Regular article

The mechanism analysis of KangBingDuKouFuYe in treating throat infection based on network pharmacology and molecular docking

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Abstract

KangBingDuKouFuYe (KBDKFY) is widely used to treat influenza, upper respiratory tract infections, mumps and other diseases. Due to their diverse active ingredients, it is believed that they may have excellent anti-inflammatory, antibacterial and antiviral effects. Therefore, we believe they may have multiple therapeutic targets for throat inflammation caused by bacterial or viral infections. This study utilizes network pharmacology methods to analyze the therapeutic effects of KBDKFY on Bacterial Pharyngeal Tonsillitis and Viral Pharyngitis, aiming to identify its active ingredients, action targets and related pathways through molecular docking. Additionally, it determines the affinity between the main active ingredient and the core target before conducting *in vitro* bacteriostatic tests. The analysis results show that KBDKFY contains multiple active ingredients and potential targets for treating Bacterial Pharyngeal Tonsillitis and Viral Pharyngitis. KEGG enrichment analysis indicates that KBDKFY may have therapeutic effects on these conditions through pathways such as pathways in cancer, Kaposi sarcoma-associated herpesvirus infection, PI3K-Akt signaling pathway, and others. This provides a theoretical basis for further exploring pharmacological effects and clinical applications of KBDKFY.

Keywords: KangBingDuKouFuYe (KBDKFY); network pharmacology; molecular docking; Bacterial Pharyngeal Tonsillitis; Viral Pharyngitis

1 Introduction

Traditional Chinese medicine has unique efficacy in both alleviating symptoms and regulating patients' immune function [1]. Yu-nv-jian decoction (YNJ) is a classic traditional Chinese medicinal formula, which has been clinically used for periodontitis treatment over four hundred years. More and more clinical and epidemiological studies show that the drugs in YNJ exhibit anti-inflammatory and osteo-protective effects [2]. In addition, Epimedium, listed as a medium-grade drug in *Shennong's Classic of Materia Medica*, has the effects of strengthening tendons and bones and dispelling rheumatism and is often used clinically to treat flaccidity of tendons and bones, rheumatic

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Received: 2024-12-13 Accepted: 2025-01-19

arthralgia, numbness and spasm. Moreover, studies have shown that Epimedium can regulate the production of inflammatory cytokines and interfere with the function of immune cells through multiple pathways and targets [3]. KangBingDuKouFuYe (KBDKFY) aids in heat and dampness clearance, blood cooling and detoxification. This over-the-counter medicine comprises 9 medicinal ingredients, namely Isatis *indigotica, Forsythia suspensa*, *Phragmites australis*, *Acorus tatarinowii*, *Curcuma wenyujin*, *Pogostemon cablin* and *Anemarrhena asphodeloides* [4]. It is widely used in treating various diseases such as cold, influenza, upper respiratory tract infection, mumps, viral conjunctivitis and hand-foot-mouth disease due to its remarkable clinical efficacy and safety profiles [5]. It is believed that their diverse active ingredients have excellent anti-inflammatory, antibacterial and antiviral effects.

Throat diseases, including bacterial pharyngitis and tonsillitis, are characterized by rapid onset of pharyngeal pain, chills and fever. Throat inflammation caused by viral infections, such as viral pharyngitis, can be classified into acute and chronic forms, of which the acute form is more prevalent and typically manifested as sore throat and fever. Both types of throat inflammation are highly contagious and represent major public health concerns.

The identification of organism systems in network pharmacology is achieved through the analysis of complex network composition relationships and characteristics. Thus, the network relationship between drug-gene-target-disease interaction is revealed, enabling prediction of drug action mechanisms based on this network relationship [6]. Network pharmacology is a powerful tool for exploring the mechanism of action, identifying active ingredient groups, and promoting the modernization of Traditional Chinese Medicine (TCM) by predicting target actions and clarifying TCM's mode of operation [7]. In this study, we employed network pharmacology to investigate the effects of KBDKFY.

2 Materials and methods

2.1 Material

The KBDKFY discussed in this article and provided by Liaoning Xingao Pharmaceutical Co., Ltd., is a formula of 9 Chinese herbs, Panax quinquefolium, Forsythia, Rehmannia, Acorus calamus, Ulmus, Patchouli, Radix et Rhizoma Dioscoreae, Rhizoma Zhi Materiae and Gypsum.

2.2 Network pharmacology prediction

2.2.1 Main component screening of KBDKFY

The principal components were screened using the TCMSP database [8], with the screening criteria set as oral bioavailability (OB) [9] and drug-likeness (DL) [10], where OB $\geq$ 30% and DL $\geq$ 0.18.

2.2.2 Acquisition of principal component genes

The principal components were queried one by one in the PubChem database, and the Smile name of the principal component molecules was obtained, which was successively imported into the Swiss target prediction database to obtain the disease-related genes of the principal components. The genes were removed if the probability of the genes concerned was > 0.

2.2.3 Acquisition of disease genes

Disgenet database and GeneCard database [11] were respectively searched for "Bacterial Pharyngeal Tonsillitis" and the data were integrated to de-process the disease genes. "Bacterial Pharyngeal

Tonsillitis" is set with the relevance score ≥ 0.4.

The above operations were repeated for "Viral Pharyngitis". Due to the large number of disease genes, the relevance score of "Viral Pharyngitis" is set as ≥ 1.0.

2.2.4 Overlapping genes of principal components and diseases

The 'Wei-sheng-xin' platform was used to de-process the disease-related genes of the principal components and the genes of Bacterial Pharyngeal Tonsillitis and Viral Pharyngitis were imported into the Venn map project of 'Wei-sheng-xin' platform respectively to generate the corresponding Venn map.

2.2.5 Construction of drug-principal component-intersection gene network

Corresponding network files and tape files were constructed on intersection gene, drug, single Chinese medicine containing the main component of the drug, drug main component, target gene corresponding to the main component of the drug, and intersection gene of Viral Pharyngitis and Bacterial Pharyngeal Tonsillitis, respectively. These files were imported then into Cytoscape_v3.10.0 [12] to build the network and delete free items.

2.2.6 Construction of intersection gene PPI network

The intersection genes of Bacterial Pharyngeal Tonsillitis and Viral Pharyngitis were imported into the STRING database, and the species was selected as Homo species. After the intersection gene (protein) PPI network map appeared, the screening condition was selected as active interaction sources. The intersection genes followed the principle that the confidence score was lower than 0.9. The tsv. files were then exported and PPI network diagram was opened in Cytoscape_v3.10.0.

2.2.7 GO-KEGG analysis

The intersection genes of Bacterial Pharyngeal Tonsillitis and Viral Pharyngitis were imported using the David database and Function Annotation Tool. Bacterial Pharyngeal Tonsillitis and Viral pharyngeal tonsillitis were downloaded and imported into the Gene_Ontology entries respectively. BP, CC and MF of pharyngitis were selected, and the top 20 items with count values from high to low were sorted out and saved for plotting.

2.2.8 Core target screening

The two common genes imported into the string database were saved in tsv. file format and imported into the software Cytoscape_v3.10. The critical values of degree, between, and closeness (the average value is used as the critical value in this study) were calculated, and targets greater than or equal to the corresponding critical values were selected as the core targets. The difference was displayed by changing the PPI protein size with degree value, and corresponding images and results were obtained.

2.3 Molecular docking

The core targets and active ingredients of Bacterial Pharyngeal Tonsillitis and Viral Pharyngitis were selected for molecular docking, and the chemical structure formula of active ingredients was queried using the Pubchem database to obtain their SDF format files. The protein structure was querried in the PDB database, the Human species item was selected for organisms, and the corresponding pdb. file for each protein was obtained. The active site for each protein was obtained from the accompanying literature.

PyMOL-2.1.0 and AutoDock tools were used for protein pretreatment, including hydrogenation, water removal, small molecule ligand removal and active site selection, and corresponding pbd. and pbdqt. files were exported. ChemDraw 20.0 was used to process the chemical structural formula of the active component so that its conformation was at the lowest energy, and the corresponding file was derived. With the key target as the receptor and the corresponding active component as the donor, AutoDock vina 2.0 was used for molecular docking, and the binding energy and output results were calculated. The 9 results with the lowest binding energy were imported into Pymol-2.1.0 for 3D diagram visualization analysis and into Discovery Studio 2020 Client for 2D diagram visualization analysis.

3 Results

3.1 Main component screening and associated disease targets of KBDKFY

Based on data from the TCMSP database and considering weight-age factors, a total of 71 KBDKFY active components were identified by determining the quantities of 25 in BLG, 16 in LQ, 1 in LG, 4 in SCP, 7 in YJ, 6 in GHX and 2 in DH. Swiss Target Prediction database was used to eliminate redundancies and provide a final list of 844 related drug targets (Table 1).

Table 1 List of active ingredients

Serial number	Chinese herb	Abbreviations	Principal component
1	*Isatisindigotica*	BLG	25
2	*Forsythiasuspensa*	LQ	16
3	*Phragmites australis*	LG	1
4	*Acorus tatarinowii*	SCP	4
5	*Curcumawenyujin*	YJ	7
6	*Pogostemon cablin*	GHX	6
7	*Rehmanniaglutinosa*	DH	2
8	*Anemarrhenaasphodeloides*	ZM	10
9	Gypsum Fibrosum	SG	0

3.2 Acquisition of disease genes

Bacterial Pharyngeal Tonsillitis was queried in the Disgenet database and GeneCard database. The Bacterial Pharyngeal Tonsillitis was screened according to a Relevance score ≥ 0.4, and 1119 disease genes were obtained.

Similarly, Viral Pharyngitis was queried in the Disgenet database and GeneCard database, and the results obtained were screened according to Relevance score ≥ 1.0, and 1864 disease genes were obtained.

3.3 Intersection genes of principal component genes and disease genes

Using the ‘Weishengxin’ platform, 172 genes of Bacterial Pharyngeal Tonsillitis and 253 genes of Viral Pharyngitis and drug target intersection were mapped and obtained (Fig. 1-A).

3.4 Drug-principal component-intersection gene-pathway network

The Drug-principal component-intersection

gene-pathway network diagram can clearly show the relationship between the main ingredients of a drug and their corresponding target genes, and the diagram can show how the drug ingredients affect various signaling pathways through cross-genes, which play a key role in the physiological functions and pathological processes of cells (Fig. 1-B).

3.5 Construction and analysis of intersection gene PPI network

STRING database was used to obtain the intersection gene (protein) PPI network diagram (Fig. 1-C). Tsv. file for Bacterial Pharyngeal Tonsillitis was opened in Cytoscape_v3.10.0 and analyzed to obtain the top target TNF, which is mainly produced by activated mononuclear/macrophage cells. It has the functions of promoting neutrophil phagocytosis, killing and inhibiting tumor cells, causing fever (internal heat source), anti-infection, inducing acute phase protein synthesis of hepatocytes, promoting cell proliferation and differentiation, and promoting differentiation of myeloid leukemia cells into macrophages. It is an important and potent pro-inflammatory factor, involved in some autoimmune diseases and related to pathological injury.

For Viral Pharyngitis, the top target EGFR was obtained by opening the corresponding tsv. file in Cytoscape_v3.10.0 and conducting analysis. EGFR is the expression product of proto-oncogene c-erbB1 and a member of the epidermal growth factor receptor (HER) family. The EGFR signaling pathway is widely distributed on the surface of mammalian keratinocytes, epithelial cells, glial cells and fibroblasts. EGFR signaling pathway plays an important role in the growth, proliferation, differentiation and other physiological processes of mammalian cells.

The common targets of Bacterial Pharyngeal Tonsillitis and Viral Pharyngitis include SRC, STAT3 and AKT1, among which SRC is widely present in human cells and plays an important role in maintaining normal physiological functions of the body by regulating various processes such as cell division, motility, adhesion, angiogenesis and survival [13]. STAT3 exists in the cytoplasm, nucleus, mitochondria and mitochondria-related endoplasmic reticulum, and it is a signal transduction protein involved in various physiological processes such as cell proliferation, differentiation, migration and immune regulation [14]. AKT, also known as PKB or Rac, can regulate cell proliferation and growth, participate in cellular processes including glucose metabolism and apoptosis, and play an important role in cell survival and apoptosis.

3.6 Screening of core targets

19 core targets related to Bacterial Pharyngeal Tonsillitis and drugs were selected through the STRING database and Cytoscape_v3.10.0 analysis. As shown in the figure, the tag size indicates the degree of the target. It can be seen that SRC, PIK3CA, STAT3, TP53, PIK3R1, AKT1, EGFR and other targets play more roles (Fig. 2-AB).

30 core targets related to Viral Pharyngitis and drugs were selected by analyzing the STRING database and Cytoscape_v3.10.0. As shown in the figure, the tag size indicates the target degree. SRC, TP53, STAT3, PIK3CA, PIK3R1, AKT1, HSP90AA1, EGFR and other targets play more roles (Fig. 2-EF).

3.7 GO-KEGG analysis

BP, CC and MF were downloaded from David database to make a three-in-one graph. The top 14 and 30 pathways were selected from the Pathway and GO-Term results, respectively, to create enrichment bubble plots.

For Bacterial Pharyngeal Tonsillitis, a total of 343 processes were screened by BP, including phosphorylation, signal transduction, protein

phosphorylation and positive regulation of transcription by RNA polymerase II. CC screened a total of 101 processes, including the plasma membrane, cytosol, cytoplasm and nucleus. MF screened a total of 156 processes, including protein binding, identical protein binding, ATP binding and metal ion binding. Besides, the top 12 items with the highest values were selected according to the count value of pathway. The results were mainly pathways in cancer, PI3K-Akt signaling pathway, Kaposi sarcoma-associated herpesvirus infection, proteoglycans in cancer and human cytomegalovirus infection, among which 12 items with good performance are shown in Table 2 and Fig. 2-CD.

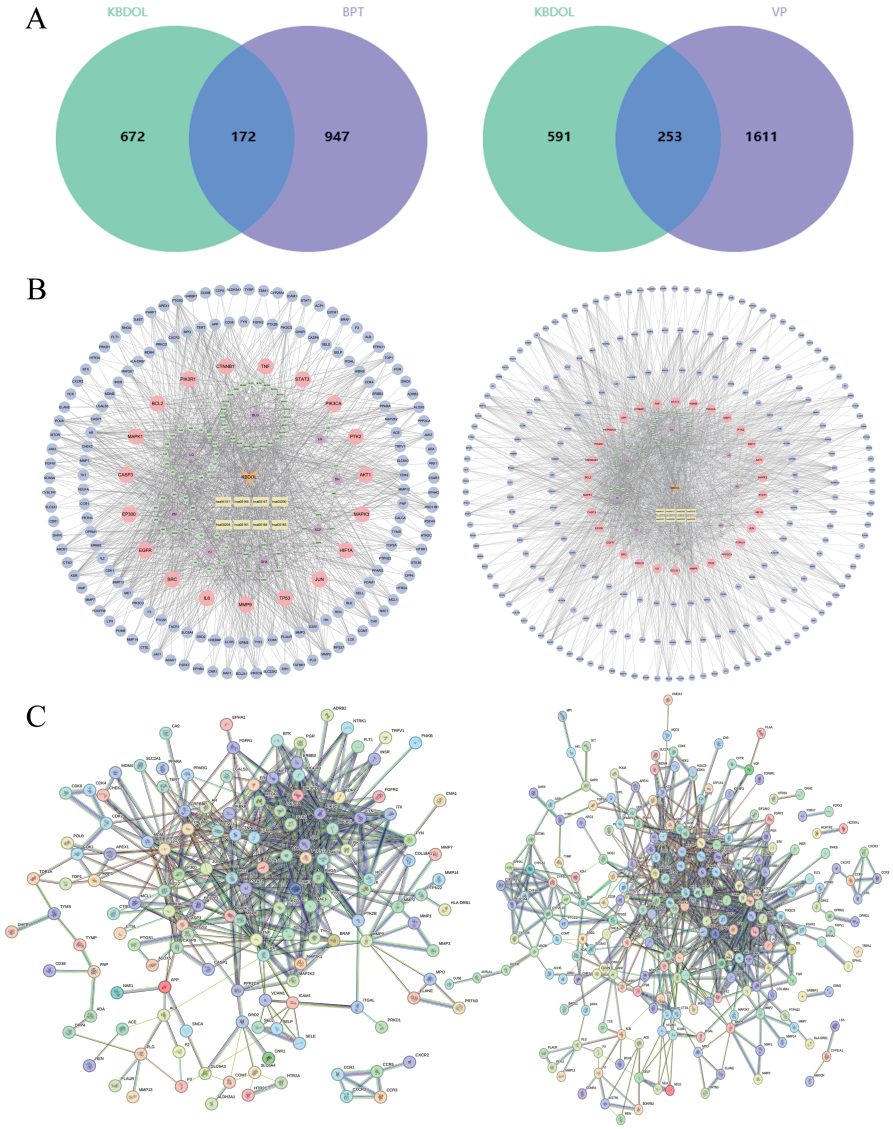

Fig. 1 Group diagram of drug-disease relationship. Left: Bacterial Pharyngeal Tonsillitis; Right: Viral Pharyngitis (A) Venn diagram of intersection gene between disease gene and drug target gene; (B) Principal component-crossover gene network diagram of antiviral oral solution with disease drugs (The two circles of blue-purple icons in the outer layer are potential targets; the third layer of pink icons from the outside to the inside is the core target; the fourth layer of icons in combination of purple and green is the single herbal medicines containing the active ingredient; and the yellow squares in the innermost layer are the pathways involved.); (C) PPI network diagram of intersection gene (protein) between disease and antiviral oral solution.

Table 2 12 items with PATHWAY performance in Bacterial Pharyngeal Tonsillitis

Term	Gene	*P*-value	Count
hsa05200	SLC2A1, PIK3CD, PIK3CB, IKBKB, SHH, CASP8, CASP3, AKT1	4.11E-30	59
hsa04151	FLT1, PIK3CD, PIK3CB, PIK3R1, EGFR, PIK3CG, PPP2CA, IKBKB	1.17E-20	41
hsa05167	SRC, PIK3CD, PIK3CB, PIK3R1, PTGS2, HIF1A, PIK3CG, ICAM1	1.09E-28	39
hsa05205	SRC, PIK3CD, PIK3CB, PIK3R1, HIF1A, TNF, EGFR, SHH	1.59E-24	36
hsa05163	SRC, PIK3CD, PIK3CB, PIK3R1, PTGS2, TNF, EGFR, IKBKB	7.56E-21	34
hsa05166	SLC2A1, XIAP, PIK3CD, PIK3CB, PIK3R1, ITGAL, TNF, ICAM1	5.43E-20	33
hsa05165	PIK3CD, PIK3CB, PIK3R1, PTGS2, TNF, EGFR, PPP2CA, IKBKB	9.38E-15	33
hsa05161	SRC, PIK3CD, PIK3CB, PIK3R1, TNF, IKBKB, CASP8, CASP3	3.72E-23	32
hsa05417	SRC, PIK3CD, PIK3CB, PIK3R1, TNF, ICAM1, IKBKB, CASP8	2.31E-18	31
hsa05206	ABCB1, PIK3CD, PIK3CB, PIK3R1, PTGS2, EGFR, IKBKB, ERBB3	7.13E-14	31
hsa04062	ITK, SRC, PIK3CD, PIK3CB, PIK3R1, PIK3CG, IKBKB, CXCR3	1.09E-17	29
hsa05215	PIK3CD, PIK3CB, PIK3R1, EGFR, IKBKB, ERBB2, AKT1, MAPK1	7.52E-25	28

For Viral Pharyngitis, BP screened a total of 979 processes, including phosphorylation, signal transduction, protein phosphorylation, negative regulation of apoptotic process and positive regulation of transcription by RNA polymerase II. CC screened a total of 122 processes, including the plasma membrane, cytosol, cytoplasm, nucleus and membrane. MF screened a total of 210 processes, including protein binding, ATP binding, identical protein binding and metal ion binding. The top 12 items with the highest value were selected according to the count value of PATHWAY. The results are mainly pathways in cancer, PI3K-Akt signaling pathway, kaposi sarcoma-associated herpesvirus infection, lipid and atherosclerosis, among which 12 items with better performance are shown in Table 3 and Fig. 2-GH.

Table 3 12 items with PATHWAY performance in Viral Pharyngitis

Term	Gene	*P*-value	Count
hsa05200	RET, GSK3B, HSP90AB1, SLC2A1, PIK3CD, PIK3CB, IKBKB, SHH	3.66E-32	73
hsa04151	RET, CHRM2, GSK3B, FLT1, HSP90AB1, PIK3CD, PIK3CB, PIK3R1	5.51E-20	48
hsa05167	GSK3B, SRC, PIK3CD, PIK3CB, PIK3R1, PTGS2, HIF1A, PIK3CG	1.37E-26	43
hsa05417	GSK3B, HSP90AB1, SRC, PIK3CD, PIK3CB, PIK3R1, TNF, ICAM1	7.71E-22	40
hsa05205	SRC, PIK3CD, PIK3CB, PIK3R1, HIF1A, TNF, EGFR, SHH	8.57E-22	39
hsa05206	HDAC4, ABCB1, HDAC1, PIK3CD, PIK3CB, PIK3R1, PTGS2, EGFR	3.10E-15	39
hsa05163	GSK3B, SRC, PIK3CD, PIK3CB, PIK3R1, PTGS2, TNF, EGFR	2.44E-18	37
hsa05165	GSK3B, HDAC1, PIK3CD, PIK3CB, PIK3R1, PTGS2, TNF, EGFR	7.06E-13	37
hsa05161	SRC, PIK3CD, PIK3CB, PIK3R1, TNF, IKBKB, CASP8, CASP3	2.89E-22	36
hsa04010	RET, FLT1, RASGRP1, TNF, EGFR, IKBKB, ERBB3, CASP3	8.52E-13	35
hsa05166	SLC2A1, XIAP, PIK3CD, PIK3CB, PIK3R1, ITGAL, TNF, ICAM1	7.83E-16	34
hsa05215	GSK3B, HSP90AB1, PIK3CD, PIK3CB, PIK3R1, EGFR, IKBKB, PLAU	1.25E-26	33

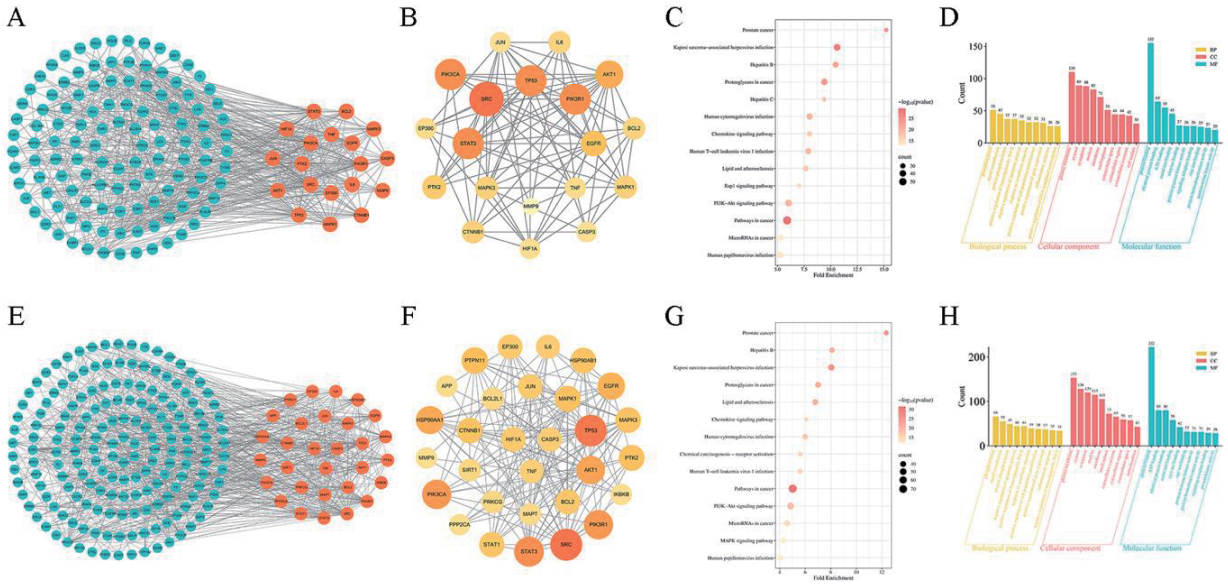

Fig. 2 Core targets and enrichment pathways (A-D) Bacterial Pharyngeal Tonsillitis; (E-H) Viral Pharyngitis.

3.8 Molecular docking

In this study, three targets shared by Bacterial Pharyngeal Tonsillitis and Viral Pharyngitis, the top five BC values, and the top three CC values, namely SRC, STAT3 and AKT1, were selected for molecular docking with the 9 drug active ingredients whose OB and DL values were higher than the average values and the highest OB values among the 30 selected active ingredients, and the corresponding molecular binding energy was obtained (Table 4).

Table 4 Minimum binding energy of active ingredients and core target of Bacterial Pharyngeal Tonsillitis

Micromolecule	Binding Energy (kcal/mol)		
	STAT3	SRC	AKT1
Diosgenin	-8.6	-6.4	-12.5
Kaempferol	-7.7	-6.3	-9.5
Sinensetin	-7.6	-5.9	-9.5
Pachypodol	-7.4	-5.9	-9.4
(-)-Phillygenin	-7.1	-5.8	-9.3
Coumaroyltyramine	-7.1	-5.7	-9
Zedoalactone_A	-6.7	-5.2	-8.9
MOL003290	-6.5	-5.1	-8.7
MOL003283	-5.9	-5.1	-8.6

Note: The proteins used are SRC_8bq3 and AKT1_6hhh; MOL003283 is (2*R*,3*R*,4*S*)-4-(4-hydroxy-3-methoxy-phenyl)-7-methoxy-2,3-dimethylol-tetralin-6-ol; MOL003290 is (3*R*,4*R*)-3,4-bis [(3,4-dimethoxy phenyl) methyl]oxolan 2-one; Table 2 shows the corresponding Chinese names of other small molecule drug active ingredients.

The optimal binding energies (AKT1 and STAT3) were selected and the corresponding molecular docking plots and tables were drawn (Fig. 3).

If the hydrogen bond length is no more than 3.5 nm, it indicates that the docking structure is stable [15]. In addition to diosgenin, the length of the intermolecular hydrogen bond of the remaining kaempferol, forsythiolate, coumaryl tyramine, (2*R*,3*R*,4*S*)-4-(4-hydroxy-3-methoxy-phenyl)-7-methoxy-2,3-dimethylol-tetralin-6-ol with AKT1 was less than 3.5 nm, indicating that the docking structure of the two is stable. The intermolecular hydrogen bond length of diosgenin, kauniol, and sweet orange flavone docking with STAT3 was less than 3.5 nm, indicating that the docking structure of diosgenin, kauniol, and sweet orange flavone was stable.

The smaller the binding energy, the better the docking result. Binding energy < -4.25 kcal/mol indicates that the binding activity of the drug ingredient to the target was good; Binding energy < -5.0 kcal/mol indicates that the drug ingredient has strong binding activity with the target [16]. The minimum binding energies of STAT3, SRC, and AKT1 were all lower than -5.0 kcal/mol after docking with the nine active ingredients, indicating that the selected active ingredients had strong binding activity with the target.

The binding energy of each drug active ingredient and the three targets of STAT3, SRC, and AKT1 showed that the binding energy of the same drug active ingredient to the AKT1 molecule was the smallest, STAT3 was the second, and SRC was the largest. Therefore, AKT1 had the highest binding activity with the selected drug active ingredient, STAT3 was the second, and SRC had the lowest binding activity.

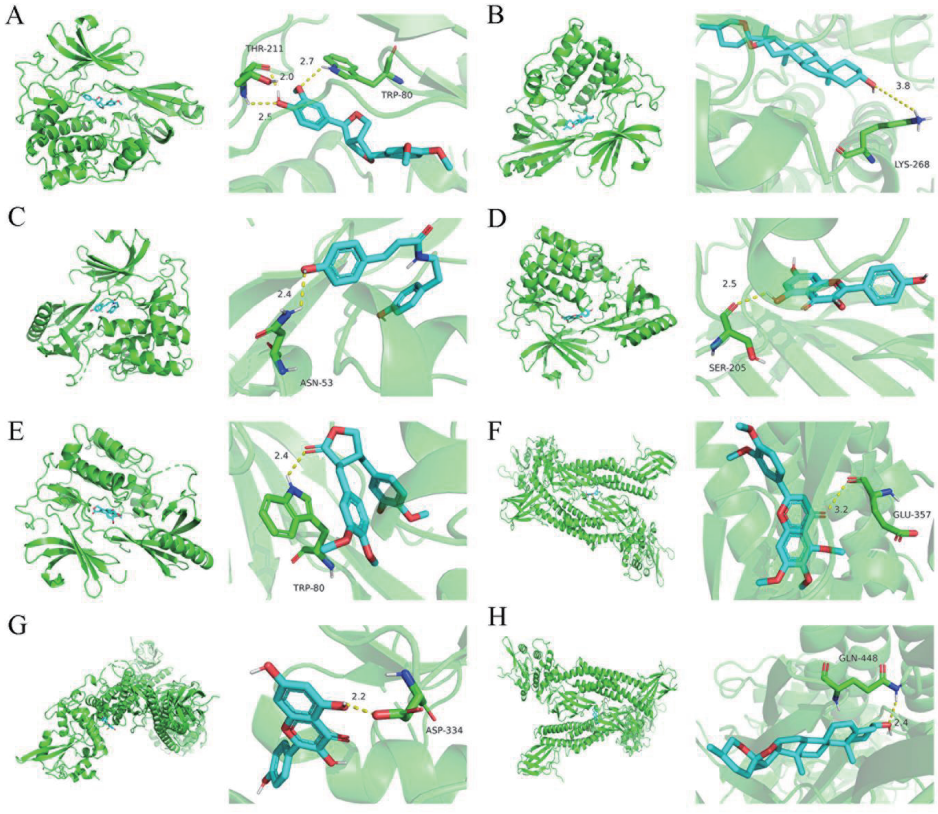

Fig. 3 Docking patterns of active ingredients with AKT1 and STAT3 molecules (A) Phillygenin-AKT1; (B) Diosgenin-AKT1; (C) Coumaroyltyramine-AKT1; (D) Kaempferol-AKT1; (E) MOL003283-AKT1; (F) Sinensetin-STAT3; (G) Kaempferol-STAT3; (H) Diosgenin-STAT3.

4 Discussion

KBDKFY was screened for 71 active ingredients by network pharmacological methods. Among them, kaempferol performed well in the analysis and molecular docking of bacterial pharyngeal tonsillitis and viral pharyngitis, and it has been shown to reduce the production of inflammatory factors, such as macrophage-derived chemokines, interferon-inducible protein-10 and interleukin-8, and to inhibit the expression of MAPK pathway [17]. Hordenine is analgesic [18] and antispasmodic to intestinal smooth muscle [19]. Besides, it has been reported to inhibit the proliferation of human GLC cells and Hela cell [20]. Furthermore, Si et al. found that quercetin inhibits the proliferation of human GLC cells by inhibiting the NF-κB subunits p50 and p65, the extracellular signal-regulated kinases (ERK1/2), and the cJUNN-terminal kinases (JNK1/2) expression inhibited inflammation in RAW264.7 cells [21].

After core target screening, the core targets of bacterial pharyngotonsillitis were non-receptor tyrosine kinase (SRC), signal transducer and activator of transcription (STAT3), phosphatidylinositol 3-kinase (PIK3R1, PIK3CA) and protein kinase (AKT1); The core targets of viral pharyngitis were non-receptor tyrosine kinase (SRC), signal transducer and activator of transcription (STAT3), phosphatidylinositol 3-kinase (PIK3R1), protein kinase (AKT1), human heat-shock protein (HSP90AA1) and epidermal growth factor receptor (EGFR). Since the two selected diseases can be triggered by multiple pathogens, the targets might be mostly related to the human immune system. By KEGG_PATHWAY analysis, bacterial pharyngotonsillitis and viral pharyngitis are jointly involved in pathways in cancer, Kaposi sarcoma-associated herpesvirus infection and PI3K-Akt signaling pathway. The pathways screened were mostly related to signaling and infection pathways in the body, including cancer pathways, which may involve cellular immunity. It can be seen that the pathways are mainly related to the immune system, especially the pathways commonly involved in bacterial pharyngotonsillitis and viral pharyngitis. Therefore, it is hypothesized that the active ingredients of the drug can affect the body's immunity to treat the disease, and the specific process needs to be further investigated for the mechanisms involved.

KBDKFY has the effects of clearing heat and dampness, cooling blood and detoxifying. Its effective components are diverse, and it is generally believed that it may have good anti-inflammatory, antibacterial and antiviral effects. One of the most obvious clinical features of bacterial pharyngotonsillitis and viral pharyngitis is the rapid onset of sore throat, inflammation and redness, and the production of inflammation. The results of this study did not clearly show that KBDKFY had different treatment pathways for the two diseases. Instead, it was found that the antiviral oral liquid relieved symptoms by regulating immunity in the inflamed area, whether it is for bacterial pharyngotonsillitis or viral pharyngitis.

In conclusion, in this study, we used network pharmacology and molecular docking methods to dock the three targets of AKT1, STAT3 and SRC with nine active ingredients of the selected antiviral oral solution and screened the mechanism of the antiviral oral solution in the treatment of bacterial pharyngotonsillitis and viral pharyngitis (Fig. 4). The study showed that multiple components, targets, and pathways existed in the treatment of bacterial pharyngotonsillitis and viral pharyngitis with KBDKFY. Network pharmacology methods are mainly used to predict the targets and active ingredients and elucidate the mechanism of action of traditional Chinese medicines [22], but the prediction results are subject to a high degree of randomness due to the influence of databases, screening conditions and software versions. In addition, due to the limitations of the test conditions, only the bacterial inhibition test was conducted on

the antiviral oral solution, and its antiviral effect needs further research. For the results obtained by screening and prediction under ideal conditions, further experimental and clinical studies are needed to verify the exact mechanism and efficacy and to prove its application value in treatment.

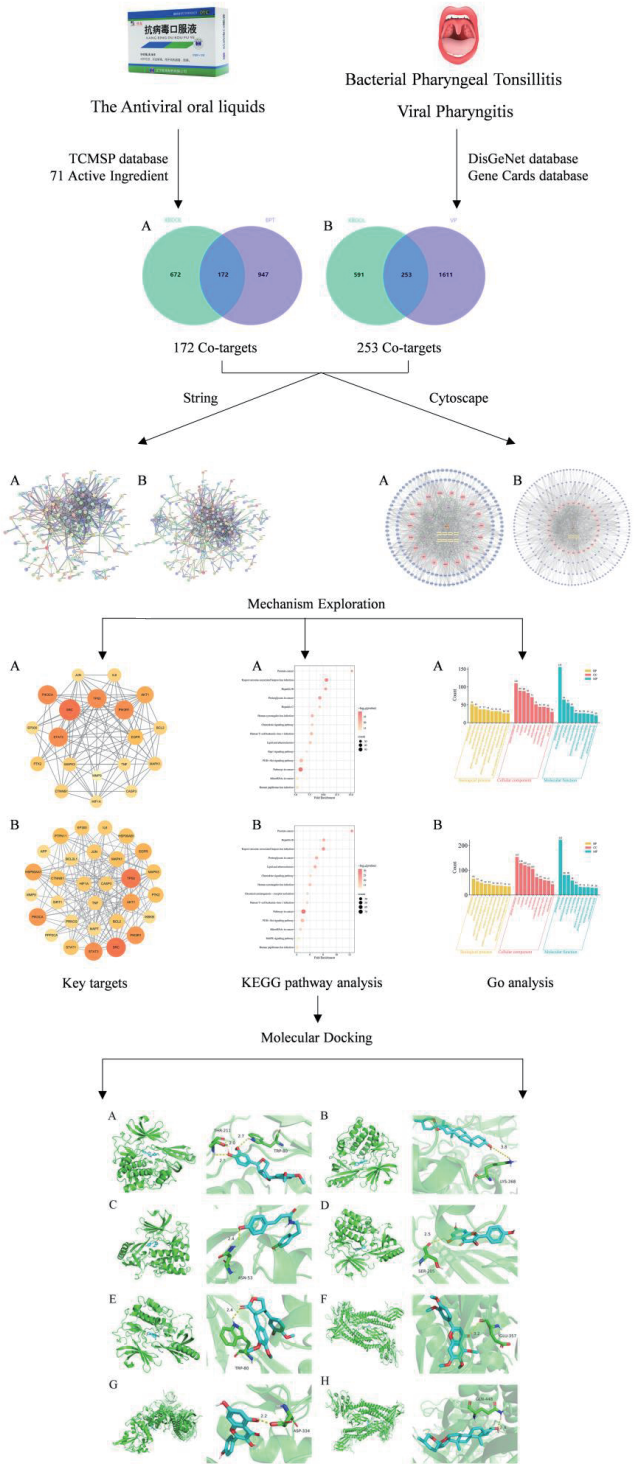

Fig. 4 Mechanisms of KBDKFY

Acknowledgments

This work was financially supported by Scientific Research Fund Project of Education Department of Liaoning Province (LJKZ0960), Science Foundation of Shenyang Pharmaceutical University (GGJJ2021105), and National College Student Innovation and Entrepreneurship Project.

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