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Mechanism of Yiqi Huoxue Compound for Treatment of Acute Myocardial Infarction Based on Network Pharmacology

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ABSTRACT

Objective: To explore the potential mechanism of Yiqi Huoxue Compound for the treatment of acute myocardial infarction (AMI) through network pharmacology.

Methods: The main active compounds and related effect targets of Yiqi Huoxue Compound were searched and screened through Traditional Chinese Medicine Systems Pharmacology Database and Analysis Platform (TCMSP). The standard names of effect targets were obtained using Uniprot database, the disease-related targets were obtained using GeneCards, Online Mendelian Inheritance in Man (OMIM) and A Database of Gene-Disease Associations (DisGeNET), and the protein interaction network of AMI-related core targets was constructed through STRING database and Cytoscape software. Gene Ontology (GO) enrichment analysis and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis were performed for core targets using R language software.

Results: Based on the screening conditions, 93 effective compounds, 140 drug targets of Yiqi Huoxue Compound and 71 potential therapeutic targets related to AMI were obtained. A total of 92 entries were excavated by GO enrichment analysis ($P<0.05$), and 42 pathways related to AMI were screened out by KEGG pathway enrichment analysis ($P<0.05$).

Conclusion: Yiqi Huoxue Compound contains a variety of active compounds, which can exert its therapeutic effect through multiple targets and multiple signaling pathways. The research results can provide a modern theoretical basis for the clinical application and mechanism research of Yiqi Huoxue Compound.

KEYWORDS: Yiqi Huoxue Compound; acute myocardial infarction; network pharmacology

INTRODUCTION

AMI is one of the common coronary arteriosclerotic types (CADs), which for a variety of reasons consist of sudden severe stenosis or a full coronary artery occlusion. The development and occurrence mechanisms of AMI have still not been fully clarified. The main mechanisms of current research are the creation, activation of leukocytes and calcium excess[1], of oxygen-free radicals. A multi-level network to analyse active compounds and potential drugs goals, disease targets and target genotypes is established in a new discipline with a view to analysing and predicting potential mechanisms for medical use in disease from a holistic point of view

Recent studies have demonstrated that traditional Chinese medicine, one of AMI therapy and research entries, has a certain protective effect on AMI. In the TCM categories AMI is one among the 'heavy duty,' 'cold-mouth pain' and 'angel pectoris.' The heart is the location of the disease, including spleen, liver and kidneys. AMI causes qi and blood deficiency, yin-yang and visceral dysfunction, including a stagnation of qi, blood stages, turbid plexemia and cold congestion. Asthenia is the main aetiology in blood vessel and surface stasis. In combination with my own experience, my supervisors have done this to treat

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AMI with excellent clinical effectiveness by way of long-term clinical practise.

My supervisor, Professor Guoheng Hu, is the instructor of inheriting academic experience of the sixth batch of nationally renowned experts in TCM, and he has been engaged in clinical work for decades and achieved great accomplishments in the field of cardiovascular and cerebrovascular diseases. He has discovered in the clinical treatment of CAD that based on the etiology of asthenia in origin and excess in superficiality, the compound method should be used in the treatment, thereby tonifying qi and activating blood circulation. Simply tonifying qi cannot dissipate blood stasis, while simply activating blood circulation cannot invigorate qi. Therefore, tonifying qi and activating blood circulation should be combined, and qi can promote blood circulation, remove stasis, benefit pulse and eliminate stagnation. Therefore, the experiential prescription Yiqi Huoxue Compound tonifying qi and activating blood circulation was prepared to invigorate qi and dredge pulse vessel. *Astragalus membranaceus* is used as the sovereign drug to promote blood circulation through strengthening qi. *Angelica sinensis* is used as the ministerial drug to replenish blood and promote blood circulation through "removing extravasated blood and nourishing new blood". *Salvia miltiorrhiza* is used to "eliminate stagnant blood, and replenish new blood", and remove blood stasis. Moreover, *Ligusticum wallichii*, as a drug promoting circulation and regulating vital energy, can dredge blood vessels, invigorate blood circulation, and activate meridians to stop pain.

The potential mechanism of Yiqi Huoxue Compound in the treatment of AMI was explored through a network of pharmacology to provide a new theoretical basis for the prevention and treatment of cardiovascular diseases with TCM.

MATERIALS AND METHODS

Screening of active ingredients and prediction of targets in Yiqi Huoxue Compound

In the research of the key wording of the active ingredient in the Yiqi Huoxue compound the traditional Pharmacological Database and Analysis Platform (TCMSP) for Chinese drugs systems, "Astragalus membranaceus," "Angelica sinensis," "Ligusticum wallichii" and "Salvia Miltiorrhiza." The active ingredients of the Yiqi HuoXue Compound were tested according to the pharmacokinetic principle using the built-in TCMSP Ingredient Scrub Tool which used to screen off and create a Database on the compounds involved with the active ingredients of Yiqi Huoxue Compound.

Establishment of drug target network for Yiqi Huoxue Compound

Using the Uniport data base (https:/www.uniprot.org/) the objective protein obtained has been converted and corrected to obtain the Yiqi Huoxue composition effect targets. The MCT and its impact targets were then imported for visualisation into the software Cytoscape (http:/www.cytoscape.org/) and the appropriate drug target network was built.

Collection of AMI-related targets

In the Human Gene database (GeneCards-https:/www.genecards.org), online Mendelian heritage at man (OMIM-https:/www.omim.org/) and in a data base of gene-disorders assocations, the keyword was the "acute myocardial infarction." AMI related targets have been searched. AMI-related targets were searched. The targets for disease were achieved after deduplication.

The drug targets and disease targets were mapped through Venny 2.1.0 (http://bioinfogp.cnb.sic.es/tools/venny/index.html). The target intersection was displayed in the form of Venn diagram, based on which the potential therapeutic targets of Yiqi Huoxue Compound in the treatment of AMI were obtained.

Establishment of protein-protein interaction (PPI) network and screening of core targets

The potential therapeutic targets obtained were entered into the Search Tool for the Retrieval of Interacting Genes/Proteins (STRING-https://string-db.org/) to get the information about protein interaction. Then the target protein intersection obtained was imported into Cytoscape software for visualization, the protein interaction network diagram was plotted, the TCM-disease protein interaction visual network was constructed, and the core targets were screened.

Gene Ontology (GO) enrichment analysis and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis

The information about TCM-disease targets obtained above was calculated using the R language software, and the results of GO enrichment analysis and KEGG pathway analysis were obtained. Then the results were presented in the form of bar graphs or bubble graphs.

RESULTS

Screened active ingredients in Yiqi Huoxue Compound

OB≥30% and DL≥0.18 were set as the conditional parameters, based on which the active ingredients of Yiqi Huoxue Compound were screened out through TCMSP. A total of 94 active compounds were screened out, including 20 in *A. membranaceus*, 2 in *A. sinensis*, 7 in *L. wallichii* and 65 in *S. miltiorrhiza*. After deduplication, the unique value 93 was retained (Table 1).

Drug target network for Yiqi Huoxue Compound

After screening and deduplication through TCMSP and standardisation in Uniprot database (Table 2), 140 target effects for the active ingredients of Yiqi Huoxue Compound were obtained. Table 2. The drug target network was built using the Cytoscape 3.6.1 software, with 137 nodes and 1,405 sides, with a single drug target each, while the target-target interactions are on every side. According to a Network Topology Analytics, the goals of the drug target network containing 51 nodes and 630 sides were chosen to be higher than the mean grade (20.51), whereby the colour of a darker node was higher (Figure 1).

AMI-related targets in Yiqi Huoxue Compound

A total of 1,148 targets related to AMI were obtained from GeneCards, OMIM and DisGeNET, with "Acute myocardial infarction" as the key word. The drug targets of Yiqi Huoxue Compound and disease targets were mapped using Venny 2.1.0, and then 71 potential therapeutic targets were obtained (Figure 2).

PPI network and core targets

The 71 intersectional objectives obtained through drug-disease mapping were analysed using Cytoscape3.6.1 software, and the network relationship was visualised. There were 59 nodes and 158 sides in the central network diagram (Figure 3). The nodes showed potential objectives, and the bigger node matched the other node-related targets. Each side represented the objective-target interaction, with the higher degree of association corresponding to the thicker lines. The grades were ranged from 1 to 19, and averaged 5.36 (the top 40-degree targets), according to network topology analyses.

GO and KEGG pathway enrichment analysis results

The seventy-one related targets obtained above were analysed for GO and KEGG pathways with R language software. Total of 92 molecular, biological and cellular function entries (P<0.05), with the top 20 GO entries in a bar and a bubble diagram (Figures 4 and 5) were excavated. Table 4. Protease Binding, serine hydrolase activity, heme binding, binding of tetrapyrrol, serine endopeptidase activity, serine peptidase activity, integrate binding, growth factor receptor binding and binding RNA Polymerase II transcript factors have been enriched with the GO entries. The KEGG enrichment analysis (P<0.05) screened 42 signalling paths and the top 20 entries were drawn into bars and bubble charts (figures 6 and7).). It has been found that the inputs were enhanced by phosphatidylinositol 3-hydroxy kinase (PI3K)-protein kinase B (AKT) pathway, toll-like receptor pathways for signalising the signalling pathway of the tumour necrosis factor (TNF), interleukin17 (IL-17), the mitogenic protein kinase (MaPK), a C-type lectin receptor, and vascular endothelial growth factor. Signal pathway of the signalised signal pathway.

DISCUSSION

AMI is one of the common types of CAD, whose pathogenesis is sudden severe stenosis or complete occlusion of one coronary artery due to various reasons. At present, the mechanism of occurrence and development of AMI has not been fully clarified. According to current research, its mechanism may be the generation of oxygen free radicals, leukocyte activation and calcium overload [1]. Recently, autophagy has been one of the hotspots of research on AMI [2]. Under normal conditions in the body, the normal function of the heart is maintained with a low level of autophagy. Under stress conditions, such as myocardial inflammation, energy deficiency, hypoxia or organelle damage, autophagy can be activated [3]. Myocardial cells in a stress state can clear the damaged mitochondria in the body through initiating autophagy timely and properly, preventing the release of apoptotic factors into the cytoplasm and blocking the apoptotic pathway. At the same time, the resistance of cells to hypoxia is improved, thereby protecting the myocardial cells [4]. Network pharmacology is an emerging discipline, in which a multi-level protein interaction visual network is constructed based on the analysis of active compounds and potential targets of drugs, disease-related targets, and target genotypes under the guidance of holistic thinking, so as to analyze and predict the potential mechanism of drug treatment of diseases.

In this study, Yiqi Huoxue is an effective prescription by Professor Hu Guoheng in long-term clinical practise guided by traditional Chinese medicine theory, which consists of A. Divranaceus,

A. Synensis, S. The Melti-orryzes and L. Waleligiii. Traditional Chinese medicine is made up of a wide variety of traditional Chinese medicines and each Chinese traditional medicine consists of rich chemical components, each of which can work towards various goals and pathways. The efficacy of traditional medicine is an important element of the multi-component multi-target-multipathway. This research examined Yiqi Huoxue Compound's active components of efficacy, effect goals, trajectories and biological functions by using a network of pharmacology; the networking of PPI associated with the MIA was built; and the potential Yiqi Huoxue Compound mechanisms were anticipated for AMI treatment.

The Yiqi Huoxue Compounds and AMI have many associated targets. In this study the Venny platform scanned a total of 71 intersectional objectives from both. The PPI interaction network test confirmed that Yiqi Huoxue Compound 's core targets in the treatment of AMI includes the transcription factor AP-1 (JUN), TN F, lymphoma-B-cells-2 (Bcl-2), epidermal growth factor receptor (EGFR), oxide synthase nitrical synthase 3 (NOS3). (PTGS2). Bcl-2 is a major autophagy protein, which can prevent the expansion of self-administered vacuoles and the conglomeration of autophagosomal membranes by inhibiting Beclin1 in the Beclin1 / Bcl-2 tract. LC3 expression was found to be inhibible and the survival rate of myocardial cells damaged could be improved through the activation of the Pathway Bcl-2 / Beclin1, which protects myocardial cells[5]. NOS3 can catalyse NO production by controlling proline and arginine metabolism, regulating blood flow, restoring blood vessels, blocking the aggregation and adherence of platelets, leukocytes and suppressing the abnormal spread of vascular, smooth muscle cells. NOS3 will be abnormally regulated in the cases of myocardial injury. This reduces NO 's production and aggravates myocardial ischemic injury. VEGFA can be involved in pathophysiological processes such as angiogenesis as well as nervous regeneration, the main way of regulating angiogenesis is the VEGFA-VEGFR2 pathway. JUN, IL-6, TNF and PTGS2 are closely linked to the development and development of atherosclerosis, cardiomyocyte apoptosis, inflammatory response and overexpression of cytokines and myocardial ischemistry reperfusion molecules. They are a cause of accurate effects. Furthermore, multiple inflammatory factors such as JUN, IL-6 and TNF may interact with one other in order to induce an inflammatory response of myocardial cells, to exacerbate an inflammatory myocardial injury and to facilitate the progression of AS, which are key risk factors for AMI. In the pathological processes, such as oxidative stress, inflammatory response and DNA damage, MAPK14 and MAPK1, members of the MAPK family, can be activated. MAPK can also have effects on the human body's coagulation and fibrinolysis system through the ERK pathways and the P38MAPK [6-7]. Yiqi Huoxue Compound can in short mediate autophagy, oxidative stress and inflamative reaction with targets such as JUN, TNF, Bcl-2, EGFR, NOS3, PTGS2, MAPK1, VEGFA, MAPK8, MAPK14 and IL-6, thus having a therapeutic effect on AMI.

The biological functions of Yiqi Huoxue Compouncture in AMI treatment, according to the results of GO enhancement analysis, included mainly protease binding, serine hydrolasses, hema-binding, tetrapyrrole-binding, serine endopeptidase activity, septidase activity, integrin binding, RNA polymerase II transcription factor binding. The results of KEGG enrichment pathway analysis showed that Yiqi Huoxue compound can regulate core targets by PI3K-AKT signal track, MAPK signalling pathway, Toll-like receptor signalling pathways, HIF-1 signalling track, IL-17 signalling pathways, C-type reading receiver, and VEGF signalling track to exert its clinical effect.

The PI3K-AKT signalling pathway can control cell proliferation, differentiation, apoptosis and transportation of glucose and can also synergize with the Toll-like signalling path to cell autophagy control. A key kinase in the downstream of the PI3K-AKT signalling pathway is the mammalian target of rapamycin (mTOR). The mTOR signalling pathway controls pathological processes such as cell growth and apoptosis primarily by regulating the signalling path PI3K-AKT-mTOR. The mTOR has been identified as a key regulator during cell autophagy development and the active mTOR can promote autophagosome development and ripening[7]. Liu[8] indicated that autophagy is involved in pathological procedures, such as ischemical-reperfusion myocardial lesions. TNF, MAPK, IL-17, and C-type lectin, receptor, pathway signals, are intricately related to immunoregulation, angiogenesis and inflammatory response. The mechanism of occurrence of AMI also regulates cell growth, differentiation and stress adaptation with the environment, as well as oxidation stress, immunoregulation, and inflammation. The VEGF pathway and HIF-1 pathway may also promote angiogenesis which both play important roles during ischemy and hypoxia. The VEGF signalling pathway in particular

is an irreplaceable part of the whole angiogenesis process. The HIF-1 signalling system can update the VEGF and its receptors' expressions in the case of cell hypoxia to lead to angiogenesis, and leads iNOS to blood flow and ischemic lesions. Simultaneously, the study shows that hypoxia as well as anoxia can lead to autophagy, and that HIF-dependent autophagy causes hypoxia[9].

Based on the differentiation of syndrome and treatment in TCM, the active ingredients, the potential aims of the Yiqi Huoxue Compound and its potential mechanism for AMI treatments were explored through network pharmacology, in order to clarificate mechanisms for the occurrence and development of AMI. The results revealed that the active ingredients of the Yiqi Huoxue Compound could act through the PI3K-AKT signalling pathway, HIF-1, Signals pathway, VEGF signalling track, TNF signalling pathway, MAPK Signals Pathway, IL-17 signals path, and C-type lectin on several targets, such as the JUN, TNF, EGFR, NOS3, PTGS2, MAPK1, VEGFA, MAPK8, MAPK1, and IL-6. The potential linkages between Yiqi Huox Compound and ischemia-hypoxia, inflammatory action, immunoregulation, and cell apoptosis in the onset of AMI can be seen. The paths and objectives provided the basis for further analysis of animals. In animal experiments the most important active ingredients, core targets and pathways of Yiqi Huoxue Compound remain to be verified.

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Table 1. **Basic information about active ingredients in Yiqi Huoxue Compound**

Mol ID	Molecule Name	OB%	DL
MOL000006	luteolin	36.16	0.25
MOL000033	(3S,8S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-[(2R,5S)-5-propan-2-yloctan-2-yl]-2,3,4,7,8,9,11,12,14,15,16,17-dodecahydro-1H-cyclopenta[a]phenanthren-3-ol	36.23	0.78
MOL000098	quercetin	46.43	0.28
MOL000211	Mairin	55.38	0.78
MOL000239	Jaranol	50.83	0.29
MOL000296	hederagenin	36.91	0.75
MOL000354	isorhamnetin	49.6	0.31
MOL000358	beta-sitosterol	36.91	0.75
MOL000359	sitosterol	36.91	0.75
MOL000371	3,9-di-O-methylnissolin	53.74	0.48
MOL000374	5'-hydroxyiso-muronulatol-2',5'-di-O-glucoside	41.72	0.69
MOL000378	7-O-methylisomucronulatol	74.69	0.3
MOL000379	9,10-dimethoxypterocarpan-3-O-β-D-glucoside	36.74	0.92
MOL000380	(6aR,11aR)-9,10-dimethoxy-6a,11a-dihydro-6H-benzofurano[3,2-c] chromen-3-ol	64.26	0.42
MOL000387	Bifendate	31.1	0.67
MOL000392	formononetin	69.67	0.21
MOL000398	isoflavanone	109.99	0.3
MOL000417	Calycosin	47.75	0.24
MOL000422	kaempferol	41.88	0.24
MOL000433	FA	68.96	0.71
MOL000438	(3R)-3-(2-hydroxy-3,4-dimethoxyphenyl) chroman-7-ol	67.67	0.26
MOL000439	isomucronulatol-7,2'-di-O-glucosiole	49.28	0.62
MOL000442	1,7-Dihydroxy-3,9-dimethoxypterocarpene	39.05	0.48
MOL000449	Stigmasterol	43.83	0.76
MOL000569	digallate	61.85	0.26
MOL001494	Mandenol	42	0.19
MOL001601	1,2,5,6-tetrahydrotanshinone	38.75	0.36
MOL001659	Poriferasterol	43.83	0.76
MOL001771	poriferast-5-en-3beta-ol	36.91	0.75
MOL001942	isoimperatorin	45.46	0.23
MOL002135	Myricanone	40.6	0.51
MOL002140	Perlolyrine	65.95	0.27
MOL002151	senkyunone	47.66	0.24
MOL002157	wallichilide	42.31	0.71
MOL002222	sugiol	36.11	0.28
MOL002651	Dehydrotanshinone IIA	43.76	0.4
MOL002776	Baicalin	40.12	0.75
MOL006824	α-amyrin	39.51	0.76
MOL007036	5,6-dihydroxy-7-isopropyl-1,1-dimethyl-2,3-dihydrophenanthren-4-one	33.77	0.29
MOL007041	2-isopropyl-8-methylphenanthrene-3,4-dione	40.86	0.23
MOL007045	3α-hydroxytanshinone IIa	44.93	0.44
MOL007048	(E)-3-[2-(3,4-dihydroxyphenyl)-7-hydroxy-benzofuran-4-yl] acrylicacid	48.24	0.31
MOL007049	4-methylenemiltirone	34.35	0.23
MOL007050	2-(4-hydroxy-3-methoxyphenyl)-5-(3-hydroxypropyl)-7-methoxy-3-benzofurancarboxaldehyde	62.78	0.4
MOL007051	6-o-syringyl-8-o-acetylshanzhisidemethylester	46.69	0.71
MOL007058	formyltanshinone	73.44	0.42
MOL007059	3-beta-Hydroxymethyllenetanshiquinone	32.16	0.41
MOL007061	Methylenetanshinquinone	37.07	0.36
MOL007063	przewalskina	37.11	0.65
MOL007064	przewalskinb	110.32	0.44
MOL007068	Przewaquinone B	62.24	0.41

MOL007069	przewaquinone C	55.74	0.4
MOL007070	(6S,7R)-6,7-dihydroxy-1,6-dimethyl-8,9-dihydro-7H-naphtho[8,7-g]benzofuran-10,11-dione	41.31	0.45
MOL007071	przewaquinonef	40.31	0.46
MOL007077	sclareol	43.67	0.21
MOL007079	tanshinaldehyde	52.47	0.45
MOL007081	Danshenol B	57.95	0.56
MOL007082	Danshenol A	56.97	0.52
MOL007085	Salvilenone	30.38	0.38
MOL007088	cryptotanshinone	52.34	0.4
MOL007093	dan-shexinkumd	38.88	0.55
MOL007094	danshenspiroketallactone	50.43	0.31
MOL007098	deoxyneocryptotanshinone	49.4	0.29
MOL007100	dihydrotanshinlactone	38.68	0.32
MOL007101	dihydrotanshinone I	45.04	0.36
MOL007105	epidanshenspiroketallactone	68.27	0.31
MOL007107	C09092	36.07	0.25
MOL007108	isocryptotanshi-none	54.98	0.39
MOL007111	Isotanshinone II	49.92	0.4
MOL007115	manool	45.04	0.2
MOL007118	microstegiol	39.61	0.28
MOL007119	miltionone I	49.68	0.32
MOL007120	miltionone II	71.03	0.44
MOL007121	miltipolone	36.56	0.37
MOL007122	Miltirone	38.76	0.25
MOL007123	miltirone II	44.95	0.24
MOL007124	neocryptotanshinoneii	39.46	0.23
MOL007125	neocryptotanshinone	52.49	0.32
MOL007127	1-methyl-8,9-dihydro-7H-naphtho[5,6-g]benzofuran-6,10,11-trione	34.72	0.37
MOL007130	prolithospermicacid	64.37	0.31
MOL007132	(2R)-3-(3,4-dihydroxyphenyl)-2-[(Z)-3-(3,4-dihydroxyphenyl)acryloyl]oxy-propionicacid	109.38	0.35
MOL007140	(Z)-3-[2-[(E)-2-(3,4-dihydroxyphenyl)vinyl]-3,4-dihydroxy-phenyl]acrylicacid	88.54	0.26
MOL007141	salvianolicacidg	45.56	0.61
MOL007142	salvianolicacidj	43.38	0.72
MOL007143	salvilenone I	32.43	0.23
MOL007145	salviolone	31.72	0.24
MOL007149	NSC122421	34.49	0.28
MOL007150	(6S)-6-hydroxy-1-methyl-6-methylol-8,9-dihydro-7H-naphtho[8,7-g] benzofuran-10,11-quinone	75.39	0.46
MOL007151	Tanshindiol B	42.67	0.45
MOL007152	Przewaquinone E	42.85	0.45
MOL007154	tanshinoneiia	49.89	0.4
MOL007155	(6S)-6-(hydroxymethyl)-1,6-dimethyl-8,9-dihydro-7H-naphtho[8,7-g]benzofuran-10,11-dione	65.26	0.45
MOL007156	tanshinone VI	45.64	0.3

Table 2. **Targets of main ingredients of Yiqi Huoxue Compound**

No.	Target	No.	Target	No.	Target	No.	Target
1	ACACA	36	CTRB1	71	ICAM1	106	PDE3A
2	ACHE	37	CTSD	72	IFNG	107	PGR
3	ACP3	38	CYP1A2	73	IL1B	108	PIK3CG
4	ADH1B	39	CYP3A4	74	IL2	109	PKIA
5	ADH1C	40	DPP4	75	IL6	110	PLAT
6	ADRA1A	41	DRD2	76	INSR	111	PLAU
7	ADRA1B	42	DRD5	77	ITGB3	112	PON1
8	ADRA1D	43	ECE1	78	JUN	113	POR
9	ADRA2A	44	EDNRA	79	KCNH2	114	ppar gamma2
10	ADRA2B	45	EGF	80	KCNMA1	115	PPARD
11	ADRA2C	46	EGFR	81	KDR	116	PPARG
12	ADRB1	47	ESR1	82	LTA4H	117	PPP3CA
13	ADRB2	48	ESR2	83	LYZ	118	PRSS1
14	AHR	49	F3	84	MAOA	119	PTGER3
15	AKR1C3	50	F7	85	MAOB	120	PTGS1
16	ALOX5	51	FASN	86	MAP2	121	PTGS2
17	APP	52	GABRA1	87	MAPK1	122	PYGM
18	AR	53	GABRA2	88	MAPK14	123	RB1
19	ATP5F1B	54	GABRA3	89	MAPK8	124	RELA
20	BCL2	55	GABRA5	90	MET	125	RXRA
21	BIRC5	56	GABRA6	91	MGAM	126	RXRB
22	CA2	57	GABRE	92	MMP1	127	SCN5A
23	CALCR	58	GABRG3	93	MMP2	128	SELE
24	CASP7	59	GJA1	94	MMP3	129	SLC6A2
25	CCL2	60	GRIA2	95	MPO	130	SLC6A3
26	CCNA2	61	GSK3B	96	MT-ND6	131	SLC6A4
27	CHEK1	62	GSTM1	97	NCOA1	132	SOD1
28	CHRM1	63	GSTM2	98	NCOA2	133	THBD
29	CHRM2	64	GSTP1	99	NOS2	134	TNF
30	CHRM3	65	HMOX1	100	NOS3	135	TOP1
31	CHRM4	66	HTR1A	101	NQO1	136	TOP2B
32	CHRM5	67	HTR1B	102	NR3C1	137	TP53
33	CHRNA2	68	HTR2A	103	NR3C2	138	VCAM1
34	COL1A1	69	HTR2C	104	ODC1	139	VEGFA
35	COL3A1	70	HTR3A	105	OPRD1	140	XDH

Table 3. **Core targets**

No.	Target	Degree	No.	Target	Degree
1	JUN	19	21	ICAM1	6
2	TNF	16	22	CHRM2	6
3	TP53	15	23	IFNG	5
4	MAPK1	14	24	EDNRA	5
5	VEGFA	13	25	KDR	4
6	MAPK8	12	26	VCAM1	4
7	MAPK14	12	27	COL1A1	4
8	IL6	12	28	NOS3	4
9	EGFR	11	29	BCL2	4
10	NR3C1	10	30	GSK3B	4
11	APP	10	31	PPARG	4
12	IL1B	9	32	MMP2	4
13	ESR1	9	33	ADRB2	4
14	IL2	8	34	NOS2	3
15	RB1	7	35	ALOX5	3
16	CCL2	7	36	SELE	3
17	PTGS2	7	37	MMP3	3
18	AR	7	38	ADRA2B	3
19	EGF	6	39	OPRD1	3
20	ITGB3	6	40	HTR2A	3

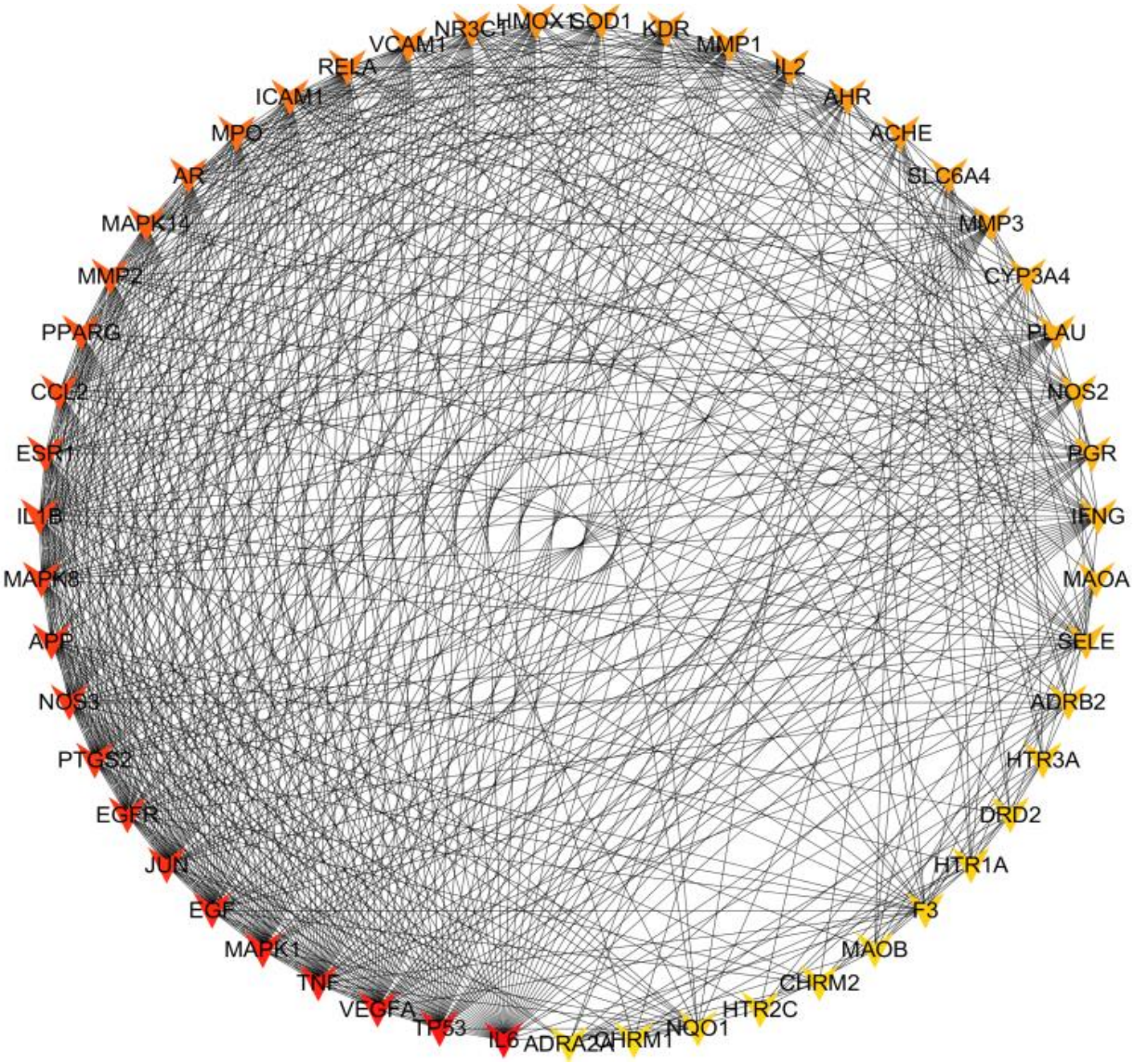

Figure 1. **Drug target network.**

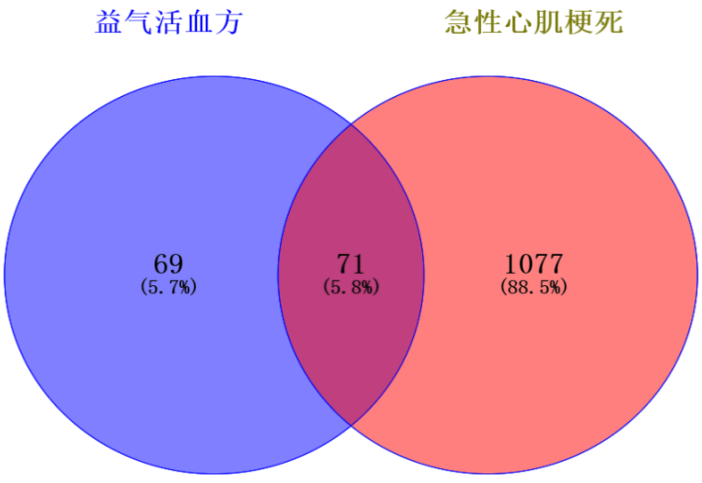

Figure 2. **AMI-related targets in Yiqi Huoxue Compound.**

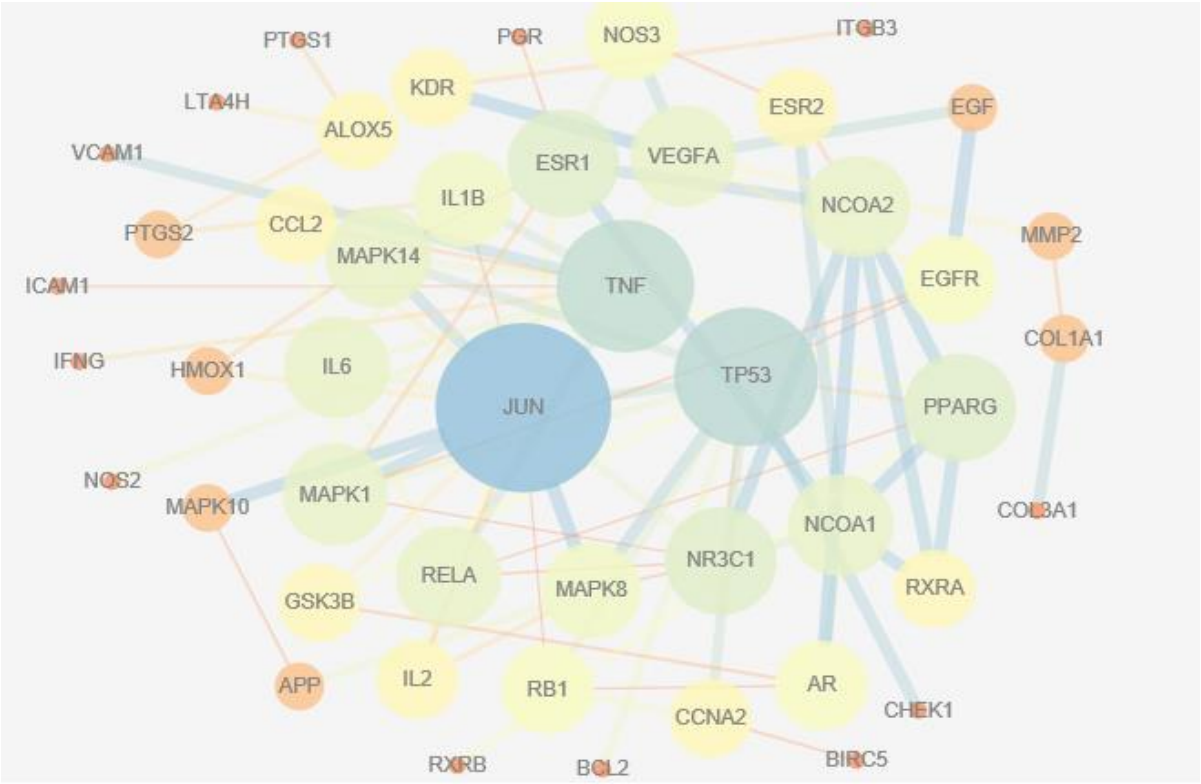

Figure 3. **PPI network of AMI-related targets for Yiqi Huoxue Compound.**

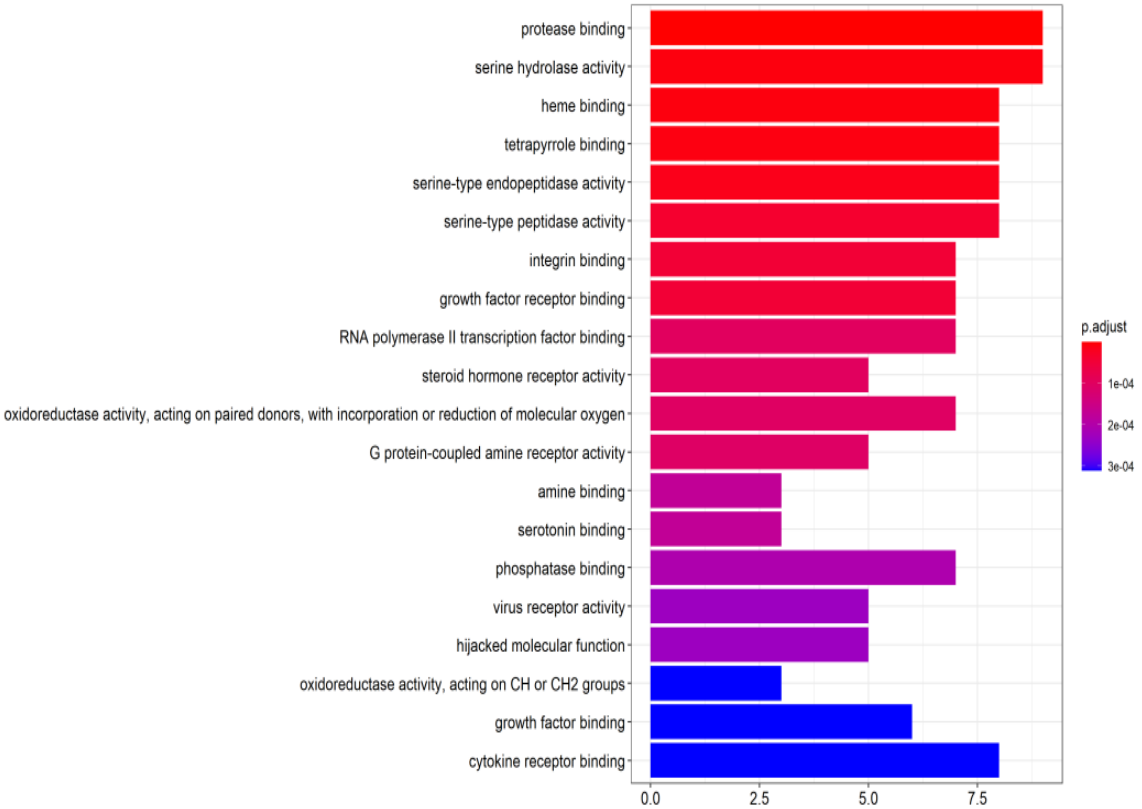

Figure 4. **Bar graph of GO enrichment analysis.**

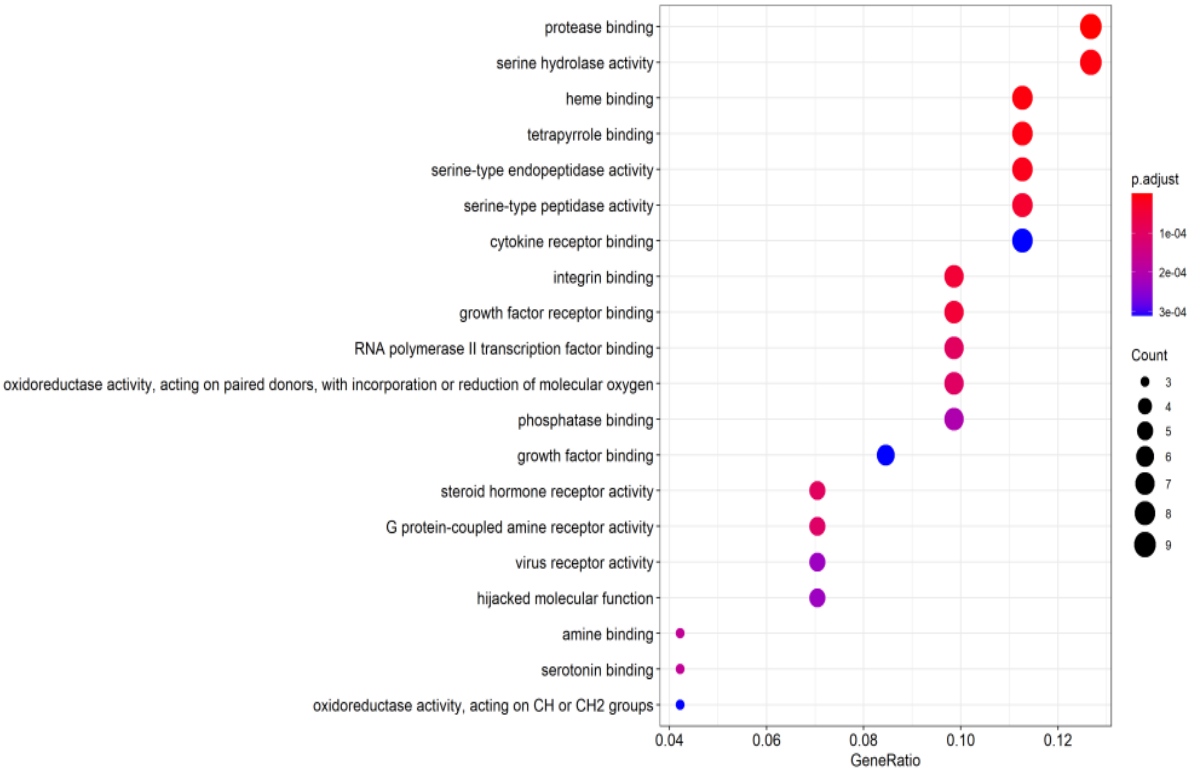

Figure 5. **Bubble graph of GO enrichment analysis.**

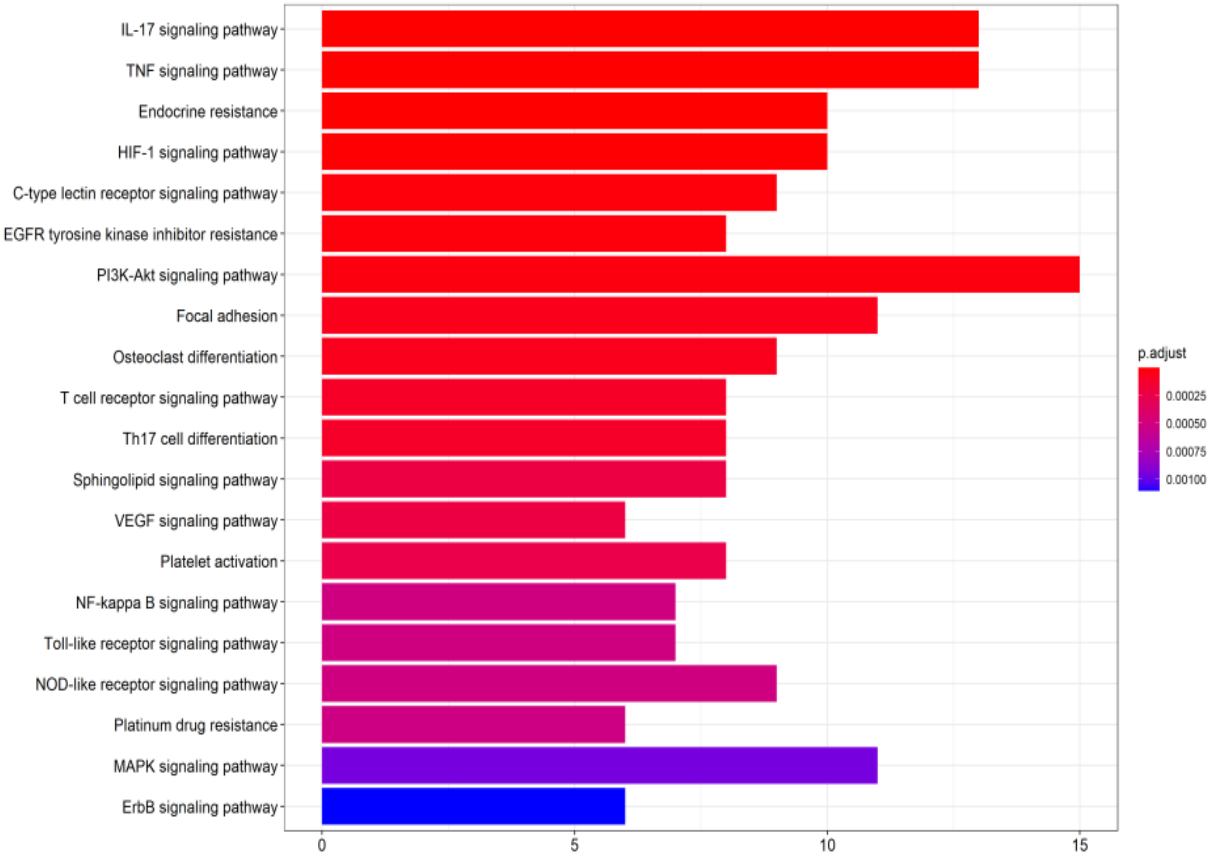

Figure 6. **Bar graph of KEGG pathway enrichment analysis.**

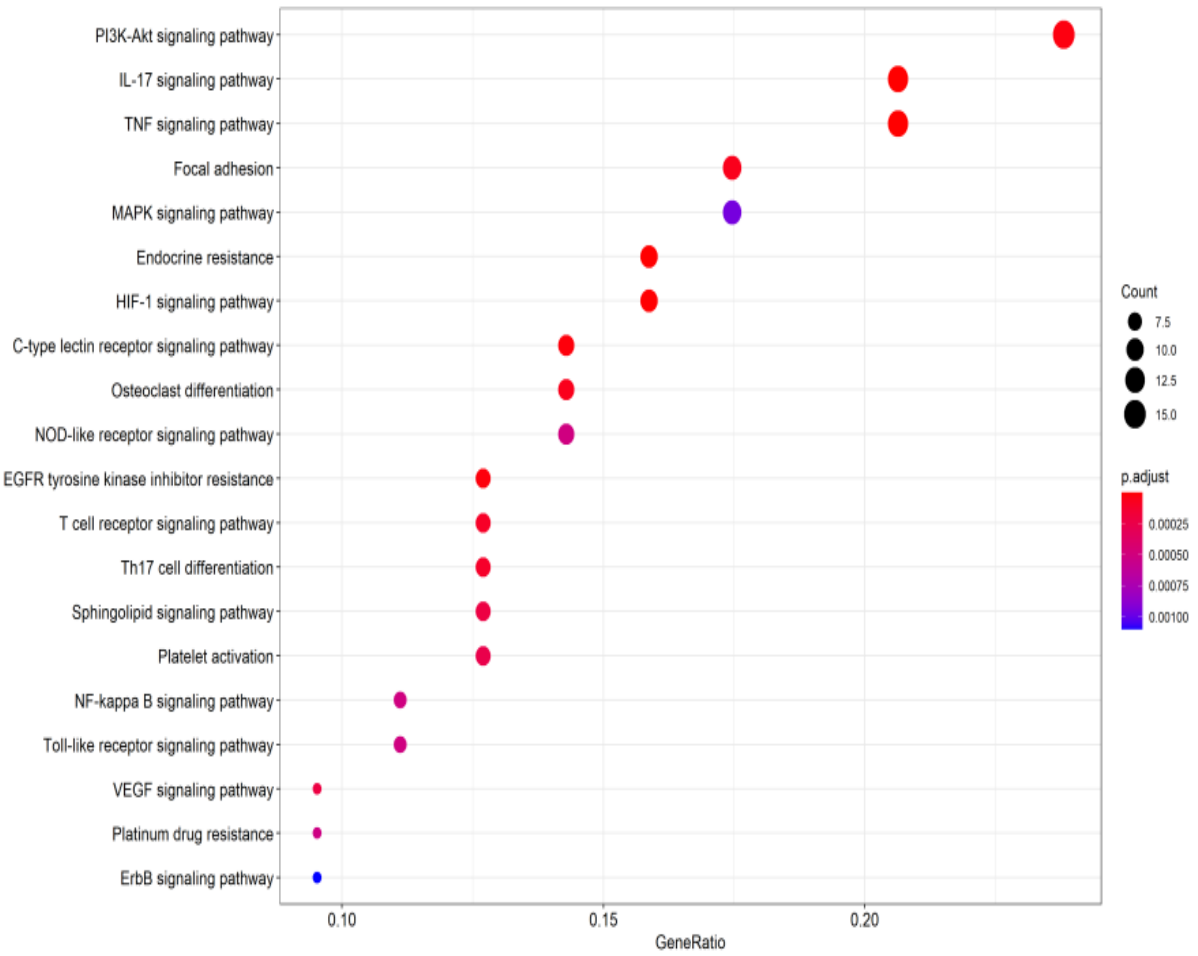

Figure 7. **Bubble graph of KEGG pathway enrichment analysis.**