Journal of Clinical and Nursing Research, 2025, Volume 9, Issue 12
http://ojs.bbwpublisher.com/index.php/JCNR
Online ISSN: 2208-3693
Print ISSN: 2208-3685

Exploring the Mechanism of Wumei Pill in the Treatment of Autoimmune Hepatitis Based on Network Pharmacology and Molecular Docking

Xinyue Shangguan[1], Shuangyue Wen[1], Silong Li[1], Chuyu Dong[1], Ruiyun Wang[1], Buyue Zhang[1], He Zhang[2]*

[1]School of Medical Technology, Qiqihar Medical University, Qiqihar 161006, Heilongjiang, China
[2]Department of Immunology, Qiqihar Medical University, Qiqihar 161006, Heilongjiang, China

**Corresponding author: Zhang He, zhanghe19930826@163.com*

Abstract: *Objective*: To explore the molecular mechanism and action pathways of Wumei Pill in the treatment of autoimmune hepatitis (AIH) using network pharmacology and molecular docking methods. *Methods*: The active components and targets of Wumei Pill, as well as AIH-related disease targets, were screened through the TCMSP, GeneCards, OMIM, and Disgenet databases. Cytoscape 3.9.1 was used to construct a series of topological networks, followed by Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis and Gene Ontology (GO) enrichment analysis. Molecular docking and visualization were performed using AutoDockTools 1.5.7 and PyMOL 2.4.0. *Results*: A total of 124 active components of Wumei Pill, 877 drug targets, 1130 disease targets, and 64 overlapping targets were obtained. GO enrichment analysis yielded 82 biological processes, 4 cellular components, and 19 molecular functions. KEGG pathway enrichment analysis identified 21 signaling pathways. *Conclusion*: Wumei Pill can act on targets such as Tumor Necrosis Factor (TNF), Caspase 3 (CASP3), C-X-C Motif Chemokine Ligand 8 (CXCL8), Nuclear Factor Kappa B Subunit 1 (NFKB1), and Transforming Growth Factor Beta 1 (TGFB1) through active components including girinimbine and (R)-tetrahydroberberine. It further regulates inflammation and apoptosis-related pathways such as tumor-related signaling pathways and Th17 cell differentiation pathway to treat AIH. This study provides a theoretical basis for in-depth research on the mechanism of Wumei Pill in the treatment of AIH and the development of therapeutic drugs.

Keywords: Wumei pill; Autoimmune hepatitis (AIH); Network pharmacology; Molecular docking technology

Online publication: Dec 31, 2025

1. Introduction

Autoimmune hepatitis (AIH) is a chronic inflammatory liver disease caused by immune abnormalities. Clinical manifestations vary among patients of different severity, mainly characterized by interface hepatitis in liver

histopathological examination, elevated serum gamma-glutamyl transpeptidase (GGT), immunoglobulin G (IgG), and positive autoantibodies such as antinuclear antibody (ANA) and anti-smooth muscle antibody (ASMA) [1]. Currently, the incidence of AIH is increasing year by year. Due to its strong concealment, it is difficult for patients to detect in the early stage, and it can easily progress to cirrhosis and liver failure if left untreated [2]. Therefore, strengthening early detection, timely medical intervention, and reducing inflammation levels are crucial to prevent disease deterioration.

After receiving AIH patients, Western medicine usually adopts the traditional treatment plan of combining glucocorticoids with immunosuppressants. This plan takes a long time, causes various adverse reactions during medication, and is prone to recurrence after drug withdrawal [3]. The therapeutic effect of this plan on AIH patients is not ideal, and long-term medication requires substantial financial resources, bringing a heavy economic burden to patients' families. Thus, exploring more effective, economical, and safe treatment plans is imperative [4].

Traditional Chinese medicine (TCM) is an important part of traditional medicine. Guided by the principles of holistic view and syndrome differentiation and treatment in clinical application, it has the advantages of fewer adverse reactions and cost-effectiveness, and has shown good efficacy in the treatment of liver diseases, providing conditions for improving AIH treatment outcomes. Wumei Pill is a TCM preparation derived from Zhang Zhongjing's Shanghan Lun (Treatise on Febrile Diseases). Its main components include 10 medicines such as *Mume Fructus*, *Asari Radix* et Rhizoma, *Zingiberis Rhizoma*, *Cinnamomi Ramulus*, *Ginseng Radix* et Rhizoma, *Angelicae Sinensis Radix*, *Phellodendri Chinensis Cortex*, *Coptis Chinensis Rhizoma*, and *Aconiti Radix Lateralis Preparata*. It has the main effects of warming the viscera to calm roundworms, soothing the liver and regulating the middle energizer, clearing heat from the upper and warming the lower, balancing pathogenic factors and healthy Qi, and treating both cold and heat syndromes. It is widely used in the treatment of multisystem diseases such as gastroenteritis and hepatorenal syndrome [5–8]. Pharmacological evidence-based research has shown that Wumei Pill can inhibit Th17 cell differentiation and regulate the NLRP3 inflammasome to improve inflammatory responses [9,10].

Network pharmacology and molecular docking technology adopt an interdisciplinary research approach, combining bioinformatics and computer technology to mine relevant network data around research topics and generate drug-disease mapping relationship networks, providing support for further analyzing the therapeutic effects of TCM on diseases. Using network pharmacology and molecular docking technology to explore the mechanism of Wumei Pill in the treatment of AIH helps enrich clinical diagnosis and treatment methods and improve the cure rate of this disease.

2. Materials and methods

2.1. Screening of active components, targets of Wumei Pill, and construction of overlapping targets with diseases

The names and 2D structures of components of Wumei Pill (*Mume Fructus*, *Asari Radix* et Rhizoma, *Zingiberis Rhizoma*, *Cinnamomi Ramulus*, *Ginseng Radix* et Rhizoma, *Angelicae Sinensis Radix*, *Phellodendri Chinensis Cortex*, *Coptis Chinensis Rhizoma*, *Aconiti Radix Lateralis Preparata*) were obtained from the TCMSP database. Active components with oral bioavailability (OB) ≥ 40% and drug-likeness (DL) ≥ 0.18 were screened. The Swiss Target Prediction database was used to predict the targets of active components, and drug component genes were obtained. AIH-related disease targets were retrieved from the GeneCards, OMIM, and Disgenet databases using

"Autoimmune hepatitis" as the index. The overlapping targets between disease genes and drug component targets were obtained using Venny 2.1.0.

2.2. Construction of protein-protein interaction (PPI) network

The overlapping targets were input into the STRING 12.0 database, with the species set to "Homo sapiens" and confidence > 0.40. The potential targets were screened and imported into Cytoscape 3.9.1 software. CentiScaPe 2.2 was used to select parameters including Degree, Closeness, and Betweenness to obtain core targets and construct the PPI network diagram.

2.3. Construction of topological networks of TCM component-target and pathway-target

Information on drugs, active components, common targets, pathways, and targets was imported into Cytoscape 3.9.1 for network structure visualization. Node colors were set as follows: TCM component-target network: drugs–purple, active components–green, common targets–orange; pathway-target topological network: targets–green, pathways–red. Node sizes were set based on node degree (from small to large with increasing degree), resulting in the drug-component-target network diagram and pathway-target topological network diagram.

2.4. Kyoto encyclopedia of genes and genomes (KEGG) and gene ontology (GO) enrichment analysis

The common drug-disease targets were imported into the DAVID platform, and enrichment analysis was performed by selecting "OFFICIAL-GENE-SYMBOL", Homo sapiens, and Gene List. Enriched biological processes (BP), cellular components (CC), and molecular functions (MF) were obtained (screened with $p < 0.05$). Microbioinformatics online mapping tools were used to draw bubble charts and bar charts for visualization of results.

2.5. Molecular docking

Based on the component-target network diagram, the top 10 active components with the highest degree values were selected, and their Mol2 structures were downloaded. Preprocessing was performed using PyMOL 2.4.0, and the pdbqt format was saved. Based on the PPI network, the top 5 targets with the highest degree values were selected as macromolecular receptor experimental objects. Crystal structures obtained by X-ray crystallography from "*Homo sapiens*" were selected from the PDB database. The crystal structures in pdb format were downloaded, and the proteins were preprocessed (e.g., water removal) using PyMOL 2.4.0, followed by hydrogenation in AutoDockTools 1.5.7 and saving in pdbqt format. Molecular docking was performed using AutoDockTools 1.5.7, and visualization was achieved using PyMOL 2.4.0.

3. Results

3.1. Screening of active components, targets, and overlapping targets

A total of 124 active components of Wumei Pill were screened from the TCMSP database. A total of 877 targets of active components of Wumei Pill were predicted through the Swiss Target Prediction website, with 51 active components obtained after screening and deduplication. AIH targets screened from the GeneCards, OMIM, and Disgenet databases were 808, 142, and 190, respectively. After data collation and deduplication, 1130 disease targets

were obtained. A total of 64 overlapping targets between Wumei Pill and AIH were obtained using Venny 2.1.0.

3.2. Core targets of PPI network

CentiScaPe 2.2 was used to screen 12 key targets with Degree > 5.388, Closeness > 0.008, and Betweenness > 89.469, resulting in 12 nodes and 33 edges. The greater the importance, the larger and brighter the circle; the higher the degree of connection, the thicker and darker the line. The results showed that the core targets included Tumor Necrosis Factor (TNF), Cytochrome P450 27B1 (CYP27B1), Transforming Growth Factor Beta 1 (TGFB1), etc. (**Figure 1**).

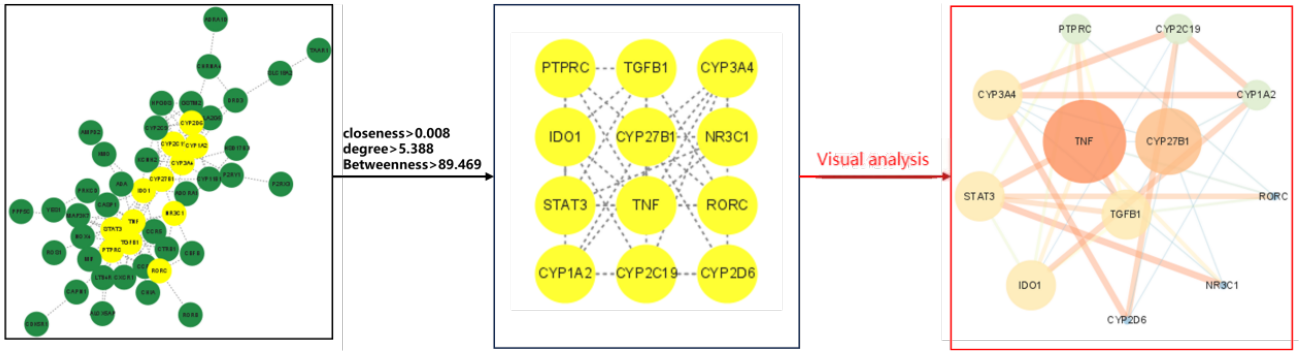

Figure 1. Protein-protein interaction (PPI) network diagram of overlapping targets between core targets of Wumei Pill and core targets of AIH.

3.3. Topological networks of drug-component-target and pathway-target

Cytoscape 3.9.1 was used for network structure visualization to obtain the drug-component-target network diagram (**Figure 2**) and pathway-target topological network diagram (**Figure 3**). The higher the degree value, the larger the node.

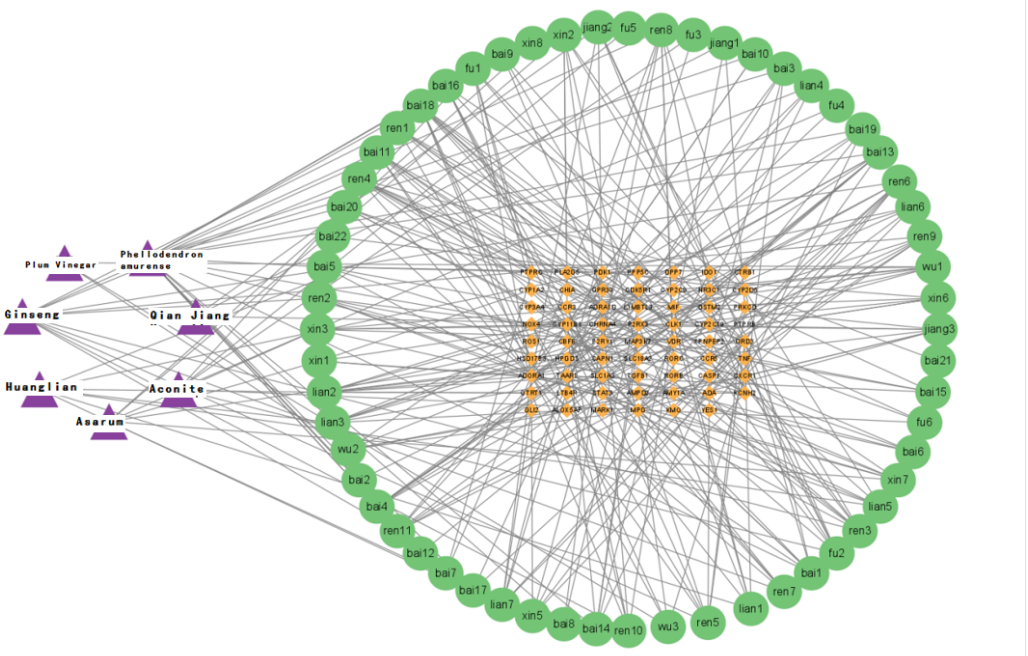

Figure 2. Drug-component-target network diagram.

Figure 3. Pathway-target topological network diagram.

3.4. GO and KEGG enrichment analysis of core targets

GO enrichment analysis of 12 key target genes using the David database yielded 105 GO terms, including 82 biological processes (mainly involved in inflammatory response, positive regulation of transcription by RNA polymerase II, positive regulation of DNA-templated transcription, etc.), 4 cellular components (cytoplasm, intracellular membrane-bounded organelle, endoplasmic reticulum membrane, cell surface), and 19 molecular functions (involving genes related to African trypanosomiasis, chemical carcinogenesis-receptor activation, proteoglycans in cancer, etc.). KEGG enrichment analysis identified 20 signaling pathways, including linoleic acid metabolism, Th17 cell differentiation, drug metabolism-cytochrome P450, etc.

3.5. Molecular docking results

The top 5 targets (TNF, CASP3, CXCL8, NFKB1, TGFB1) with the highest degree values in the PPI network were selected for molecular docking simulation with the main components (girinimbine, calyachine, (R)-tetrahydroberberine, cavidine, (-)-isocorydine) (**Table 1**). The binding strength between compounds and ligands was judged based on binding energy. The lower the binding energy, the tighter the binding between the compound and the ligand. The results showed that all binding energies were less than 0 kcal/mol, indicating that the core

active components of Wumei Pill had good binding activity with AIH-related targets and high potential biological activity. Combinations with good binding ability and hydrogen bonds were selected for visualization analysis (**Figure 4**).

Table 1. Molecular docking binding energies

Target	Girinimbine	Calyachine	(R)-Tetrahydroberberine	Cavidine	(-)-Isocorydine
CASP3	-5.17	-4.73	-6.04	-4.52	-3.75
TNF	-6.11	-5.68	-5.47	-5.1	-3.84
NFKB1	-6.64	-5.1	-5.04	-5.3	-5.21
TGFB1	-5.04	-4.75	-4.37	-4.72	-3.73
CXCL8	-5.0	-5.0	-4.41	-5.36	-3.69

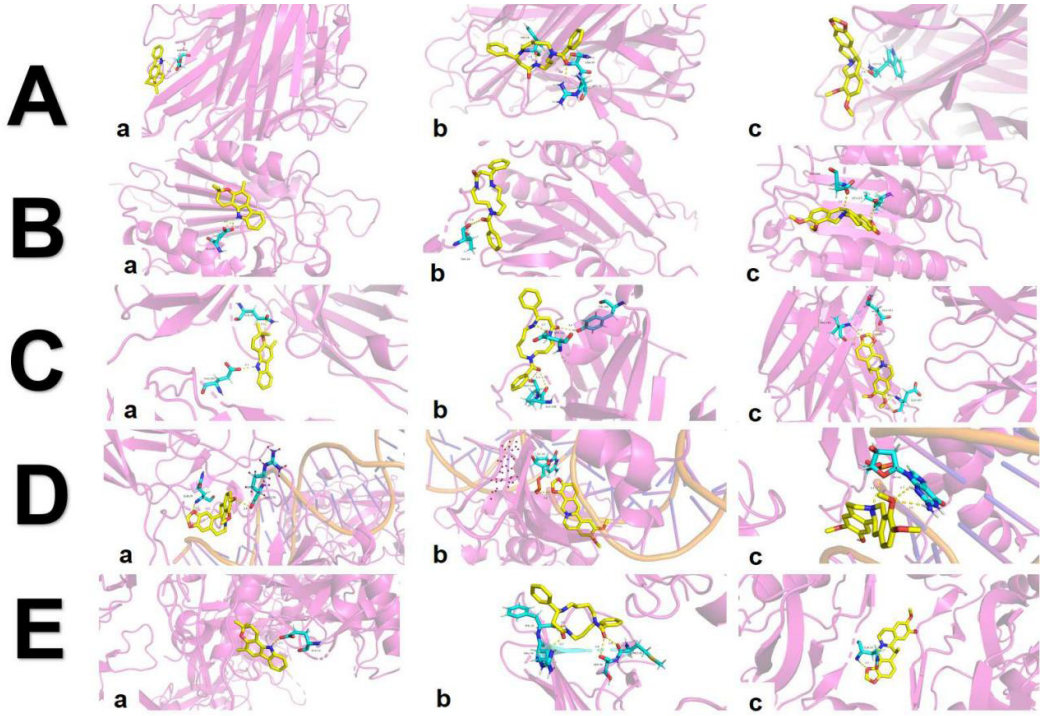

Figure 4. Molecular docking results 6A: a: TNF–Girinimbine; b: TNF–Calyachine; c: TNF–(R)-Tetrahydroberberine;6B: a: CASP3–Girinimbine; b: CASP3–Calyachine; c: CASP3–(R)-Tetrahydroberberine;6C: a: CXCL8–Girinimbine; b: CXCL8–Calyachine; c: CXCL8–Cavidine;6D: a: NFKB1–(R)-Tetrahydroberberine; b: NFKB1–Cavidine; c: NFKB1–(-)-Isocorydine;6E: a: TGFB1–Girinimbine; b: TGFB1–Calyachine; c: TGFB1–Cavidine.

4. Discussion

Autoimmune hepatitis is mainly caused by factors such as living environment, drug use, and viral invasion. During the immune system response, antibodies produced by hepatocytes and T cell-mediated immune responses lead to inflammatory reactions in the liver [11]. Since AIH was introduced in the clinical field, treatment methods have been relatively limited, and the main treatment goals are to slow down liver fibrosis and relieve liver inflammation [12]. Studies have found that Wumei Pill has the effects of reducing inflammation and enhancing immune function in the treatment of this disease [13].

In this study, a total of 124 main active components of Wumei Pill, corresponding to 877 targets, and 64 overlapping targets involved in the treatment of AIH were obtained. The main components such as girinimbine, calyachine, (R)-tetrahydroberberine, cavidine, and (-)-isocorydine were obtained by constructing the component-target network diagram. The top 5 core targets were screened through the PPI network, and it was concluded that the mechanism of Wumei Pill on AIH is mainly related to TNF, CASP3, CXCL8, NFKB1, and TGFB1. Molecular docking of the top 5 main active components with the 5 core targets showed that the core active components of Wumei Pill had good binding activity with AIH-related targets and high potential biological activity.

TNF is secreted by macrophages and T cells, and its main function is to regulate inflammatory immune responses. High doses of TNF can stimulate MAPK and NF-κB signaling pathways, activate local inflammatory genes and mediate cell life activities, leading to inflammatory reactions [14,15]. TNF plays an important role in multiple cellular functions such as immune regulation and inflammation. Relevant studies have shown that under the induction of TNF-α blockers, the human body is prone to drug-induced autoimmune hepatitis [16,17]. CASP3 is a protease that can cause DNA cleavage and promote cell apoptosis. Based on bioinformatics and proteomic identification, CASP3 is one of the main types of liver-protective target proteins [18]. In addition, studies have found that berberine hydrochloride can inhibit the CASP3 signaling pathway to alleviate liver injury caused by acute hypoxia exposure, and CASP3 can also participate in liver regeneration [19,20], further confirming that CASP3 is related to liver injury diseases. During inflammation mediation, CXCL8 has the function of promoting the formation of Mallory-Denk bodies in the liver. Abnormal regulation of its receptors is related to many inflammation-mediated diseases, and its expression is significantly upregulated in various inflammatory liver diseases [21]. NF-κB subunits regulate innate and adaptive immunity, cell proliferation, stress response, and cell apoptosis. After the deletion of p105 and p50 of NFKB1, organ damage and inflammatory reactions will be aggravated [22]. Studies have suggested that NFKB1 is related to rheumatoid arthritis, and TGF-β1 is related to systemic lupus erythematosus, indicating that they may be related to autoimmune diseases [23,24].

KEGG enrichment results indicated that the process of Wumei Pill in the treatment of AIH may be related to pathways such as inflammatory bowel disease, drug metabolism-cytochrome P450, linoleic acid metabolism, proteoglycans in cancer, and Th17 cell differentiation. Core targets are highly enriched in the above pathways, mainly related to processes such as inflammatory response, positive regulation of transcription by RNA polymerase II, and positive regulation of DNA-templated transcription. According to investigation and analysis, AIH has the risk of developing into hepatocellular carcinoma [25]. Both drug metabolism-cytochrome P450 and proteoglycan-related pathways are closely related to hepatocellular carcinoma [26,27]. According to the KEGG analysis of therapeutic targets, the number of targets enriched in drug metabolism-cytochrome P450 and proteoglycan-related signaling pathways is relatively high. Cell surface proteoglycans are important regulatory factors in inflammatory reactions and serve as attractive pharmacological targets in cancer for cancer immunotherapy, reflecting that the use of Wumei Pill is related to the clinical remission of AIH transformation to hepatocellular carcinoma [28]. Linoleic acid is a major positive regulator of CD8+ T cell activity, enhancing anti-tumor ability by improving metabolic adaptability, so linoleic acid can be used as an enhancer for adoptive cell therapy in tumor treatment [29]. In addition, linoleic acid can reduce apoptosis through NF-κB [30]. As a key mediator of inflammatory reactions, the transcription factor NF-κB can regulate multiple aspects of immune function. Loss-of-function mutations in negative regulators of the NF-κB pathway are also the cause of autoimmune or inflammatory diseases [31]. The NF-κB signaling pathway can not only promote hepatocyte survival in the liver but also control the expression of a series of growth factors and cytokines, participating in liver inflammatory reactions [32]. Therefore, it can be

inferred that linoleic acid plays an important role in the treatment of AIH by regulating NF-κB. Th17 cells are related to many inflammatory reactions and autoimmune diseases, and the increased differentiation of pathogenic T helper 17 cells plays an important role in the occurrence and development of AIH [33]. Regulating Th17 cell balance provides a feasible treatment method for AIH patients [34,35].

Analysis of molecular docking results showed that the main active components of Wumei Pill had good docking effects with key targets of autoimmune hepatitis, and all binding energies were < 0 kJ/mol, indicating that there is a stable interaction between them. Based on this finding, we have reason to speculate that Wumei Pill may have potential efficacy in the treatment of AIH.

5. Conclusion

In summary, this study predicted the active components and targets of Wumei Pill using network pharmacology methods, analyzed the protein PPI network interaction, cellular components, signaling pathways, and biological processes of the targets of Wumei Pill in the treatment of AIH, and initially clarified the mechanism of Wumei Pill in the treatment of AIH. Molecular docking technology was used to construct a docking model of the interaction between active components in Wumei Pill and key targets for the treatment of AIH, further verifying the results of network pharmacology analysis, providing a reference basis for subsequent experimental research and clinical application.

Funding

University-Level College Student Innovation and Entrepreneurship Training Program of Qiqihar Medical University; Exploring the Mechanism of Ganjiang Huangqin Huanglian Renshen Decoction on AIH Mice Based on Network Pharmacology and In Vivo Experiments (Project No.: X202311230039)

Disclosure statement

The authors declare no conflict of interest.

References

[1] Chen H, Zhou Y, 2023, Progress in the Diagnosis and Treatment of Autoimmune Hepatitis. Guangzhou Medical Journal, 54(6): 1–6 + 16.

[2] Reau N, Lammert C, Weinberg E, 2024, Autoimmune Hepatitis: Current and Future Therapies. Hepatology Communications, 8(6): e0458.

[3] Ma X, Wang Q, Xiao X, et al., 2022, Guidelines for the Diagnosis and Treatment of Autoimmune Hepatitis (2021). Journal of Clinical Hepatology, 38(1): 42–49.

[4] Schmeltzer P, Russo M, 2018, Clinical Narrative: Autoimmune Hepatitis. American Journal of Gastroenterology, 113(7): 951–958.

[5] Li Z, He X, Xu J, et al., 2024, Clinical Observation of Wumei Pill in the Treatment of Gastroesophageal Reflux Disease of Cold-Heat Complex Type. Hebei Journal of Traditional Chinese Medicine, 46(3): 410–414.

[6] Wang K, Lü L, 2023, One Case of Acute Optic Neuritis Treated with Modified Wumei Pill. Chinese Journal of

Ophthalmology of Traditional Chinese Medicine, 33(9): 864–866.

[7] Sun J, Huang S, Liu T, et al., 2023, Efficacy of Wumei Pill Combined with Anti-Hp Quadruple Eradication Therapy in the Treatment of Hp-Infected Chronic Atrophic Gastritis of Cold-Heat Complex Type and Its Effects on Hp Eradication Rate and Levels of IL-1β and IL-6. Journal of Guangzhou University of Chinese Medicine, 40(8): 1916–1922.

[8] Xu Z, Wu Y, 2022, Progress in the Clinical Application of Wumei Pill. Guide of Traditional Chinese Medicine, 28(1): 143–146.

[9] Wu F, Chen G, Fang K, et al., 2023, Network Pharmacology Research Indicates That Wu-Mei-Wan Treats Obesity by Inhibiting Th17 Cell Differentiation and Alleviating Metabolic Inflammation. Combinatorial Chemistry and High Throughput Screening, 26(1): 30–48.

[10] Li K, Wang Z, Wang J, 2024, Wumei Pill Improves Intestinal Mucosal Inflammatory Response and Pyroptosis in Rats with Ulcerative Colitis by Regulating NLRP3 Inflammasome. Chinese Journal of Immunology, 40(1): 97–102 + 109.

[11] Li Z, Duan Z, Wu Q, et al., 2021, Study on the Mechanism of Kuhuang Granule in the Treatment of Autoimmune Hepatitis Based on Network Pharmacology and Molecular Docking. Beijing Medicine, 43(9): 894–898.

[12] Reau N, Lammert C, Weinberg E, 2024, Autoimmune Hepatitis: Current and Future Therapies. Hepatology Communications, 8(6): e0458.

[13] Zhu Y, Zhang H, 2022, Progress in Clinical Application of Wumei Pill. Journal of Practical Traditional Chinese Medicine, 38(12): 2249–2253.

[14] Webster J, Vucic D, 2020, The Balance of TNF-Mediated Pathways Regulates Inflammatory Cell Death Signaling in Healthy and Diseased Tissues. Frontiers in Cell and Developmental Biology, 8: 365.

[15] Ren J, Ding Y, Li S, et al., 2023, Predicting the Anti-Inflammatory Mechanism of Radix Astragali Using Network Pharmacology and Molecular Docking. Medicine, 102(35): e34945.

[16] Pasquereau S, Kumar A, Herbeis G, 2017, Targeting TNF and TNF Receptor Pathway in HIV-1 Infection: From Immune Activation to Viral Reservoirs. Viruses, 9(4): 64.

[17] Efe C, 2013, Drug-Induced Autoimmune Hepatitis and TNF-α Blocking Agents: Is There a Real Relationship? Autoimmunity Reviews, 12(3): 337–339.

[18] Ma X, Zhang M, Fang G, et al., 2021, Ursolic Acid Reduces Hepatocellular Apoptosis and Alleviates Alcohol-Induced Liver Injury via Irreversible Inhibition of CASP3 In Vivo. Acta Pharmacologica Sinica, 42(7): 1101–1110.

[19] Zhang Z, Dong Q, Guan R, et al., 2022, Berberine Hydrochloride Alleviates Liver Injury Caused by Acute Hypoxia Exposure by Inhibiting the TNF-α/Caspase-8/Caspase-3 Signaling Pathway. Chinese Journal of Cellular and Molecular Immunology, 38(1): 48–53.

[20] Di-Iacovo N, Pieroni S, Piobbico D, et al., 2023, Liver Regeneration and Immunity: A Tale to Tell. International Journal of Molecular Sciences, 24(2): 1176.

[21] Ha H, Debnath B, Neamati N, 2017, Role of the CXCL8-CXCR1/2 Axis in Cancer and Inflammatory Diseases. Theranostics, 7(6): 1543–1588.

[22] Cartwright T, Perkins N, Wilson C, 2016, NFKB1: A Suppressor of Inflammation, Ageing and Cancer. FEBS Journal, 283(10): 1812–1822.

[23] Elkhawaga S, Gomaa M, Elsayed M, et al., 2021, NFKB1 Promoter −94 Insertion/Deletion ATTG Polymorphism (rs28362491) Is Associated with Severity and Disease Progression of Rheumatoid Arthritis Through Interleukin-6 Levels Modulation in Egyptian Patients. Clinical Rheumatology, 40(7): 2927–2937.

[24] Stadtlober N, Flauzino T, Santos L, et al., 2021, TGFB1 + 869 T > C (rs1800470) Variant Is Independently Associated with Susceptibility, Laboratory Activity, and TGF-β1 in Patients with Systemic Lupus Erythematosus. Autoimmunity,

54(8): 569–575.

[25] Guo W, Zhang H, Liu L, 2022, Research Progress on Autoimmune Hepatitis-Related Hepatocellular Carcinoma. Journal of Clinical Hepatology, 38(6): 1431–1435.

[26] Tang L, Wei R, Chen R, et al., 2022, Establishment and Validation of a Cholesterol Metabolism-Related Prognostic Signature for Hepatocellular Carcinoma. Computational and Structural Biotechnology Journal, 20: 4402–4414.

[27] Baghy K, Tátrai P, Regős E, et al., 2016, Proteoglycans in Liver Cancer. World Journal of Gastroenterology, 22(1): 379–393.

[28] Espinoza-Sánchez N, Göttte M, 2020, Role of Cell Surface Proteoglycans in Cancer Immunotherapy. Seminars in Cancer Biology, 62: 48–67.

[29] Nava Lauson C, Tiberti S, Corsetto P, et al., 2023, Linoleic Acid Potentiates CD8+ T Cell Metabolic Fitness and Antitumor Immunity. Cell Metabolism, 35(4): 633–650.e9.

[30] Lee D, Choi K, Oh J, et al., 2022, Linoleic Acid Reduces Apoptosis via NF-κB During the In Vitro Development of Induced Parthenogenic Porcine Embryos. Theriogenology, 187: 173–181.

[31] Barnabei L, Laplantine E, Mbongo W, et al., 2021, NF-κB: At the Borders of Autoimmunity and Inflammation. Frontiers in Immunology, 12: 716469.

[32] He G, Karin M, 2011, NF-κB and STAT3: Key Players in Liver Inflammation and Cancer. Cell Research, 21(1): 159–168.

[33] Yasuda K, Takeuchi Y, Hirota K, 2019, The Pathogenicity of Th17 Cells in Autoimmune Diseases. Seminars in Immunopathology, 41(3): 283–297.

[34] Zhao H, 2023, Study on All-Trans Retinoic Acid Regulating Treg/Th17 Cell Balance to Improve Autoimmune Hepatitis in Mice, thesis, Lanzhou University.

[35] Yu Q, Tu H, Yin X, et al., 2022, Targeting Glutamine Metabolism Ameliorates Autoimmune Hepatitis via Inhibiting T Cell Activation and Differentiation. Frontiers in Immunology, 13: 880262.