

Study on Molecular Mechanism of Yiqing Capsule in Treating Upper Respiratory Tract Infection Based on Network Pharmacology

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Abstract

Objective: To investigate the possible mechanism of Yiqing Capsules in the treatment of upper respiratory tract infection based on network pharmacology. **Methods:** The main active components of Yiqing Capsules were selected on TCMSP database; the targets of upper respiratory tract infection were selected on GeneCards database. The drug-compound-target network and PPI network were constructed through STRING database and soft Cytoscape 3.7.2. Soft R was used to perform GO enrichment analysis and KEGG pathway enrichment analysis of main targets. **Results:** According to the screening conditions, 48 active compounds and 171 related targets were obtained. GO enrichment analysis obtained 2333 items, KEGG pathway enrichment analysis obtained 2248 items, including Kaposi sarcoma-associated herpesvirus infection, Human cytomegalovirus infection, Epstein-Barr virus infection, PI3K-Akt signaling pathway, etc. **Conclusion:** Yiqing capsules play a therapeutic role in upper respiratory tract infection through multi-target and multi-pathway.

Keywords

Yiqing Capsule, Upper Respiratory Tract Infection, Network Pharmacology

1. Introduction

Upper respiratory infection is a general term that includes acute inflammation of the nasal cavity, pharynx, or larynx. Generalized sense is not a diagnosis of a disease, but a group of diseases, including the common cold, viral pharyngitis, laryngitis, herpetic pharyngitis, eustachian conjunctiva fever, and bacterial pha-

ryngo-tonsillitis. At present, there is no specific drug treatment for upper respiratory tract infection, but antibiotics and antiviral drugs are used according to the relevant examination results. Research shows that traditional Chinese medicine (TCM) with heat-clearing, detoxification and antiviral effects can also be selected, which helps to improve symptoms and shorten the course of disease. Yiqing Capsule is a Chinese herbal medicine compound preparation which is composed of *Scutellaria baicalensis*, *Coptis chinensis*, and *Rheum officinale*. The capsule has functions of heat-clearing and detoxicating, removing blood stasis, hemostasis, etc. It is suitable for the treatment of body heat irritability, eye red sore of mouth, sore throat and gingival swelling pain, and constipation [1]. The capsule is used for clinical treatment on acute and chronic pharyngitis [2] [3] [4], acne [5], periodontitis [6], etc. It is also reported that Yiqing Capsule has good therapeutic effect in the acute stage of upper respiratory tract infection [7]. However, the relevant molecular mechanisms are unclear and unreported. Therefore, our study explored and predicted the relevant targets and molecular mechanisms of Yiqing Capsule in the treatment of upper respiratory tract infection based on network pharmacology, in order to provide theoretical data for clinical application.

2. Materials and Methods

2.1. Selected the Compounds and Targets of Yiqing Capsule

Searched chemical components of *Scutellaria baicalensis*, *Coptis chinensis*, *Rheum officinale* through Traditional Chinese Medicine Systems Pharmacology Database and Analysis Platform (TCMSP) database, used oral bioavailability (OB) $\geq 30\%$ and drug-likeness (DL) ≥ 0.18 as screening conditions to get the relevant compounds and targets.

2.2. Constructed the Drug-Compound-Target Network and PPI Network

Use “upper respiratory tract infection” as a keyword to screen the target genes on GeneCards database (www.genecards.org). Then make comparison with the target genes of the main chemical components of Yiqing Capsule, screened out the same target genes. Then construct drug-compound-target network and PPI network through soft Cytoscape 3.7.2 and STRING database.

2.3. Target Pathway Analysis

The key genes to the main chemical components of Yiqing Capsules in treating upper respiratory tract infection were used for Gene Ontology (GO) enrichment analysis and Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analysis. GO enrichment analysis included biological process (BP), molecular function (MF), cellular component (CC). Then screen the gene-pathway by KEGG enrichment analysis. All analysis used soft R, “org.Hs.eg.db”, “clusterProfiler”, “enrichplot” and “ggplot2”, p-value < 0.5 .

3. Results

3.1. Compounds and Targets of Yiqing Capsule

Searched chemical components of *Coptis chinensis*, Radix Scutellariae and Rhubarb through TCMSP database, after eliminated the same compounds, we selected out 48 active compounds, 30 for *Scutellaria baicalensis*, 11 for *Coptis chinensis*, 7 for *Rheum officinale*, the results are shown in **Table 1**. Search 6391 target genes on GeneCards database with the keyword “upper respiratory tract infection”. 171 target genes of Yiqing Capsule in treating upper respiratory tract infection were obtained through matching, the results are shown in **Figure 1**.

Table 1. Basic information of active components in Yiqing Capsule.

NO	Mol ID	components	MW	OB (%)	DL
<i>Scutellaria baicalensis</i> (30 components)					
1	MOL000073	ent-Epicatechin	290.29	48.96	0.24
2	MOL000173	wogonin	284.28	30.68	0.23
3	MOL000228	(2R)-7-hydroxy-5-methoxy-2-phenylchroman-4-one	270.3	55.23	0.2
4	MOL000358	beta-sitosterol	414.79	36.91	0.75
5	MOL000359	sitosterol	414.79	36.91	0.75
6	MOL000449	Stigmasterol	412.77	43.83	0.76
7	MOL000525	Norwogonin	270.25	39.4	0.21
8	MOL000552	5,2'-Dihydroxy-6,7,8-trimethoxyflavone	344.34	31.71	0.35
9	MOL001458	coptisine	320.34	30.67	0.86
10	MOL001490	bis[(2S)-2-ethylhexyl] benzene-1,2-dicarboxylate	390.62	43.59	0.35
11	MOL002714	baicalein	270.25	33.52	0.21
12	MOL002879	Diop	390.62	43.59	0.39
13	MOL002897	epiberberine	336.39	43.09	0.78
14	MOL002909	5,7,2,5-tetrahydroxy-8,6-dimethoxyflavone	376.34	33.82	0.45
15	MOL002910	Carthamidin	288.27	41.15	0.24
16	MOL002913	Dihydrobaicalin_qt	272.27	40.04	0.21
17	MOL002914	Eriodyctiol (flavanone)	288.27	41.35	0.24
18	MOL002915	Salvigenin	328.34	49.07	0.33
19	MOL002917	5,2',6'-Trihydroxy-7,8-dimethoxyflavone	330.31	45.05	0.33
20	MOL002925	5,7,2',6'-Tetrahydroxyflavone	286.25	37.01	0.24
21	MOL002927	Skullcapflavone II	374.37	69.51	0.44
22	MOL002928	oroxylin a	284.28	41.37	0.23
23	MOL002932	Panicolin	314.31	76.26	0.29
24	MOL002934	NEOBAICALEIN	374.37	104.34	0.44
25	MOL002937	DIHYDROOROXYLIN	286.3	66.06	0.23

Continued

26	MOL008206	Moslosooflavone	298.31	44.09	0.25
27	MOL010415	11,13-Eicosadienoic acid, methyl ester	322.59	39.28	0.23
28	MOL012245	5,7,4'-trihydroxy-6-methoxyflavanone	302.3	36.63	0.27
29	MOL012246	5,7,4'-trihydroxy-8-methoxyflavanone	302.3	74.24	0.26
30	MOL012266	rivularin	344.34	37.94	0.37
<i>Coptis chinensis</i> (11 components)					
31	MOL000098	quercetin	302.25	46.43	0.28
32	MOL000622	Magnograndiolide	266.37	63.71	0.19
33	MOL000785	palmatine	352.44	64.6	0.65
34	MOL001454	berberine	336.39	36.86	0.78
35	MOL001458	coptisine	320.34	30.67	0.86
36	MOL002668	Worenine	334.37	45.83	0.87
37	MOL002894	berberrubine	322.36	35.74	0.73
38	MOL002897	epiberberine	336.39	43.09	0.78
39	MOL002903	(R)-Canadine	339.42	55.37	0.77
40	MOL002904	Berlambine	351.38	36.68	0.82
41	MOL002907	Corchoroside A Qt	404.55	104.95	0.78
<i>Rheum officinale</i> (7 components)					
42	MOL000096	(-)-catechin	290.29	49.68	0.24
43	MOL000358	beta-sitosterol	414.79	36.91	0.75
44	MOL000471	aloe-emodin	270.25	83.38	0.24
45	MOL002235	EUPATIN	360.34	50.8	0.41
46	MOL002268	rhein	284.23	47.07	0.28
47	MOL002281	Toralactone	272.27	46.46	0.24
48	MOL002297	Daucosterol Qt	386.73	35.89	0.7

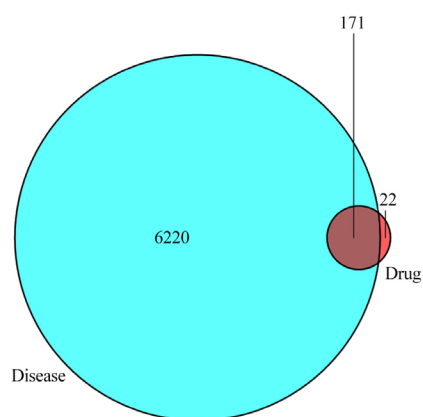


Figure 1. Venny figure for Yiqing Capsule in treating upper respiratory tract infection. (The aquamarine blue circle shows 6391 target genes of upper respiratory tract infection, the red circle shows 193 targets in Yiqing Capsule. The overlap represents a total of 171 genes in Yiqing Capsule in treating the disease.)

3.2. Constructed the Drug-Compound-Target Network and PPI Network

We constructed the drug-compound-target network of Yiqing Capsule in treating upper respiratory tract infection on soft Cytoscape, at last we got 227 nodes and 798 edges, as is shown in **Figure 2**. PPI network was constructed through STRING database, the result is shown in **Figure 3**.

3.3. Target Pathway Analysis

Our research got 2333 GO items of 48 main targets, with 68 CC items, 2117 BP items and 148 MF items, such as nuclear receptor activity, transcription factor activity, direct ligand regulated sequence-specific DNA binding and cytokine receptor binding, etc. The top 20 items are shown in **Figure 4**. We also got 2248 gene-pathway by KEGG enrichment analysis, such as Hepatitis B, IL17 signaling pathway, Kaposi sarcoma-associated herpesvirus infection, Human cytomegalovirus infection, Epstein-Barr virus infection, PI3K-Akt signaling pathway, etc, the results are shown in **Figure 5**. In **Figure 4** and **Figure 5**, the colour of column nodes shows the P value, from blue to red indicates that P value is smaller, the gradual change of column shape from long to short indicates that there are more enrichment targets.

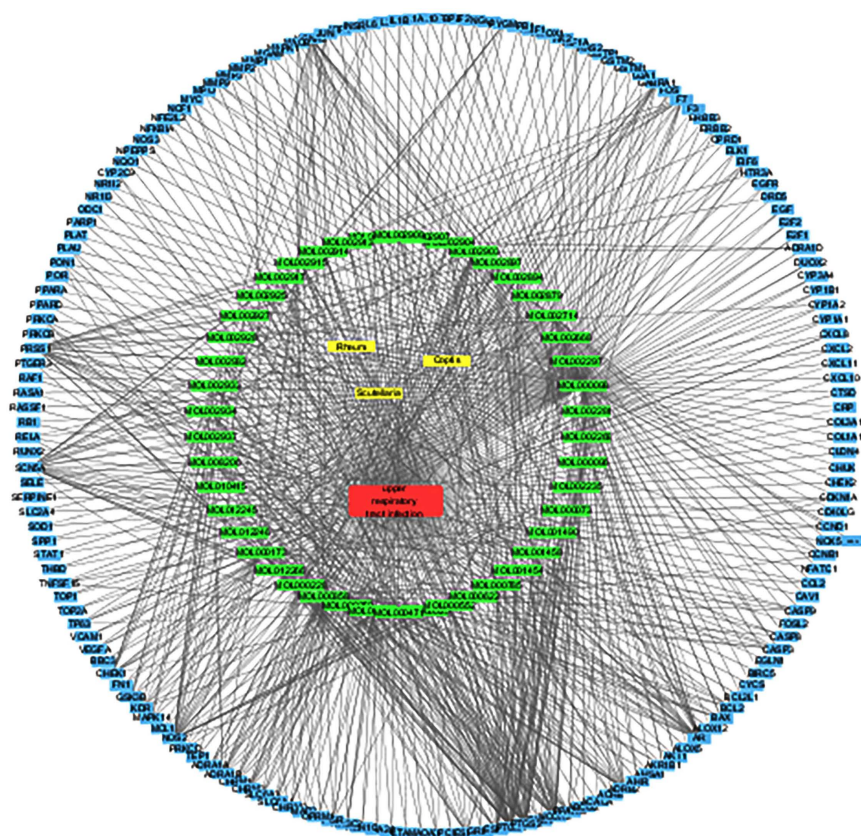


Figure 2. Compound-target-pathway network of Yiqing Capsule in treating upper respiratory tract infection. (The red is disease, the yellow is Chinese medical herbs of Yiqin Capsule, the green is main compounds, the blue is gene targets.)

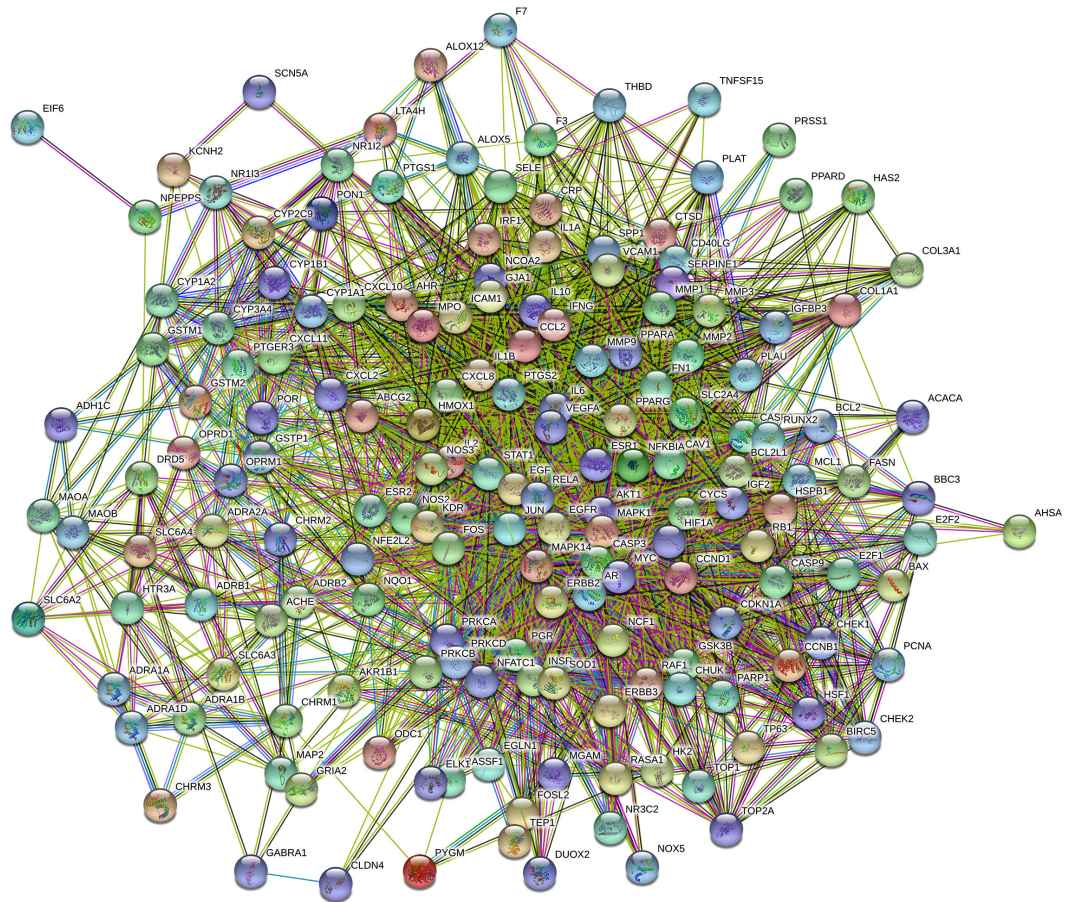


Figure 3. PPI network of Yiqing Capsule.

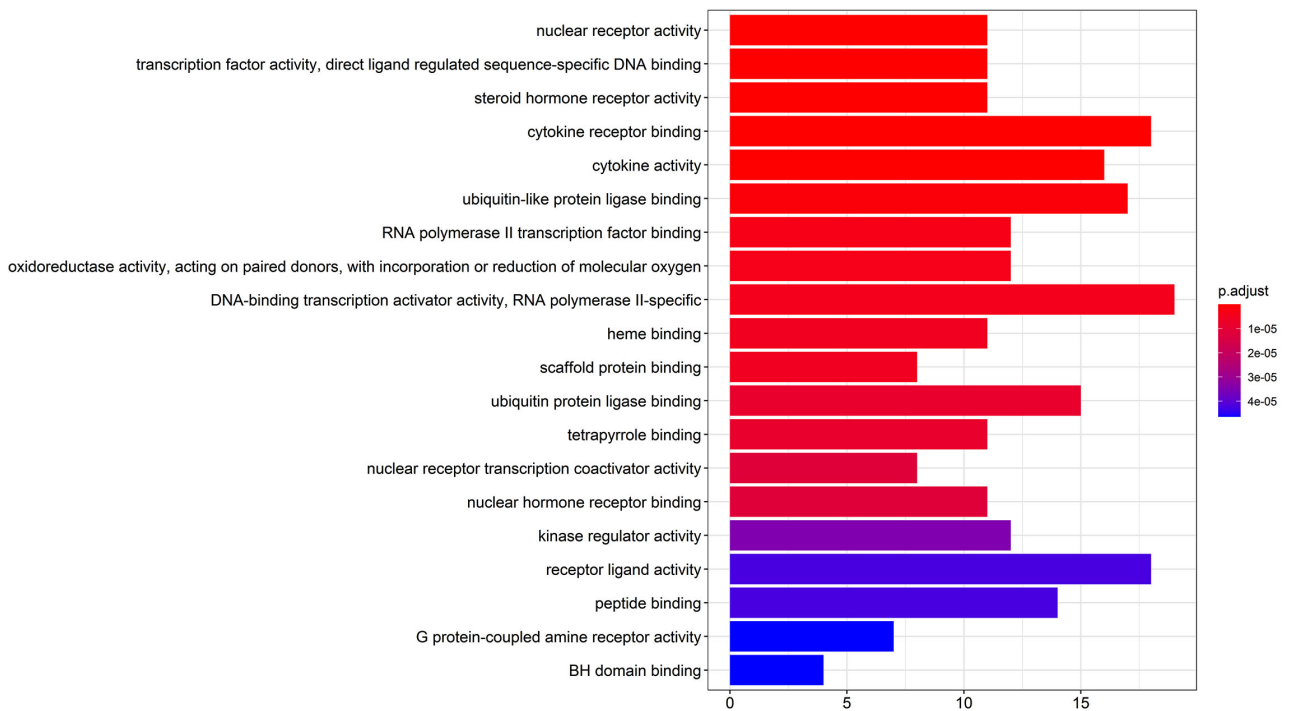


Figure 4. GO enrichment analysis of targets of Yiqing Capsule.

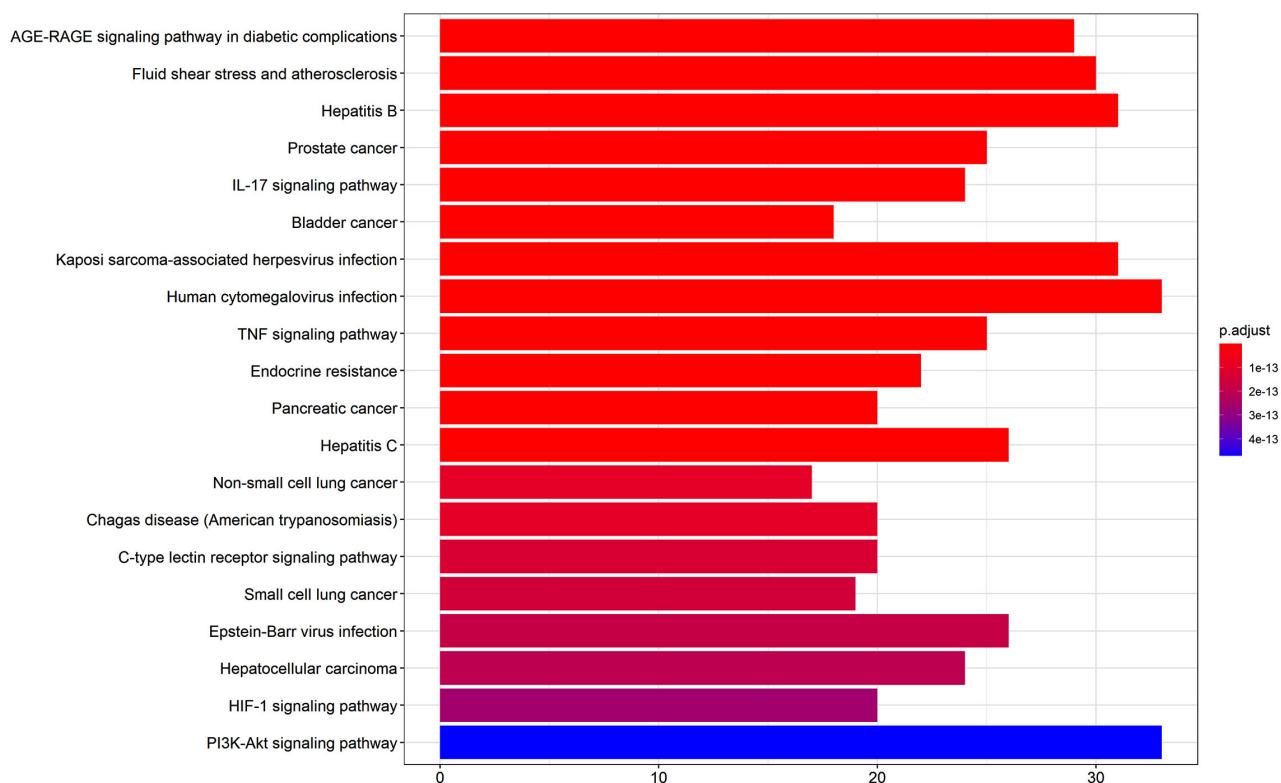


Figure 5. KEGG enrichment analysis of targets of Yiqing Capsule.

4. Discussion

Network pharmacology is a method to study the network relationship among drugs, diseases and targets, which has been widely used in pharmacology research, and is helpful to quickly find the targets and molecular mechanisms of drugs. Our study analyzed the main active compounds and related targets of Yiqing Capsule in the treatment of upper respiratory tract infection through network pharmacology. The result is shown that Yiqing Capsule plays an important role in the treatment of upper respiratory tract infection through multiple compounds, multiple targets and multiple pathways. Liu Wei found that the serum level of il-17 in children with recurrent upper respiratory tract infection was significantly higher than that in healthy children. The result of his study showed that il-17 was an independent factor in the occurrence of children with upper respiratory tract infection by Cox statistical analysis [8]. In our study, we found that the active component pathway of Yiqing Capsule includes il-17 signaling pathway. Therefore, combined with the characteristics of il-17 expression level in the above clinical reports, certain theoretical basis can be provided for the treatment of upper respiratory tract infection by Yiqing Capsule.

Our study also explored the potential components, targets and signaling pathways of Yiqing Capsule in the treatment of upper respiratory tract infection by network pharmacology, providing a theoretical basis for the study of molecular signaling pathways and clinical applications. However, the complex relationship between Yiqing Capsule and diseases still needs further clinical verification.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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