ISSN 2618-1584 Vol. 7, Issue 2: 103-111, DOI: 10.25236/FMSR.2025.070215

Mechanism exploration of Zanthoxyli Radix in Parkinson's disease treatment via network pharmacology and molecular docking

Shuya Gao[1], Shunli Liu [1], Jianjun Huang[2,*]

[1]Youjiang Medical University for Nationalities, Baise, Guangxi, 533000, China
[2]Affiliated Hospital of Youjiang Medical University for Nationalities, Baise, Guangxi, 533000, China
**Corresponding author*

Abstract: *By employing network pharmacology and molecular docking approaches, we aim to investigate the interactions between the bioactive constituents present in Zanthoxylum nitidum and the specific targets within the human body, with the ultimate goal of modulating the pathological mechanisms associated with Parkinson's Disease (PD). Relevant chemical components of Zanthoxylum nitidum were searched in TCSMP, CNKI, and Wanfang databases to obtain effective active components and predicted target genes. The component-gene target network was constructed using Cytoscape 3.7.2 software. Major targets of PD were obtained from the GEO database and compared with core gene targets of Zanthoxylum nitidum using a Venn diagram. Protein-protein interaction (PPI) network analysis was conducted on the intersection targets, and functional enrichment analysis was performed based on Gene Ontology (GO). Kyoto Encyclopedia of Genes and Genomes (KEGG) resources were used for enrichment studies on biological pathways to predict biological processes and pathways. The "drug-target-pathway" network was constructed using Cytoscape 3.7.2 software, and molecular docking was performed on core components and key targets using AutoDock vina software. A total of 38 compounds related to Zanthoxylum nitidum, 672 component targets, and 86 common targets between Zanthoxylum nitidum and PD were obtained. Network analysis revealed that the core active components of Zanthoxylum nitidum for treating PD are ethyl ferulate, dihydrochelerythrine, diosmetin, apigenin, and nitidine chloride. Core targets include AKT1, GAPDH, BCL2, EGFR, STAT3, and CASP3. GO and KEGG analyses showed that the pathways of Zanthoxylum nitidum in treating PD are mainly enriched in PI3K-Akt signaling pathway, Ras signaling pathway, and apoptosis signaling pathway. Its functions mainly include protein tyrosine kinase activity, transmembrane receptor protein kinase activity, and protein phosphatase binding. Molecular docking was performed between the top five key components of Zanthoxylum nitidum and six core genes screened by PPI. The chemical components in Zanthoxylum nitidum act on multiple pathways and targets to exert therapeutic effects on PD.*

Keywords: *Zanthoxyli Radix; Parkinson's disease; Network pharmacology; Molecular docking*

Parkinson's disease (PD), also known as tremor paralysis, is a common degenerative disease among the elderly[1]. This disease is prevalent among the elderly over 65 years old. With the increasingly serious issue of aging in society, the incidence of PD is expected to keep rising in the future, imposing a heavy burden on society[2]. Given that there are currently no effective treatments for PD, it is particularly urgent and important to develop more new therapeutic methods for PD. Radix Zanthoxyli is the dried root of the plant DC of the Rutaceae family. In traditional Chinese medicine theory, Radix Zanthoxyli has the functions of promoting blood circulation and removing blood stasis, regulating qi and relieving pain, dispelling wind and unblocking meridians, and detoxifying and reducing swelling[3]. The currently discovered components of Dichroa febrifuga include alkaloids, coumarins, lignins, sterols and inorganic elements, etc[4-8]. Among them, the main component is alkaloids[9].Previous studies have shown that camphorin has therapeutic potential for Parkinson's disease in vitro through targeting α-Syn[10]. The research conducted by LIU Y P et al. has provided scientific evidence for the neuroprotective effect of carbazole alkaloids [11]. However, regarding the potential active ingredients contained in the Radix Zanthoxyli and their mechanism of action, further in-depth exploration is still needed. Network pharmacology adopts the "multi-compound, multi-target and multi-pathway" approach, integrating systems biology, bioinformatics and pharmacology, which is conducive to revealing the systemic effects of traditional Chinese medicine and is regarded as a new strategy for drug development [12, 13] . Therefore, in this study, we employed network pharmacology and molecular docking techniques to conduct a

ISSN 2618-1584 Vol. 7, Issue 2: 103-111, DOI: 10.25236/FMSR.2025.070215

preliminary exploration and analysis of the potential therapeutic mechanism of the active ingredients of Radix Zanthoxyli in treating PD.

1. Materials and Methods

1.1 Screening of Chemical Components Related to Radix Zanthoxyli

Through the search on the TCMSP (Traditional Chinese Medicine Systems Pharmacology Database and Analysis Platform) and the CNKI (China National Knowledge Infrastructure) databases, the relevant active components of Radix Zanthoxyli were identified. After merging and removing duplicates from the active components of Radix Zanthoxyli in TCMSP and the literature-related ones, first, the CSA (Chemical Substance Abstract) numbers were retrieved and obtained from the websites of ChemSrc (https://www.chemsrc.com) and GuideChem (https://china.guidechem.com). Then, using the Pubchem database, the corresponding Canonical SMILES were searched for based on the CSA numbers. Finally, these Canonical SMILES were input into the Swiss ADME platform (https://www.swissadme.ch) [14, 15]. Set the following filtering conditions to screen for core active ingredients: 1. The lipophilicity value should be less than 5, and the gastrointestinal absorption (Glabsoption) rating should be "High". These two conditions jointly ensure that the compounds have good oral bioavailability. 2. In the drug similarity assessment, at least three or more results should be "Yes". This further enhances the reliability of the compounds as potential drugs. Import the twigs-related chemical components screened out into the Swisstargetprediction platform (website: www.Swisstargetprediction.ch), and select the target proteins with Probability values greater than 0, because these proteins are more likely to interact with the compounds.

1.2 Construction of the Network of Core Targets for the Active Ingredient of Radix Zanthoxyli

The genes for screening the active components of Radix Zanthoxyli were imported into STRING (https://www.string-db.org/) for obtaining the data of protein-related networks. Then, they were imported into Cytoscape 3.9.1 and processed with the CytoNCA plugin. The conditions such as BC (betweenness centrality), CC (closeness centrality), and DC (degree) were set. After importing the corresponding files, the median value was set. Those with values greater than the median were regarded as the core genes for screening the active components of Radix Zanthoxyli. Then the core genes were imported into Cytoscape 3.7.2. Subsequently, through this software tool, the "degree value" was obtained to identify the core active ingredients of the two-faced fern[16], Construct a network diagram of the active ingredients and target points of the Radix Zanthoxyli traditional Chinese medicine.

1.3 Screening of PD-related targets

Based on the keyword "Parkinson's Disease" in the GeneCards database, NCBI database and Uniport database, the target genes and target proteins of Parkinson's disease were retrieved. The screening conditions for each database are as follows: in the GeneCards database, the correlation between drugs and targets is > 20; in the NCBI database and Uniport database, the category selection of drugs and targets is set as human. After merging and removing duplicates, it is defined as the PD dataset. The gene datasets of "Parkinson's Disease" and "Zanthoxyli Radix" were processed using the R software package "venn" (R software packages (version 4.2.0)), and a Venn diagram was drawn to obtain the common targets of the two.

1.4 Constructing protein-protein interaction network (PPI)

Input the selected core genes into the STRING database (https://www.string-db.org/) to obtain the protein-protein interaction (PPI) data corresponding to these core genes. Subsequently, import the PPI data into Cytoscape 3.9.1 software for visualization processing, so as to analyze and understand the relationships among these proteins more intuitively.

1.5 Functional enrichment analysis of core targets

By using multiple packages on the Bioconductor platform in R3.6.2 software environment, such as org.Hs.eg.db, colorspace, stringi, pathview, ggplot2 and limma, etc., GO and KEGG functional enrichment analysis was conducted. The enrichment results of GO and KEGG were visualized and

ISSN 2618-1584 Vol. 7, Issue 2: 103-111, DOI: 10.25236/FMSR.2025.070215

plotted by using Cytoscape 3.9 software.

1.6 Construction of Radix Zanthoxyli-Target-Pathway Network

In order to further explore the therapeutic mechanism of the active components of Radix Zanthoxyli on PD, the top 20 key pathways from KEGG, the active components of Radix Zanthoxyli and the core targets screened were imported into Cyto-scape 3.7.2 to construct a component-target-pathway network structure.

1.7 Molecular docking of the active components of Radix Zanthoxyli with key targets

Select the six most important protein targets in the PPI network and the five key main compounds of the Radix Zanthoxyli active ingredients. Use Autodock Tools 1.5.7 software and PyMOL 2.5.2 for molecular docking and visualization processing.

2. Result

2.1 Prediction of the components of "Radix Zanthoxyli"

The initial screening conditions for the TCMSP database were: OB% $\geqslant$ 30 and DL $\geqslant$ 0.18, which yielded 20 active components related to Radix Zanthoxyli. Through the search in the CNKI database, 53 compound information related to Radix Zanthoxyli was collected. After merging and deduplication, a total of 57 active ingredients were obtained. According to the screening criteria in 1.1, a total of 38 effective compounds were screened out (as shown in Table 1). The relevant active ingredients of Radix Zanthoxyli were input into the Swisstargetprediction platform to obtain the names of drug targets, and the target proteins with a predicted probability (Probability) greater than 0 were selected. After deleting the duplicate items, a total of 672 gene targets were obtained. Through CytoNCA in Cytoscape 3.9.1, 230 core genes were acquired (Figure 1).

Table 1 Information on the relevant active ingredients of the Zanthoxyli Radix

Project	CAS Number	Molecular name	Project	CAS Number	Molecular name	Project	CAS Number	Molecular name
LMZ1	3486-66-6	Coptisine	**LMZ14**	6900-99-8	Norchelerythrine	**LMZ27**	2141-09-5	magnoflorine
LMZ2	2447-54-3	Sanguinarine	**LMZ15**	21080-31-9	Angoline	**LMZ28**	3072-13-7	9, 12-octadecadienamide
LMZ3	607-80-7	Sesamin	**LMZ16**	475-75-2	Liriodenine	**LMZ29**	51152-20-6	Episyringaresinol
LMZ4	2543-94-4	Phellopterin	**LMZ17**	54354-62-0	decarine	**LMZ30**	116498-58-9	5, 5'-Dimethoxylariciresinol
LMZ5	83-95-4	Skimmianin	**LMZ18**	133-04-0	asarinin	**LMZ31**	92-61-5	scopoletin
LMZ6	520-34-3	Diosmetin	**LMZ19**	6216-81-5	syringaresinol	**LMZ32**	93-35-6	umbelliferone
LMZ7	66056-18-6	Glycyrin	**LMZ20**	6880-91-7	bocconoline	**LMZ33**	4335-12-0	Toddaculin
LMZ8	1260382-72-6	7-Chloro-6-Methoxy-5-Methyl1H-indole	**LMZ21**	6872-57-7	nitidine	**LMZ34**	487-06-9	5,7-Dimethoxycoumarin
LMZ9	111407-29-5	xanthoxylol	**LMZ22**	484-29-7	Dictamnine	**LMZ35**	482-27-9	isopimpinellin
LMZ10	520-33-2	5,7-dihydroxy-2-chroman-4-one	**LMZ23**	5876-17-5	haplopine	**LMZ36**	2543-94-4	Phellopterin
LMZ11	548-31-2	Oxynitidine	**LMZ24**	55-21-0	benzamide	**LMZ37**	520-36-5	Apigenin
LMZ12	79559-55-0	Ethoxychelerythrine	**LMZ25**	32262-18-3	4 -methoxy -1 -methyl -2 -quinolone	**LMZ38**	22329-76-6	Methyl ferulate
LMZ13	34316-15-9	chelerythrine	**LMZ26**	64190-94-9	Zanthobungeanine			

2.2 Construction of the Component-Target Network of Radix Zanthoxyli

The component-target network of Radix Zanthoxyli contains 268 nodes (38 nodes for active ingredients, 229 nodes for gene targets, and 1 node for traditional Chinese medicine) and 544 edges (as shown in Figure 1). In this network, the network of dihydrogen phloroglucinol has the highest degree of connection, connecting with 47 gene targets. The next are magnolol and dichlorophyllin alkaloid chloride, which are respectively connected with 46 and 43 gene targets (Figure 1).

ISSN 2618-1584 Vol. 7, Issue 2: 103-111, DOI: 10.25236/FMSR.2025.070215

2.3 Screening of PD-related targets

Based on the keyword "Parkinson's Disease" in GeneCards database, NCBI database and Uniport database, 1836 target genes and target proteins of Parkinson's disease were identified. The gene datasets of "Parkinson's Disease", "Mog V" and the two were used to draw a Venn diagram by R software package "venn" (R software packages (version 4.2.0)), and the common target points of the two were obtained (Figure 2).

2.4 Analysis of potential target protein-protein interaction (PPI) networks

The 86 active ingredients of 86-Radix Zanthoxyli were imported into the String database together with the common targets of PD, and a PPI network consisting of 86 protein nodes was constructed. Among them, 1982 edges represented the interaction relationships between these proteins. The average node degree value of the protein network was 46.1, and the local clustering average coefficient was 0.73. To further analyze this network, the built-in Network Analyzer function of Cytoscape 3.7.2 was used. The analysis of the network showed that the top 6 targets ranked by degree values were AKT1 (v-akt murine thymoma viral oncogene homolog 1), GAPDH (glyceraldehyde-3-phosphate dehydrogenase), BCL2 (B-cell lymphoma-2), EGFR (epidermal growth factor receptor), STAT3 (Signal Transducer and Activator of Transcription 3), and CASP3 (Apoptosis-Related Cysteine Peptidase). The degree values were 83, 82, 78, 78, 77, and 75 respectively, suggesting that the mechanism of action of 86-two-faced-needle active ingredients in treating PD might be related to these core proteins. See Figure 3.

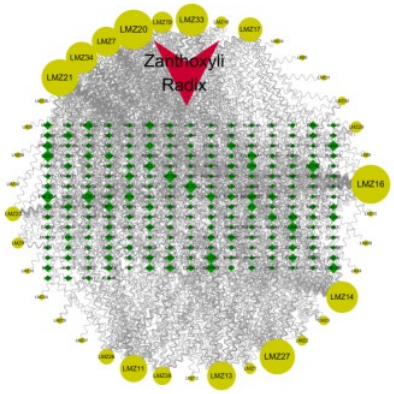

Figure 1 Compound component-target diagram: red V-shape represents Zanthoxyli Radix; Orange circles represent related compounds of the Zanthoxyli Radix,Green diamonds represent the Zanthoxyli Radix related components (see Table 1 for the ID of each component

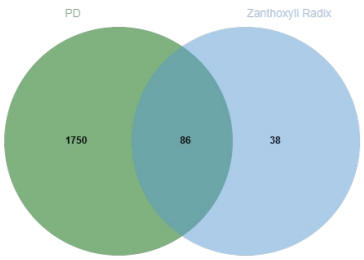

Figure 2 Venn diagram of Zanthoxyli Radix -PD active targets

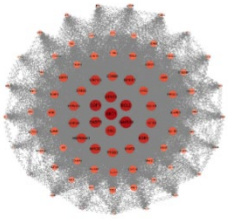

Figure 3 Potential PPI network for Zanthoxyli Radix treatment of Parkinson's disease

ISSN 2618-1584 Vol. 7, Issue 2: 103-111, DOI: 10.25236/FMSR.2025.070215

2.5 Enrichment analysis of potential targets GO and KEGG pathways

The GO (Gene Ontology) and KEGG (Kyoto Encyclopedia of Genes and Genomes) pathway enrichment analyses were conducted using the R language toolkit on the potential targets of the active components of Radix Zanthoxyli in the process of treating PD. The GO enrichment results indicated that the biological processes (BP) of these potential targets mainly included: response to oxidative stress, regulation of neuron death, peptidyl-tyrosine phosphorylation, etc. The involved cellular components (CC) included membrane raft, membrane region, cell-substrate junction, nuclear envelope, glutamatergic synapse, etc. The related molecular functions (MF) included protein tyrosine kinase activity, transmembrane receptor protein kinase activity, protein phosphatase binding, etc., as shown in Figure 4.

To further investigate the biological processes of these targets, KEGG pathway analysis was conducted. The results showed that the therapeutic targets of the active components of Bajianpi were significantly enriched in 239 KEGG pathways. After screening with $P < 0.05$, the PI3K-Akt signaling pathway and Ras signaling pathway were relatively prominent among the pathways. Other related pathways mainly involved apoptosis (Neurotrophin signaling pathway), neurotrophic signaling pathway (Thyroid hormone signaling pathway), thyroid hormone signaling pathway, estrogen signaling pathway, and Parkinson disease (Parkinson disease), as shown in Figure 5

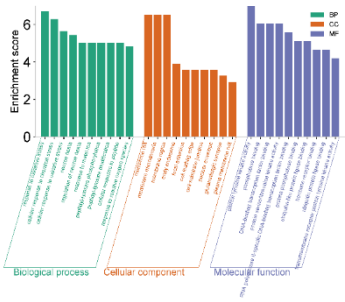

Figure 4 GO analysis of intersection genes of Zanthoxyli Radix-Parkinson's disease

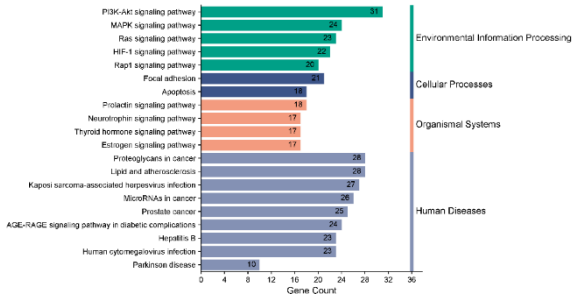

Figure 5 Predicted pathways for the active ingredients of the Zanthoxyli Radix in the treatment of PD

2.6 Construct a network diagram of "Radix Zanthoxyli Active Ingredient - Core Target - Key Pathway"

In the ranking of target points in network analysis, the top five target points based on Degree values are PIK3CA, PIK3CD, EGFR, GSK3B and AKT1. In the ranking of Degree values of active ingredients of effective components, the top five active ingredients of two-faced fern are ferulic acid ethyl ester, dihydro linalool lignan, camphene, apigenin and chloro two-faced fern alkaloid. Network analysis suggests that these two-faced fern active ingredients and core genes may be important components and targets for treating PD, as shown in Figure 6.

2.7 The molecular docking of the active ingredients of Radix Zanthoxyli with the core genes

The top five active components of Radix Zanthoxyli were selected from the component-target pathway and docked with the six potential core targets (AKT1, GAPDH, BCL2, EGFR, STAT3 and CASP3) obtained from the PPI network analysis. The specific information of the active components of Radix Zanthoxyli is shown in Table 2. A binding energy value less than 0 indicates that the ligand molecule can spontaneously bind to the receptor protein, while a binding energy value greater than 5.0 kJ/mol indicates that the ligand molecule has an ideal binding affinity [17]. The results of molecular

ISSN 2618-1584 Vol. 7, Issue 2: 103-111, DOI: 10.25236/FMSR.2025.070215

docking analysis showed that the binding energies of the active components to the core targets were all within the range of -6.2 to -10.0 kcal/mol (1 kcal = 4.186 kJ) (as shown in Table 3). The lower the binding energy value, the better the docking effect of the active component to the gene target. The 2D and 3D structures of the specific binding energies are shown in Figures 7, respectively.

Table 2 Core components of Zanthoxyli Radix polyphenols

Molecular name	Degree	Source	Molecular name	Degree	Source
Methyl ferulate	27	LMZ38	Apigenin	23	LMZ37
Bocconoline	25	LMZ20	Nitidine	21	LMZ21
Diosmetin	24	LMZ6			

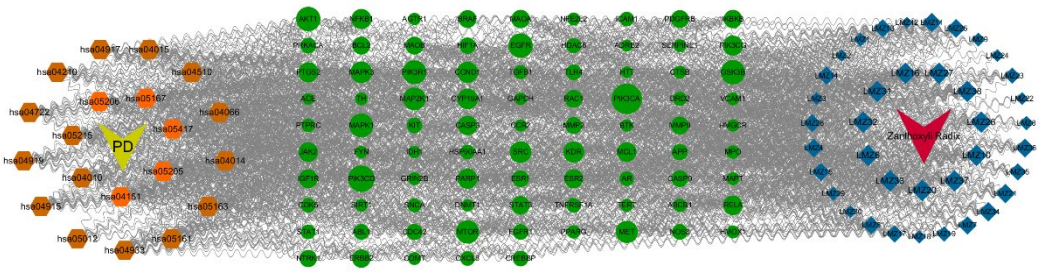

Figure 6 Core target-active ingredient-pathway diagram: the blue diamond represents the active ingredient of the Zanthoxyli Radix; The orange triangle represents the signaling pathway; The green circles represent the core targets

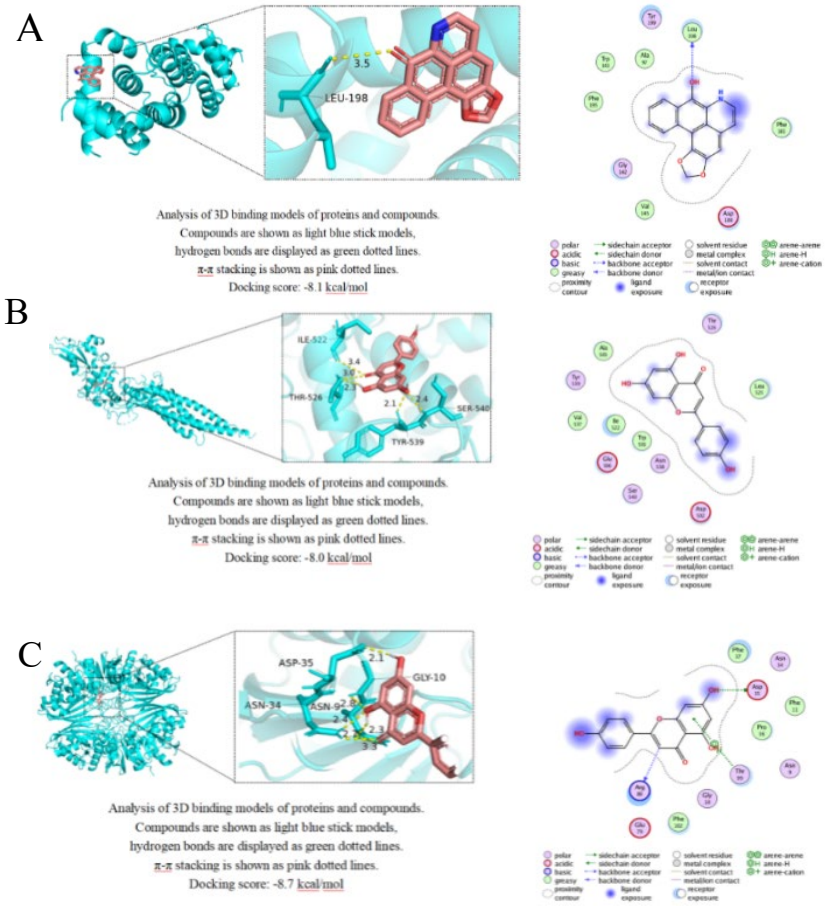

Figure 7 2D and 3D structures of key active components docking with core target proteins in Zanthoxyli Radix

ISSN 2618-1584 Vol. 7, Issue 2: 103-111, DOI: 10.25236/FMSR.2025.070215

Table 3 Binding energy of the core active component of the Zanthoxyli Radix to the core protein

Molecular name	AKT1 (kJ/mol)	GAPDH (kJ/mol)	BCL2 (kJ/mol)	EGFR(kJ/mol)	STAT3(kJ/mol)	CASP3 (kJ/mol)
Methyl ferulate	-4.2	-4.8	-5.3	-5.4	-5.3	-4.4
Bocconoline	-7.0	-6.2	-7.7	-7.5	-7.0	-5.7
Diosmetin	-6.3	-8.7	-7.2	-7.6	-8.0	-6.3
Apigenin	-7.9	-7.4	-8.2	-7.7	-7.8	-6.3
Nitidine	-6.8	-6.9	-6.8	-6.9	-6.7	-6.4

3. Discussion

In this study, network pharmacology and molecular docking techniques were employed to predict the active components, potential targets and related pathways of the effective ingredients of Radix Zanthoxyli in the treatment of PD. The analysis of the targets of active ingredients in traditional Chinese medicine indicated that the chemical components with a relatively high correlation with Gastrodia elata included eugenol acetate, dihydro geniposide, limonin, apigenin and chlorogenic gastrodin. The pathogenesis of Parkinson's disease is rather complex. Most experts generally believe that it is closely related to various factors such as mitochondrial dysfunction, abnormal protein aggregation, oxidative stress response, immune mechanism imbalance, and senescence and apoptosis[18, 19]. Ethinyl ferulic acid (EFE) is a natural lipophilic derivative of ferulic acid. It has pharmacological effects such as anti-thrombosis formation, anti-inflammation and antioxidation[20, 21]. Research indicates that EFE can induce the expression of heme oxygenase-1 (HO-1) and protect rat neurons from oxidative stress [22]. EFE also protects neurons from oxidative stress and neurotoxicity induced by β-amyloid protein 1-42 (Aβ1-42) [23]. Hydroxycitrosin dihydroxy has not only the analgesic effect but also the anti-inflammatory effect similar to hydrocortisone[24]. The effect of camphor saponin on MPP+ -induced damage in human neuroblastoma cell line SH-SY5Y cells. Camphor saponin can inhibit cell viability, promote cell proliferation, and inhibit cell apoptosis, thereby improving the effect of PD[25]. The extract of celery can reduce the oxidative stress indicators in patients with Parkinson's disease and improve their clinical prognosis. This suggests that celastrol may have the effect of improving the mitochondrial function of neurons in PD patients[26]. Chlorogenic acid of Pterocarpus angustifolius can regulate the activities of downstream proteins in the mitochondrial apoptotic pathway by inhibiting the Akt signaling pathway and the Januskinase/signal transducer and activator of transcription 3 (JAK/STAT3) signaling pathway, thereby inducing cell apoptosis. This suggests that it may exert protective effects on PD by regulating mitochondrial apoptosis [27]

The PPI network analysis indicates that the active components of Liangmiangui may exert their biological effects through core genes such as AKT1, GAPDH, BCL2, EGFR, STAT3 and CASP3. Relevant studies have shown that senescence apoptosis and mitochondrial dysfunction are considered to be the main contributors to PD [28-30]. GAPDH is a redox-sensitive protease. Under oxidative stress, GAPDH can regulate the permeability of mitochondrial membranes through voltage-dependent ion channels, facilitating the release of cytochrome and various pro-apoptotic proteins from mitochondria, thereby further increasing the oxidative stress level of cells and promoting apoptosis [31] . Research shows that phosphorylation of STAT3 can promote cell proliferation, inhibit cell apoptosis, and also facilitate angiogenesis, thereby providing nutritional support for new neurons and synapses[32]. The mitochondrial apoptotic pathway is an intrinsic apoptotic pathway triggered by intracellular factors (such as toxins, oxidative stress, etc.). In this pathway, the expression of BCL2 family proteins is interfered by intracellular factors, thereby affecting the permeability of the mitochondrial membrane[33]; Subsequently, some pro-apoptotic molecules such as Cytochrome C are released from mitochondria, thereby activating Caspase-3 and inducing Caspase-dependent cell apoptosis [34]. Mitochondria are important regulators involved in apoptosis. When stimulated by pathological or physiological signals, the expression of BCL2 and BAX is imbalanced, resulting in changes in mitochondrial function. Apoptosis-inducing factor is released outside the mitochondria and activates the downstream Caspase cascade reaction, ultimately leading to apoptosis of the cells [35, 36]. The GAPDH gene, GAPDH enzyme protein and Lewy bodies are the pathological markers of PD. The formation of Lewy bodies in the substantia nigra and striatum is the residual pigment neurons of PD. α-synuclein is the main component of Lewy bodies[37]. The above

ISSN 2618-1584 Vol. 7, Issue 2: 103-111, DOI: 10.25236/FMSR.2025.070215

studies have demonstrated that GAPDH is also one of the key potential main targets for PD treatment.

GO biological process enrichment analysis indicated that the potential targets were mainly concentrated in the responses to oxidative stress, regulation of neuronal death, and phosphorylation of tyrosine residues of peptides. At the molecular function level, they mainly involved protein tyrosine kinase activity, transmembrane receptor protein kinase activity, and protein phosphatase binding. Protein tyrosine kinase phosphorylates with common receptor EGFR and thereby generates a series of enzymatic catalytic effects[38]. The KEGG analysis results indicate that the pathways related to PD are ranked relatively high, including the PI3K-Akt signaling pathway and the Ras signaling pathway. Other related pathways mainly involve apoptosis, neurotrophic signaling pathways, thyroid hormone signaling pathways, estrogen signaling pathways, and Parkinson's disease signaling pathways. In conclusion, through the methods of network pharmacology and molecular docking technology, this study conducted a preliminary exploration and analysis of the mechanism of action of Radix Zanthoxyli in treating Parkinson's disease (PD) from multiple perspectives. It suggested that the intervention of Radix Zanthoxyli in PD might exert potential effects through the above-mentioned key chemical components and core genes. This article's analysis demonstrated a complex network intervention mode involving multiple components, multiple targets, and multiple pathways. This not only provided a scientific basis for the application of related components of Radix Zanthoxyli in clinical treatment of PD, but also pointed out the research direction and ideas for subsequent experimental verification of the potential mechanism of Radix Zanthoxyli.

References

[1] CURRIM F, SINGH J, SHINDE A, et al. Exosome Release Is Modulated by the Mitochondrial-Lysosomal Crosstalk in Parkinson's Disease Stress Conditions [J]. Mol Neurobiol, 2021, 58(4).
[2] PéREZ DE LA CRUZ S. Effectiveness of aquatic therapy for the control of pain and increased functionality in people with Parkinson's disease: a randomized clinical trial [J]. Eur J Phys Rehabil Med, 2017, 53(6).
[3] CHAN Y T, WANG N, FENG Y. The toxicology and detoxification of Aconitum: traditional and modern views [J]. Chin Med, 2021, 16(1).
[4] LIANG M, ZHANG W, HU J, et al. Simultaneous analysis of alkaloids from Zanthoxylum nitidum by high performance liquid chromatography-diode array detector-electrospray tandem mass spectrometry [J]. J Pharm Biomed Anal, 2006, 42(2).
[5] MIRZAYEVA T, ČOPíKOVá J, KVASNIČKA F, et al. Screening of the Chemical Composition and Identification of Hyaluronic Acid in Food Supplements by Fractionation and Fourier-Transform Infrared Spectroscopy [J]. Polymers (Basel), 2021, 13(22).
[6] LO S F, MULABAGAL V, CHEN C L, et al. Bioguided fractionation and isolation of free radical scavenging components from in vitro propagated chinese medicinal plants Dendrobium tosaense Makino and Dendrobium moniliforme SW [J]. J Agric Food Chem, 2004, 52(23).
[7] YANG ZHONGDUO Z D, REN JIN. Skimmianine,a furoquinoline alkaloid from Emphasis Zanthoxylum nitidum/Emphasis as a potential acetylcholinesterase inhibitor[J]. J Med Chem res, 2012,21(6),722-725.
[8] BAO Y, GAO Y, CUI X. Effect of Shufeng Jiedu capsules as a broad-spectrum antibacterial [J]. Biosci Trends, 2016, 10(1).
[9] SCHMIDT D R, PATEL R, KIRSCH D G, et al. Metabolomics in cancer research and emerging applications in clinical oncology [J]. CA Cancer J Clin, 2021, 71(4).
[10] JAVED H, NAGOOR MEERAN M F, AZIMULLAH S, et al. Plant Extracts and Phytochemicals Targeting α-Synuclein Aggregation in Parkinson's Disease Models [J]. Front Pharmacol, 2018, 9.
[11] LIU Y P, GUO J M, WANG X P, et al. Geranylated carbazole alkaloids with potential neuroprotective activities from the stems and leaves of Clausena lansium [J]. Bioorg Chem, 2019, 92.
[12] NOGALES C, MAMDOUH Z M, LIST M, et al. Network pharmacology: curing causal mechanisms instead of treating symptoms [J]. Trends Pharmacol Sci, 2022, 43(2).
[13] LI S, ZHANG B. Traditional Chinese medicine network pharmacology: theory, methodology and application [J]. Chin J Nat Med, 2013, 11(2).
[14] DASHTI H, WEDELL J R, WESTLER W M, et al. Automated evaluation of consistency within the PubChem Compound database [J]. Sci Data, 2019, 6.
[15] DAINA A, MICHIELIN O, ZOETE V. SwissADME: a free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules [J]. Sci Rep, 2017, 7.
[16] SHANNON P, MARKIEL A, OZIER O, et al. Cytoscape: a software environment for integrated models of biomolecular interaction networks [J]. Genome Res, 2003, 13(11).

ISSN 2618-1584 Vol. 7, Issue 2: 103-111, DOI: 10.25236/FMSR.2025.070215

[17] YANG L, XU H, CHEN Y, et al. Melatonin: Multi-Target Mechanism Against Diminished Ovarian Reserve Based on Network Pharmacology [J]. Front Endocrinol (Lausanne), 2021, 12.
[18] TOULORGE D, SCHAPIRA A H, HAJJ R. Molecular changes in the postmortem parkinsonian brain [J]. J Neurochem, 2016, 139 Suppl 1.
[19] KAUR K, GILL J S, BANSAL P K, et al. Neuroinflammation - A major cause for striatal dopaminergic degeneration in Parkinson's disease [J]. J Neurol Sci, 2017, 381.
[20] ULANOWSKA M, OLAS B. Biological Properties and Prospects for the Application of Eugenol-A Review [J]. Int J Mol Sci, 2021, 22(7).
[21] WU Y X, WANG Y Y, GAO Z Q, et al. Ethyl ferulate protects against lipopolysaccharide-induced acute lung injury by activating AMPK/Nrf2 signaling pathway [J]. Acta Pharmacol Sin, 2021, 42(12).
[22] SCAPAGNINI G, BUTTERFIELD D A, COLOMBRITA C, et al. Ethyl ferulate, a lipophilic polyphenol, induces HO-1 and protects rat neurons against oxidative stress [J]. Antioxid Redox Signal, 2004, 6(5).
[23] SULTANA R, RAVAGNA A, MOHMMAD-ABDUL H, et al. Ferulic acid ethyl ester protects neurons against amyloid beta- peptide(1-42)-induced oxidative stress and neurotoxicity: relationship to antioxidant activity [J]. J Neurochem, 2005, 92(4).
[24] XIAO Y, SHAO K, ZHOU J, et al. Structure-based engineering of substrate specificity for pinoresinol-lariciresinol reductases [J]. Nat Commun, 2021, 12(1).
[25] OSHIMA T, ITO M. Sedative effects of l-menthol, d-camphor, phenylethyl alcohol, and geraniol [J]. J Nat Med, 2021, 75(2).
[26] CHANGKEB V, NOBSATHIAN S, LE GOFF G, et al. Insecticidal efficacy and possibility of Combretum trifoliatum Vent. (Myrtales: Combretaceae) extracts in controlling Spodoptera frugiperda (J.E. Smith) (Lepidoptera: Noctuidae) [J]. Pest Manag Sci, 2023, 79(12).
[27] DESHAIES R J, JOAZEIRO C A. RING domain E3 ubiquitin ligases [J]. Annu Rev Biochem, 2009, 78.
[28] CHUANG D M, HOUGH C, SENATOROV V V. Glyceraldehyde-3-phosphate dehydrogenase, apoptosis, and neurodegenerative diseases [J]. Annu Rev Pharmacol Toxicol, 2005, 45.
[29] MOON H E, YOON S H, HUR Y S, et al. Mitochondrial dysfunction of immortalized human adipose tissue-derived mesenchymal stromal cells from patients with Parkinson's disease [J]. Exp Neurobiol, 2013, 22(4).
[30] LI L, NADANACIVA S, BERGER Z, et al. Human A53T α-synuclein causes reversible deficits in mitochondrial function and dynamics in primary mouse cortical neurons [J]. PLoS One, 2013, 8(12).
[31] TARZE A, DENIAUD A, LE BRAS M, et al. GAPDH, a novel regulator of the pro-apoptotic mitochondrial membrane permeabilization [J]. Oncogene, 2007, 26(18).
[32] XIA M L, XIE X H, DING J H, et al. Astragaloside IV inhibits astrocyte senescence: implication in Parkinson's disease [J]. J Neuroinflammation, 2020, 17(1).
[33] SINGH R, LETAI A, SAROSIEK K. Regulation of apoptosis in health and disease: the balancing act of BCL-2 family proteins [J]. Nat Rev Mol Cell Biol, 2019, 20(3).
[34] LEMASTERS J J. Dying a thousand deaths: redundant pathways from different organelles to apoptosis and necrosis [J]. Gastroenterology, 2005, 129(1).
[35] YIN F, ZHOU H, FANG Y, et al. Astragaloside IV alleviates ischemia reperfusion-induced apoptosis by inhibiting the activation of key factors in death receptor pathway and mitochondrial pathway [J]. J Ethnopharmacol, 2020, 248.
[36] LU H Y, CHEN X Q, TANG W, et al. GRP78 silencing enhances hyperoxia-induced alveolar epithelial cell apoptosis via CHOP pathway [J]. Mol Med Rep, 2017, 16(2).
[37] MEHRA S, SAHAY S, MAJI S K. α-Synuclein misfolding and aggregation: Implications in Parkinson's disease pathogenesis [J]. Biochim Biophys Acta Proteins Proteom, 2019, 1867(10).
[38] HUBBARD S R, TILL J H. Protein tyrosine kinase structure and function [J]. Annu Rev Biochem, 2000, 69.