Exploring the Mechanism of Jianzhong Chubi Decoction in Treating Comorbidity of Knee Osteoarthritis and Chronic Gastritis by Network Pharmacology and Molecular Docking

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Abstract [**Objectives**] To explore the mechanisms of Jianzhong Chubi Decoction in treating comorbid knee osteoarthritis (KOA) and chronic gastritis (CG) based on network pharmacology and molecular docking approaches. [**Methods**] Active components and their corresponding targets of Jianzhong Chubi Decoction were retrieved from the TCMSP and SymMap databases. Disease targets for KOA and CG were collected from GeneCards. Overlapping targets were used to construct a "drug-active component-target" network and a protein-protein interaction (PPI) network. Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analyses were performed. Molecular docking was subsequently conducted to validate the binding affinities between the core active components and key targets. [**Results**] A total of 104 active components and 440 targets were obtained for Jianzhong Chubi Decoction, along with 1 500 KOA targets and 1 000 CG targets, yielding 98 intersecting targets. The core components were quercetin, kaempferol, and feruloyltyramine; the key targets included TNF, AKT1, IL-6, and IL-1β. KEGG enrichment analysis mainly involved cancer pathways, lipid and atherosclerosis pathways, and the AGE-RAGE signaling pathway. Molecular docking showed that the binding energies of the core components with the key targets were all below -5 kcal/mol. [**Conclusions**] Jianzhong Chubi Decoction exerts anti-inflammatory, cartilage-protective, and gastric mucosa-protective effects through multiple components, multiple targets, and multiple pathways. This provides a pharmacological basis for the concept of "treating different diseases with the same therapy" in KOA and CG comorbidity.

Key words Jianzhong Chubi Decoction, Knee osteoarthritis (KOA), Chronic gastritis (CG), Network pharmacology, Molecular docking, Comorbidity

1 Introduction

Knee osteoarthritis (KOA) is a chronic, degenerative, inflammatory joint disease marked by pain and progressive loss of mobility, imposing a substantial burden on the quality of life of middle-aged and older adults[1]. In China, the prevalence of symptomatic KOA has reached 8.1%[2], and its disease burden has escalated into a major public health challenge over the last 30 years[3]. Existing treatments, mainly including analgesics, anti-inflammatory agents, and surgical interventions, fail to reverse the underlying pathological changes of KOA, leaving prevention as the most effective approach[4]. As a condition in which Traditional Chinese Medicine (TCM) has demonstrated pronounced therapeutic strengths, TCM-based therapies can deliver meaningful improvements in pain, joint function, and quality of life, along with a strong safety record[2,5].

Osteoarthritis (OA) is frequently comorbid with chronic gastritis (CG)[6]. KOA is the most common form of OA, and approximately 40% of KOA patients experience concomitant gastric inflammation[7-8]. Treating the comorbidities concurrently can markedly improve clinical symptoms in patients with both KOA and CG[9]. The concept of "comorbidity" aligns with the holistic approach of TCM and is rooted in the "body-organ combined impediment" theory, combined with the understanding that rheumatic diseases involve multiple systems and manifest complex and variable clinical features[10]. Clinical studies have confirmed that Jianzhong Chubi Decoction can significantly alleviate symptoms in patients with comorbid KOA and CG, demonstrating clear clinical advantages in comprehensive comorbidity management; however, its immune-related mechanisms remain unclear. This study aims to systematically analyze the active components of Jianzhong Chubi Decoction and their target-mediated mechanisms in treating KOA comorbid with CG using network pharmacology and molecular docking approaches.

2 Data and methods

2.1 Information extraction of effective active components and action targets of Jianzhong Chubi Decoction The herbal composition of Jianzhong Chubi Decoction, comprising Ramulus Cinnamomi (Guizhi, 12 g), Radix Paeoniae Alba (Baishao, 36 g), Radix et Rhizoma Glycyrrhizae (Gancao, 18 g), Fructus Jujubae (Dazao, 18 g), Radix et Rhizoma Ginseng (Renshen, 18 g), Rhizoma Zingiberis Recens (Shengjiang, 18 g), Rhizoma Pinelliae (Banxia, 12 g), Radix Scutellariae (Huangqin, 12 g), Rhizoma Coptidis (Huanglian, 12 g), Radix Astragali (Huangqi, 18 g), Radix Achyranthis Bidentatae (Niuxi, 18 g), Flos Lonicerae Japonicae (Jinyinhua, 15 g), Radix Polygalae (Yuanzhi, 10 g), and Herba Dendrobii (Shihu, 15 g), was searched in the TCMSP

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(https://old.tcmsp-e.com/tcmsp.php) and SymMap (http://www.symmap.org/) databases. Active components were filtered using oral bioavailability (OB) ≥30% and drug-likeness (DL) ≥ 0.18 as selection criteria. All resulting target proteins were standardized via UniProt (https://www.uniprot.org). For active components lacking target information, their canonical SMILES notations were retrieved from PubChem (https://pubchem.ncbi.nlm.nih.gov) and then submitted to Swiss Target Prediction (http://swisstargetprediction.ch) for target prediction, retaining only those with a prediction probability ≥0.1. Duplicate entries were subsequently removed to yield the final set of potential drug targets.

2.2 Information extraction of disease-related target The GeneCards database (https://www.genecards.org) was searched using "Knee Osteoarthritis" and "Chronic Gastritis" as keywords to retrieve disease-related targets. After collection and removal of duplicate targets, the target information for KOA and CG was obtained.

2.3 Screening of intersection targets and construction of a drug-active component-target network The Venny 2.1.0 online platform (https://bioinfogp.cnb.csic.es/tools/venny/index.html) was used to identify the intersecting targets among Jianzhong Chubi Decoction, KOA, and CG. The intersection targets were imported into Cytoscape 3.10.4 software to construct a "drug-active component-target" visualization network. Topological analysis of the network nodes was performed using the CytoNCA plugin, and the nodes were ranked according to their degree values.

2.4 Construction of the protein-protein interaction (PPI) network and extraction of core targets The intersection targets between the Chinese herbal formula and the diseases were input into the STRING database (https://cn.string-db.org/) with the confidence threshold set to 0.40. The resulting network was then exported to Cytoscape 3.10.4 for topological analysis and network construction. Targets were screened based on betweenness centrality (BC), degree centrality (DC), and closeness centrality (CC). Genes with values above the median for all three selected indicators were subjected to further analysis to obtain the key targets.

2.5 GO and KEGG enrichment analysis The intersecting targets of the three (the herbal formula, KOA, and CG) were input into the Metascape database (http://metascape.org/) for Gene Ontology (GO) functional and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis. GO analysis encompassed three domains: biological process (BP), molecular function (MF), and cellular component (CC). The most significantly enriched terms were selected for further analysis and processing. Visualization was performed online using the WeChat-based bioinformatics platform Shengxin (http://www.bioinformatics.com.cn/).

2.6 Molecular docking analysis The top three core components from the "drug-active component-target" network and the top four key targets from the PPI network, ranked by degree, were selected for molecular docking analysis. The molecular structures of the active components were downloaded from PubChem as receptors, and the target protein structures were obtained from the PDB database (https://www.rcsb.org/) as ligands. Molecular docking was performed using the CB-Dock2 online platform (https://cadd.labshare.cn/cb-dock2/index.php). A docking binding energy of < -5.0 kcal/mol was used as the criterion for assessing binding affinity. Visualization analysis was conducted in PyMOL software.

3 Results and analysis

3.1 Active components of the drug and their target information A total of 104 active components of Jianzhong Chubi Decoction were identified from the TCMSP and SymMap databases, among which 18 were common active components (Table 1). A "drug-active component-target" network was constructed using Cytoscape 3.10.4, comprising 559 nodes and 1 889 edges (Fig. 1). Topological analysis identified the top five active components with the highest degree values (Table 2), among which quercetin (Que), kaempferol (Kae), and moupinamide (NTF) were identified as the core components.

3.2 Screening of disease-related targets and intersection targets A total of 1 500 KOA-related targets and 1 000 CG-related targets were retrieved from the GeneCards database. These were analyzed together with the 440 targets of Jianzhong Chubi Decoction using the Venny 2.1.0 online platform, yielding 98 intersection targets (Fig. 2).

3.3 PPI network construction and analysis Analysis of the 98 intersecting targets in the STRING database generated a PPI network that was subsequently visualized in Cytoscape 3.10.4. The initial network contained 98 nodes and 2 386 edges. After filtering with the median values of degree centrality (DC), betweenness centrality (BC), and closeness centrality (CC), a refined network of 12 nodes and 66 edges was retained (Fig. 3). The top four targets ranked by degree, namely tumor necrosis factor (TNF), interleukin-6 (IL-6), interleukin-1β (IL-1β), and AKT serine/threonine kinase 1 (AKT1), were identified as the core targets (Table 3).

3.4 GO functional enrichment analysis and KEGG pathway enrichment analysis GO functional enrichment analysis was categorized into three types: BP, CC, and MF. For each GO category, statistically significant GO terms were first screened based on statistical significance (p-value) and then ranked by enrichment counts (Counts). The top 10 terms in each category were selected for enrichment analysis and visualization (Fig. 4A). For KEGG pathway enrichment analysis, statistically significant pathways were first screened by p-value, followed by ranking according to enrichment factor and Counts, and the top 20 core pathways were ultimately identified (Fig. 4B).

Table 1 Common active components

MOL	No.	Drugs				
MOL000449	A1	Fructus Jujubae	Radix Scutellariae	Radix Achyranthis Bidentatae	Radix et Rhizoma Ginseng	Rhizoma Zingiberis Recens	Rhizoma Pinelliae
MOL000422	A1	Radix Paeoniae Alba	Radix et Rhizoma Glycyrrhizae	Radix Astragali	Flos Lonicerae Japonicae	Radix Achyranthis Bidentatae	Radix et Rhizoma Ginseng
MOL000098	A3	Fructus Jujubae	Radix et Rhizoma Glycyrrhizae	Radix Astragali	Flos Lonicerae Japonicae	Radix Achyranthis Bidentatae	Flos Lonicerae Japonicae
MOL000358	B1	Radix Paeoniae Alba	Ramulus Cinnamomi	Radix Scutellariae	Radix Achyranthis Bidentatae	Rhizoma Zingiberis Recens	
MOL000492	C1	Radix Paeoniae Alba	Fructus Jujubae	Radix et Rhizoma Glycyrrhizae	Ramulus Cinnamomi		
MOL000359	C2	Radix Paeoniae Alba	Radix et Rhizoma Glycyrrhizae	Ramulus Cinnamomi	Radix Scutellariae		
MOL000211	C3	Radix Paeoniae Alba	Fructus Jujubae	Radix et Rhizoma Glycyrrhizae	Radix Astragali		
MOL002914	D1	Radix Scutellariae	Flos Lonicerae Japonicae	Radix Achyranthis Bidentatae			
MOL002714	D2	Radix Scutellariae	Radix Achyranthis Bidentatae	Rhizoma Pinelliae			
MOL001454	D3	Fructus Jujubae	Radix Achyranthis Bidentatae	Rhizoma Coptidis			
MOL008647	E1	Rhizoma Coptidis	Fructus Jujubae				
MOL005376	E2	Radix et Rhizoma Ginseng	Herba Dendrobii				
MOL000787	E3	Radix et Rhizoma Ginseng	Fructus Jujubae				
MOL000392	E4	Radix et Rhizoma Glycyrrhizae	Radix Astragali				
MOL000354	E5	Radix et Rhizoma Glycyrrhizae	Radix Astragali				
MOL000239	E6	Radix et Rhizoma Glycyrrhizae	Radix Astragali				
MOL000173	E7	Radix Scutellariae	Radix Achyranthis Bidentatae				
MOL002773	E8	Flos Lonicerae Japonicae	Fructus Jujubae				

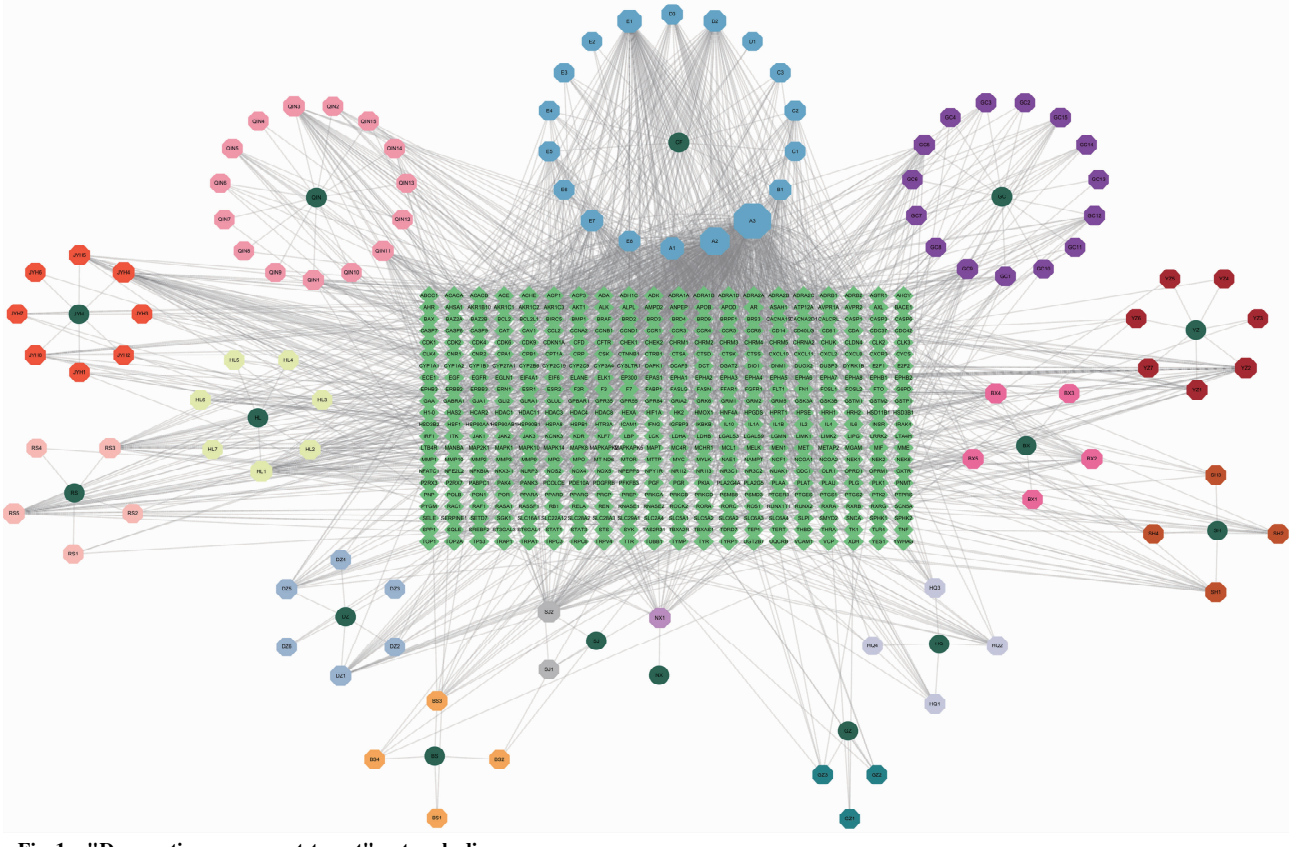

Fig. 1 "Drug-active component-target" network diagram

Table 2 Top 5 active components in "drug-active component-target" network

MOL-ID	Component	Degree
MOL000098	Quercetin	367
MOL000422	Kaempferol	200
MOL008647	Moupinamide	88
MOL000449	Stigmasterol	75
MOL002714	Baicalein	80

Table 3 Core targets of PPI network

Target	Full name of target	Degree
TNF	Tumor Necrosis Factor	91
IL-6	Interleukin 6	91
IL-1β	Interleukin 1 Beta	89
AKT1	AKT Serine/Threonine Kinase 1	87

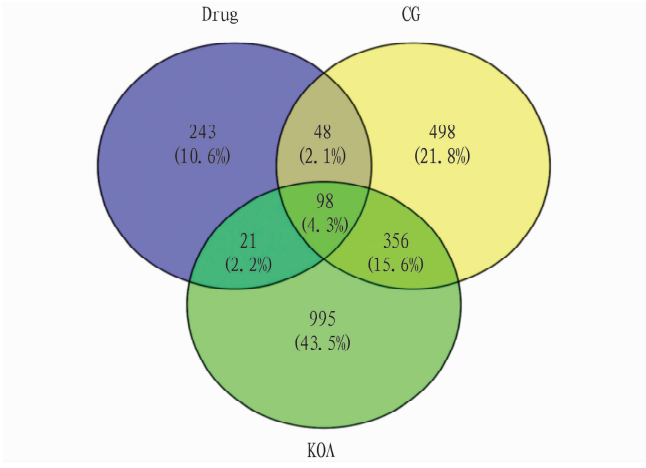

Fig. 2 Venn diagram for drug-disease targets

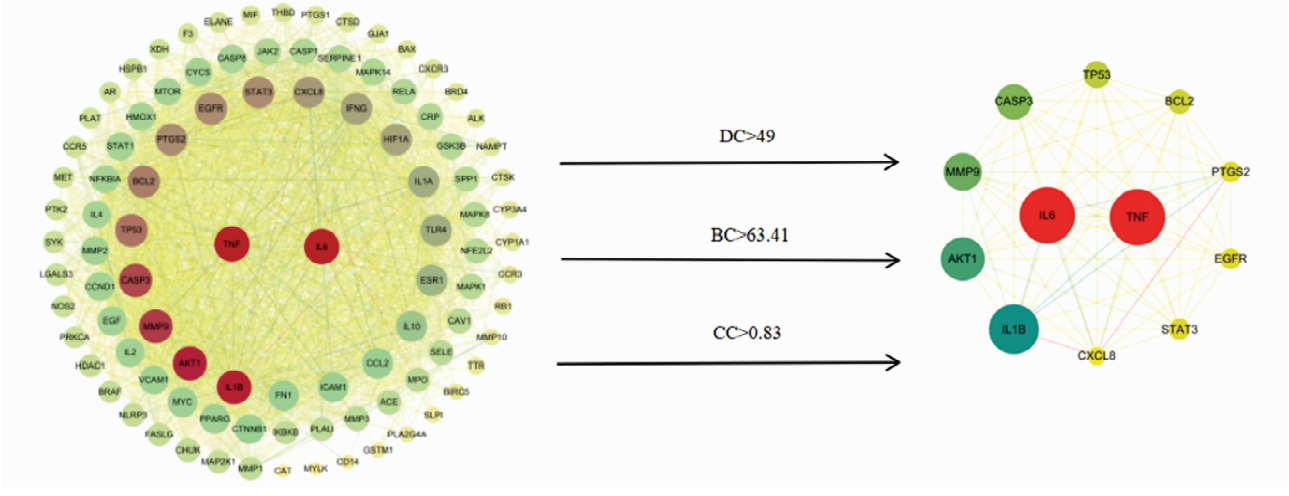

Fig. 3 Flow chart of screening

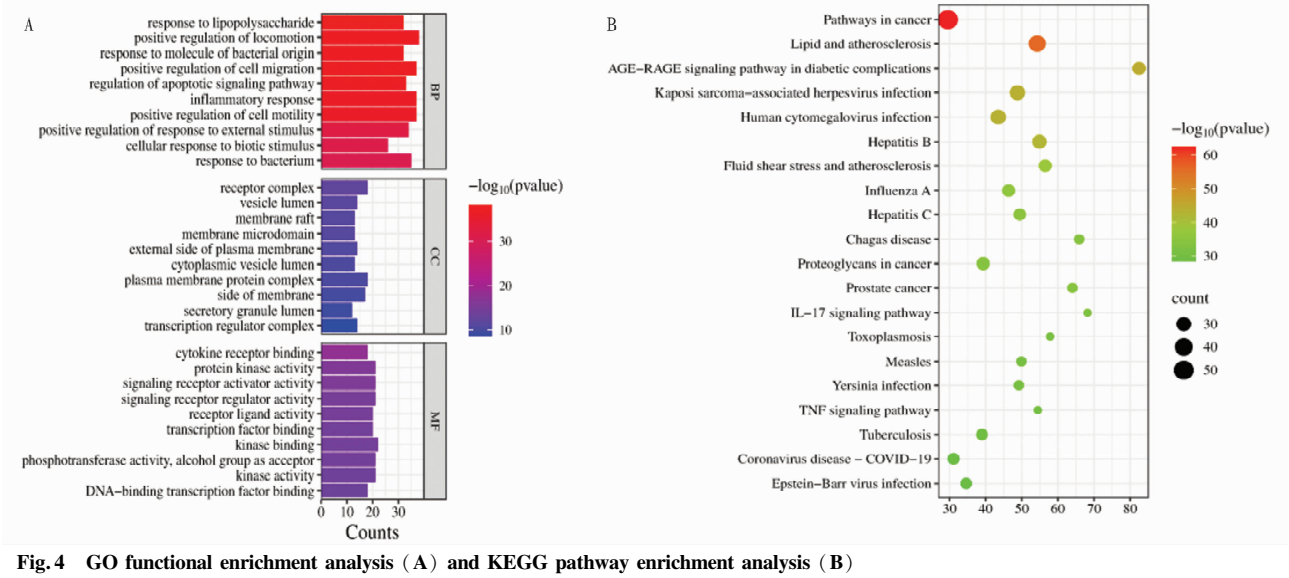

Fig. 4 GO functional enrichment analysis (A) and KEGG pathway enrichment analysis (B)

3.5 Molecular docking verification Molecular docking was performed between the three core components (Que, Kae, NTF) and the four core targets (TNF, AKT1, IL-6, IL-1β). Published evidence indicates that a lower binding energy between ligand and receptor reflects stronger binding affinity and the ability to form stable hydrogen bonds[11]. The docking results showed that the

binding energies of all core component-key target pairs were below −5 kcal/mol (Table 4). The docking complexes with better binding affinity, including Kae-TNF, Kae-IL-1β, Kae-AKT1, and NTF-IL-6, were selected for visual analysis (Fig. 5) to explore the binding modes between the receptor proteins and small-molecule ligands.

Table 4 Binding energies of key targets and core components

Core components	Key targets	Binding energy//KcaL/mol
Que	TNF	8.6
	AKT1	8.3
	IL-6	9.2
	IL-1β	7.9
Kae	TNF	11.1
	AKT1	10.4
	IL-6	9.6
	IL-1β	10.4
NTF	TNF	8.2
	AKT1	7.6
	IL-6	10
	IL-1β	−7.7

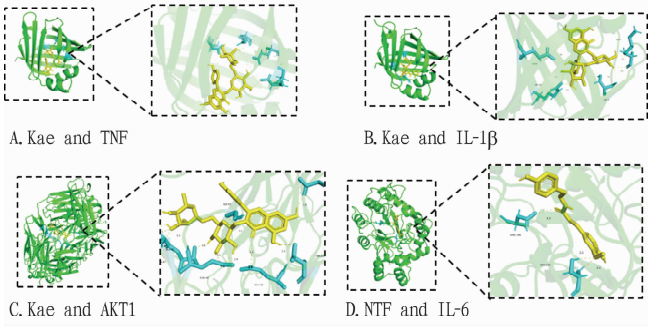

Fig. 5 Molecular docking conformation of core components and key targets

4 Discussion

KOA is a multifactorial whole-joint disease, the pathological hallmark of which is the progressive fibrosis, fissuring, ulceration, and eventual loss of articular cartilage[5]. In the framework of traditional Chinese medicine, KOA is classified as "bone bi" (bone impediment) and is fundamentally regarded as a disease of "concurrent sinew-bone involvement with coexisting atrophy and impediment," presenting as root deficiency with branch excess, namely, root atrophy (wei) and branch impediment (bi)[2]. Clinical observations show that knee joint damage in CG patients tends to occur earlier and with greater severity than in age-matched controls. Also, medications that target both gastritis and arthritis can concurrently relieve gastric symptoms and reduce joint inflammation[9]. A meta-analysis has further suggested that CG may contribute to the onset and pathological progression of KOA via a "stomach-knee joint" axis, thus giving rise to a conceptual axis that bridges the visceral organ and the limb[9].

The above findings align with the theories of "treating atrophy by selecting Yangming alone" and "body-organ combined impediment"[10]. The knee joint depends on the nourishment of qi and blood from the stomach meridian; deficiency of the stomach and its associated meridians or spleen-stomach dampness-heat can impair knee joint function[12]. The stomach is located in the middle energizer (middle jiao), corresponding to the knee joint at the mid-segment of the limbs, and the foot Yangming stomach meridian forms an internal-external interconnected system with the knee joint. Physiologically, the stomach and the knee joint are closely linked through the meridian and sinew systems. The *Plain Questions – Treatise on Atrophy* states: "The Yangming··· governs the moistening of the ancestral sinews; the ancestral sinews control the binding of bones and the smooth movement of joints." Disorders of the foot Yangming stomach meridian often lead to knee pain and impediment. As recorded in the *Spiritual Pivot – Meridians*: "When the (stomach foot Yangming) meridian is affected by disease··· the knee and patella become swollen and painful." Yang Shangshan of the Sui Dynasty, in the *Grand Simplicity of the Yellow Emperor's Inner Canon*, noted: "When the stomach pulse is soft and scattered, it indicates food impediment and patellar pain," and explained that "stomach deficiency fails to digest water and grain, leading to food accumulation in the stomach, causing impediment and pain; moreover, the meridian traverses the knee, hence knee and patellar pain arise." Shen Jin'ao of the Qing Dynasty, in the *Tracing the Source and Course of Miscellaneous Diseases – Source and Course of Knee Diseases*, recorded: "Crane-knee wind··· in its early stages must involve Yangming dampness-heat." Grounded in the principles of "treating atrophy by selecting Yangming alone" and "body-organ combined impediment," the therapeutic strategy of this formula is to strengthen the middle jiao and replenish the stomach, unblock collaterals, and eliminate impediment.

Jianzhong Chubi Decoction is derived from modified formulations of Jianzhong Bupi Decoction, Xiao Gouteng Decoction, and Sishen Jian. In this formula, Radix et Rhizoma Ginseng (Renshen) and Radix Astragali (Huangqi) serve as the sovereign (Jun) medicinals, aiming to restore the spleen and stomach as the root of acquired constitution. Ramulus Cinnamomi (Guizhi) and Radix Paeoniae Alba (Baishao) act as the minister (Chen) medicinals, softening the liver to relieve pain and assisting the sovereign medicinals in fortifying the spleen and harmonizing the nutrient and defensive aspects. Rhizoma Pinelliae (Banxia), Radix Scutellariae (Huangqin), and Rhizoma Coptidis (Huanglian), characterized by acrid opening and bitter downbearing, together with Radix Achyranthis Bidentatae (Niuxi), Flos Lonicerae Japonicae (Jinyinhua), Caulis Dendrobii (Shihu), and Radix Polygalae (Yuanzhi), which supplement the liver and kidney, clear residual toxins, and nourish the stomach yin, jointly serve as the adjuvant (Zuo) medicinals. Rhizoma Zingiberis Recens (Shengjiang), Radix et Rhizoma Glycyrrhizae (Gancao), and Fructus Jujubae (Dazao) function as the courier (Shi) medicinals, boosting qi, supplementing the center, and harmonizing the actions of all ingredients. The whole formula combines cold and warm properties and applies both supplementation and draining simultaneously, thereby jointly achieving the effects of fortifying the middle jiao and replenishing the stomach, unblocking collaterals, and eliminating impediment. Clinical practice has demonstrated that Jianzhong Chubi Decoction can significantly alleviate the clinical symptoms of pa-

tients with comorbid KOA and CG, offering distinct advantages in comprehensive comorbidity management.

The above analyses identified three core components of Jianzhong Chubi Decoction (quercetin, kaempferol, and moupinamide) which possess anti-inflammatory, gastric mucosa- and cartilage-protective, and cell-repair functions. Quercetin is a potent anti-inflammatory agent with sustained action[13]. It exhibits biological properties of stabilizing mast cell activity and protecting gastrointestinal cells[14], and it can exert bidirectional regulatory effects on inflammatory responses and immune functions, maintaining physiological balance through dynamic regulatory mechanisms[15]. Kaempferol is an anti-inflammatory and antioxidant flavonoid. One study found that kaempferol can modulate the gut microbiota and multiple metabolites[16]; it also protects bone by inhibiting adipogenesis, inflammatory responses, oxidative stress, osteoclast autophagy, and osteoblast apoptosis, while concurrently activating osteoblast autophagy pathways, exerting significant bone-protective effects through multidimensional synergistic regulation[17]. Predictive models indicate that moupinamide is a natural anti-inflammatory agent[18], and its anti-inflammatory effects may be attributed to the downregulation of cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS) expression via inhibition of activator protein-1 (AP-1) and the c-Jun N-terminal kinase (JNK) signaling pathway in RAW264.7 mouse macrophages[19].

PPI network analysis identified TNF, AKT1, IL-6, and IL-1β as the core cytokines in KOA and CG comorbidity. TNF is primarily mediated by tumor necrosis factor-alpha (TNF-α) and its receptors. Elevated TNF-α levels are closely associated with the degree of inflammation and disease severity in KOA patients[20]. TNF-α drives cartilage degradation by stimulating IL-1β and matrix metalloproteinases (MMPs), which degrade aggrecan and type II collagen, thereby compromising cartilage elasticity and integrity[21-22]. AKT1 plays a critical role in the pathogenesis of KOA. Inhibition of AKT1 can enhance autophagy in articular chondrocytes, protecting them from KOA-related inflammation, whereas activation of AKT1 is essential for chondrocyte proliferation and protection against apoptosis[23]. In addition, by orchestrating the PI3K/AKT1 cascade, elevating antioxidant enzyme activity, maintaining mitochondrial homeostasis, and suppressing pro-apoptotic and pro-inflammatory signals, AKT1 can mitigate gastric mucosal injury and delay the progression of CG[24]. IL-6 plays a key role in KOA pathophysiology and cartilage degradation. In articular chondrocytes, IL-6 induces the expression of matrix metalloproteinases (*e.g.*, MMP-3 and MMP-13) and a disintegrin and metalloproteinase with thrombospondin motifs (*e.g.*, ADAMTS-4 and ADAMTS-5)[25]. Moreover, IL-6 is central to immune regulation, inflammatory responses, and the initiation and progression of apoptosis. Studies have detected elevated IL-6 levels in the gastric tissues of CG patients, which leads to the accumulation of neutrophils and lymphocytes in the gastric mucosa and disrupts the regulation of inflammatory cytokines[26]. In the pathogenesis of KOA, excessive activation of fibroblasts secretes the key inflammatory mediator IL-1β, sustaining the inflammatory environment within the joint; therefore, inhibiting IL-1β can effectively delay the progression of KOA[27]. A systematic review of case-control studies has indicated an association between IL-1β promoter polymorphisms and the risk of gastritis[28].

GO and KEGG pathway enrichment analysis revealed that the core targets of Jianzhong Chubi Decoction were predominantly enriched in Pathways in cancer, Lipid and atherosclerosis, and the AGE-RAGE signaling pathway. These pathways are intertwined and jointly participate in the pathological processes of KOA and CG comorbidity. Within the cancer pathway, inflammatory signaling networks involving mitogen-activated protein kinases (MAPK) and nuclear factor-κB (NF-κB) not only drive cartilage degeneration and osteophyte formation in KOA but also contribute to chronic inflammation and precancerous transformation of the gastric mucosa in CG[28-29]. Regarding the Lipid and atherosclerosis pathway, dyslipidemia can promote lipid deposition and mitochondrial dysfunction in KOA cartilage[30], while CG patients also exhibit lipid metabolism disorders—including abnormalities in total cholesterol and high-density lipoprotein cholesterol (HDL-C)—that are independent of Helicobacter pylori infection[31]. The AGE-RAGE signaling pathway exacerbates meniscal calcification in aging-related KOA by activating the mTOR-ATF4 circuit[32], and in chronic atrophic gastritis, it aggravates gastric mucosal injury by regulating ferroptosis and inflammatory responses[33]. The interplay of these three pathways reveals the molecular basis by which Jianzhong Chubi Decoction achieves "treating different diseases with the same therapy" through the regulation of an "inflammation-metabolism-aging" network.

Molecular docking results provided further confirmation that the core components of Jianzhong Chubi Decoction bound strongly to the key target proteins enriched in the above pathways. In particular, kaempferol and moupinamide displayed particularly robust binding affinities, reinforcing the multi-pathway mechanism by which Jianzhong Chubi Decoction exerts its therapeutic effects on KOA-CG comorbidity.

The integrated results indicate that Jianzhong Chubi Decoction achieves the "treating different diseases with the same therapy" effect on KOA and CG by synergistically modulating TNF, AKT1, IL-6, and IL-1β through its three principal components (quercetin, kaempferol, and moupinamide) and by targeting the intersecting Pathways in cancer, Lipid and atherosclerosis, and AGE-RAGE signaling axes. Quercetin supplies anti-inflammatory and immunomodulatory actions; kaempferol contributes antioxidant and bone-metabolism-balancing properties; and moupinamide suppresses the JNK/COX-2/iNOS cascade. Collectively, these ingredients counteract TNF-α-, IL-6-, and IL-1β-driven cartilage breakdown and gastric mucosal damage, while AKT1-mediated autophagy and antioxidant reinforcement are concurrently boosted. The three pathways offer a multi-dimensional interpretation of comorbidity through the lenses of inflammation, metabolic dysregulation, and aging. Overall, Jianzhong Chubi Decoction operates via a multi-component, multi-target mechanism to produce anti-inflammatory, cartilage- and gastric mucosa-protective, and cytoprotective effects.

5 Conclusions

The present study, based on network pharmacology and molecular

docking, confirmed that Jianzhong Chubi Decoction exerts synergistic therapeutic effects on KOA-CG comorbidity through multi-component, multi-target, and multi-pathway mechanisms. The therapeutic strategy of Jianzhong Chubi Decoction fully embodies the "middle-for-middle" principle rooted in the theories of "treating atrophy by selecting Yangming alone" and "body-organ combined impediment," emphasizing the integrated regulation of inflammatory responses, immune homeostasis, metabolic function, and tissue repair. Through its cold-and-warm, supplementing-and-draining formula composition, it simultaneously promotes the nourishment of articular cartilage and the protection of gastric mucosa, driving the dynamic balance of qi, blood, and fluid metabolism and the inflammatory network. This effectively alleviates the pathological states of joint degenerative inflammation in KOA and gastric mucosal injury in CG. The study identified the core targets and key signaling pathways of Jianzhong Chubi Decoction in treating KOA-CG comorbidity, providing a solid pharmacological basis for its clinical application in managing such complex comorbidities.

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(To page 39)

that OSR has inhibitory effect on the central nervous system.

Yu Jianqiang *et al.* [7] administered different doses of OSR to mice, observed their appearance and behavioral manifestations, and recorded the number of spontaneous locomotor activities within 10 min. The results showed that the drugtreated mice exhibited reduced activity, lying still with eyes closed, and sluggish responses. Photoelectric counting revealed that the number of spontaneous locomotor activities decreased significantly in a dosedependent manner (250, 500, and 1 000 mg/kg), indicating that OSR markedly suppressed spontaneous exploratory behavior and exerted central inhibitory and sedative effects. In addition, a synergistic hypnotic experiment with pentobarbital sodium was conducted in mice to observe the influence on the hypnotic effect of pentobarbital sodium and the synergistic effect at a subthreshold hypnotic dose, and to record sleep latency, sleep duration, and the rate of induced sleep. The results showed that OSR significantly shortened sleep latency, significantly prolonged sleep duration, and, when combined with a certain dose (40 mg/kg) of pentobarbital sodium, induced sleep in more than half of the animals, indicating that OSR itself possesses hypnotic potential and can enhance the hypnotic effect of central depressants. Its sedativehypnotic effect is related to the activation or enhancement of endogenous sleep/inhibitory neural pathways, and a significant synergistic effect exists. Further, a pentylenetetrazol (PTZ) induced convulsion antagonism experiment was performed to observe the protective effect of the drug against clonic convulsions induced by the chemical convulsant PTZ. The results revealed that OSR did not significantly reduce the number of animals developing PTZ induced convulsions, indicating that its central inhibitory action is pathwayselective, primarily affecting mechanisms related to sedation and hypnosis, while exhibiting no significant effect on convulsive pathways associated with the targets of PTZ. In summary, OSR is a natural compound with clear central inhibitory activity, demonstrating that OSR exerts inhibitory effects on the central nervous system and holds promise for development as a novel hypnotic drug.

7 Conclusions and prospects

OSR exhibits significant multiple pharmacological activities, including analgesic, antitumor, antiarrhythmic, anti-inflammatory, and CNS inhibitory activities. In particular, it exerts favorable inhibitory effects on tumor cell proliferation, migration, and invasion, holding broad prospects for drug development and clinical application. However, as a natural compound derived from traditional Chinese medicine, research on its pharmacological mechanisms and clinical application remains at a preliminary stage. It is therefore necessary to continually integrate knowledge, theories, and experimental techniques from disciplines such as molecular biology, cell biology, laboratory animal science, pharmacology, and basic medicine, and to conduct more comprehensive and in-depth investigations of OSR at the molecular, cellular, and animal levels, so as to elucidate its precise molecular targets and regulatory signaling networks. These efforts will provide a theoretical basis and data support for the future development of OSR-based herbal preparations, clinical translation, and the design of rational combination drug regimens.

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(From page 36)

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