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Study on the Protective Effect and Mechanism of BaiheWuyao Decoction on Non-alcoholic Fatty Liver Disease Based on Network Pharmacology

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Abstract: To explore the protective effect and mechanism of Baihe Wuyao Decoction (BWD) on non-alcoholic fatty liver disease (NAFLD) by using network pharmacology and molecular docking technology. The main active ingredients of Baihe and Wuyao were screened through the TCM Systematic Pharmacology Database Platform (TCMSP) database, The Swiss Target Prediction database, UniProt database and PharmMapper database screened the gene targets of Baihe and Wuyao; The GeneCards database and the OMIM database were used to obtain the relevant gene targets for NAFLD; Using Venn2. 1 Acquisition of drug-disease common targets; The String 11.5 database was used to construct a protein-protein interaction (PPI) network for the treatment of NAFLD in Baihe Wuyao Decoction to screen the core targets; Based on the Metascape gene function annotation analysis tool, the gene ontology (GO) and Kyoto Encyclopedia of Genomes (KEGG) pathway enrichment analysis of the intersection targets were performed; The active ingredient-drug target and active ingredient-target-pathway interaction network were constructed using Cytoscape 3.7.2 software to obtain the core active ingredient; AutoDockTools-1.5.6 software was used to select six of the top 30 genes in the PPI network and five core active components for molecular docking to verify the binding performance, and visualized with PyMOL. A total of 7 active ingredients and 286 related targets of Baihe were obtained, a total of 509 targets were collected after removing duplicate targets and gene annotation. A total of 1864 NAFLD-related targets were screened through the GeneCards database and the OMIN database,a total of 78 intersecting targets were obtained through Venn diagrams, and there were 78 intersecting targets between Baihe Wuyao Decoction and NAFLD, The main active ingredients involved are β-sitosterol, quercetin, isohexaturonic acid, norisopordine, 6,7-dimethoxy-2-(phenyethyl) chromone among others. The core targets are PPAR (peroxisome proliferation activation receptor α), JUN (chromosomal gene), NOS3 (nitric oxide synthase), ESR1 (estrogen receptor), etc. KEGG pathway enrichment analysis showed that PPAR signaling pathway and endocrine resistance may be the key signaling pathways in the treatment of non-alcoholic fatty liver disease (NAFLD) by Baihe Wuyao Decoction. The molecular docking results showed that the binding energy of the five core pharmaceutical active ingredients and the corresponding key targets was less than -

4.0kJ/mol. Among them, β-sitosterol and 3DMC could be well combined with six core targets, and it was predicted that they were important active ingredients for the intervention of non-alcoholic fatty liver disease in Baihe Wuyao Decoctionn. BWD can protect NAFLD through multiple targets and pathways, The core active ingredients of BWD includes β-sitosterol, quercetin, isohaipineic acid, norisopordine, 6,7-dimethoxy-2-(phenylethyl) chromoneand 3DMC, which can act on multiple key targets such as AKT1, PPARA, BCL2, and ESR1, regulate PPAR signaling pathway, endocrine resistance and other signaling pathways. The mechanism of BWD protects againstNAFLDisrelated to the improvement of glucose-lipid metabolism and insulin resistance, as well as anti-inflammatory effects and enhancing autophagy functions.

Nonalcoholic fatty liver disease (NAFLD) is a clinical syndrome characterized by an abnormal accumulation of liver fat due to a well-defined hepatocompromising trigger other than alcohol [1-4]. The incidence of NAFLD is increasing globally and has now replaced viral hepatitis as the leading chronic liver disease worldwide [3,4]. By 2030, the number of people with NAFLD globally is estimated to rise dramatically to 314.58 million, which is the highest increase of chronic diseases in the world [5].The pathogenesis of NAFLD is associated with metabolic syndrome (MS) such as lipid accumulation, insulin resistance (IR), inflammation, and autophagy, but the exact etiology of the disease is not fully understood [6].

Modern pharmacological studies have shown that a variety of components in Lilium and Aconitum have hypoglycemic effects [6-8], and have a good protective effect against liver injury [9-12]. Lily (Lilii Bulbus) contains a variety of pharmacologically active components such as polysaccharides, polyphenols, saponins and alkaloids, which have the effects of clearing the heart and tranquilizing the mind, nourishing yin and moistening the lungs, and are sweet, moist and slightly cold in nature [6]. Wu yao, derived from Linderae Radix, family Camphoraceae, is often used as dried tuberous roots in medicine for the treatment of chest and abdominal distension and pain, gas reversal and shortness of breath, and cold condensation and stagnation of qi [11]. The intake of Wu Yao extract inhibited the elevation of blood glucose and slowed down the progressive deterioration of functional and pathological aspects of diabetic nephropathy in db/db mice [9,13]. In addition, the total alkaloids in aconite not only block the NF-κB and MAPKs signaling pathways, but also inhibit the inflammatory mediators produced by macrophages, which in turn ameliorates liver injury [14]. All these suggest that Wu Yao may have potential hepatoprotective activity. Therefore, BWD Tang has a theoretical basis for the treatment of NAFLD.

Network pharmacology (network pharmacology) of traditional Chinese medicine (TCM) is a new discipline that explores the complex relationship between constituent targets and disease targets with TCM targets and disease targets as the core [15,16]. Through the screening of network big data, the systematic and comprehensive analysis of drug interventions and effects on diseases can be used to target drug targets and disease targets more precisely. In this study, network pharmacology was applied to find the interaction relationship between the components of BWD and its potential targets and NAFLD targets. It will provide potential herbal prescriptions for the clinical prevention and treatment of NAFLD, and at the same time provide a reference for revealing the pathophysiological mechanisms of NAFLD.

1. Materials and methods

1.1 Potential active ingredients and gene targets in BWD

Firstly, the chemical components of Baihe and Wuyao were retrieved through the TCM Network Pharmacology Database and Analysis Platform (TCMSP).Then, according to the four criteria of absorption, distribution, metabolism and excretion (ADME), the potential active substances of Baihe and Wuyao were comprehensively screened.After that, the intestinal absorption utilization (Caco-2) ≥-0.4, oral bioavailability (OB) ≥30%, and drug-likeness (DL) ≥ 0.18 were used as screening criteria,Potential candidate active ingredients in Baihe and Wuyao were obtained.Then, the Swiss Target Prediction database was used to screen out the potential active ingredients and drug treatment targets of BWD in combination with literature review.

1.2 NAFLD target prediction

With the help of Genecards and OIOM databases, the known disease targets were searched, and the correspondence between the targets and diseases was determined with the keyword "non-alcoholic fatty liver disease".

1.3 Access to drugs - disease common targets with Venn2.1

Based on the key targets of the active ingredients of BWD and the targets of NAFLD screened above, Venn2.1 was used to draw a Venn diagram to obtain the common targets of BWD and NAFLD.

1.4 Protein interaction network (PPI) and core target analysis

Protein -protein interaction (PPI) analysis of potential targets of BWD active ingredients with NAFLD targets was performed by String database to construct protein-protein interaction network. The relevant parameters were set as follows: species restriction to human and confidence > 0.40. Discrete targets were deleted and TSV files were downloaded and imported into Cytoscape 3.7.2 software to draw the PPI network diagram. The core active ingredients and targets of BWD for NAFLD were screened according to node size and colour shades, Degree value.

1.5 GO and KEGG enrichment analysis

Import candidate targets into Metascape (http://metascape.org/), make gene ontology (GO) enrichment, and draw notes on the path of Kyoto Gene and Genome Encyclopedia (KEGG). Finally, draw a bubble chart.

1.6 Construction of drug core ingredient-target-pathway map

Imported the drug active ingredients, intersecting targets and the top 20 pathways enriched by KEGG enrichment analysis into Cytoscape 3.7.2 software to construct the drug ingredient-target-pathway network map of BWD.

1.7 Molecular docking

To validate the binding affinity between core target sites and key active ingredients, molecular docking was conducted. The MOL2 structures of the docked small molecules were obtained from the TCMSP database, while the crystal structures of the docked receptor proteins were retrieved from the

Protein Data Bank (PDB) (http://www.rcsb.org) in PDB format. AutoDock Tools 1.5.6 was employed for molecular docking of ligands and receptors, followed by visualization of selected docking results using PyMOL software.

2. Result

2.1 Information on potential active ingredients in BWD and NAFLD targets

According to the screening conditions, the TCMSP database was used to screen the potential active chemical components of BWD and obtain the target information corresponding to its compounds. The UniProt database and PharmMapper database were used to supplement the target information and the Swiss Target Prediction database, combined with literature review, to screen out the potential active ingredients and drug treatment targets of Baihe Wuyao Decoction. A total of 7 active ingredients and 286 related targets were obtained, Wuyao has 9 active ingredients and 276 related targets,A total of 509 targets were collected after BWD removed duplicate targets and gene annotation. In Table 1, the main potential ingredients are listed. Among them, there are 7 Baihe and 9Wuyao.

Deriving the relationship between potential targets and related diseases from TCMSP. A total of 1864 NAFLD disease targets were found according to the GeneCards database and the OMIM database.

Table 1: Information on the main potential active ingredients in BWD

Mol ID	Herb	OB (%)	Caco-2	DL
MOL000358	Lilii Bulbus	36.91	1.32	0.75
MOL000449	Lilii Bulbus	43.83	1.44	0.76
MOL002039	Lilii Bulbus	36.2	1.12	0.28
MOL009449	Lilii Bulbus	32.43	-0.17	0.8
MOL009458	Lilii Bulbus	39.34	0.12	0.57
MOL009465	Lilii Bulbus	35.11	-0.02	0.81
MOL009471	Lilii Bulbus	32.43	-0.04	0.8
MOL010495	Linderae Radix	31.93	1.12	0.3
MOL010496	Linderae Radix	32.38	1	0.39
MOL010907	Linderae Radix	40.92	0.75	0.46
MOL010913	Linderae Radix	77.09	0.72	0.25
MOL010916	Linderae Radix	42.55	-0.21	0.19
MOL010917	Linderae Radix	31.18	1.05	0.51
MOL000358	Linderae Radix	36.91	1.32	0.75
MOL000359	Linderae Radix	36.91	1.32	0.75
MOL000098	Linderae Radix	46.43	0.05	0.28

2.2 Drug-disease common target Venn diagram

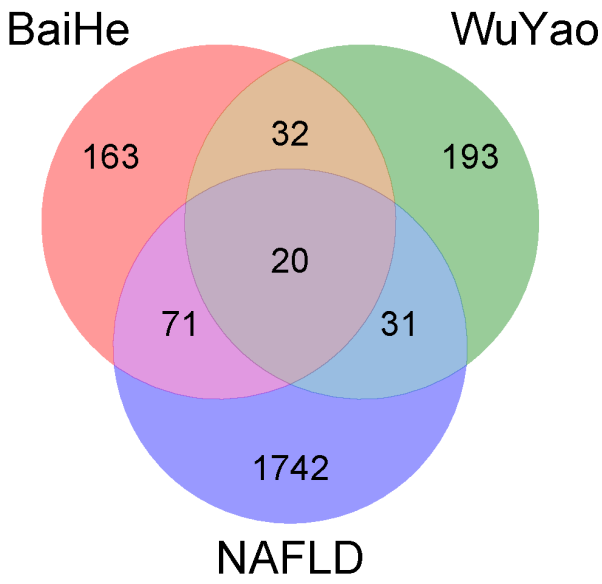


Figure 1: Venn diagram of the potential active ingredient of BWD and the NAFLD target

Deriving the relationship between potential targets and related diseases from TCMSP, a total of 1864 NAFLD disease targets were found according to the GeneCards database and the OMIM database. Organize the target information corresponding to BWD and intersect with the BWD component targets, a total of 122 drug-disease intersection target genes of BWD and NAFLD were obtained.Among them, there were 91 Baihe and 51 Wuyao, of which 20 target genes were shared by Baihe Wuyao (Fig. 1).

2.3 The analysis results of the core targets between BWD and NAFLD

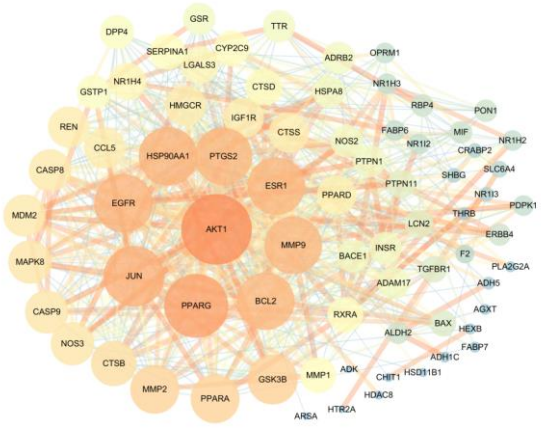


Figure 2: The PPI network selection diagram of active ingredients in BWD and core targets of NAFLD was illustrated

String was used to analyze protein-protein interactions of 78 potential targets. According to the results extracted with a reliability >0.40, the TSV file was imported into Cytoscape 3.7.2 to draw a PPI network diagram (Figure 2). According to the results of PPI analysis, there were 75 nodes and 582 edges. Using the MCC algorithm of the cytoHubba plug-in, 9 core targets (Degree value >30)

were found, which were AKT1, PPARG, JUN, EGFR, HSP90AA1, BCL2, PTGS2, MMP9, and ESR1. The information of the top 10 potential targets is shown in Table 2. Using the MCC algorithm of the cytoHubba plug-in and analyzing the relationship between active ingredients and potential targets (Figure 3), β-sitosterol, quercetin, isophorbide, and norepinephrine had high Degree values, which were the key active ingredients of BWD.

Table 2: Presents information on the top 10 potential targets

Target	Full name	Degree
AKT1	1 AKT serine/threonine kinase 1	48
PPARG	PPAR gamma	42
JUN	JUN Jun Proto-Oncogene, AP-1 Transcription Factor Subunit	39
EGFR	epidermal growth factor receptor	37
HSP90AA1	90α heat shock protein HSP 90-alpha	37
BCL2	B-cell lymphoma-2	36
PTGS2	PTGS2 - prostaglandin-endoperoxide synthase 2	36
MMP9	9 Matrix metalloproteinase-9	36
ESR1	estrogen receptor 1	36
GSK3B	GSK-3β	29

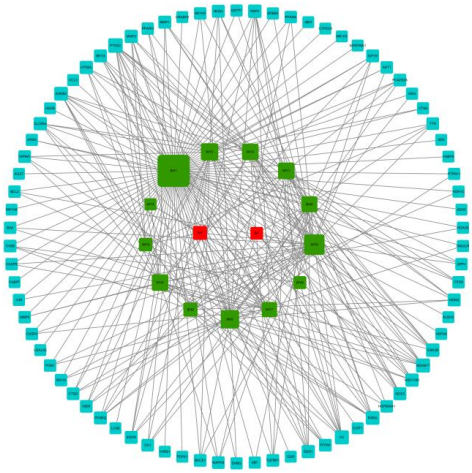


Figure 3: The compound-target network diagram of BWD was presented

2.4 GO and KEGG enrichment analysis to determine the potential BWD channel

GO analysis results show that there are 917 biological process pathways , including response to hormone , positive regulation of phosphorus metabolic process , etc ; Among the 59cell components expressed , they mainly involve the vesicle lumen , membrane raft , etc .101molecular function related processes mainly include nuclear receptor activities , ligand activated transcription factor activities , carboxylic acid binding , etc , whuch is suggested that Baihe Wuyao Decoction may treat NAFLD by regulating the above processes . The GO enrichment analysis diagram (Figure 4) and KEGG enrichment analysis results are sorted according to the P value to get the first 30 pathways (Figure 5). Combined with the pathogenesis of NAFLD, it suggests that BWD and NAFLD have the highest concentration in PPAR signaling pathway, endocrine resistance, IL -17 signaling pathway, insulin resistance and other pathways. These results all support that BWD protects NAFLD through multi

target and multi - channel cooperation, which is in line with the concept of multi target and multi - channel coordinated treatment.

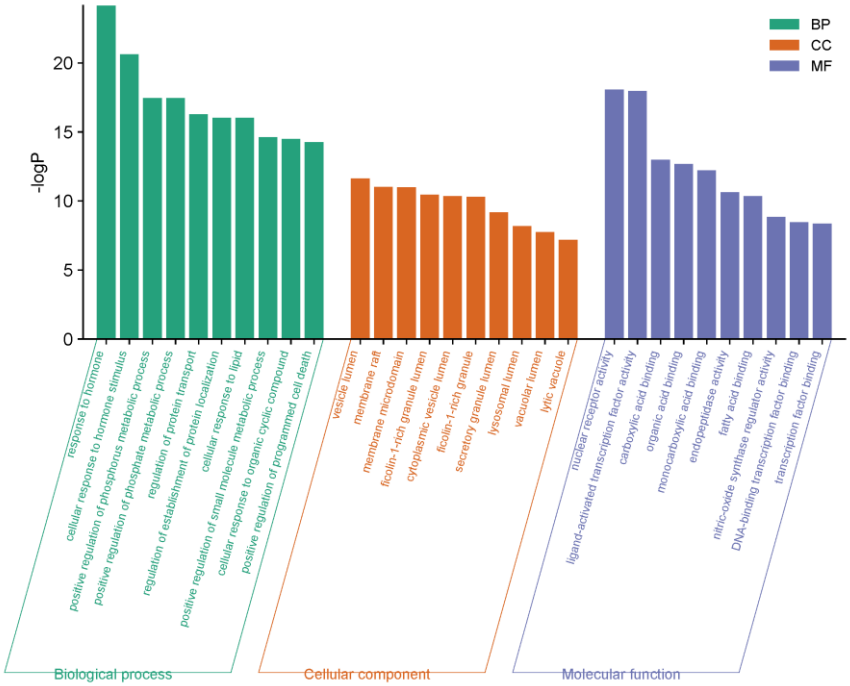


Figure 4: The graphical representation of Gene Ontology (GO) enrichment analysis is depicted

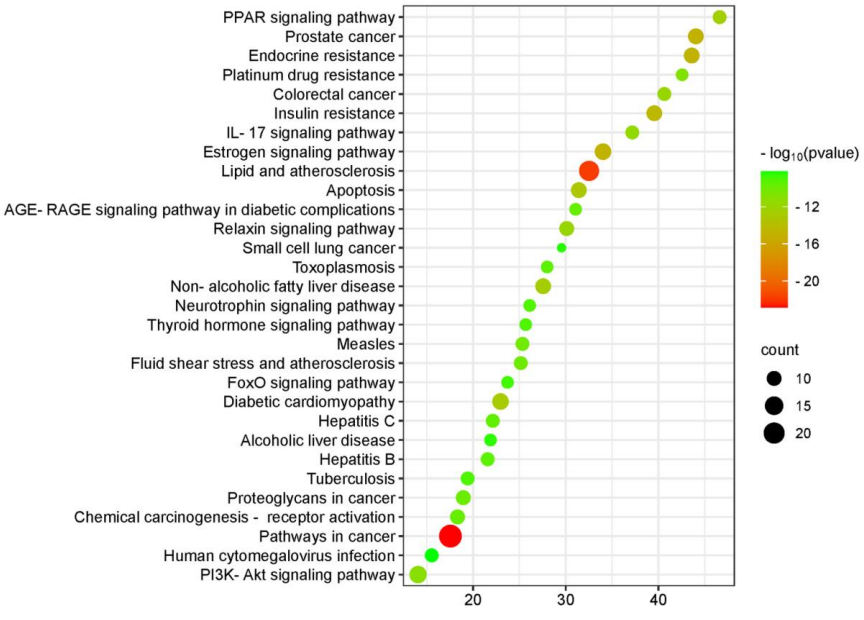


Figure 5: The bubble plot depicting KEGG enrichment analysis was presented

2.5 Drug core ingredient-target-pathway map

Cytoscape 3.7.2 software was used to construct an "active ingredient-target-pathway" network diagram of BWD (Figure 6), and the core active ingredients of BWD for NAFLD were screened

according to the node sizes and color shades, and the Degree value in the network diagram, and the results showed that the top five core active ingredients of BWD were β-sitosterol, quercetin, isohippuric acid, desmethylisoboldine, and 6,7-dimethoxy-2-(phenylethyl)chromone (Table 3), which may play an important role in the protection against NAFLD.

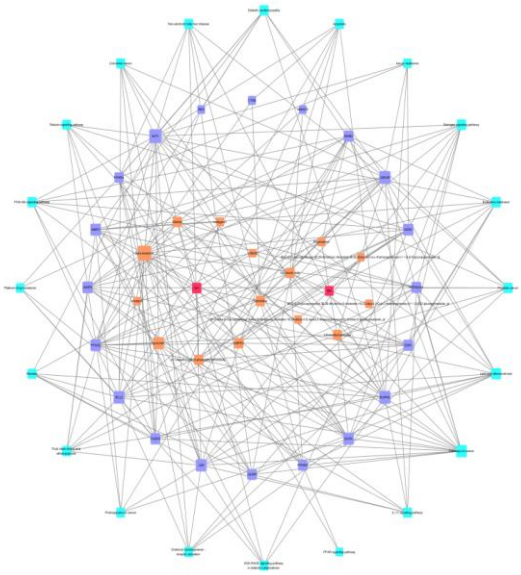


Figure 6: The "active ingredient-target-pathway" network of the effect of BaiHe of the valley on non-alcoholic fatty liver disease.

Table 3: Topological analysis of BWD core active ingredients

MOL	Name	OB/%	DL	Degree	BC	CC
MOL000358	beta-sitosterol	36.91	0.75	25	0.16346507	0.57142857
MOL000098	quercetin	46.43	0.28	14	0.05624433	0.5
MOL002039	Isopimaric acid	36.2	0.28	8	0.0655001	0.4375
MOL010907	Norboldine	40.92	0.46	8	0.02216981	0.44444444
MOL010495	6,7-dimethoxy-2-(2-phenylethyl)chromone	31.93	0.3	8	0.0192098	0.4516129

2.6 Molecular docking result

Using AutoDock Vina software, molecular docking was performed to validate the binding of five core drug active ingredients with six core target sites. A binding energy of ≤-5.0 kJ/mol between ligands and receptors was considered effective molecular docking. The docking results demonstrated that the docking energies between key targets and important compounds were all below -5.0 kJ/mol, indicating stable docking conformations, as shown in Figure 7. Among the effective compounds with lower binding energies, β-sitosterol, 3DMC, and quercetin were selected along with their corresponding effective targets BCL2, AKT1, and JUN, respectively. Visualization using PyMOL software revealed the formation of hydrogen bonds during the binding process, enhancing binding stability. The results confirm the favorable binding ability of key active ingredients from BWD with core targets of NAFLD, as depicted in Figure 8. The molecular docking results indicate that the binding energies of the five core drug active ingredients with their corresponding key target sites are all less than -4.0 kJ/mol. Among them, β-sitosterol and 3DMC demonstrate favorable binding with all six core target sites. This suggests that they may serve as important active ingredients for the

intervention of non-alcoholic fatty liver disease (NAFLD) by Baihe Wu Yao Decoction.

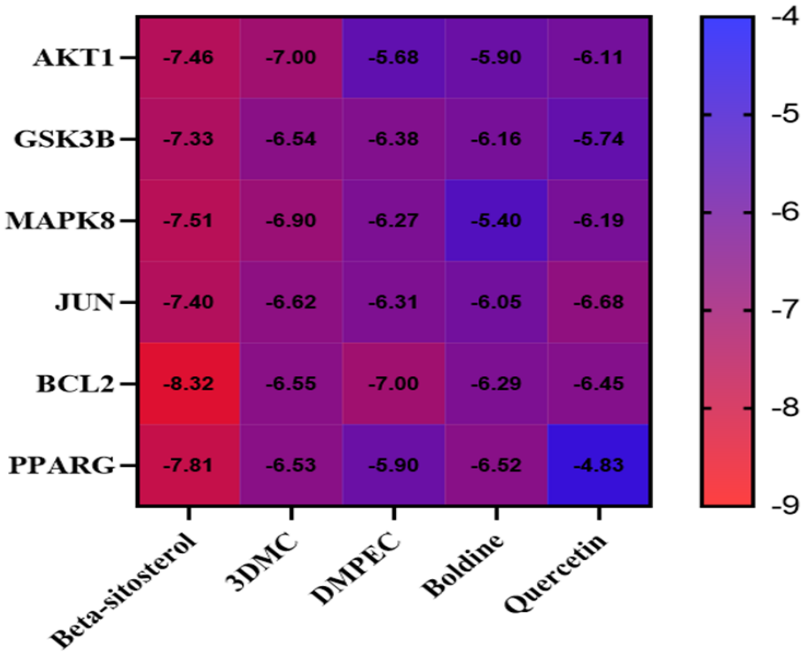
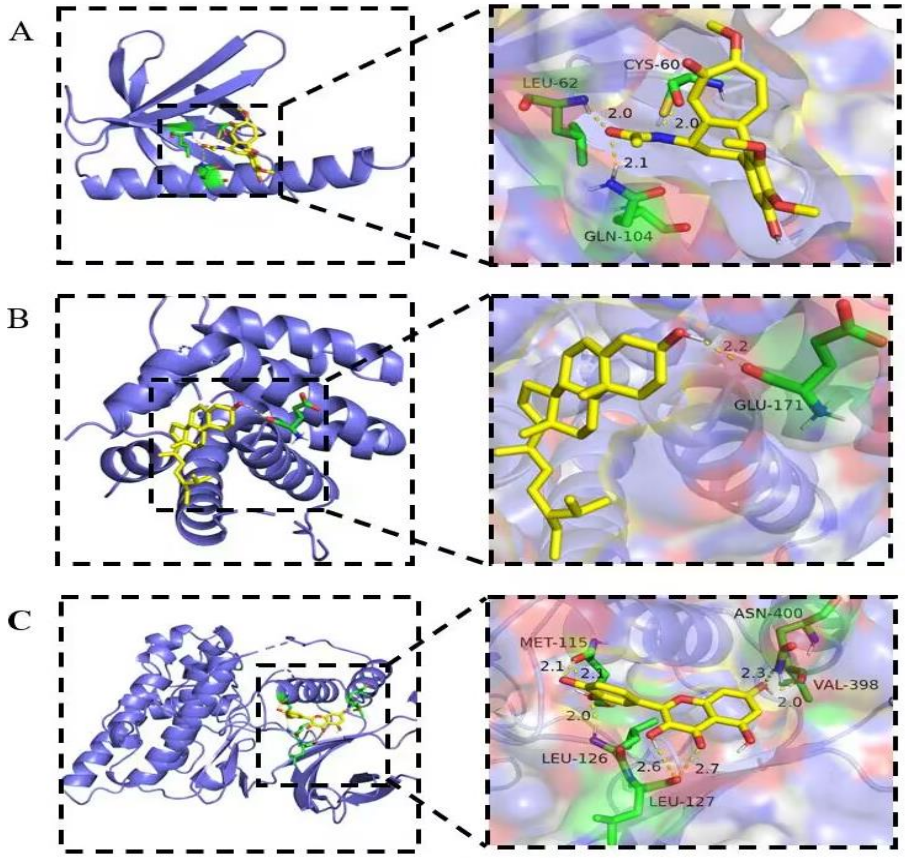


Figure 7: Molecular docking heat map



A: Beta-sitosterol-BCL2 B: 3DMC-AKT1 C:Quercetion-JUN

Figure 8: Molecular docking diagram of partial active ingredients with core target

3. Discuss

3.1 Analysis of the traditional Chinese medicine theory of BWD in the treatment of NAFLD

There is no such thing as "NAFLD" in traditional Chinese medicine, and it can be classified into the categories of "hypochondriac", "hepatic accumulation", "fattening", "liver turbidity" and "hepatic fetish" according to its clinical manifestations. In the 11th Five-Year Plan, the TCM Liver Disease Collaboration Group of the State Administration of Traditional Chinese Medicine identified the TCM disease name of NAFLD as "hepatosis" [17]It is believed that NAFLD is mostly due to improper diet, excessive fat and sweet taste, or loss of work and rest, or loss of emotional will, resulting in loss of spleen health, liver leakage, water and fluid internal arrest, and phlegm turbidity and endogenous,Qi stagnation and blood stasis, resulting in phlegm drinking, dampness, and blood stasis accumulating in the body and beating in the liver, is a disease [18].The disease is mainly located in the liver, which is closely related to the spleen and kidney, and its pathological factors are mainly phlegm, dampness, and stasis [19].The classic prescription for the treatment of NAFLD is also a hot spot at present, and the Qing Dynasty's "Chen Xiuyuan Medical Book Complete Works" has been recorded in BWD, which is a small compound of traditional Chinese medicine, which is composed of two flavors of Baihe and Wuyao.It is mainly used for the treatment of superficial gastritis and stomach pain.However, there are no studies of BWD for the treatment of NAFLD.Modern pharmacology shows that Baihe is a medicinal and edible homologous Chinese medicine, containing polysaccharides, polyphenols, saponins and alkaloids and other pharmacologically active components.Its main effects include: (1) anti-inflammatory, antioxidant, immunomodulatory activities; (2) Hepatoprotective, cholesterol-lowering and hypoglycemic active BaiHe is a traditional Chinese medicine with medicinal and edible homologous properties, containing a variety of pharmacologically active components such as polysaccharides, polyphenols, saponins and alkaloids.These effects of Baihe Wuyao Decoction suggest thatBaihe Wuyao Decoction may have potential hepatoprotective, hypoglycemic and anti-inflammatory activities.The research group has confirmed that Baihe Wuyao Decoction has a good improvement effect on carbon tetrachloride (CCl4)-induced chronic liver injury and liver fibrosis,It has an ameliorating effect on type 1 diabetes and its complicated liver injury, and its mechanism is related to anti-inflammatory, antioxidant, anti-apoptosis, etc.Considering the above-mentioned pharmacological effects of Baihe Wuyao Decoction,many of them are consistent with the pathological mechanisms of NAFLD, which indicates that Baihe Wuyao Decoction is likely to be effective against NAFLD [20].

3.2 Analysis of the core active ingredients of the Baihe Wuyao Decoction

It has been shown that β -sitosterol significantly reduces triglyceride (TG) content and lipid peroxide MDA levels and increases antioxidant GSH levels in fatty liver cells. [21]. Quercetin (Que) is a natural flavonoid, which is the main component of the biological therapeutic effects of many Chinese herbal medicines, such as Chai Hu, Mulberry leaf and Ginkgo biloba [22].Que has preventive and therapeutic effects on a variety of diseases, and its mechanism is reflected in antioxidant, anti-inflammatory, anticancer, and enhancement of immunity, etc. [23]. Some studies have shown that Que has a significant intervention effect on NAFLD models in vivo and in vitro, and the mechanisms involved mainly include the inhibition of inflammation and the regulation of autophagy [24]. Isopimaric acid (IPA) is a structurally specialized resin acid singly isolated from the natural product rosin and belongs to the diterpenoids, whose biological activities are mostly focused on the participation in the regulation of several functions of the organism as an opener of K+ and Ca2+ channels, with potential therapeutic effects on hypertension, analgesia, atrial fibrillation, arrhythmia, and Alzheimer's disease. In addition, there are biological activities such as anticancer and enzyme

inhibition [25]. Desmethylisoboldine can significantly reduce tumor necrosis factor (TNF-α) and interleukin-1β (IL-1β), and its mechanism of action is to inhibit the release of inflammatory factors by down-regulating the activity of the MAPKs signaling pathway [26].6, 7-Dimethoxy-2-(phenylethyl)chromone is one of the 2-(2-phenylethyl)chromone derivatives of sedum [27]. Modern pharmacological studies have shown that the chemical constituents in incense have anti-inflammatory, anti-tumor, hypoglycemic, antibacterial and sedative-analgesic effects [28, 29]. The above findings suggest that BWD may have a protective effect against NAFLD.

3.3 Analysis of the core targets of BWD

In this study, the core targets of BWD were predicted by PPI network and cytoHubba's MCC algorithm. The results showed that protein kinase B1 (AKT1), peroxisome proliferator-activated receptor γ (PPARG), JUN, epidermal growth factor receptor (EGFR), heat shock protein 90α (HSP90AA1), Bcl-2 protein (BCL2), prostaglandin H2 synthase-2 (PTGS2), matrix metalloproteinase 9 (MMP9), and estrogen receptor 1 (ESR1) may be the key targets of BWD for the treatment of non-alcoholic fatty liver disease.

The AKT1 family is a kind of serine-threonine protein kinase AKT, which is a key factor in the PI3K-AKT signaling pathway [30].Experimental studies have shown that IR and protein kinase B levels are decreased in NAFLD/NASH rats, and up-regulating the expression of protein kinase B in the liver can improve insulin resistance and have a therapeutic effect on NAFLD/NASH [31].PPARγ is not only a key regulator of lipid synthesis, differentiation, and metabolism, but also an essential molecule for maintaining insulin sensitivity, which plays an important role in blood glucose and lipid stability, lipid metabolism, and adipogenesis [32].PPARγ affects glucose and lipid metabolism by regulating the expression and activity of liver X receptor alpha, which plays an important role in glucose and lipid metabolism [33].HSP90AA1 is a member of the HSP90 family. HSP90AA1 undergoes a functional cycle related to its ATPase activity, which may cause conformational changes in specific proteins and activate them. In addition, HSP90AA1 can interact with a variety of common chaperones, regulating its substrate recognition, ATPase cycle, and chaperone function [34,35]. In vivo studies have shown that the overexpression of Hsp90 in hepatocyte lines is associated with lipid accumulation, and blocking the biological activity of Hsp90 can reduce fat production, indicating that Hsp90 plays an important role in the development of NAFLD [40]. BCL2, as a mitochondrial outer membrane protein, plays an anti-apoptotic role in the apoptotic pathway because it can bind to the pro-apoptotic factor BAX, preventing its conformational change during apoptosis and controlling cell apoptosis [36]. One of the important functions of PTGS2 gene is to participate in the regulation of inflammatory responses. The cyclooxygenase translated by PTGS2 is the main mediator of inflammation by catalyzing the initial steps of arachidonic acid metabolism and prostaglandin synthesis, and can be used as a therapeutic target for inflammatory diseases [37]. MMP9 is an important mediator of high blood sugar-induced apoptosis, and inhibiting MMP9 can reduce apoptosis and enhance cell viability [38]. In the absence of estrogen, it may increase visceral tissue fat and promote systemic insulin resistance [39]. Many sex hormones are synthesized by pregnenolone and are mainly metabolized in the liver, including estrogen, progesterone, and testosterone [40]. Estrogen Receptor a (ESR1) mediates the liver's response to estrogen, and the destruction of ESR1 expression leads to insulin resistance, increased obesity, impaired glucose tolerance, hepatic steatosis, and inflammatory infiltration [41]. An animal study showed that ESR1-/- male rats had little change in body weight, but regulated the expression of genes involved in liver fat and carbohydrate metabolism, showing increased liver fat deposition and impaired glucose tolerance [42]. Therefore, this study demonstrates that BWD can treat NAFLD through multiple pathways, including insulin resistance pathway, PPAR pathway, lipid and atherosclerosis pathway,

and cancer pathway

3.4 Core Pathway Analysis of BWD

The KEGG enrichment analysis results, combined with the pathogenesis of NAFLD, suggest that BWD and NAFLD had the highest enrichment degree in PPAR signaling pathway, IL -17 signaling pathway, insulin resistance and other pathways. Among them , BWD treats NAFLD through PPAR related pathways , mainly by promoting the oxidative decomposition of fatty acids , which occurs in the mitochondrial β Oxidation plays a leading role in fatty acid oxidation , which plays an important role in regulating energy metabolism and lipid metabolism disorder [431.IL-17A can increase liver lipid deposition and inhibit liver lipid β Oxidation , enhance the inflammatory damage of liver , and inhibit the IL -17A downstream target NF k - Activation of B can down regulate the expression of hepatic inflammatory factors 144]. IL -17A gene knockout may also reduce the inflammatory liver injury effect 145l by reducing the hemotaxis of neutrophils andmonocytes, promoting the anti - inflammatory (M2) polarization of macrophages, and inhibiting the activation of liver macrophages.

4. Conclusion

In summary, this paper analyzed the mechanism of the main active ingredients in BWD extracts for the treatment of NAFLD using network pharmacology and molecular docking techniques Combined with the above network pharmacology analysis, it was concluded that the core active ingredients of BWD, such as β-sitosterol, quercetin, isohydrocinnamic acid, desmethylisopoldine, 6, 7-dimethoxy-2-(phenylethyl)chromone, and 3DMC, regulate PPAR signaling pathway; endocrine resistance, and other signaling pathways, by being able to act on multiple key targets, such as , AKT1,PPARA, BCL2, and ESR1. The core active ingredients, such as PPARA, JUN, NOS3, ESR1 and other key targets, regulate PPAR signaling pathway, endocrine resistance and other signaling pathways to play a protective role against NAFLD, and its mechanism may be related to the improvement of glucose-lipid metabolism and insulin resistance, as well as anti-inflammatory effects. Resistance, as well as anti-inflammatory and and enhangcing autophagy functions.

Acknowledgements

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