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Exploring Potential Mechanisms of *Atractylodes lancea* in Chronic Pancreatitis by Network Pharmacology and Molecular Docking

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Abstract [**Objectives**] To explore the mechanism of *Atractylodes lancea* in the treatment of chronic pancreatitis (CP). [**Methods**] The network pharmacology and molecular docking techniques were applied. The active components of *A. lancea* were screened through the TCMSP database, and the potential targets of *A. lancea* were predicted using the SwissTargetPrediction database. Disease-related targets of chronic pancreatitis were collected from the GeneCards and OMIM databases. Cytoscape software was used to construct and analyse the "drug component-target" network. The intersecting targets between the active component targets of *A. lancea* and CP-related targets were identified, and a protein-protein interaction (PPI) network was constructed and analysed using the STRING database and Cytoscape software to obtain the core targets. GO functional enrichment analysis and KEGG pathway enrichment analysis of the intersecting targets were performed using RStudio software. Finally, AutoDock Tools software was employed to validate the molecular docking between the major active components and the core targets. [**Results**] A total of 9 active components of *A. lancea*, 279 component-related targets, 1 160 disease-related targets, and 94 intersecting drug-disease targets were identified. The core genes involved in the treatment of CP by *A. lancea* mainly included *IL6*, *TNF*, *STAT3*, *TP53*, and *EGFR*. The major signalling pathways included the PI3K-Akt signalling pathway, lipid and atherosclerosis, and proteoglycans in cancer. The intervention of *A. lancea* in CP involves a complex biological process with multiple targets and pathways. [**Conclusions**] This study elucidates the mechanism of *A. lancea* against CP from the perspectives of multi-component and multi-target actions, and provides a theoretical basis as well as directions for subsequent molecular biological experiments.

Key words *Atractylodes lancea*, Chronic pancreatitis (CP), Network pharmacology, Molecular docking

0 Introduction

Chronic pancreatitis (CP) is a progressive chronic inflammatory disease of the pancreas mediated by multiple factors, characterized by recurrent pancreatic parenchymal injury, acinar cell atrophy, inflammatory cell infiltration, and fibrotic tissue proliferation. Ultimately, it leads to both exocrine and endocrine insufficiency, significantly impairing patients' quality of life and long-term prognosis[1-3]. In recent years, risk factors such as alcohol consumption, smoking, metabolic disorders, and pancreatobiliary diseases have continued to contribute to the increasing burden of pancreatitis-related diseases[4]. Due to its prolonged course, high recurrence rate, and increased risk of pancreatic cancer, CP has become an important research focus in digestive system diseases[5]. Current clinical management primarily relies on symptomatic support, nutritional intervention, pain control, and endoscopic or surgical treatment; however, effective therapeutic agents for suppressing persistent inflammation, delaying pancreatic fibrosis progression, and improving the pancreatic microenvironment remain limited[6].

Traditional Chinese medicine (TCM) demonstrates unique advantages in the prevention and treatment of chronic inflammatory diseases through its multi-component, multi-target, and multi-pathway synergistic effects[7]. Atractylodis Rhizoma (the dried rhizome of *Atractylodes lancea* or *Atractylodes chinensis*) is a commonly used herbal medicine in clinical practice, known for its functions of drying dampness, strengthening the spleen, and dispelling wind and cold, and is widely applied in spleen-stomach disorders and various digestive system-related diseases[8]. Modern pharmacological studies have shown that Atractylodis Rhizoma contains abundant bioactive components, including volatile oils, sesquiterpenoids, and polysaccharides, which exhibit anti-inflammatory, antioxidant, immunomodulatory, and tissue-protective effects[9-11]. Among them, atractylone, a major sesquiterpenoid constituent of Atractylodis Rhizoma, has been reported to exhibit anti-inflammatory activity[12]. Recent studies have further indicated that polysaccharides derived from Atractylodis Rhizoma may regulate the microbiota and improve barrier function in inflammatory disease models[13]. These findings suggest that Atractylodis Rhizoma may intervene in the development and progression of CP by modulating inflammation, oxidative stress, and cellular signaling pathways; however, its precise mechanisms in CP remain to be systematically elucidated.

Network pharmacology, based on the concept of "holistic-network-multi-target" analysis, enables systematic exploration of the complex interactions among herbal active compounds, potential targets, and diseases[14]. Molecular docking further validates the binding affinity between active compounds and key target proteins at the molecular level[15]. The combined application of these approaches has become an important strategy for elucidating the mechanisms of traditional Chinese medicines and has been widely used in studies of digestive system diseases[16]. Therefore, this study aims to employ network pharmacology combined with molecular docking to identify the active components and potential core targets of *A. lancea* in the treatment of CP, and to systematically

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analyze the associated biological processes and signaling pathways, thereby providing a theoretical basis for mechanistic research and subsequent experimental validation.

2 Materials and methods

2.1 Screening of active components and targets of *A. lancea* The chemical constituents of *A. lancea* were retrieved from the Traditional Chinese Medicine Systems Pharmacology Database (TCMSP, http://tcmspw.com/tcmsp.php). Active compounds were screened based on the criteria of oral bioavailability (OB) ≥ 30% and drug-likeness (DL) ≥0.18. The corresponding targets of these compounds were collected. Canonical SMILES of the selected active compounds were obtained from the PubChem database. These SMILES structures were then imported into the SwissTargetPrediction database (http://www.swisstargetprediction.ch/) to predict potential targets, with the screening condition set as Probability > 0. All predicted targets were subsequently standardized using the UniProt database (https://www.uniprot.org/). Targets that could not be matched in UniProt were excluded, and the remaining targets were merged and duplicates were removed.

2.2 Identification of disease-related targets Using "chronic pancreatitis" as the keyword, disease-related targets were collected from the GeneCards (https://www.genecards.org/) and OMIM (https://www.omim.org/) databases. Targets with a relevance score > 15 were retained to construct the disease target dataset. The intersection between disease-related targets and *A. lancea* targets was identified using the Venny 2.1.0 tool (https://bioinfogp.cnb.csic.es/tools/venny/index.html).

2.3 Construction of the protein-protein interaction (PPI) network The intersecting targets were imported into the STRING database (https://string-db.org/) to obtain protein-protein interaction (PPI) information. The species was limited to Homo sapiens, and the confidence score was set to 0.4, with other parameters kept as default. The PPI network was visualized and analyzed using Cytoscape 3.9.1. Topological parameters, including degree centrality (DC), betweenness centrality (BC), and closeness centrality (CC), were calculated using the CytoNCA plugin. Nodes with higher values indicate greater connectivity and are more likely to play key roles in the network.

2.4 Construction of the "herb-active compound-target" network The intersecting target data were imported into Cytoscape 3.9.1 (https://cytoscape.org/) to construct the "herb-active compound-target" network, which visually represents the interactions between active components and targets. Topological analysis of the network was performed using the CytoNCA plugin by calculating DC, BC, and CC values.

2.5 GO functional enrichment and KEGG pathway analysis Gene Ontology (GO) enrichment analysis and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis were performed using RStudio with the packages "ggplot2", "clusterProfiler", "enrichplot", and "org.Hs.eg.db". A threshold of adjusted P value (P_{adj}) < 0.05 was applied to identify significantly enriched terms and pathways. The results were subsequently visualized.

2.6 Molecular docking The three-dimensional (3D) structures of the selected active compounds were obtained from the PubChem database and converted into MOL2 format using OpenBabel 3.1.1. The crystal structures of core target proteins were downloaded from the RCSB Protein Data Bank (PDB). PyMOL 2.5 software was used to remove water molecules, add hydrogen atoms, and prepare the protein structures. Molecular docking was then performed using AutoDock Tools.

3 Results and analysis

3.1 Identification of active compounds and prediction of potential targets of *A. lancea* Based on the TCMSP platform, active compounds of *A. lancea* were screened using the criteria of oral bioavailability (OB) ≥30% and drug-likeness (DL) ≥0.18. A total of nine active compounds were identified (Table 1).

Table 1 Active compounds of *Atractylodes lancea*

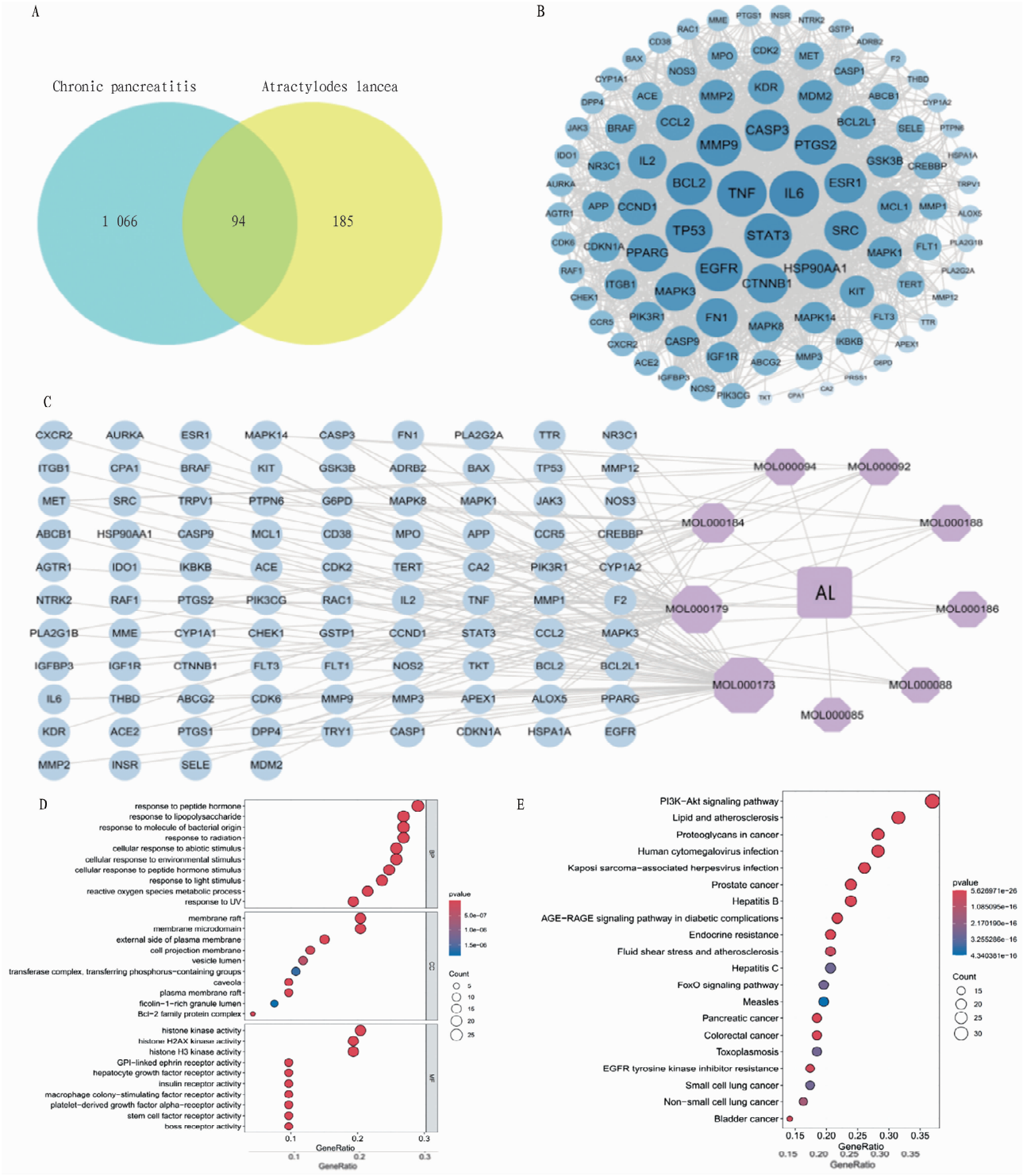
MOL ID	Molecule name	*OB*	*DL*
MOL000173	wogonin	30.684 567 06	0.229 42
MOL000184	NSC63551	39.253 645 86	0.759 40
MOL000188	3β-acetoxyatractylone	40.572 334 74	0.219 13
MOL000085	beta-daucosterol_qt	36.913 905 83	0.753 82
MOL000179	2-Hydroxyisoxypropyl-3-hydroxy-7-isopentene-2,3-dihydrobenzofuran-5-carboxylic	45.199 122 14	0.204 96
MOL000186	Stigmasterol 3-O-beta-D-glucopyranoside_qt	43.829 851 58	0.758 12
MOL000088	beta-sitosterol 3-O-glucoside_qt	36.913 905 83	0.754 90
MOL000092	daucosterin_qt	36.913 905 83	0.755 49
MOL000094	daucosterol_qt	36.913 905 83	0.755 79

Subsequently, the potential targets of these compounds were obtained from the TCMSP database and further predicted using the SwissTargetPrediction platform. After integration and removal of duplicates, a total of 279 potential targets associated with the active compounds of *A. lancea* were identified.

3.2 Identification of disease-related targets Using "chronic pancreatitis" as the search term, disease-related targets were retrieved from the GeneCards and OMIM databases. A total of 1 160 potential gene targets associated with chronic pancreatitis were identified, and their corresponding standardized gene names were collected for further analysis.

3.3 Construction of the core target PPI network The targets of *A. lancea* active compounds were intersected with chronic pancreatitis-related targets, and a Venn diagram was generated

(Fig. 1A) to illustrate the relationship between drug targets and disease targets. A total of 94 overlapping targets were identified. These common targets were subsequently imported into the STRING 11.5 platform to construct the protein-protein interaction (PPI) network (Fig. 1B), which consisted of 94 nodes and 1 626 edges. Among them, the top five targets ranked by network parameters were IL6, TNF, STAT3, TP53, and EGFR.



NOTE (A) Venn diagram of active compound targets of *A. lancea* and CP-Related. (B) PPI network diagram of active components of *A. lancea* and CP core targets. (C) *A. lancea* component-target network diagram. (D) GO biological function enrichment analysis. (E) KEGG pathway enrichment analysis.

Fig. 1 Exploring the mechanisms of *Atractylodes lancea* in the treatment of CP Based on network pharmacology

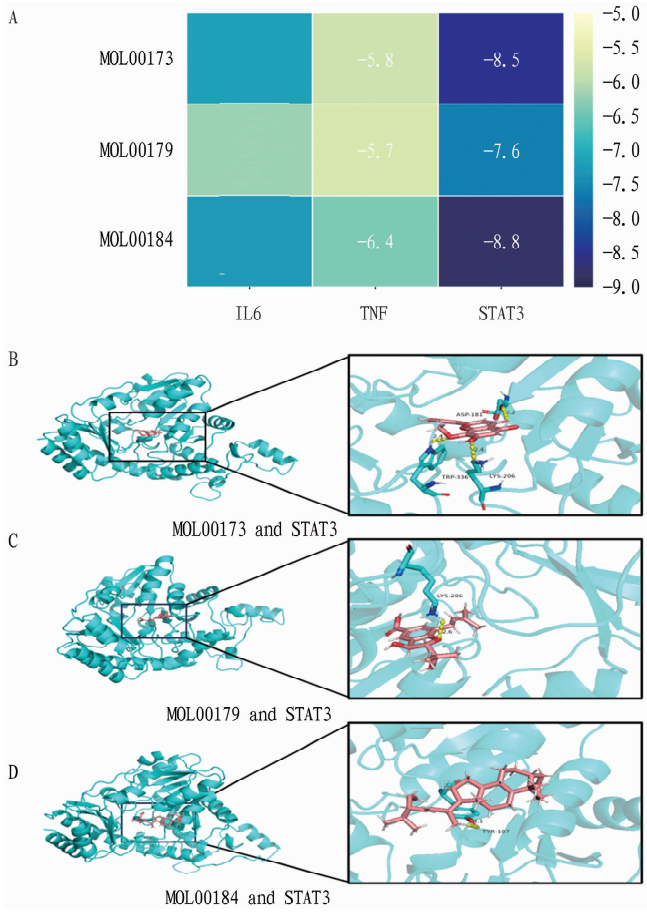
3.4 Construction and analysis of the target network of *A. lancea* components Import the 9 active components of *A. lancea* and 94 intersecting targets into Cytoscape software for analysis, and draw the component-target network diagram (Fig. 1C). A total of 104 nodes and 136 edges were obtained. Among them, 1 herb node and 9 compound nodes were shown in purple of *A. lancea*, 94 blue nodes represent the potential targets of *A. lancea* active components against CP, and 136 edges represent the interactions between active components and targets. The larger the node, the more active components are connected to the target. The top 3 active components are: MOL000173 (wogonin), MOL000179(2-Hydroxyisoxypropyl-3-hydroxy-7-isopentene-2, 3-dihydrobenzofuran-5-carboxylic), MOL000184 (NSC63551). These three components may be the main components of *A. lancea* against chronic pancreatitis.

3.5 GO and KEGG enrichment analysis GO functional enrichment and KEGG pathway analyses were performed on the 94 core targets using RStudio.

A total of 2 494 GO terms were identified, including 2 177 biological process (BP) terms, 92 cellular component (CC) terms, and 225 molecular function (MF) terms. The BP category was mainly enriched in processes such as response to peptide hormone, response to lipopolysaccharide, response to molecule of bacterial origin, response to radiation, and cellular response to abiotic stimulus. For CC, the enriched terms were primarily associated with membrane raft, membrane microdomain, external side of plasma membrane, cell projection membrane, and vesicle lumen. In the MF category, the enriched terms mainly included histone kinase activity, histone H2AX kinase activity, histone H3 kinase activity, GPI-linked ephrin receptor activity, and hepatocyte growth factor receptor activity (Fig. 1D).

KEGG pathway enrichment analysis identified a total of 182 signaling pathways, of which the top 20 pathways were selected for visualization. The major enriched pathways included the PI3K-Akt signaling pathway, lipid and atherosclerosis, proteoglycans in cancer, and human cytomegalovirus infection. These results suggest that the active compounds of *A. lancea* may exert therapeutic effects on chronic pancreatitis through multi-pathway synergistic regulation (Fig. 1E).

3.6 Molecular docking of key active compounds and core targets Molecular docking analysis was performed between the top three active compounds ranked by target connectivity and the key core targets. The binding energy heatmap was constructed to visualize the interactions (Fig. 2A). The docking results showed that the binding energies between the three major active compounds and the core targets were all lower than −5 kcal/mol, indicating favorable binding affinity and suggesting potential interactions between these compounds and targets. Furthermore, the optimal binding conformations between the active compounds and their corresponding targets were visualized. Specifically, the interactions included MOL000173-STAT3, MOL000179-STAT3, and MOL000184-STAT3 (Fig. 2B – D).



NOTE (A) Heatmap of binding energies between active components of *A. lancea* and core targets. (B – D) Schematic diagram of molecular docking results.

Fig. 2 Molecular docking of key active compounds and core targets

4 Discussion

CP is a chronic disorder characterized by persistent inflammatory responses, recurrent pancreatic tissue injury, and progressive fibrosis. Its pathogenesis involves complex processes including the release of inflammatory mediators, enhanced oxidative stress, dysregulated cellular apoptosis, and aberrant activation of multiple signaling pathways[17]. Recently, accumulating evidence has demonstrated that pancreatic stellate cells play a pivotal role in the development of fibrosis in chronic pancreatitis, acting as critical effector cells linking inflammatory responses to extracellular matrix deposition[18]. Meanwhile, the infiltration of immune cells and abnormal activation of the associated inflammatory network also contribute to tissue injury and microenvironmental remodeling in chronic pancreatitis[19]. Accordingly, interventions targeting inflammatory regulation, inhibition of pancreatic stellate cell activation, and fibrosis-related signalling pathways are regarded as promising therapeutic strategies for chronic pancreatitis[20].

In the present study, we systematically analyzed the potential mechanisms underlying the effects of *A. lancea* against chronic

pancreatitis using network pharmacology and molecular docking approaches. The results revealed that 9 bioactive components and 279 potential targets were screened from *A. lancea*. Intersection with 1 160 disease-related targets of chronic pancreatitis yielded 94 common targets, suggesting that *A. lancea* may exert comprehensive therapeutic effects via multiple components acting on diverse disease-associated targets.

Component-target network analysis indicated that wogonin, 2-Hydroxyisoxypropyl-3-hydroxy-7-isopentene-2,3-dihydrobenzofuran-5-carboxylic acid, and NSC63551 might be the key bioactive components responsible for the effects of *A. lancea* on chronic pancreatitis. Among them, wogonin exhibited a higher degree of connectivity, implying its crucial contribution to the pharmacological efficacy of *A. lancea*. In network pharmacology research, components with superior topological parameters are generally considered potential key pharmacodynamic substances[21]. Furthermore, accumulating evidence indicates that Atractylodis Rhizoma exhibits anti-inflammatory, antioxidant, and tissue-protective effects, which pharmacologically support its potential application in chronic inflammatory diseases[22]. We therefore hypothesize that these key components may collaboratively intervene in chronic pancreatitis by modulating inflammatory responses, cellular stress, and signal transduction processes.

PPI network analysis further identified IL6, TNF, STAT3, TP53, and EGFR as core hub targets, which are primarily implicated in inflammatory responses, cell proliferation and apoptosis, tissue injury repair, and fibrogenic processes. IL6 and TNF are canonical pro-inflammatory cytokines whose sustained overexpression exacerbates inflammatory cascades and pancreatic tissue damage[19]. STAT3 participates in the expression of inflammation-related genes, cell survival, and tissue remodeling, and is essential for maintaining the chronic inflammatory microenvironment[23]. TP53 is closely associated with cell cycle regulation, apoptosis, and cell fate determination relevant to fibrosis[24]. EGFR-related signalling is involved in the activation, proliferation, and fibrogenic progression of pancreatic stellate cells[25]. These findings suggest that *A. lancea* may ameliorate chronic pancreatitis by regulating the inflammatory cytokine network and molecular events related to injury repair.

GO enrichment analysis demonstrated that the common targets were mainly enriched in responses to inflammatory stimuli, regulation of cellular stress, and receptor-mediated signal transduction. Most of these targets were localized to membrane rafts, membrane microdomains, and the outer side of the plasma membrane, indicating that *A. lancea* may modulate pathological processes in chronic pancreatitis by regulating membrane receptors and their downstream signalling networks. KEGG pathway enrichment analysis revealed that the 94 common targets were significantly enriched in the PI3K-Akt signalling pathway, lipid and atherosclerosis, proteoglycans in cancer, among others, with the PI3K-Akt pathway being particularly prominent. The PI3K/Akt pathway exerts critical functions in inflammation, cell survival, and fibrogenesis[26]. Previous studies have shown that abnormal PI3K and Hippo signaling can synergistically induce chronic pancreatitis-like lesions via upregulation of CTGF[27]. Other evidence suggests that targeting the PI3K/AKT/FOXO1 axis promotes apoptosis of pancreatic stellate cells and alleviates pancreatic fibrosis[28]. In addition, endoplasmic reticulum stress-related pathways are also involved in the regulation of fibrosis in chronic pancreatitis[29]. We therefore propose that *A. lancea* may attenuate inflammatory responses, ameliorate cellular injury, and delay pancreatic fibrosis by modulating the PI3K/Akt pathway and its downstream effector molecules.

Molecular docking results confirmed favorable binding activities between key bioactive components of *A. lancea* and core targets. In particular, the three components with high connectivity exhibited strong binding tendencies toward STAT3, suggesting that STAT3 may represent an important target for *A. lancea* in the treatment of chronic pancreatitis. These findings provide molecular evidence supporting the reliability of the network pharmacology predictions. Nevertheless, the present study is mainly based on in silico database predictions and molecular docking analyses, lacking experimental validation *in vitro* and *in vivo*. Further experimental investigations are therefore warranted to verify these findings.

5 Conclusions

This study systematically explored the potential mechanisms of Atractylodis Rhizoma in chronic pancreatitis using network pharmacology and molecular docking. The results suggest that Atractylodis Rhizoma may exert therapeutic effects through multiple active components, multiple targets, and multiple pathways, with IL6, TNF, STAT3, TP53, and EGFR identified as key candidate targets, and the PI3K-Akt signaling pathway as a major potential regulatory pathway. These findings provide a preliminary theoretical basis for understanding the pharmacological actions of Atractylodis Rhizoma in chronic pancreatitis and may support future experimental validation.

References

[1] THIERENS N, VERDONK RC, LÖHR JM, *et al.* Chronic pancreatitis [J]. Lancet, Dec 21 2025, 404(10471): 2605 – 2618.

[2] BEHRMAN SW, FOWLER ES. Pathophysiology of chronic pancreatitis [J]. Surgical Clinics of North America, Dec 2007, 87(6): 1309 – 1324.

[3] DE RIJK FEM, VAN VELDHUISEN CL, KEMPENEERS MA, *et al.* Quality of life in patients with definite chronic pancreatitis: A nationwide longitudinal cohort study [J]. American Journal of Gastroenterology, Aug 1, 2023, 118(8):1428 – 1438.

[4] LI T, QIN C, ZHAO B, *et al.* Global and regional burden of pancreatitis: Epidemiological trends, risk factors, and projections to 2050 from the

global burden of disease study 2021[J]. BMC Gastroenterology, Nov 8, 2024, 24(1): 398.
[5] GANDHI S, DE LA FUENTE J, MURAD MH, *et al.* Chronic pancreatitis is a risk factor for pancreatic cancer, and incidence increases with duration of disease: A systematic review and meta-analysis[J]. Clinical and Translational Gastroenterology, Mar 28, 2022, 13(3): e00463.
[6] TŁUSTOCHOWICZ K, KRAJEWSKA A, KOWALIK A, *et al.* Treatment strategies for chronic pancreatitis (CP)[J]. Pharmaceuticals (Basel), Feb 24, 2025, 18(3): 311.
[7] ZHOU X, SETO SW, CHANG D, *et al.* Synergistic effects of Chinese herbal medicine: A comprehensive review of methodology and current research [J]. Frontiers in Pharmacology, 2016, 7: 201.
[8] ZHANG WJ, ZHAO ZY, CHANG LK, *et al.* Atractylodis Rhizoma: A review of its traditional uses, phytochemistry, pharmacology, toxicology and quality control [J]. Journal of Ethnopharmacology, Feb 10, 2021, 266: 113415.
[9] ZHANG W, BAI Q, CUI G, *et al.* Recent progress and ongoing challenges in *Rhizoma atractylodis* research: Biogeography, biosynthesis, quality formation and control[J]. Medicinal Plant Biology, 2023, 2(1): 19.
[10] GUO D, XU K, WAN Q, *et al.* Different processing methods and pharmacological effects of Atractylodis Rhizoma[J]. Chinese Journal of Natural Medicines, Aug 2024, 22(8): 756 – 768.
[11] LIN X, GUO X, QU L, *et al.* Preventive effect of Atractylodis Rhizoma extract on DSS-induced acute ulcerative colitis through the regulation of the MAPK/NF-κB signals *in vivo* and *in vitro*[J]. Journal of Ethnopharmacology, Jun 28, 2022, 292: 115211.
[12] YAO Y, SHEN G, LUO J, *et al.* Research Progress with Atractylone as an antitumor agent[J]. Molecules, Nov 19, 2024, 29(22): 5450.
[13] SUN J, JIANG Y, WANG B, *et al.* Structural characterization of the polysaccharides from *Atractylodes chinensis* (DC.) Koidz. and the protective effection against alcohol-induced intestinal injury in rats[J]. International Journal of Biological Macromolecules, Dec 2024, 282(Pt 1): 136641.
[14] ZHENG S, LIANG Y, XUE T, *et al.* Application of network pharmacology in traditional Chinese medicine for the treatment of digestive system diseases[J]. Frontiers in Pharmacology, 2024, 15: 1412997.
[15] JIAO X, JIN X, MA Y, *et al.* A comprehensive application: Molecular docking and network pharmacology for the prediction of bioactive constituents and elucidation of mechanisms of action in component-based Chinese medicine[J]. Computational Biology and Chemistry, Feb 2021, 90: 107402.
[16] GONG S, LU R, FAN Y, *et al.* The potential mechanism of *Bletilla striata* in the treatment of ulcerative colitis determined through network pharmacology, molecular docking, and *in vivo* experimental verification [J]. Naunyn-Schmiedeberg's Archives of Pharmacology, May 2023, 396 (5): 983 – 1000.
[17] BURZYŃSKI J, FICHNA J, TARASIUK A. Putative molecular targets for vitamin A in neutralizing oxidative stress in acute and chronic pancreatitis: A systematic review[J]. Naunyn-Schmiedeberg's Archives of Pharmacology, Jul 2023, 396(7): 1361 – 1370.
[18] KONG F, PAN Y, WU D. Activation and regulation of pancreatic stellate cells in chronic pancreatic fibrosis: A potential therapeutic approach for chronic pancreatitis [J]. Biomedicines, Jan 4, 2024, 12(1): 108.
[19] IYER S, ENMAN M, SAHAY P, *et al.* Novel therapeutics to treat chronic pancreatitis: Targeting pancreatic stellate cells and macrophages [J]. Expert Review of Gastroenterology & Hepatology, Apr-May 2024, 18 (4 – 5): 171 – 183.
[20] CHANG M, CHEN W, XIA R, *et al.* Pancreatic stellate cells and the targeted therapeutic strategies in chronic pancreatitis [J]. Molecules, Jul 22, 2023, 28(14): 5586.
[21] LI S, ZHANG B. Traditional Chinese medicine network pharmacology: Theory, methodology and application[J]. Chinese Journal of Natural Medicines, Mar 2013, 11(2): 110 – 120.
[22] YUN EH, BASHIR KMI, LEE J, *et al.* Protective effects of Atractylodis Rhizoma extracts on lung injury induced by particulate matter 2.5 in mice[J]. Antioxidants (Basel), Jan 23, 2025, 14(2): 127.
[23] YU H, PARDOLL D, JOVE R. STATs in cancer inflammation and immunity: A leading role for STAT3[J]. Nature Reviews Cancer, Nov 2009, 9(11): 798 – 809.
[24] MCELHINNEY K, IRNATEN M, O'BRIEN C. p53 and Myofibroblast apoptosis in organ fibrosis[J]. International Journal of Molecular Sciences, Apr 4 2023, 24(7): 6737.
[25] BLAINE SA, RAY KC, BRANCH KM, *et al.* Epidermal growth factor receptor regulates pancreatic fibrosis[J]. The American Journal of Physiology-Gastrointestinal and Liver Physiology, Sep 2009, 297 (3): G434 – 441.
[26] Fruman DA, Chiu H, Hopkins BD, *et al.* The PI3K Pathway in Human Disease[J]. Cell, Aug 10, 2017, 170(4): 605 – 635.
[27] TAMURA T, KODAMA T, SATO K, *et al.* Dysregulation of PI3K and Hippo signaling pathways synergistically induces chronic pancreatitis via CTGF upregulation[J]. Journal of Clinical Investigation, Jul 1, 2021, 131(13): e143414.
[28] WANG QY, XU BY, WANG Y, *et al.* Sodium aescinate promotes apoptosis of pancreatic stellate cells and alleviates pancreatic fibrosis by inhibiting the PI3K/Akt/FOXO1 signaling pathways [J]. Frontiers in Pharmacology, 2025, 16: 1554260.
[29] BEN-HAROSH Y, ANOSOV M, SALEM H, *et al.* Pancreatic stellate cell activation is regulated by fatty acids and ER stress[J]. Experimental Cell Research, Oct 1, 2017, 359(1): 76 – 85.