DOI: 10.53469/jcmp.2024.06(06).29

Research Focusing on How Qinge Pill Functions in Managing Stress Urinary Incontinence, Utilizing Network Pharmacology

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Abstract: ***Objective:*** ***Investigating how Qing-e pill aids in managing stress urinary incontinence through network pharmacology.*** ***Methods:*** ***Utilizing the TCM system's pharmacological database and analytical framework (TCMSP), along with literature exploration, the active components and their respective targets for Qing-e pill were identified, leading to the creation of a network of compound TCM - active ingredients - targets. The focus of SUI was identified using the GeneCards and OMIM databases. The active ingredient SUI-target network model was developed and examined using the Cytoscape 3.10.1 software. The protein interaction network (PPI) was created using the STRING database, incorporating gene ontology functional annotation (GO) and Tokyo Genome Encyclopedia (KEGG) pathway enrichment analysis on key targets through DAVID online, with molecular docking performed using Surflex software.*** ***Results:*** ***Screening yielded 86 active components, 461 possible targets, 2551 SUI targets, and 187 typical targets for Qing-e pill and SUI. The outcomes of network analysis revealed Qing-e pill's primary targets for SUI treatment were AKT1, IL6, JUN, TNF, HSP90AA1, ESR1, CTNNB1, EGFR, among others. The primary biological mechanisms encompassed reactions to lipopolysaccharide, molecules originating from bacteria, metal ions, growth of epithelial cells, and the control of membrane potential, among others. KEGG enrichment primarily aims to utilize the AGE-RAGE signaling pathway in treating a range of conditions, including diabetes complications, prostate cancer, fluid shear stress, atherosclerosis, lipid and atherosclerosis, IL-17 signaling pathway, and more.*** ***Conclusion:*** ***Initially, network pharmacology shed light on the foundational materials and operational methods of Qing-e pill in treating SUI, offering a theoretical foundation for their clinical use.***

Keywords: Qing-e pill, Stress urinary incontinence, Network pharmacology, Mechanism of action, Signaling pathway.

1. Introduction

Stress Urinary Incontinence (SUI) refers to a clinical syndrome in which urine leakage occurs under the condition of increased abdominal pressure due to damage to the pelvic floor muscles or nerve structures [1-2]. The incidence of SUI is quite high, with the prevalence of urinary incontinence in adult women ranging from 18.5% to 57.5%, and this ratio gradually increases with age, so the prognosis is usually not optimistic [1]. Currently, Western medicine treats SUI mainly with drugs such as Duloxetine and estrogen. Duloxetine induces significant side effects on gastrointestinal function and the central nervous system, leading to a high discontinuation rate of treatment; while estrogen carries the risk of increasing cardiovascular disease, breast cancer, endometrial cancer, and ovarian cancer with long-term use [3]. In comparison, traditional Chinese medicine theory places more emphasis on holistic thinking, syndrome differentiation, and treatment, with minimal side effects from Chinese herbal medicine, making the treatment of SUI safe and reliable.

In traditional Chinese medicine theory, SUI is classified as a disease type of 'bladder cough' and 'urinary difficulties,' with its pathological mechanism mainly characterized by deficiency in the root with excess in the branch, usually based on qi deficiency and yang deficiency, while various pathological factors such as phlegm, dampness, and blood stasis intertwine as manifestations; its onset is closely related to the kidneys. This disease manifests in various types, with complex symptoms, mainly showing kidney qi deficiency, lung-spleen qi deficiency, and liver channel depression heat as the main types. In the later stages of SUI, kidney yang deficiency leads to an imbalance in the transformation of bladder qi, where fluids cannot be steamed, resulting in the phenomenon of coughing and urinary incontinence. The Song Dynasty's '*Taiping Hui Min He Ji Ju Fang*' has the earliest record of Qing-e pill, now included in the 'Chinese Pharmacopoeia,' which clearly indicates that Eucommia ulmoides and salt-processed psoralea can guide the medicine into the kidneys, helping to strengthen the function of 'the kidneys govern storage' to consolidate the effect of securing the bladder and stopping urinary leakage. Clinical studies have found that this formula has shown certain efficacy in treating diseases with symptoms of kidney qi deficiency, with the whole formula focusing on warming yang, transforming qi, securing the bladder, and stopping urinary leakage. Based on modern pharmacological studies, Qing-e pill have been shown to promote estrogen production [7-8], and estrogen is an effective treatment for SUI [3]. Therefore, the research team speculates that Qing-e pill may help alleviate clinical symptoms such as urinary leakage caused by increased abdominal pressure in SUI patients, thereby improving their quality of life. However, due to the lack of a clear explanation of the mechanism of Qing-e pill in treating SUI from the perspective of traditional Chinese medicine, their promotion and application in clinical practice face significant challenges.

Network pharmacology combines systems biology and computer science technology to comprehensively analyze and predict the targets and pathways of drugs in diseases, thereby promoting the advancement of treating different diseases with the same treatment. Therefore, this study uses the methods of network pharmacology to deeply analyze the drug components, therapeutic targets, and action pathways of

Qing-e Pill in the treatment of SUI, aiming to provide scientific theoretical support for the clinical use of Qing-e Pill in treating SUI.

2. Materials and Methods

2.1 Information on Chemical Components and Target Acquisition of Qing-e pill

Using the Traditional Chinese Medicine Systems Pharmacology Database and Analysis Platform (TCMSP) [9] (http://ibts.hkbu.edu.hk/LSP/tcmsp.php), we searched for components of Eucommia, ensuring their oral bioavailability (OB) reaches or exceeds 30%, while their drug-likeness (DL) reaches or exceeds 0.18 [10]. After identifying the active components, we used Mol.ID numbers to find the gene targets of single drug components. Compound data was downloaded from the Uniprot (http://www.uniprot.org/) database, and the 'VLOOKUP' function was used to match the target gene names. Finally, our research team provided detailed annotations of the target proteins related to the identified chemical components through the Uniprot (https://www.uniprot.org) database. Ineffective components without target points were filtered out.

Collected garlic, walnut kernel, and psoralea corylifolia components again through the SYMmap database (http://www.symmap.org/), set the screening criteria as OB value ≥ 30%, and used PubChem data (https://pubchem.ncbi.nlm.nih.gov) in combination with SMILES (Simplified Molecular Input Line Entry System). SMILES data can be distributed across various networks, facilitating the creation of SwissTargetPrediction (http://www.swisstargetprediction.ch) and predicting effective targets.

2.2 Search for Potential Therapeutic Targets for SUI

In the GeneCards database (https://www.genecards.org), the OMIM database (https://www.omim.org), and the DisGenet database (https://www.disgenet.org), target genomes closely related to SUI were retrieved for the study. These genomes were then integrated and sorted, with overlapping gene entries removed, ultimately identifying disease targets for SUI. Subsequently, a Venn diagram was created using Venny 2.1.0 (https://bioinfogp.cnb.csic.es/tools/venny/) to analyze the intersection between the targets of Qing-e Pill and the targets for SUI, thereby identifying potential therapeutic targets for SUI treatment with Qing-e Pill.

2.3 Construction of the Active Ingredient-SUI-Target Network for Qing-e pill

By integrating the active ingredients and therapeutic targets of the drug, and importing them into the Cytoscape 3.10.1 software [11], a network diagram of the ingredients and target genes of Qing-e pill was created. Degree centrality and degree distribution were used to determine the relationships and key nodes between each point. In this network, the degree value is often used to evaluate the importance of a node; the number of connections a node has with other nodes is positively correlated with its importance. The shortest path lengths between components were calculated based on degree values, thus obtaining the relative relationships between components and the overall network structure characteristics. Network Analysis software was used to analyze the topological structure, from which numerical data was obtained, and the top five active ingredients were selected as the core components of Qing-e pill for improving SUI.

2.4 Construction of Protein-Protein Interaction (PPI) Networks

As we all know, the STRING database (https://string-db.org/) is a specialized protein database for analyzing known and predicted protein-protein interactions [12]. This study focuses on amino acid residues and uses random sequence search techniques to select candidate genes for enrichment screening from published literature. In the STRING database, a protein interaction network model was designed, consisting of the screened intersecting target proteins. This network structure has a good topological structure and node degree distribution, indicating that this method can effectively predict protein-protein interaction forces and conduct quantitative structure-activity relationship studies. By selecting 'Homo sapiens' as the screening species and setting the medium confidence level to a minimum interaction threshold of 0.4, candidate nodes were clustered to identify key proteins. All other parameters were preset, resulting in a network diagram describing the interactions between proteins.

2.5 GO Enrichment Analysis and KEGG Enrichment Analysis

Studies generally consider the DAVID database (https://david.ncifcrf.gov/) to be a frequently used tool database in the field of bioinformatics [13-14]. To better predict the structure of protein sequences, the research group utilized the significant advantages demonstrated in biology, using co-expression between selected candidate genes and target proteins as the research subject. The cross-targets selected were input into the DAVID database for GO enrichment analysis (including biological processes, cellular components, molecular functions) and KEGG pathway analysis. All possible protein sequence information involved in metabolic pathways was stored in an index table, and then pathways were identified based on the biological characteristics of these proteins. Using GO enrichment techniques, the research group plotted bar charts for three sections. Each region's genes and proteins were annotated with functional and therapeutic information, thereby successfully establishing a data-driven platform for studying and developing the mechanisms of active ingredients in traditional Chinese medicine. Through in-depth research on KEGG pathways, the research team identified pathways related to Qing-e Pill treatment of SUI and accordingly plotted the distribution map of KEGG bubbles. The enrichment quantity of targets can be reflected by the size of the nodes, and a lower P-value indicates higher reliability of the signaling pathway.

3. Results

3.1 Screening Results of Active Ingredients in Qing-e pill

By utilizing the TCMSP database and conducting relevant

literature searches, the basic chemical component information of Qing-e Pill was successfully obtained. Through the screening of OB and DL values, 28 active components in Eucommia, 26 active components in walnut kernels, 13 active components in Psoralea, and 19 active components in garlic were identified. After removing 86 major duplicate active components, 461 target genes were successfully screened. These proteins were standardized through the SwissTargetPrediction database, among which 86 were effective active components. After summarizing and deduplication, a total of 461 unique target genes were ultimately obtained.

3.2 SUI Disease Target Prediction Results

Using 'Stress Urinary Incontinence' as the search keyword in the GeneCards and OMIM databases, we searched for SUI targets. By merging and deduplicating the targets related to SUI in the databases, we successfully identified 2551 disease targets associated with SUI. Subsequently, by cross-referencing the targets of drugs and diseases, we determined 187 potential therapeutic targets of Qing-e Pill for SUI. By intersecting the target genes of 461 compounds with the 2551 SUI target genes, we identified 187 common target genes, as shown in Figure 1.

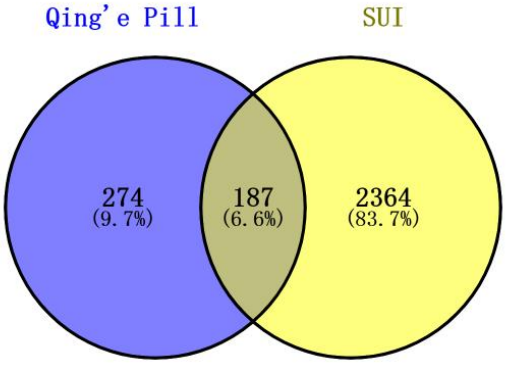

Figure 1: Venn Diagram

3.3 Qing-e Pill Active Ingredients and Their Corresponding Target Network Diagram

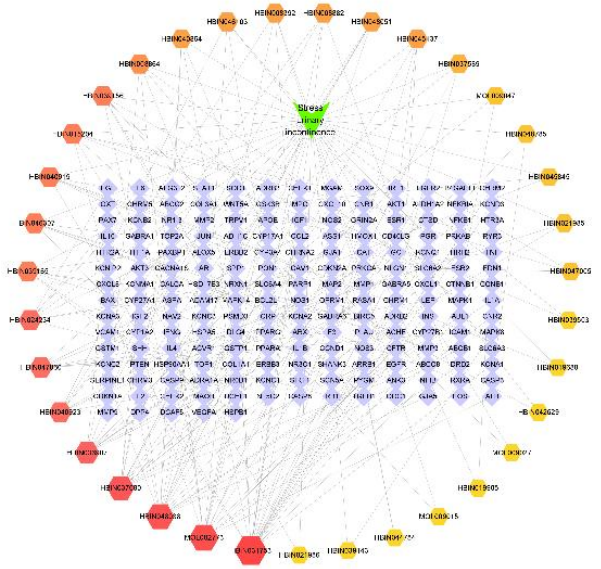

Figure 2: Active ingredients-target interaction network diagram of Qing-e pill

By re-integrating the preliminary data, a network diagram of traditional Chinese medicine-component-target was drawn (Figure 2), ultimately evaluating 461 nodes and 1111 edges. Transparency and node size were assessed, with the degree value chosen as the primary evaluation criterion. The larger the node size, the more prominent its color, resulting in a correspondingly higher degree value, as shown in Figure 2. Among all active components, the top five are considered the main active components: kaempferol, beta-carotene, vitamin B, N-methylcytisine, and nicotinic acid, with evaluations of 25, 20, 18, 16, and 11 respectively.

3.4 Results of PPI Network Construction

The 187 target proteins collected in the early stage were uploaded to the STRING database, thus constructing a protein-protein interaction network, as shown in Figure 3. In the diagram, the nodes represent proteins, and the edges represent functional associations. There are a total of 187 nodes and 3,640 edges, with an average node degree of 38.9 and an average local clustering coefficient of 0.596. The PPI enrichment p-value is less than 1.0e-16. Based on the frequency of gene connections, the top 10 core genes, selected by higher Degree values, are: AKT1, IL6, JUN, TNF, HSP90AA1, ESR1, CTNNB1, EGFR, IL1B, MAPK1. These 10 targets are key targets for the treatment of SUI with Qing-e Pill, as shown in Figure 4.

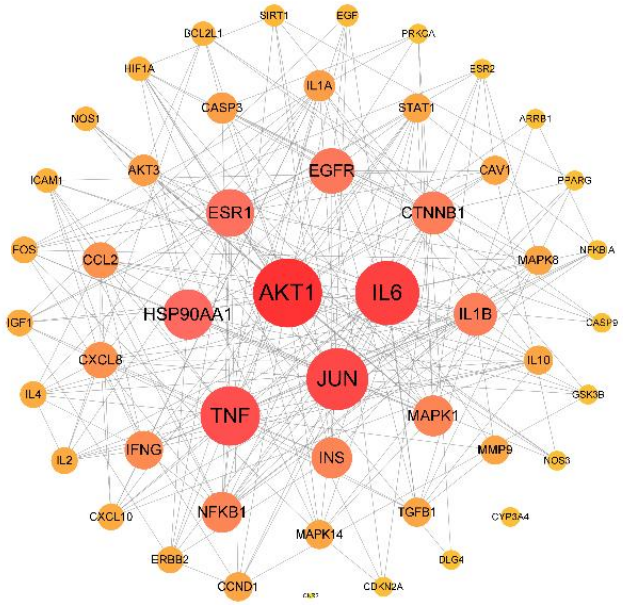

Figure 3: PPI network of Qing-e pill target protein

3.5 GO Functions and KEGG Pathway Enrichment Analysis

The 187 common targets obtained earlier were imported into the DAVID database, and 187 gene sequences were successfully detected. Subsequently, an in-depth GO functional analysis was conducted. Through GO functional analysis, we obtained 89 enrichment results with $P<0.05$. Among these results, there are 3072 Biological Process (BP) terms, 148 Cellular Component (CC) terms, and 250 Molecular Function (MF) terms. These results were sorted by p-value, with the top 10 visualized on the Bioinformatics website (see Figure 4). BP mainly studied the response to lipopolysaccharide, response to molecule of bacterial origin,

and response to metal ion, epithelial cell proliferation, regulation of membrane potential, regulation of epithelial cell proliferation, response to drug, vascular process in circulatory system, response to mechanical stimulus, and regulation of tube diameter. of tube diameter); In CC, it mainly involves the synaptic membrane, postsynaptic membrane, presynaptic membrane, the integral component of the presynaptic membrane, membrane raft, membrane microdomain, integral component of the synaptic membrane, intrinsic component of the presynaptic membrane, and intrinsic component of the synaptic membrane, etc. In MF, it mainly involves gated channel activity, channel activity, passive transmembrane transporter activity, receptor ligand activity, signaling receptor activator activity, voltage-gated cation channel activity, ion channel activity, voltage-gated ion channel activity, voltage-gated channel activity, and cation channel activity. Based on the ranking of P-values, the top 10 entries from biological processes, molecular functions, and cellular components are screened and referenced in Figure 4.

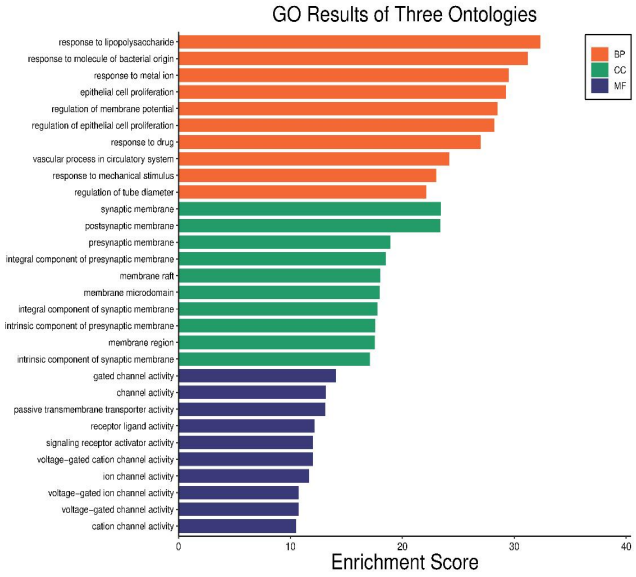

Figure 4: GO analysis of key potential targets against SUI of Qing-e pill

Through KEGG analysis, 264 pathways were successfully identified. The herbal medicine-component-target network diagram in Figure 2 was ranked according to p-value criteria, and the top 10 pathways were visualized (Figure 5). In the diagram, a lower p-value (indicated in red) corresponds to a higher number of enriched genes in the pathway, which implies greater significance. The effectiveness of Qing-e Pill in treating SUI may be related to various signaling pathways, including AGE-RAGE signaling in diabetic complications, fluid shear stress and atherosclerosis, lipid and atherosclerosis signaling pathways, IL-17 signaling pathway, TNF signaling pathway, Chagas disease, and relax in signaling pathway. This suggests that Qing-e Pill can improve SUI symptoms through the combined effects of multiple signaling pathways. Additionally, in the DAVID database, KEGG pathway regulation maps were retrieved, highlighting that key targets are mainly enriched in the atherosclerosis pathway (Figure 6).

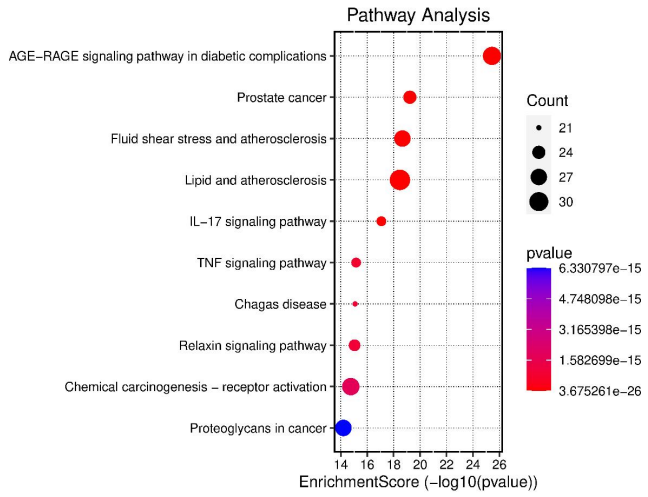

Figure 5: KEGG Pathway Enrichment Analysis Diagram

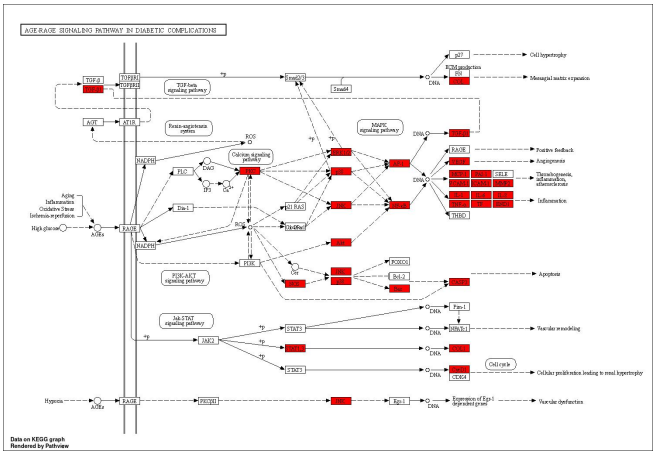

Figure 6: Core Targets and Regulatory Pathways

4. Discussion

In the theoretical system of traditional Chinese medicine (TCM), stress urinary incontinence does not have a specific name, but based on its symptoms, it can generally be classified as 'incontinence,' 'bladder cough,' or 'difficult urination'. TCM believes this condition is often caused by kidney qi deficiency, kidney essence deficiency, or kidney yang deficiency, and is closely related to emotional factors. Treatment should mainly focus on tonifying the kidneys and replenishing essence. SUI is a common form of urinary incontinence, primarily manifesting as involuntary leakage of urine from the urethra after actions that may cause a sudden increase in abdominal pressure, such as coughing, exercising, or laughing. In severe cases, this may also occur during daily activities, directly reducing the patient's health status and potentially harming their psychological well-being [15-17]. From the perspective of TCM, the causes and mechanisms of SUI are spleen and kidney qi deficiency and weakened control, thus the treatment plan should emphasize tonifying the kidneys, consolidating control, and strengthening the spleen and benefiting qi. The '*Jingyue Complete Works with Annotations*' states: 'This condition may be due to excessive labor during childbirth, sinking of heat due to depression, or qi

deficiency leading to prolapse. The treatment should mainly focus on raising yang, replenishing qi, and consolidating true yin' [18]. For the treatment of 'bladder cough,' starting with the accumulation of water in the Bladder meridian of the Taiyang and using Wuling Powder is not uncommon [19-20]. However, the use of Qing-e pill is rarely seen. Qing-e pill use Eucommia as the principal ingredient, which is mild in nature and flavor, and has the effects of regulating and stabilizing the Chong and Ren meridians, tonifying the liver and kidneys, and strengthening muscles and bones. According to the *Shen nong Ben cao Jing* [21], 'Eucommia can treat lumbar and spinal pain, tonify the middle, enhance vital energy, strengthen muscles and bones, boost willpower, and relieve itching and dampness in the genital area, as well as residual urine dripping.' Psoralea, being warm in nature and entering the spleen and kidney meridians, can warm the spleen, tonify the kidneys, consolidate essence, reduce urination, and help the kidneys absorb Qi to alleviate asthma, acting as a minister drug. The *Ben Cao Jing Shu* [22] also mentions that it can warm and tonify kidney Yang, warm kidney water, and spleen earth, thus enhancing the Yang of the spleen and kidneys. Additionally, salt-roasting can guide the drug to the kidneys directly reaching the lower part of the body. Garlic, warm in nature, can warm and promote heart Yang, facilitating the connection between the heart and kidneys. Walnut kernels, also warm in nature, can tonify the kidneys and consolidate essence, and they warm the lungs, acting as an adjuvant. The combination of these herbs achieves the effects of warming the kidneys, assisting Yang, consolidating the bladder, and stopping leakage. Modern pharmacological studies have found that Eucommia can tonify the liver and kidneys, strengthen muscles and bones, and contains flavonoids and other substances that have anti-aging and stress-relief effects [23]. Psoralea corylifolia contains numerous active components, including psoralen, isopsoralen, and bakuchiol in the coumarin series; bavachin in the flavonoid class; and bakuchiol in the monoterpenophenol class, all of which exhibit estrogen-like effects [24]. Walnut kernels can warm the lungs and tonify the kidneys, with pharmacological studies showing that they are rich in fatty acids and linoleic acid, which have good antioxidant effects [25]. Garlic, with its pungent and warm properties, can detoxify and unblock the meridians. Allicin and garlic oil in garlic have anti-inflammatory and vasodilatory effects [26]. Therefore, Qing-e pill are promising as a new treatment option for kidney qi deficiency-type stress urinary incontinence (SUI). This study used various data on the chemical composition, target genes, and pathways of Qing-e pill to build a network for functional analysis and systematically predict their potential molecular mechanisms on the multi-component and multi-gene targets of SUI.

Currently, estrogen replacement is one of the main treatments for SUI in Western medicine. The use of selective estrogen receptor modulators can effectively promote the growth of the urethral epithelium, enhance the blood supply to the venous plexus of the urethral mucosa, influence the function of the connective tissue around the bladder and urethra, and increase the tension of the pelvic floor muscles [3]. Yang RP et al. [27] and Sun GY et al. [28] found that after studying the estrogen-like effects and kidney yang deficiency treatment efficacy of different purified parts of Qing-e pill, the decoction of the whole Qing-e pill exhibited significant estrogen-like effects, with particularly notable efficacy in treating kidney yang deficiency. This study shows that Qing-e pill contain 86 active ingredients, with kaempferol, beta-carotene, vitamin B, N-methylcytisine, and nicotinic acid ranking high after screening for potency. Kaempferol, a bioflavonoid found in Eucommia, has ERα and ERβ agonist abilities, participates in the estrogen signaling pathway, improves neuronal function, and inhibits cell apoptosis and autophagy [29-30]. In addition, this substance also plays a role in regulating signaling pathways such as NF-κB and Notch, and it exhibits multiple pharmacological effects including anticancer, antioxidant, antiviral, anti-inflammatory, antibacterial, and immune-boosting properties [31-33]. Beta-carotene, another active component found in Eucommia, plays an important role in neurodevelopment and anti-apoptosis [34-35]. Research by Chen et al [36] indicates that beta-carotene can trigger antioxidant response elements and transcription factors such as NRF2, while also enhancing downstream targets containing antioxidant response elements, thereby reducing oxidative stress reactions. Vitamin B plays a crucial role in the synthesis of nucleic acids, proteins, and lecithin, promoting the formation of myelin and the regeneration of axons, which are indispensable for the repair of damaged nerve cells [37]. N-methylcytisine, a tricyclic quinolizidine alkaloid extracted from garlic, possesses various pharmacological activities including hypoglycemic, analgesic, and anti-inflammatory effects [38-39]. Niacin is a key active substance in garlic. Besides its anti-inflammatory and antioxidant functions, it also plays a role in lipid metabolism by lowering cholesterol and is closely linked to estrogen signaling pathways [40-41]. Oxidative damage and the decline in estrogen levels are considered critical pathological causes of SUI. Esculetin, β-carotene, Vitamin B, N-methylcytidine, and Niacin have significant antioxidant and anti-aging effects, making it a key active ingredient in the treatment of kidney qi deficiency-type SUI.

In the PPI network analysis, the core targets identified were AKT1, IL6, JUN, TNF, and HSP90AA1. AKT serine/threonine kinase 1 (AKT1) plays a critical role in many cellular activities, including cell proliferation and apoptosis. Numerous studies have shown that AKT1 is closely associated with estrogen signaling pathways and provides protective effects on neurons after ischemic injury [42], which is important for improving the repair of SUI nerve injuries. Interleukin 6 (IL-6) is the founding cytokine of the neurotrophin family, produced by neurons and glial cells, and signals as a neurocytokine under injury and regeneration conditions [43]. The expression of IL-6 is usually restricted to traumatic conditions, providing temporary nutritional support to initiate repair responses. A study indicates that preconditioning damage before sciatic nerve injury can stimulate IL-6 induced GAP-43 upregulation, subsequently enhancing the regeneration of damaged nerves. The results show that the nerve regeneration response is weakened in IL-6 KO mice, confirming the crucial role of IL-6 in regulating nerve regeneration [44]. Jun is a key transcription factor involved in Schwann cell remodeling, capable of activating Schwann cells to differentiate into myelinating Schwann cells with regenerative functions. Research demonstrates [45] that acupuncture, through needle-induced mechanical signals, reduces Jun phosphorylation, increases the expression of the apoptosis-related protein Bcl-2 in nerve cells, and the

increased expression of Bcl-2 can feedback to affect the JNK signaling pathway. This exerts an inhibitory effect on neuron apoptosis, preventing the occurrence of SUI. Tumor necrosis factor (TNF) is a cytokine that can cause cell death. It is expressed in various tissues and is related to the body's immune response, inducing the host to produce corresponding antibodies to resist foreign pathogenic microorganisms. Yoshikawa and his team [46] observed a significant increase in TNFR-1, IL6, MMP-9, and collagen in model rats during simulated vaginal dilation and parturition-related SUI experiments. This indicates that these proteins play a crucial role in maintaining normal pregnancy processes. HSP90, as a key chaperone protein, is mainly responsible for ensuring proper protein folding inside cells, with two main subtypes in mammals: HSP90AB1 and HSP90AA1. As an inducible molecular chaperone, it is involved in stress responses [47-48]; while the HSP90AA1 protein is a key factor in exacerbating synaptic degeneration through glial cells, closely related to SUI-related pelvic nerve damage [49]. The etiology of SUI is related to factors such as vaginal delivery, menopause, and aging, which can lead to metabolic imbalance, oxidative stress, and hypoxia in pelvic floor nerve and muscle cell matrix, causing various pathological damages. GO functional enrichment analysis involves multiple biological processes, including responses to lipopolysaccharides, bacterial-derived molecules, metal ions, epithelial cell proliferation, membrane potential regulation, all of which are closely related to the pathogenic mechanisms of SUI perineal nerve damage. Enrichment analysis of the KEGG pathway reveals involvement in various pathways, including tumor, inflammation, and endocrine systems. Shinohara et al[50] found that TNF-α has an inhibitory effect on urethral smooth muscle cells, suggesting that inhibiting TNF-α may have some effect on potential treatments for urinary incontinence. The AGE-RAGE signaling pathway is closely associated with diabetes and its complications, and in the study by SAKAKIBARA et al[51], they found that bladder dysfunction in diabetic patients is related to peripheral nerve damage, and high glucose levels may affect the function of perineal and sacral nerves. The mechanism of pelvic autonomous nerve damage is currently unclear, but most researchers believe it may be due to the interaction of multiple factors. The anal sphincter is a core structure supporting pelvic floor function, controlled by perineal nerves. If there is an abnormality in neural function, it may lead to muscle malnutrition, atrophy, and reduced contraction ability, ultimately resulting in symptoms of urinary incontinence. Akbar A et al[36] indicated through a study on the prevalence of urinary incontinence and the racial differences in related diseases such as atherosclerosis that there is a correlation between atherosclerosis and SUI. Additionally, potential therapeutic target genes for SUI are concentrated in lipid and atherosclerosis signaling pathways, and obesity is considered a common risk factor for SUI. Therefore, this study suggests that Qing-e Pill may effectively treat SUI by reducing lipid accumulation in the patient's body, thereby repairing nerve damage, improving obesity, alleviating inflammation, and reducing oxidative stress.

Overall, this study extensively explores the multi-component and multi-target effects of Qing-e Pill in the treatment of Kidney Qi Deficiency type Stress Urinary Incontinence (SUI), and identifies multiple potential pathways that may impact SUI. In particular, Qing-e Pill may accelerate the growth of urinary tract epithelium, restore the function of periurethral connective tissue, and improve damage to the pelvic nerve, possibly by stimulating estrogen production, further demonstrating the effectiveness of Qing-e Pill in clinically treating Kidney Qi Deficiency type SUI. Additionally, it was found to have anti-inflammatory and antioxidant stress effects, providing new evidence for the important clinical significance of Qing-e Pill in the prevention and treatment of diseases. This research was conducted on a theoretical basis, and further experimental verification is needed in various aspects such as cells and animals.

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