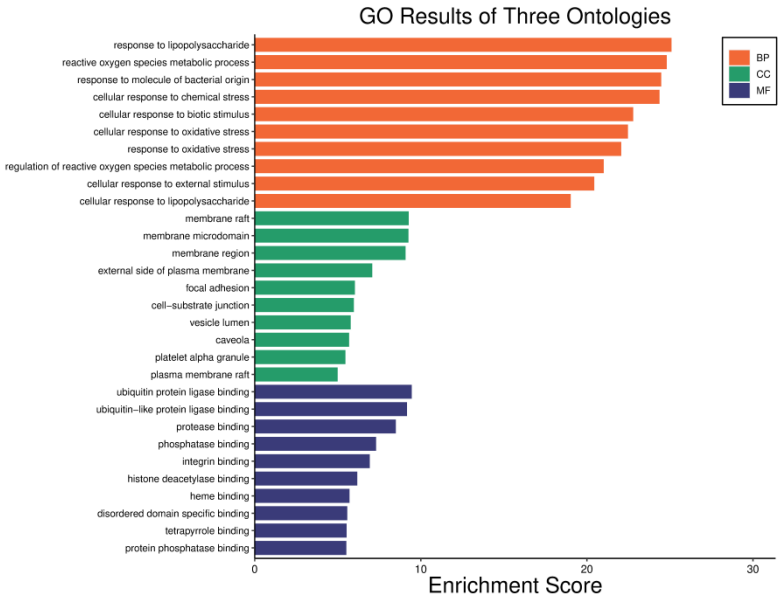

Figure 4: GO enrichment analysis of YQHD treated CAG

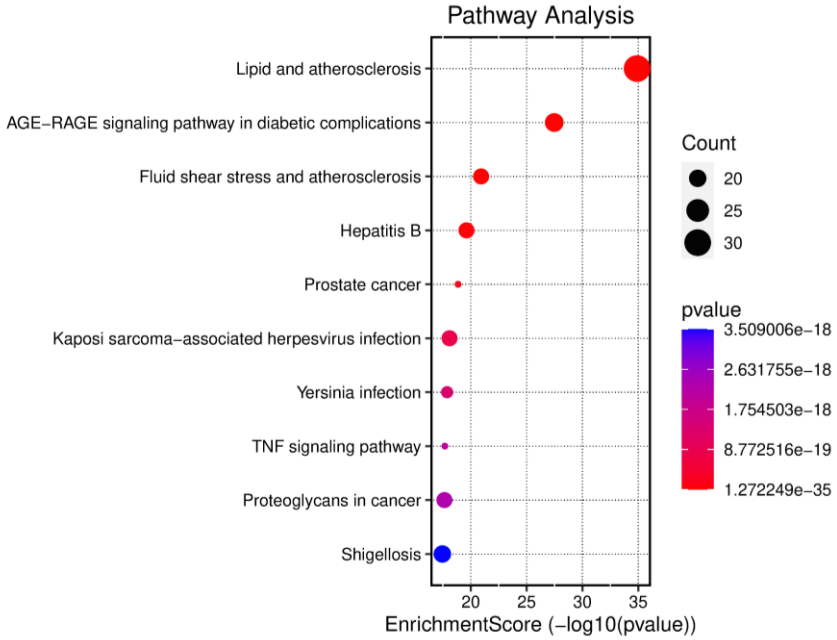

Figure 5: KEGG pathway enrichment analysis of YQHD for CAG treatment

4. Discussion

In traditional Chinese medicine (TCM), chronic atrophic gastritis (CAG) can be categorized under syndromes such as "Wei Pi" (gastric fullness), "Cao Za" (noisy stomach), and "Wei Tong" (gastric pain). The primary affected organ is the stomach, but it is closely related to the liver, spleen, and gallbladder[6]. According to TCM theory, the spleen functions optimally when it ascends, promoting health, while the stomach's function thrives when it descends, ensuring harmony. The spleen and stomach are crucial organs for the absorption and digestion of food and the distribution of nutrients.

The liver regulates the free flow of Qi, and when liver Qi either rises excessively or fails to ascend adequately, it can disrupt the spleen and stomach, leading to dysfunction. The pathogenesis of CAG is largely attributed to the impaired transportation and transformation functions of the spleen and stomach, disrupted gastric motility, and obstructed gastric Qi.

The progression of CAG is a prolonged pathological process in which the weakness of the spleen and stomach results in poor Qi and blood circulation, leading to blood stasis. This stasis generates heat, which accumulates and transforms into toxicity, further exacerbating blood stasis and ultimately damaging the gastric mucosa. This process culminates in mucosal atrophy. Based on this pathogenesis, the Second Department of Spleen and Stomach Diseases at Shaanxi Provincial Hospital of Traditional Chinese Medicine has achieved significant clinical efficacy using Yangwei Qingre Huayu Decoction in the treatment of CAG.

Yangwei Qingre Huayu Decoction consists of 11 herbs, including Salvia miltiorrhiza, Oldenlandia diffusa, vinegar-processed Corydalis yanhusuo, Scutellaria barbata, Dendrobium, Atractylodes macrocephala, Amomum villosum, sandalwood, licorice slices, Panax notoginseng powder, and Lilii Bulbus. In this formula, Salvia miltiorrhiza, Corydalis yanhusuo, and Panax notoginseng work together to invigorate blood and relieve pain. Atractylodes macrocephala and Amomum villosum tonify Qi and harmonize the spleen and stomach, while sandalwood regulates Qi and alleviates pain. Scutellaria barbata and Oldenlandia diffusa clear heat and detoxify, and Lilium brownii and Dendrobium nourish Yin and enhance stomach function. The combination of these herbs effectively nurtures the stomach, clears heat, invigorates blood, and alleviates pain.

Although Yangwei Qingre Huayu Decoction has demonstrated notable clinical efficacy, its broader application and utilization are hindered by a lack of comprehensive analysis of its material basis.

In this study, UHPLC-Q Exactive Focus MS/MS combined with network pharmacology was employed to scientifically analyze the chemical constituents, relevant targets, and mechanisms of action of the Yangwei Qingre Huayu Decoction (YQHD) in the treatment of chronic atrophic gastritis (CAG). A total of 162 chemical compounds were identified, including salvianolic acids, ursolic acid, tetrahydropalmatine, apigenin, atractylenolide, quercetin, isoglycyrrhizin, and ginsenoside. Salvianolic acids, primarily derived from Salvia miltiorrhiza, represent key active hydrophilic constituents of this herb. Extensive research has demonstrated that salvianolic acids exert anti-inflammatory, antioxidant, and anti-tumor effects, with a significant inhibitory impact on the growth of transplanted colon cancer in mice [8]. Ursolic acid, which is abundant in Oldenlandia diffusa and other herbs, effectively suppresses gastric cancer cell proliferation and migration, induces apoptosis, and enhances immune function by modulating the JAK/STAT signaling pathway in lymphocytes [9-10]. Tetrahydropalmatine alleviates pain through D2 receptor blockade in the spinal cord and significantly inhibits the proliferation of malignant glioma cells by disrupting their cell cycle and promoting apoptosis [11-12]. Apigenin induces apoptosis by decreasing the Bcl-2/Bax protein expression ratio and halts gastric cancer xenograft development by generating ROS and causing cell cycle arrest through inhibition of the STAT3/JAK2 pathway [13]. Atractylenolide promotes the migration and proliferation of IEC-6 intestinal epithelial cells through polyamine-mediated Ca2+ signaling, thereby protecting against gastrointestinal mucosal injury [14]. Quercetin, a compound widely present in various traditional Chinese herbs, has been shown to inhibit gastric cancer cell proliferation and invasion [15]. Isoglycyrrhizin improves cisplatin resistance in gastric cancer by enhancing apoptosis in vitro and inhibiting tumor growth in vivo [16]. Ginsenosides suppress tumor growth by promoting necrosis and apoptosis of BGC-823 cells and inducing autophagy, which inhibits gastric cancer cell proliferation [17].

The PPI network diagram suggests that the core targets of the Yangwei Qingre Huayu Decoction (YQHD) in the treatment of CAG may include tumor protein P53 (TP53), HSP90AA1, signal

transducer and activator of transcription 3 (STAT3), serine/threonine kinase (AKT1), fibronectin (FN1), tumor necrosis factor (TNF), sarcoma gene (SRC), heat shock protein 70 protein 5 (HSPA5), intercellular adhesion molecule 1 (ICAM1), and C-X-C chemokine receptor type 4 (CXCR4). Recent studies have indicated that the expression of TNF-α is significantly elevated in the gastric mucosal tissues of patients with gastritis. TNF is a cytokine that promotes the release of inflammatory factors and induces apoptosis [18]. TP53 is involved in regulating physiological processes such as apoptosis, and mutations in TP53 during the early stages of gastric cancer can accelerate cancer progression [19]. HSP90AA1, a functional gene of HSP90α, plays a role in the proliferation and metastasis of gastric cancer [20]. Based on the above core targets, it is speculated that YQHD exerts its therapeutic effects on CAG primarily through the regulation of proto-oncogenes and tumor suppressor genes.

KEGG pathway enrichment analysis indicated that the treatment of CAG with YQHD involves multiple pathways, including lipid and atherosclerosis, AGE-RAGE signaling pathway in diabetic complications, prostate cancer, TNF signaling pathway, and proteoglycans in cancer. Notably, several of these pathways are associated with cancer development and progression, suggesting that YQHD has significant potential in treating CAG with precancerous lesions. Lipid and atherosclerosis is a key factor in the formation of atherosclerosis, and the TNF signaling pathway regulates the expression of various cytokines and inflammatory factors, playing a critical role in the inflammatory response and being closely associated with atherosclerosis [21]. According to the literature, AGEs can induce oxidative stress, accelerate inflammation, and promote thrombosis in various cells. Inhibiting the formation of AGEs and blocking their interaction with their receptor (RAGE), as well as suppressing RAGE-mediated signaling pathways, can help mitigate the progression of inflammation and thrombosis [22]. These findings align with the traditional Chinese medicine effects of YQHD, which "clear heat and resolve stasis." Therefore, the analysis of the pharmacological substances and mechanisms of YQHD in the treatment of CAG demonstrates that its therapeutic significance lies in its ability to regulate the expression of various inflammatory factors, inhibit cancer cell proliferation, and promote cancer cell apoptosis.

5. Conclusion

In conclusion, this study, based on mass spectrometry combined with network pharmacology, demonstrates that YQHD can treat chronic atrophic gastritis with precancerous lesions through multi-component, multi-target, and multi-pathway mechanisms. These findings provide valuable insights and a foundation for future research.

Acknowledgements

Clinical Observation of Jue Shu Gao in Treating Cold-Heat Complex Chronic Atrophic Gastritis with Insomnia and Its Effects on the Gut Microbiota. (SZY-KJCYC-2023-020).

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