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Exploration of the Mechanism of Shegan Qingwen Fuzheng Oral Liquid in Treating Respiratory Infections Based on Network Pharmacology and Molecular Docking

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Abstract: *Respiratory diseases are prevalent and frequently occur in various parts of the respiratory system. More and more studies have revealed the key role of traditional Chinese medicine (TCM) in treatment of respiratory diseases, but the active components of its function are still unclear and need to be further explored. In this study, the main components and potential targets of Shegan Qingwen Fuzheng Oral Liquid (SQFOL) were obtained through the TCMSP, HERB, and SwissTargetPrediction databases. The PPI network was constructed by combining STRING, and targets related to respiratory viral infections were screened using GeneCards, DisGeNET, and OMIM to establish a "component-target-disease" network. GO and KEGG enrichment analysis were then performed with the help of DAVID, and molecular docking was used to verify and visualize the core components and key proteins. PPI network analysis indicated that GAPDH, AKT1, TNF, IL6, and TP53 were potential hub proteins. The "drug–core target–disease" network identified quercetin, deacetylmatricarin, and linolenic acid as potential core active compounds. GO and KEGG analysis showed enrichment in the MAPK, PI3K–Akt, HIF-1, cancer, and human cytomegalovirus infection signaling pathways. Molecular docking confirmed that quercetin exhibited stable binding with hub proteins, particularly GAPDH. The therapeutic mechanism of SQFOL against respiratory viral infections may involve multi-component, multi-target, and multi-pathway regulation. These mechanisms are likely to contribute to the inhibition of viral replication, regulation of inflammatory responses, and maintenance of immune homeostasis.*

Keywords: *Shegan Qingwen Fuzheng Oral Liquid; Respiratory Infection; Quercetin; Network Pharmacology; Core Targets; Molecular Docking*

1. Introduction

Respiratory infections rank highest in mortality among all infectious diseases, with over 90% caused by respiratory viruses such as respiratory syncytial virus (RSV), influenza virus, parainfluenza virus, rhinovirus, adenovirus, and coronaviruses [1]. Currently, there are no specific clinical therapies for respiratory viral infections, with management primarily symptomatic. Modern medicine emphasizes single-target drug-microorganism interactions, yet drug development lags behind pathogen evolution. Existing antiviral drugs exhibit significant side effects, narrow applicability, and high susceptibility to resistance [2]. To address emerging or mass outbreaks of respiratory infectious diseases, there is an urgent need to develop drugs with proven efficacy and low safety risks.

Traditional Chinese medicine (TCM) has a long history of effectively treating respiratory infectious diseases. Records of preventing and treating respiratory infections (such as rashes, fever, and cough) can be found in classical texts like Treatise on Cold Damage, Treatise on Warm Diseases, and Distinctions of Warm Diseases. TCM's approach to combating respiratory viral infections is rooted in its holistic philosophy and syndrome differentiation. The therapeutic principle centers on expelling pathogens while fortifying the body's defenses, emphasizing the triadic relationship between the host, virus, and medication. This dual-pronged strategy directly targets viruses to eliminate pathogens while simultaneously modulating the immune system to enhance the body's inherent potential, thereby achieving antiviral effects [3-4]. Furthermore, due to the synergistic effects of multiple components in

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TCM, it exhibits broad-spectrum antiviral activity and is less likely to induce drug-resistant viral strains [5-6]. The Shegan Qingwen Fuzheng Oral Liquid (SQFOL) was developed by our research team based on the clinical formula [Shegan Qingwen Fuzheng Formula]. The formulation includes 10 herbs: Belamcandae rhizoma, Lonicerae Japonicae Flos, Isatidis Radix, Isatidis Folium, Taraxaci Herba, Eupatorii Herba, Bupleuri Radix, Astragali Radix, Ligustri Lucidi Fructus, Artemisiae Scopariae Herba. It possesses the effects of clearing heat and detoxifying, strengthening the spleen and transforming turbidity, and fortifying the body while expelling pathogens. The research team has completed studies on extraction and formulation processes. To better serve clinical applications, investigating its pharmacodynamic basis and mechanism of action is particularly important.

In recent years, network pharmacology and molecular docking techniques have provided powerful tools for unraveling the “black box” mystery of TCM mechanisms. Network pharmacology constructs “drug component-target-disease” interaction networks to analyze the potential mechanisms of TCM formulas from a holistic and systemic perspective, effectively revealing the associative patterns between groups of active components and disease-related biological networks [7]. Molecular docking technology simulates the affinity and binding patterns of TCM small molecules with target proteins, providing preclinical validation at the molecular level for potential targets predicted by network pharmacology [8]. This study aims to employ network pharmacology and molecular docking techniques to conduct a multi-level analysis of Shegan Qingwen Fuzheng Oral Liquid. This analysis will encompass its active components, the relationships among drugs, key targets, and diseases, major signaling pathways, and the binding patterns between core components and core targets, thereby providing a foundation for subsequent research.

2. Materials and methods

2.1 Collecting the chemical components of TCMs from public databases

The chemical components of the TCMs used in this study were collected from the TCMSP and HERB databases. Chemical components of Belamcandae rhizoma (Shegan, SG), Lonicerae Japonicae Flos (Jinyinhua, JYH), Isatidis Radix (Banlangen, BLG), Isatidis Folium (Daqingye, DQY), Eupatorii Herba (Peilan, PL), Bupleuri Radix (Caihu, CH), Astragali Radix (Huangqi, HQ), Ligustri Lucidi Fructus (Nüzhenzi, NZZ), and Artemisiae Scopariae Herba (Yinchen, YC) were collected using the TCMSP database, while the chemical components of Pugongying (PGY) were collected from the HERB database. The selection of active ingredients was based on the following criteria: oral bioavailability (OB)≥30% and drug-likeness (DL)≥0.18.

2.2 Obtaining the targets of active ingredients

We obtained the targets of the 9 TCMs (see section 2.1)from the TCMSP database, and further filtered them using the Uniprot database with the criteria "Human" and "Reviewed". For the component of Pugongying, the targets were downloaded and filtered from the SwissTarget Prediction database (Probability>0). All obtained targets were further organized.

2.3 Obtaining the targets related to respiratory diseases

In this study, targets related to respiratory diseases were collected using the keywords "severe acute respiratory syndrome coronavirus 2, influenza virus, respiratory syncytial virus, human parainfluenza virus, immunity, anti-inflammation, and Anti-Virus" from the GeneCards, DisGeNET, and OMIM disease databases.

2.4 Construction of PPI network for drug and efficacy intersection targets

On the one hand, we used the Venny 2.1.0 online platform to obtain the intersection of the targets for the action targets and efficacy targets of TCMs. On the other hand, based on the String database, we constructed a PPI network for the intersection targets, with "Homo sapiens" as the filter and "highest confidence" as the threshold setting.

2.5 Screening of key compounds for the treatment of respiratory diseases

Cytoscape 3.8.0 software was used to build the “drug-critical target-disease” network to screen

ISSN 2618-1584 Vol. 7, Issue 6: 70-78, DOI: 10.25236/FMSR.2025.070608

compounds with a high Degree as key compounds for the treatment of respiratory diseases.

2.6 Molecular docking

Using PubChem and PDB databases, the sdf files of core components and the pdb files of target proteins were obtained. Autodock Vina software was used for pre-processing and molecular docking of compounds and proteins, with the output of the top 10 docking scores for conformations.

2.7 Functional enrichment

The DAVID database (https://david-d.ncifcrf.gov/) was used for GO enrichment analysis and KEGG pathway enrichment analysis of key targets. The top 10 entries for each type of enrichment score and pathways with "P<0.05" were displayed.

3. Results

3.1 Collection of active ingredients and action targets of 10 kinds of TCMs

The chemical components of 10 kinds of TCMs were collected from the TCMSP and HERB databases, and the total number of active ingredients was 6 kinds of SG, 23 kinds of JYH, 39 kinds of BLG, 10 kinds of DQY, 35 kinds of PGY, 11 kinds of PL, 17 kinds of CH, 20 kinds of HQ, 13 kinds of NZZ and 13 kinds of YC. Next, we collected and sorted out 230 action targets of 9 kinds of TCMs ingredients from the TCMSP database. A total of 503 targets from PGY were collected using SwissTarget Prediction database. Finally, a total of 651 drug targets were obtained for follow-up study.

3.2 Acquisition of targets related to respiratory diseases

This study collected disease-related targets from GeneCards, DisGeNET, and OMIM databases with "severe acute respiratory syndrome coronavirus 2, influenza virus, respiratory syncytial virus, human parainfluenza virus, immunity, anti-inflammation, and Anti-Virus" as keywords. After deduplication, a total of 11,874 efficacy-related targets were obtained.

3.3 Obtaining the intersection targets between drugs and efficacy

As shown in Figure 1A, the Venn diagram of drug and efficacy intersection targets was obtained. From the diagram, we can see that 564 intersection target genes were obtained after 651 drug targets were intersected with 11874 efficacy related targets. In addition, a total of 564 intersection target genes were input into the String database to construct the PPI network, as shown in Figure 1B. We also found that the top 5 targets were GAPDH (degree: 298), AKT1 (degree: 297), TNF (degree: 281), IL6 (degree: 273) and TP53 (degree: 265).

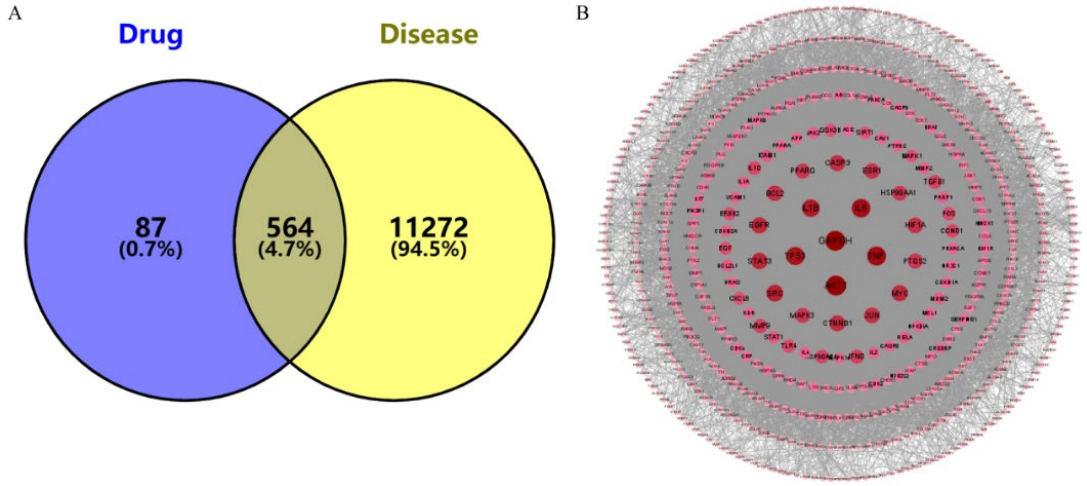

Figure 1: Venn diagram(A) and PPI network(B) of intersection targets.

ISSN 2618-1584 Vol. 7, Issue 6: 70-78, DOI: 10.25236/FMSR.2025.070608

3.4 Screening of key compounds for the treatment of respiratory diseases

In this study, we first constructed a "drug-key targets-disease" network using Cytoscape 3.8.0 software, as shown in Figure 2. The constructed network had a total of 690 nodes and 2467 edges, in which triangular nodes represent Chinese herbal medicines, circular nodes represent constituents, diamond nodes denote shared constituents among different herbs, inverted triangle nodes indicate key targets, and hexagonal nodes represent diseases. The chemical constituents of the 10 herbs in the network are detailed in Table 1. Further analysis of the "drug-chemical components-key targets-disease" network showed that the average degree value in the network is 7.15, with a median of 3. There are 158 compounds with a degree value greater than the average. The top-ranked compounds based on Degree were C26 (quercetin), C84 (desacetylmatricarin), and C90 (linolenic acid), indicating that these three compounds may be key compounds for treating respiratory system diseases.

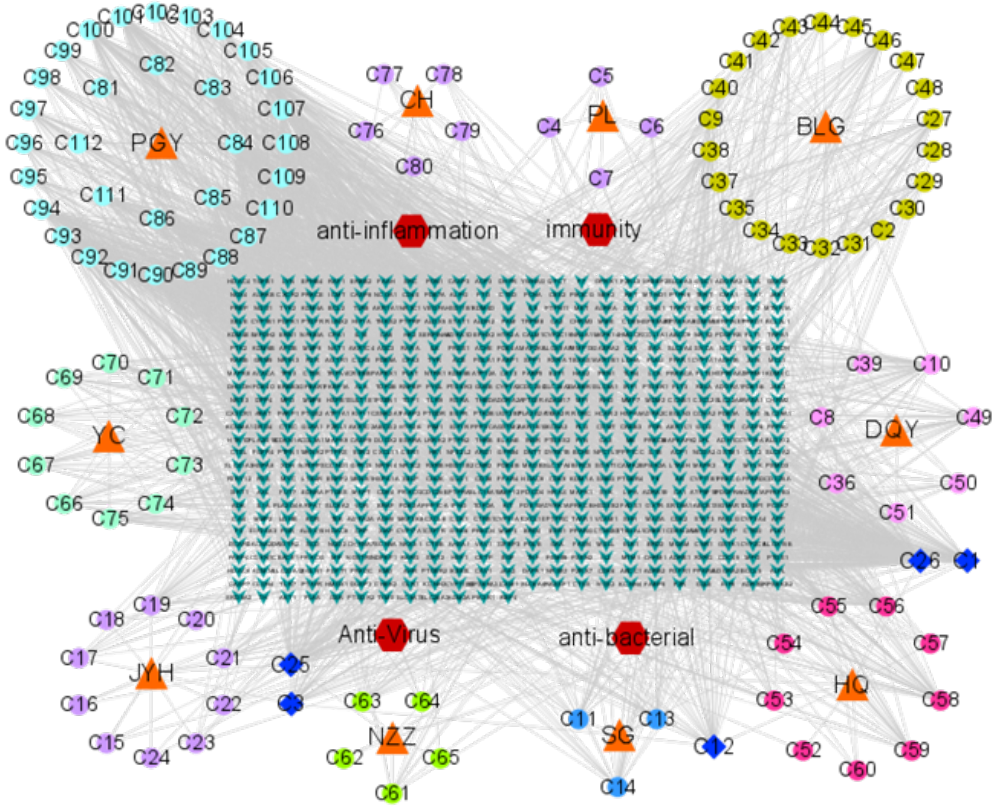

Figure 2: "Drug - key target- disease" network.

Table 1: Chemical components of 10 Chinese medicinal herbs.

No.	Molecule Name	MOL ID	Herb	No.	Molecule Name	MOL ID	Herb
C1	luteolin	MOL000006	PL, JYH, NZZ	C57	Bifendate	MOL000387	HQ
C2	sitosterol	MOL000359	PL, BLG	C58	formononetin	MOL000392	HQ
C3	Stigmasterol	MOL000449	PL, JYH, BLG, CH	C59	Calycosin	MOL000417	HQ
C4	7-acetoxy-8-hydroxy-9-isobutyryloxythymol	MOL000584	PL	C60	FA	MOL000433	HQ
C5	9-acetoxy-8,10-epoxy-6-hydroxythymol 3-O-angelate	MOL000588	PL	C61	taxifolin	MOL004576	NZZ
C6	Eupatoriopicrin	MOL000595	PL	C62	Lucidumoside D	MOL005146	NZZ
C7	Eupaformosanin	MOL000604	PL	C63	Lucidumoside D_qt	MOL005147	NZZ
C8	isovitexin	MOL002322	BLG, DQY	C64	eriodictyol	MOL005190	NZZ
C9	Dinatin	MOL001735	BLG	C65	Olitoriside_qt	MOL005212	NZZ
C10	beta-sitosterol	MOL000358	SG, JYH, BLG, DQY, NZZ, YC	C66	Areapillin	MOL004609	YC, CH
C11	Rhamnazin	MOL000351	SG	C67	Genkwanin	MOL005573	YC
C12	isorhamnetin	MOL000354	HQ, YC, CH	C68	Skrofulein	MOL007274	YC
C13	Iristectorigenin (9CI)	MOL003758	SG	C69	Isoarcapillin	MOL008039	YC
C14	Iristectorigenin A	MOL003759	SG	C70	Eupalitin	MOL008040	YC

ISSN 2618-1584 Vol. 7, Issue 6: 70-78, DOI: 10.25236/FMSR.2025.070608

C15	Mandenol	MOL001494	JYH	C71	Eupatolitin	MOL008041	YC
C16	Ethyl linolenate	MOL001495	JYH	C72	capillarisin	MOL008043	YC
C17	Eriodyctiol (flavanone)	MOL002914	JYH	C73	4'-Methylcapillarisin	MOL008045	YC
C18	secologanic dibutylacetal_qt	MOL003014	JYH	C74	Demethoxycapillarisin	MOL008046	YC
C19	beta-carotene	MOL002773	JYH	C75	Artepillin A	MOL008047	YC
C20	ZINC03978781	MOL003036	JYH	C76	Baicalin	MOL002776	CH
C21	Chryseriol	MOL003044	JYH	C77	Cubebin	MOL013187	CH
C22	Centauroside_qt	MOL003111	JYH	C78	Longikaurin A	MOL004624	CH
C23	Ioniceracetalides B_qt	MOL003117	JYH	C79	(+)-Anomalin	MOL004653	CH
C24	dinethylsecologanoside	MOL003128	JYH	C80	petunidin	MOL000490	CH
C25	kaempferol	MOL000422	JYH, HQ, NZZ, CH	C81	chlorogenic acid	HBIN020363	PGY
C26	quercetin	MOL000098	JYH, HQ, NZZ, YC, CH, PGY	C82	Chrysanthemaxanthin	HBIN020427	PGY
C27	acacetin	MOL001689	BLG	C83	cichoric acid	HBIN020526	PGY
C28	Isaindigodione	MOL001721	BLG	C84	desacetylmatricarin	HBIN023435	PGY
C29	EUPATORIN	MOL001733	BLG	C85	esculetin	HBIN025796	PGY
C30	(-)-taxifolin	MOL001736	BLG	C86	Ethyl caffeate	HBIN025897	PGY
C31	ZINC03860434	MOL001749	BLG	C87	ethyl p-hydroxyphenylacetate	HBIN025971	PGY
C32	glucobrassicin	MOL001750	BLG	C88	Flavoxanthin	HBIN026570	PGY
C33	24-Ethylcholest-4-en-3-one	MOL001755	BLG	C89	inositol	HBIN030188	PGY
C34	quindoline	MOL001756	BLG	C90	linolenic acid	HBIN033339	PGY
C35	hydroxyindirubin	MOL001767	BLG	C91	luteolin-7-O-galactoside	HBIN033862	PGY
C36	poriferast-5-en-3beta-ol	MOL001771	BLG, DQY	C92	Methyl caffeate	HBIN035129	PGY
C37	Ineketone	MOL001774	BLG	C93	myristic acid	HBIN036159	PGY
C38	Sinoacutine	MOL001779	BLG	C94	palmitic acid	HBIN038680	PGY
C39	Indigo	MOL001781	BLG, DQY	C95	phenylacetic acid	HBIN039500	PGY
C40	(2Z)-2-(2-oxoindolin-3-ylidene)indolin-3-one	MOL001782	BLG	C96	p-hydroxybenzoate	HBIN039673	PGY
C41	Linarin	MOL001790	BLG	C97	p-hydroxyphenylpropionic acid	HBIN039707	PGY
C42	DFV	MOL001792	BLG	C98	protocatechuic aldehyde	HBIN040911	PGY
C43	(E)-2-[(3-indole)cyanomethylene-]-3-indolinone	MOL001793	BLG	C99	rutin	HBIN042670	PGY
C44	neohesperidin_qt	MOL001798	BLG	C100	scopoletin	HBIN043442	PGY
C45	rosasterol	MOL001800	BLG	C101	stearic acid	HBIN044730	PGY
C46	Sinensetin	MOL001803	BLG	C102	(+)-Syringaresinol	HBIN045261	PGY
C47	Glucobrassicin-1-Sulfonate_qt	MOL001833	BLG	C103	taraxacoside	HBIN045521	PGY
C48	CLR	MOL000953	BLG	C104	taraxasterol	HBIN045530	PGY
C49	indirubin	MOL002309	DQY	C105	taraxasterol palmitate	HBIN045534	PGY
C50	Glycyrol	MOL002311	DQY	C106	Taraxerol	HBIN045541	PGY
C51	C05837	MOL002318	DQY	C107	taraxinic acid	HBIN045548	PGY
C52	Mairin	MOL000211	HQ	C108	taraxinic acid β-glucopyranosyl ester	HBIN045550	PGY
C53	Jaranol	MOL000239	HQ	C109	trans-p-coumaryl alcohol	HBIN046806	PGY
C54	hederagenin	MOL000296	HQ	C110	1,6,6-trimethyl-7-(3-oxobut-1-enyl)-3,8-dioxatricyclo[5.1.0.0(2,4)]octan-5-one	HBIN001773	PGY
C55	3,9-di-O-methylnissolin	MOL000371	HQ	C111	arsanin	HBIN016904	PGY
C56	7-O-methylisomucronulatol	MOL000378	HQ	C112	benzenecarboxylic acid	HBIN017758	PGY

3.5 GO and KEGG enrichment analysis results

As shown in Figure 3A, the results of GO enrichment analysis showed that BP of 10 TCMs treating respiratory diseases by targeting AKR1B1, AKR1B10, MMP13, MMP2, MMP12, APP, ELANE3 and other key targets included response to xenobiotic stimulus, protein phosphorylation, inflammatory response, negative regulation of apoptosis process, and positive regulation of MAPK cascade. Besides, there were 10 CC including plasma membrane, membrane raft, receptor complex, macromolecular complex and nucleoplasm. We also found 10 MF including enzyme binding, protein kinase activity, ATP binding and protein serine/threonine kinase activity,etc.Then we further analyzed the key signaling pathways of 10 TCMs in regulating respiratory diseases, as shown in Figure 3B. The main pathways enriched were pathways in cancer, lipid and atherosclerosis, hepatitis B, MAPK signaling pathway, human cytomegalovirus infection, HIF-1 signaling pathway, PI3K-Akt signaling pathway, hepatitis C and so on.

ISSN 2618-1584 Vol. 7, Issue 6: 70-78, DOI: 10.25236/FMSR.2025.070608

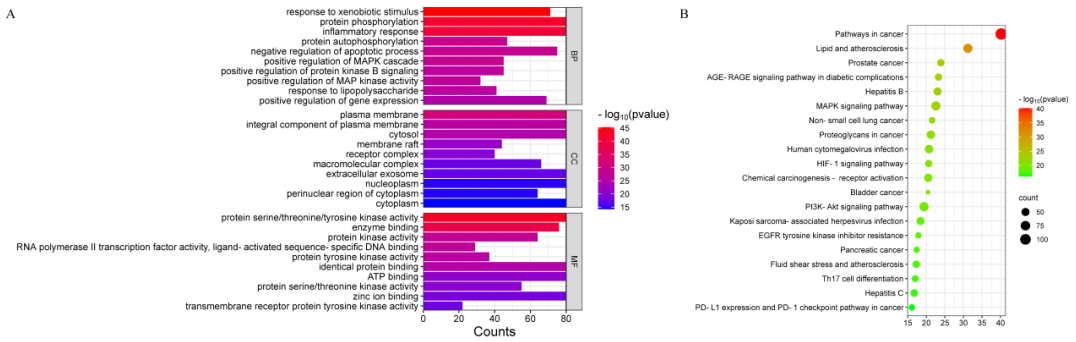

Figure 3: Functional enrichment analysis. (A)GO enrichment analysis; (B)KEGG enrichment analysis.

3.6 Molecular docking of core targets

The binding between core components and core targets was investigated by building a molecular docking model, and the results were shown in Figure 4. The binding free energy of quercetin with the protein AKT1 was -7.60 kcal/mol, with 4 intermolecular bonds existing between quercetin and the amino acid residues GLY 16, GLU 17, and THR 87 of AKT1. The binding free energy of quercetin with GAPDH was -9.03 kcal/mol, with 5 intermolecular bonds existing between quercetin and the amino acid residues ALA 183, ALA 238, SER 98, and ASN 316 of GAPDH. The binding free energy of quercetin with the protein IL6 was -7.77 kcal/mol, with 2 intermolecular bonds existing between quercetin and the amino acid residues GLU 42 and ASP 160 of IL6.In addition, the binding free energy of quercetin with the TNF was -7.68 kcal/mol, with 3 intermolecular bonds existing between quercetin and the amino acid residues GLN 67, CYS 69, and GLU 110 of TNF. The binding free energy of quercetin with TP53 was -8.35 kcal/mol, with 4 intermolecular bonds existing between quercetin and the amino acid residues SER 1749, ASP 1743, LYS 1744, and GLN 1808 of TP53.The above molecular results further indicated that quercetin can bind to the core target protein stably.

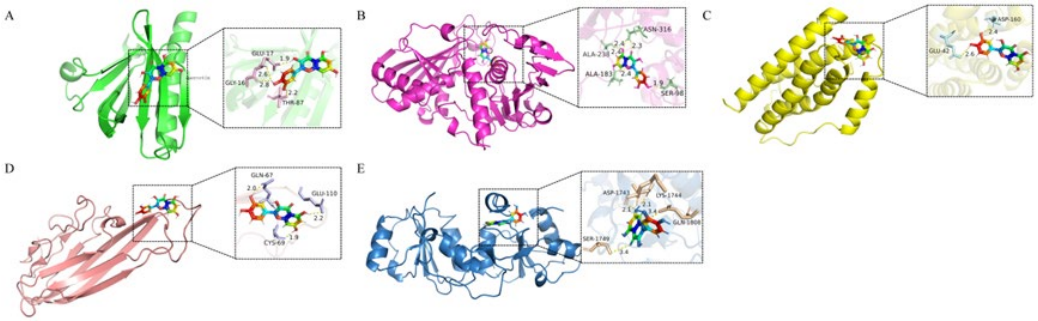

Figure 4: Molecular docking results. (A) quercetin with AKT1; (B)aquercetin with GAPDH; (C)quercetin with IL6; (D)quercetin with TNF; (E)quercetin with TP53.

4. Discussion

The results of this study indicate that components such as quercetin, apigenin, and alpha-linolenic acid exhibit high association with core target proteins, with quercetin demonstrating the strongest correlation. Molecular docking results further reveal that quercetin can stably bind to five core target proteins. As a natural flavonoid compound, quercetin has been extensively reported to exhibit significant antiviral activity against respiratory viruses (e.g., influenza virus, respiratory syncytial virus). Its mechanism involves inhibiting viral entry, replication, and assembly, while modulating signaling pathways such as MAPK and NF-κB signaling pathways to suppress virus-induced cytokine storms (e.g., excessive expression of IL-6, TNF-α, IL-1β), thereby alleviating airway inflammatory damage [9-13]. Demethyledaulopin, a sesquiterpene lactone commonly found in Asteraceae plants, has been shown in existing studies to exhibit pharmacological effects primarily in anti-liver fibrosis, anti-allergy, anti-inflammation, anti-infection, antispasmodic, and analgesic activities [14-17]. However, currently available data primarily consist of in vitro cell experiments or studies using crude plant extracts, with a lack of systematic in vivo pharmacodynamic and clinical data. Alpha-linolenic acid demonstrates multifaceted beneficial effects in respiratory viral infections. Research indicates it exerts antiviral activity by inhibiting

ISSN 2618-1584 Vol. 7, Issue 6: 70-78, DOI: 10.25236/FMSR.2025.070608

viral entry and replication, directly destroying viral particles, and suppressing key viral enzyme activity [18-20]. It also mitigates inflammation and cytokine storms induced by viral infection by suppressing pro-inflammatory cytokine expression (e.g., IL-6, IL-1β), thereby reducing pulmonary damage [18]. Furthermore, it enhances the body's antiviral immune response by activating immune cell functions [21].

From the functional characteristics of key target genes, AKR1B1 and AKR1B10 both belong to the aldehyde reductase family. They are rapidly upregulated during viral infection and act as “pro-inflammatory-oxidative stress amplifiers.” Through the “lipid peroxidation-inflammation amplification-cytokine storm” axis, they exacerbate tissue damage. In patients with comorbidities such as chronic obstructive pulmonary disease (COPD) and diabetes, AKR1B1 exhibits higher baseline expression, making it a key factor in viral-induced severe disease. -inflammation amplification-cytokine storm“ axis to exacerbate tissue damage. In patients with comorbidities such as COPD and diabetes, AKR1B10 exhibits higher baseline expression, establishing a ”susceptibility background" for virus-induced severe disease. Inhibiting its enzymatic activity or expression levels holds promise as a novel strategy to mitigate acute lung injury and multiple organ dysfunction following viral infection [22-24]. Persistently elevated MMP2 and MMP13 expression compromises alveolar-capillary basement membrane integrity, facilitating viral trans-epithelial migration. Concurrently, virus-induced MMP13 overexpression initiates post-infection pulmonary fibrosis [25]. MMP12, massively secreted by RSV- or influenza-induced M2-type alveolar macrophages, amplifies inflammatory cell infiltration and cytokine storms, serving as a critical node in airway remodeling [26]. Inhibiting MMPs may emerge as a novel therapeutic strategy to mitigate airway inflammation, reduce viral load, and alleviate acute lung injury [27-28]. Virus-induced ROS activates the non-amyloid cleavage pathway of APP (Amyloid-β precursor protein), generating sAPPα with neuroprotective and immunomodulatory effects that suppress excessive macrophage inflammation [29]. Conversely, persistent excessive ROS leads to abnormal metabolism, amplifying oxidative stress and inflammation while promoting tissue destruction [30]. ELANE3 (neutrophil elastase) exerts protective effects by directly lysing viruses during early respiratory viral infection. However, uncontrolled release in later stages leads to hypermucus secretion, tissue injury, amplified inflammation, and fibrotic promotion, making it a key driver of subsequent bacterial co-infection [31-33]. These key targets collectively shape the viral infection microenvironment characterized by “oxidative stress-matrix remodeling-cytokine storm.” This suggests that SQFOL may reverse this microenvironment through multi-targeted synergistic mechanisms, thereby blocking disease progression.

KEGG pathway analysis revealed that the drug's target sites were significantly enriched in multiple pathways closely associated with viral infection, immune inflammation, and cell survival, including well-established virus-host interaction axes such as the “MAPK signaling pathway,” “HIF-1 signaling pathway,” and “PI3K-Akt signaling pathway.” The MAPK pathway extensively participates in cell proliferation, differentiation, stress responses, and inflammatory reactions. It is rapidly activated upon viral recognition, promoting antiviral cytokine expression while also inducing inflammatory cell death [34]. The HIF-1 pathway regulates gene expression under hypoxic and inflammatory conditions, influencing immune cell function [35]. The PI3K-Akt pathway is closely associated with cell survival, metabolism, and viral replication processes [36]. Additionally, pathways including “Cancer,” “Lipids and Atherosclerosis,” “Hepatitis B,” “Human Cytomegalovirus Infection,” and “Hepatitis C” were simultaneously enriched. This suggests the compound may possess broad antiviral and immunomodulatory effects, with mechanisms overlapping pathways associated with certain cancers or metabolic diseases. Long-term complications following viral infection (e.g., pulmonary fibrosis, cardiovascular events) may also correlate with abnormal activation of these pathways.

In summary, this study reveals that the herbal components in SQFOL collectively target the inflammation-immunity-metabolism cross-network, exhibiting a synergistic “multi-component-multi-target-multi-pathway” pattern. This synergistic effect endows traditional Chinese medicine with unique advantages in addressing rapid viral mutations and multi-organ damage in hosts by simultaneously regulating inflammatory responses, eliminating pathogens, and enhancing immune function. It compensates for the limitations of modern single-target drugs in treating viral mutations and multi-system complications, providing a theoretical basis for understanding the molecular mechanisms of traditional Chinese medicine compound formulations in treating viral respiratory diseases. It also points the way for further experimental validation and drug development. Future research should integrate in vitro and in vivo experiments to functionally validate these key targets and pathways, thereby deepening our understanding of the mechanisms underlying TCM's therapeutic effects.

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References

[1] Zhou LR, Cui XL, Shi YJ. Research progress on common respiratory viruses and antiviral drugs[J]. Chinese Journal of Pharmacovigilance, 2023, 20(02):225-230.
[2] Ma QH, Xing XF, Luo JB. Research progress on heat-clearing and detoxifying traditional Chinese medicines against respiratory viruses[J]. Journal of Guangdong Pharmaceutical University, 2016, 32(05):658-661.
[3] Wei QJ, Chen J, Zhou Q, et al. A review on traditional Chinese medicine against respiratory viral infectious diseases[J]. Journal of Nanjing University of Traditional Chinese Medicine, 2024, 40(10): 1141-1148.
[4] Ma WM, Li WJ, Wang P, et al. Research progress on traditional Chinese medicine compounds against respiratory viral diseases[J]. Biomedical Transformation, 2024, 5(01):37-47.
[5] Li B, Zhang HC, Yang ZF, et al. Value and pathways for developing broad-spectrum anti-respiratory viral traditional Chinese medicines[J]. Chinese Journal of New Drugs, 2022, 31(01):33-38.
[6] Wang YX, Cui XL, Guo SS. Research progress in prevention and treatment of respiratory viral infectious diseases with traditional Chinese medicine[J]. Chinese Journal of Pharmacovigilance, 2021, 18(06):592-596.
[7] Tao L, Ke ZP, Wang TJ, et al. Frontier technologies and development trends in network pharmacology: A bibliometric analysis of patents[J]. China Journal of Chinese Materia Medica, 2025, 50(11):3070-3078.
[8] Pinzi L, Rastelli G. Molecular Docking: Shifting Paradigms in Drug Discovery[J]. Int J Mol Sci. 2019, 20(18):4331.
[9] An L, Zhai Q, Tao K, et al. Quercetin induces itaconic acid-mediated M1/M2 alveolar macrophages polarization in respiratory syncytial virus infection[J]. Phytomedicine. 2024, 130:155761.
[10] Di Petrillo A, Orrù G, Fais A, et al. Quercetin and its derivates as antiviral potentials: A comprehensive review[J]. Phytother Res. 2022, 36(1):266-278.
[11] Mehrbod P, Hudy D, Shyntum D, et al. Quercetin as a Natural Therapeutic Candidate for the Treatment of Influenza Virus[J]. Biomolecules. 2020, 11(1):10.
[12] Guang Q, Zhang LZ, Tang X, et al. Quercetin alleviates inflammation induced by porcine reproductive and respiratory syndrome virus in MARC-145 cells through the regulation of arachidonic acid and glutamine metabolism[J]. Vet Med Sci. 2024, 10(4):e1536.
[13] Wu W, Li R, Li X, et al. Quercetin as an Antiviral Agent Inhibits Influenza A Virus (IAV) Entry[J]. Viruses. 2015, 8(1):6.
[14] Nubiya A, Qin DM, Hu LP, et al. Anti-hepatic fibrosis effect of matricin from Cichorium glandulosum in vitro[J]. Herald of Medicine, 2021,40(12):1679-1683.
[15] Sachurengui, Yilina. Preliminary study on the chemical constituents and pharmacological effects of Mongolian medicine Achillea alpina[J]. Modern Health, 2017, 18:1.
[16] Cheong H, Choi EJ, Yoo GS, et al. Desacetylmatricarin, an anti-allergic component from Taraxacum platycarpum[J]. Planta Med. 1998, 64(6):577-578.
[17] Anibogwu R, Jesus K, Pradhan S, et al. Sesquiterpene Lactones and Flavonoid from the Leaves of Basin Big Sagebrush (Artemisia tridentata subsp. tridentata): Isolation, Characterization and Biological Activities[J]. Molecules. 2024, 29(4):802.
[18] McGill AR, Markoutsa E, Mayilsamy K, et al. Acetate-encapsulated Linolenic Acid Liposomes Reduce SARS-CoV-2 and RSV Infection[J]. Viruses. 2023, 15(7):1429.
[19] Goc A, Sumera W, Rath M, et al. Linoleic acid binds to SARS-CoV-2 RdRp and represses replication of seasonal human coronavirus OC43[J]. Sci Rep. 2022, 12(1):19114.
[20] Goc A, Niedzwiecki A. & Rath M. Polyunsaturated ω-3 fatty acids inhibit ACE2-controlled SARS-CoV-2 binding and cellular entry[J]. Sci Rep 2021, 11:5207.
[21] Das UN. Bioactive lipid-based therapeutic approach to COVID-19 and other similar infections[J]. Archives of Medical Science. 2023, 19(5):1327-1359.
[22] Chabert C, Vitte AL, Iuso D, et al. AKR1B10, One of the Triggers of Cytokine Storm in SARS-CoV2 Severe Acute Respiratory Syndrome[J]. Int J Mol Sci. 2022, 23(3):1911.
[23] Gao C, Hu W, Liu F, et al. Aldo-keto reductase family 1 member B induces aortic valve calcification by activating hippo signaling in valvular interstitial cells[J]. J Mol Cell Cardiol. 2021, 150:54-64.
[24] Banerjee S. Aldo Keto Reductases AKR1B1 and AKR1B10 in Cancer: Molecular Mechanisms and Signaling Networks[J]. Adv Exp Med Biol. 2021, 1347:65-82.

ISSN 2618-1584 Vol. 7, Issue 6: 70-78, DOI: 10.25236/FMSR.2025.070608

[25] Lee HS, Kim WJ. The Role of Matrix Metalloproteinase in Inflammation with a Focus on Infectious Diseases[J]. Int J Mol Sci. 2022, 23(18):10546.
[26] Makino A, Shibata T, Nagayasu M, et al. RSV infection-elicited high MMP-12-producing macrophages exacerbate allergic airway inflammation with neutrophil infiltration[J]. iScience. 2021, 24(10): 103201.
[27] Marchant DJ, Bellac CL, Moraes TJ, et al. A new transcriptional role for matrix metalloproteinase-12 in antiviral immunity[J]. Nat Med. 2014 May;20(5):493-502.
[28] Lara Ravanetti, Tamara Dekker, Lihui Guo, et al. Efficacy of FP-025: A novel matrix metalloproteinase-12 (MMP-12) inhibitor in murine allergic asthma[J]. Allergy. 2023, 78(02): 559-562.
[29] Yang, X., Liu, X., Nie, Y. et al. Oxidative stress and ROS-mediated cellular events in RSV infection: potential protective roles of antioxidants[J]. Virol J 2023, 20: 224.
[30] Kayesh MEH, Kohara M, Tsukiyama-Kohara K. Effects of oxidative stress on viral infections: an overview[J]. Npj Viruses. 2025, 3(1):27.
[31] Fragoso JM, Vargas-Alarcón G, Martínez-Flores ÁE, et al. ELANE rs17223045C/T and rs3761007G/A variants: Protective factors against COVID-19[J]. Biomol Biomed. 2024, 24(3):665-672.
[32] Neuenfeldt F, Schumacher JC, GrieshabeNr-Bouyer R, et al. Inflammation induces pro-NETotic neutrophils via TNFR2 signaling[J]. Cell Rep. 2022, 39(3):110710.
[33] Ren JJ, Li RH, Jin XT, et al. Research status of neutrophil elastase in acute respiratory distress syndrome[J]. Practical Journal of Clinical Medicine, 2024,21(04):53-56.
[34] Mohanta TK, Sharma N, Arina P, et al. Molecular Insights into the MAPK Cascade during Viral Infection: Potential Crosstalk between HCQ and HCQ Analogues[J]. Biomed Res Int. 2020, 2020:8827752.
[35] Ren LH. Mechanism of H1N1 influenza A virus activating host HIF-1 signaling pathway to promote viral replication[D]. Shanghai Jiao Tong University. 2019.
[36] Lekshmi VS, Asha K, Sanicas M, et al. PI3K/Akt/Nrf2 mediated cellular signaling and virus-host interactions: latest updates on the potential therapeutic management of SARS-CoV-2 infection[J]. Front Mol Biosci. 2023, 10:1158133.