Background. Although traditional Chinese medicine (TCM) has good efficacy in the treatment of mild cognitive impairment (MCI), especially memory improvement and safety, its substance basis and intervention mechanism are particularly complex and unknown. Therefore, based on network pharmacology and data mining, this study aims to explore the rules, active ingredients and mechanism of TCM in the treatment of MCI. Methods. By searching the GeneCard, OMIM, DisGeNET and DrugBank databases, we obtained the critical targets associated with MCI. We matched the components and herbs corresponding to the important targets in the TCMSP platform. Using Cytoscape 3.7.2 software, we constructed a target-component-herb network and conducted a network topology analysis to obtain the core components and herbs. Molecular docking was used to preliminarily analyze and predict the binding activities and main binding combinations of the core targets and components. Based on the analysis of the properties, flavor and meridian distribution of herbs, the rules of herbal therapy for MCI were summarized. Results. Twenty-eight critical targets were obtained after the screening. Using the TCMSP platform, 492 components were obtained. After standardization, we obtained 387 herbs. Based on the target-composition-herb network analysis, the core targets were ADRB2, ADRA1B, DPP4, ACHE and ADRA1D. According to the screening, the core ingredients were beta-sitosterol, quercetin, kaempferol, stigmasterol and luteolin. The core herbs were matched to Danshen, Yanhusuo, Gancao, Gouteng and Jiangxiang. It was found that the herbs were mainly warm in nature, pungent in taste and liver and lung in meridian. The molecular docking results showed that most core components exhibited strong binding activity to the target combination regardless of the in or out of network combination. Conclusion. The results of this study indicate that herbs have great potential in the treatment of MCI. This study provides a reference and basis for clinical application, experimental research and new drug development of herbal therapy for MCI.

1. Introduction

In 1997, Petersen in the United States first proposed the diagnostic standard of mild cognitive impairment (MCI), which is mismatched between memory loss and normal aging but relatively reserved in other cognitive functional domains [1]. This standard is mainly used to describe MCI types that eventually transform into AD clinically [2]. In 2011, the National Institute on Ageing-Alzheimer’s Association Task Force proposed new guidelines stating that MCI, as the second stage in the course of AD, should be classified under the AD concept and not as a separate disease [3]. Currently, mild cognitive impairment, which is a transitional condition between normal aging and dementia, is characterized by a progressive decline in memory and other cognitive functions accompanied by a slight impairment in the instrumental living ability [2, 4]. In terms of epidemiology, a systematic review of 123,766 patients showed that the prevalence of MCI among the elderly in China was approximately 15.4%, which varied depending on the demographics, lifestyle, morbidity, screening tools and diagnostic criteria [5]. MCI is an important risk factor for
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dementia. Studies have shown that approximately 10 to 15 percent of MCI patients progress to dementia each year compared with 1 to 2 percent in the normal elderly population and age-matched controls [6, 7]. The risk of AD in MCI patients was 3.17 times higher than that in the normal elderly, and 5-year and 10-year MCI follow-up studies showed that the probability of MCI converting to AD was 33% and 55.5%, respectively [8, 9]. Therefore, for MCI, early intervention is an important way to effectively delay or block cognitive decline and prevent the occurrence of dementia.

MCI interventions aim to prevent, delay or even reverse the process of AD transformation. According to the latest international MCI guidelines, currently, no drugs or foods are approved by the Food and Drug Administration (FDA) for the treatment of MCI [10–12]. Additionally, relevant evidence-based studies have shown that cholinesterase inhibitors do not lead to significant improvement in cognitive function in MCI; in contrast, the early application of cholinesterase inhibitors may cause cognitive impairment [13, 14]. Traditional Chinese medicine (TCM) has a long history of treating memory loss. Pharmacological studies and clinical trials have confirmed that TCM, including single drugs and compound TCM preparations, have a positive effect on improving cognitive impairment and enhancing memory function [15, 16]. For example, in a 24-month randomized placebo-controlled study, Bushen capsules, a Chinese herb compound, improved multiple cognitive domains and increased functional local and global connectivity in the right precuneus default mode network [17]. In patients with amnestic mild cognitive impairment, Qing-gongshoutao (QGST) pill had significant benefits in improving the overall cognitive ability and reducing the rate of progression of Alzheimer’s disease. Relevant review studies have shown that some active extracts or components of Chinese herbs, such as ginseng, Polygala, Schisandra sphenanthera, Andrographis paniculata, Gynostemma pentaphylli herba and Lycium barbarum, can prevent and treat AD by reducing Aβ production, inhibiting cell apoptosis, inhibiting neuroinflammation, regulating autophagy, resisting oxidative stress and improving mitochondrial dysfunction [18, 19].

Network pharmacology is a new analysis that reveals the multidimensional mechanism between drugs and diseases by constructing and analyzing the complex network of “drug-gene-target-disease” from the perspective of the system level and biological network overall [20–22]. This approach is widely used in the discovery of drugs and active compounds of TCM, the interpretation of the mechanism of action of traditional Chinese medicine compounds, the compatibility of prescriptions, etc. [23]. Network pharmacology aims to explore the interaction between drugs and the body from a systematic and holistic perspective, which is consistent with the characteristics of integration and systematization and consideration of the interaction of TCM [24]. Network pharmacology not only provides new ideas for the study of the complex systems of TCM but also provides a new method for rational clinical drug use and new drug development [25]. Therefore, on the basis of network pharmacology, this study screened important targets related to MCI through disease databases and further identified and analyzed the corresponding compounds and herbs. By analyzing the complex network of targets, components and herbs, we explored the core components and herbs important for the treatment of MCI. The results of this study are expected to provide new ideas and a basis for the development of new therapies and drugs for MCI. The overall research idea of this study is shown in Figure 1.

2. Materials and Methods

2.1. Collection and Screening of MCI Disease Targets. We used the GeneCard [26] (https://www.genecards.org/), OMIM [27] (http://www.omim.org/), DisGeNET [28] (http://www.disgenet.org/) and DrugBank [29] databases to search and access MCI disease targets. In DisgeNet, the confidence score is determined by the number of times that the gene-disease association appears repeatedly in all data sources, reflecting the reliability of the gene-disease association [30]. The GeneCard database established a correlation ranking of genes and diseases through the Gifts algorithm [31]. Based on the relevance score, targets with a higher relevance degree can be further screened from many targets corresponding to specific diseases.

2.2. Acquisition of Candidate Components Corresponding to Targets. The UniProt database was used to obtain the protein names of the targets. TC MSP (http://ibts.hkbu.edu.hk/LSP/tcmsp.php) was used to obtain the targets corresponding to potential active ingredients. After setting the ADME screening conditions to oral bioavailability (OB) ≥30% and drug-like property (DL) ≥0.18 [32], the candidate ingredients were obtained. The targets and candidate components were imported into Cytoscape 3.7.2 software to construct a target-component network. We carried out a network topology analysis of the target-component network to obtain the core components and targets.

2.3. Herbal Acquisition and Target-Component-Herb Network Construction. Herbs with candidate ingredients were collected from the TC MSP. The names of herbal medicines are standardized and unified in accordance with the Chinese Pharmacopoeia (2020), Traditional Chinese Medicine (“Thirteenth Five-Year Plan” textbook) and Chinese Clinical Medicine Dictionary [33]. Furthermore, we obtained the characteristics of Chinese herbal medicines, including their properties, flavor, and channel tropism, to obtain frequency statistics and analyze and summarize the rules. We performed a network topological analysis based on the construction of a target-component-herb network to identify the key nodes and evaluate the efficacy of herbs and candidate components in the treatment of MCI.

2.4. Molecular Docking of Core Target Components. The MOL2 structure of the core components (ligand) was downloaded from the TC MSP database and saved as a “PDBQT” lattice document after setting the rotatable key
through AutoDock Tools. We downloaded the core target protein structure from the PDB database (http://www.rcsb.org/) and used PyMOL 1.8 software to remove water molecules and isolate the primary ligand. After preservation, the protein structure was imported into AutoDock Tools 1.5.6 software to hydrogenate, calculate the total charge, and set the atomic type, and the file was saved in “PDBQT” format. Finally, AutoDock4 software was used for molecular docking to calculate the minimum binding energy between the active ingredients and the targets. PyMOL 2.3 and Ligplot 2.2 were used for visualization and the docking conformation analysis.

3. Results

3.1. Acquisition of Targets in MCI. Using the GeneCard database, we obtained 8019 targets related to MCI. Due to the large number of targets, we screened targets with strong relationships by using an association score greater than 0.2. Ultimately, 97 targets were acquired. After screening with a score greater than 0.02, we obtained 138 targets in the DisGeNET database. Thirty-three and 100 targets were obtained from the DrugBank database and OMIM database, respectively. After combining the targets obtained from the above four databases and eliminating duplications, in total, 190 targets were obtained. Among these 190 targets, in total, 28 underlying targets were successfully matched with compounds that met the ADME criteria as shown in Table 1.

| Gene symbol | Uniprot ID | Protein name |
|-------------|------------|--------------|
| IL6         | P05231     | Interleukin-6 |
| BACE1       | P56817     | Beta-secretase 1 |
| IL1B        | P01584     | Interleukin-1 beta |
| TNF         | P01375     | Tumor necrosis factor |
| ADIPOQ      | Q15848     | Adiponectin |
| RUNX1T1     | Q06455     | Protein CBFA2T1 |
| ACHE        | P22303     | Acetylcholinesterase |
| SOD1        | P00441     | Superoxide dismutase [Cu–Zn] |
| SLC6A3      | Q01959     | Sodium-dependent dopamine transporter |
| IL10        | P22301     | Interleukin-10 |
| MTOR        | P42345     | Serine/threonine-protein kinase mTOR |
| HTT         | P42858     | Huntingtin |
| NOS3        | P29474     | Nitric oxide synthase, endothelial |
| COL1A2      | P08123     | Collagen alpha-2(I) chain |
| GLB1        | P16278     | Beta-galactosidase |
| DPP4        | P27487     | Dipeptidy peptidase 4 |
| TP53        | P04637     | Cellular tumor antigen p53 |
| VEGFA       | P15692     | Vascular endothelial growth factor A |
| ADRB1       | P08588     | Beta-2 adrenergic receptor |
| ADRB2       | P07350     | Beta-2 adrenergic receptor |
| ADRA1A      | P35348     | Alpha-1A adrenergic receptor |
| CYP3A4      | P08684     | Cytochrome P450 3A4 |
| ADRA2C      | P18825     | Alpha-2C adrenergic receptor |
| ADRA2B      | P18089     | Alpha-2B adrenergic receptor |
| ADRA2A      | P08913     | Alpha-2A adrenergic receptor |
| ADRA1D      | P25100     | Alpha-1D adrenergic receptor |
| ADRA1B      | P35368     | Alpha-1B adrenergic receptor |

3.2. Acquisition of Potential Compounds and Construction of the Target-Component Network. After the ADME condition screening, 492 potential compounds were identified from 28 targets in the TCMSP database. We constructed a target-component network by using 28 underlying targets and 492 potential components as shown in Figure 2. There are 745 nodes and 2026 edges in the network diagram. The red nodes in the network represent the targets, the green nodes represent the components, and the edges represent the relationships between the targets and components. The
A topological analysis of the network showed that the top 5 targets were ADRB2, ADRA1B, DPP4, ACHE and ADRA1D, and their corresponding degree values were 411, 329, 319, 191 and 171, respectively. Therefore, the above targets play an important role in improving cognitive impairment and are important targets for TCM intervention for mild cognitive impairment.

### 3.3. Construction of Target-Component-Herbal Networks

In total, 449 herbs containing candidate ingredients were obtained from the TCMSP database. After standardization according to the Chinese Pharmacopoeia (2020), Traditional Chinese Medicine (“Thirteenth Five-Year Plan” textbook) and Chinese Clinical Medicine Dictionary, we finally obtained 387 herbs. We constructed a target-component-herb network using Cytoscape 3.7.2 software to explore the interrelationships of the network. The target-component-herb network contains 1189 nodes with 4173 edges. The network topology analysis showed that the top 10 herbs ranked by degree were Gancao (Glycyrrhiza uralensis fisch), Danshen (Salvia miltiorrhiza bunge), Yanhusuo (Corydalis yanhusuo), Gouteng (Uncaria rhynchophylla), Jiangxiang (Dalbergia odorifera), Wuzhuyu (Tetradium ruticarpum), Leigongteng (Tripterygium wilfordii hook.f.), Huangqin (Scutellaria baicalensis georgi), Kushen (Sophora flavescens aiton) and Lianqiao (Forsythia suspensa). As shown in Figure 3, these herbs contain 59, 41, 37, 24, 22, 19, 18, 17, 16, and 16 components. Due to the large number of components in the network, we identified the components with a strong correlation by calculating the median of their degree values. After two calculations, the median was 4 and 6, respectively. Therefore, components with degrees greater than or equal to 12 are considered potential core components in our study. The top 5 components are beta-sitosterol, quercetin, kaempferol, stigmastanol and luteolin, and the remaining components are shown in Table 2.

To more clearly show the relationship among the targets, compounds and herbs, we selected targets, compounds and herbs with a degree greater than 8 to reconstruct the target-compound-herbal network as shown in Figure 4.
Using ingredients as a bridge, we constructed a target-herb network to explore the relationship between targets and herbal medicine. The results of the network analysis showed that the herbs with the most targets were Danshen (Salvia miltiorrhiza bunge), Yanhusuo (Corydalis yanhusuo), Gancao (Glycyrrhiza uralensis fisch), Gouteng (Uncaria rhynchophylla), Jiangxiang (Dalbergia odorifera), Wuzhuyu (Tetradium ruticarpum), Yangjinhua (Datura metel L.), Banzhilian (Scutellaria barbata D. don), Kudiding (Corydalis bungeana turcz.) and Huangbai (Phellodendron amurense rupr.). As shown in Figure 5, their degree values are 154, 152, 134, 103, 69, 65, 60, 59, 56, and 56. Therefore, based on

| Mol ID     | Mol name             | Degree | OB    | DL  |
|------------|----------------------|--------|-------|-----|
| MOL000358  | Beta-sitosterol      | 246    | 36.91 | 0.75|
| MOL000098  | Quercetin            | 201    | 46.43 | 0.28|
| MOL000422  | Kaempferol           | 139    | 41.88 | 0.24|
| MOL000449  | Stigmasterol         | 138    | 43.83 | 0.76|
| MOL000006  | Luteolin             | 98     | 36.16 | 0.25|
| MOL000354  | Isoflavone           | 42     | 49.60 | 0.31|
| MOL002773  | Beta-carotene        | 31     | 37.18 | 0.58|
| MOL004328  | Naringenin           | 24     | 59.30 | 0.21|
| MOL001689  | Acacetin             | 24     | 34.97 | 0.24|
| MOL000392  | Formononetin         | 23     | 69.67 | 0.21|
| MOL000546  | Diosgenin            | 18     | 80.88 | 0.81|
| MOL000296  | Hederagenin          | 17     | 36.91 | 0.75|
| MOL001439  | Arachidonic acid     | 16     | 45.57 | 0.20|
| MOL002881  | Diosmetin            | 16     | 31.14 | 0.27|
| MOL000173  | Wogonin              | 15     | 30.68 | 0.23|
| MOL003044  | Chryseriol           | 15     | 35.85 | 0.27|
| MOL001749  | Zinc03860434         | 15     | 43.59 | 0.35|
| MOL002879  | Diop                 | 15     | 43.59 | 0.39|
| MOL001941  | Ammiinid             | 14     | 34.55 | 0.22|
| MOL002714  | Baicalein            | 14     | 33.52 | 0.20|
| MOL002322  | Isovitexin           | 13     | 31.29 | 0.71|
| MOL000787  | Fumarine             | 13     | 59.26 | 0.83|
| MOL004545  | Berberine            | 13     | 36.86 | 0.78|
| MOL000471  | Aloe-emodin          | 12     | 83.38 | 0.24|
| MOL001735  | Dinatin              | 12     | 30.97 | 0.27|
| MOL000217  | (s)-Scoulerine       | 12     | 32.28 | 0.54|
| MOL005406  | Atropine             | 12     | 45.97 | 0.19|
| MOL000785  | Palmatine            | 12     | 64.60 | 0.65|

Table 2: Information of the potential core components (degree ≥ 12).

Figure 4: Target-component-herbal network diagram.
the results of the above network analysis, we speculate that the abovementioned herbs play a very important role in the treatment of MCI.

3.4. Analysis of the Properties, Flavor and Meridian Distribution of Herbal Medicine. We analyzed the properties, taste and meridian tropism of 387 herbs that could interfere with MCI. The results showed that herbs with a bitter, pungent or sweet taste accounted for 81.22%; among these herbs, bitter herbs had the highest frequency, followed by pungent and sweet herbs. Most herbs used to treat MCI are warm, cold, or mild-natured. The results of the meridian tropism analysis showed that among the 387 herbs, those belonging to the liver meridian were the most frequent, accounting for 22.66%. The proportions of herbs belonging to the lung meridian, stomach meridian and spleen meridian were 17.5%, 12.64% and 11.41%, respectively. The results are presented in Table 3 and Figure 6.

3.5. Molecular Docking Results. In total, 140 receptor–ligand combinations were obtained by the molecular docking of 28 core components with five core targets, namely, beta-2 adrenergic receptor (ADRB2), alpha-1B adrenergic receptor (ADRA1B), dipeptidyl peptidase 4 (DPP4), acetylcholinesterase (ACHE) and alpha-1D adrenergic receptor (ADRA1D). The lower the binding energy (affinity), the better the docking effect. In general, a binding energy (affinity) less than −5.0 kcal/mol indicates good binding activity, while a binding energy less than −7 kcal/mol demonstrates exceptionally strong binding activity. The affinity of 65 receptor–ligand combinations was between −7 kcal/mol and −5 kcal/mol, accounting for 46.43%. There were 39 groups with an affinity less than −7 kcal/mol, accounting for 27.68%; among these, diosgenin (MOL000546) had the lowest affinity with the ADRA1D target. Therefore, the molecular docking results showed that 74.29% of the receptor–ligand combinations had good binding ability. The molecular docking results are shown in a heatmap (Figure 7).

Of the 140 combinations, 39 combinations existed in the target-compound network. Among the 39 combinations, there were 27 groups with binding energies between −7 kcal/mol and −5 kcal/mol and 5 groups with binding energies less than −7 kcal/mol, indicating that most combinations had good binding activity. To some extent, the results support the reliability of the interaction between the components and targets in the target-compound network.

The molecular docking results show that there are 101 new combinations outside the target-component network. The affinity of 72 new combinations was less than −5 kcal/mol, indicating good docking activity. Among the 72 new combinations, the top 5 combinations with the strongest combination ability were ADRA1D-diosgenin (−10.45 kcal/mol), ADRA1D-beta-sitosterol (−9.72 kcal/mol), ADRA1D-stigmasterol (−9.63 kcal/mol), ADRA1D-hederagenin (−9.19 kcal/mol) and DPP4-diosgenin (−8.82 kcal/mol). The binding ability of these 5 combinations is better than that of most combinations in the target-compound network, indicating that these combinations are more likely to have strong drug-target relationships. Therefore, the docking results can provide a reference for the subsequent experimental screening and design of relevant Chinese medicines and components.

Regarding the combinations in the network, five ideal combinations were selected by considering the molecular docking affinity value and the degree of the target-composition-herb network as shown in Figures 8(a)–8(e). Regarding the combinations outside the network, we selected 5 ideal combinations according to the strength of the combination ability as shown in Figures 8(f)–8(j).

4. Discussion

It is of great clinical significance to explore the pathogenesis of MCI in relation to TCM and Western medicine for the prevention and treatment of dementia. There is no exact name for MCI in Chinese medicine. According to its core symptoms of memory loss, MCI can be classified as "forgetfulness" in Chinese medicine. According to the theory of TCM, the main pathogenesis of MCI is the obstruction of brain collateral, an underfilled brain marrow, mind disusing and the deactivation of mental machinery [15]. Western medicine believes that the Aβ neurotoxicity mechanism, Tau protein hyperphosphorylation mechanism, cholinergic mechanism, oxidative stress injury mechanism, cellular inflammatory factors and other mechanisms play an important role in the pathogenesis of MCI [34–36].

4.1. Core Targets. The results of the target-component network analysis showed that ADRB2, ADRA1B, DPP4, ACHE and ADRA1D played a key role in the treatment of mild cognitive impairment. ADRB2, also known as β 2-adrenergic receptor (β2AR), is a subtype of β-adrenergic receptor that is mainly distributed in the hippocampus and cortex in the brain and is associated with memory formation [37, 38]. Studies have shown that the activation of β2AR can affect learning and memory function by promoting various forms of long-term enhancement (LTP) [39–41]. Meanwhile, the activation of β2ARs can also overcome the adverse effects of Aβ on LTP [42]. Furthermore, it has been shown that blocking β2-AR exacerbates cognitive deficits and
reduces dendrite branching in AD mice and increases Aβ accumulation by enhancing APP phosphorylation [43]. Studies have shown that α-1B knockout mice exhibit impaired spatial learning of novelty and exploration [44], which is closely related to the α-1B adrenergic receptor-mediated norepinephrine pathway. In terms of nonspatial memory function, α-1B knockout mice show a decrease in short-term delay and a significant decrease in long-term delay in a passive avoidance test, suggesting that alpha (1B)-AR may be involved in the regulation of memory consolidation and fear-driven exploration [45, 46]. Dipeptidyl peptidase 4 (DPP4) is a multifunctional exopeptidase that plays a key role in GLP-1 degradation [47], inflammation [48], and oxidative stress responses [49], which are closely associated with the onset of cognitive decline [50, 51]. DPP4 inhibitors have been shown to control blood glucose levels and prevent the exacerbation of cognitive impairment in older type 2 diabetes patients with mild cognitive impairment [52]. Acetylcholinesterase (AChE) is involved in inflammatory reactions, neuronal apoptosis, oxidative stress and the aggregation of pathological proteins, which are closely related to the pathogenesis of neurodegenerative diseases [53]. Studies have shown that low doses of donepezil (2.5 mg/d) can improve cognitive function, especially memory function, in patients with aMCI [54]. ADRA1D is not involved in spatial learning and memory but plays an important role in attention and working memory [55]. The above studies indicate that the above targets play an important role in improving cognitive impairment and are the preferred targets for TCM treatment of mild cognitive impairment.

4.2. Core Components. By analyzing the target-composition-herbal network, the core ingredients we obtained included beta-sitosterol, quercetin, kaempferol, stigmasterol and luteolin. Beta-sitosterol, a phytosterol that can easily penetrate the blood–brain barrier and accumulate in the brain, alleviates memory and behavior deficits by inhibiting cholinesterase-mediated acetylcholine degradation [56]. The evidence suggests that β-sitosterol improves memory and learning disabilities and may reduce Aβ deposition in amyloid protein precursor/presenilin 1 (APP/PS1) double transgenic mice [57]. Quercetin is a flavonoid that has been shown to have a wide range of activities against a variety of diseases and disorders. Quercetin has biological effects, such as anti-apoptosis, inhibition of oxidative stress, inflammation and promotion of neurogenesis, and has potential

| Flavor           | Frequency | Proportion (%) | Properties   | Frequency | Proportion (%) |
|------------------|-----------|----------------|--------------|-----------|----------------|
| Bitter           | 4140      | 33.47          | Warm         | 1975      | 24.90          |
| Pungent          | 3154      | 25.50          | Cold         | 1806      | 22.77          |
| Sweet            | 2752      | 22.25          | Mild-natured | 1514      | 19.09          |
| Astringent       | 643       | 5.20           | Slight cold  | 1152      | 14.52          |
| Slightly bitter  | 576       | 4.66           | Cool         | 754       | 9.50           |
| Sour             | 537       | 4.34           | Slight warm  | 494       | 6.23           |
| Salty            | 222       | 1.79           | Hot          | 208       | 2.62           |
| Light            | 173       | 1.40           | Great cold   | 25        | 0.32           |
| Slightly pungent | 80        | 0.65           | Great hot    | 4         | 0.05           |
| Slightly sweet   | 65        | 0.52           |              |           |                |
| Slightly sour    | 28        | 0.22           |              |           |                |

**Figure 6:** The meridian distribution of herbs.
therapeutic effects in various neurodegenerative diseases [58]. Experimental studies have shown that quercitin can improve cognitive deficits and enhance learning and memory ability, which is related to a reduction in senile plaques and improvement in mitochondrial dysfunction, and has antioxidant and anti-apoptosis properties [59, 60]. Furthermore, quercitin ameliorates cognitive impairment in aging mice by inhibiting NLRP3 inflammasome activation [61]. Kaempferol, as a flavonoid, has been recognized as having antioxidant, anti-inflammatory and antineurotoxic properties [59, 60]. Experimental studies have shown that quercitin can improve cognitive impairment in chronic cerebral hypoperfusion rats by scavenging oxygen free radicals, enhancing the antioxidant capacity, reducing the production of lipid peroxides, and inhibiting the inflammatory response of the cerebral cortex and hippocampus induced by chronic cerebral hypoperfusion [68]. In summary, the above core ingredients can be used for the treatment of mild cognitive impairment and have the potential for further drug development.

4.3. Herbal Medicine. Regarding the unique characteristics of herbal medicine, namely, the performance and function of the medicine, there are four properties, five flavors and meridian tropism. The results showed that the herbal medicines with therapeutic effects on MCI were mainly bitter, spicy and sweet in taste and warm in nature. The theory of meridian tropism reflects the selective effect of herbal medicine on specific zang-fu organs or meridians of the human body, which plays a major or special therapeutic effect on lesions in these parts. In this study, meridian tropism was mainly observed in the liver meridian and lung meridian. In traditional Chinese medicine, the liver is believed to store blood, regulate the blood volume and prevent bleeding, and the lungs regulate the movement of qi. Therefore, the herbs that belong to the liver and lung channels have the effects of regulating qi movement and promoting blood circulation in the treatment of MCI.
Figure 8: Continued.
Figure 8: Continued.
Through the target-component-herb network analysis using components as media, it was found that the core herbs were mainly Danshen (*Salvia miltiorrhiza* bunge), Yanhusuo (*Corydalis yanhusuo*), Gancao (*Glycyrrhiza uralensis* fisch), Gouteng (*Uncaria rhynchophylla*) and Jiangxiang (*Dalbergia odorifera*). *Salvia miltiorrhiza* bunge, a traditional Chinese medicine commonly used for cardiovascular and cerebrovascular diseases, has attracted increasing attention in the treatment of cognitive disorders, especially AD [69]. Studies have shown that various components of *Salvia miltiorrhiza* bunge have a variety of pharmacological effects related to improving cognitive impairment, such as anti-inflammatory, antioxidant, anti-apoptotic, and anti-Aβ effects and the regulation of the cholinergic system [70–73]. Tan IIA plays an anti-inflammatory and neuroprotective role by inhibiting astrocyte proliferation, upregulating Akt expression, and inhibiting NF-κB and caspase-3 production in an AD model [74, 75]. However, in terms of adverse reactions, studies have found that desipside salt injection made from *Salvia miltiorrhiza* bunge have a variety of pharmacological effects related to improving cognitive impairment, such as anti-inflammatory, antioxidant, anti-apoptotic, and anti-Aβ effects and the regulation of the cholinergic system [70–73]. Tan IIA plays an anti-inflammatory and neuroprotective role by inhibiting astrocyte proliferation, upregulating Akt expression, and inhibiting NF-κB and caspase-3 production in an AD model [74, 75]. However, in terms of adverse reactions, studies have found that desipside salt injection made from *Salvia miltiorrhiza* bunge has some side effects, such as headache, head distension, dizziness, facial flushing, skin itching, etc. [76].

*Corydalis yanhusuo* is a traditional Chinese medicine that promotes blood circulation and removes blood stasis, and its main active ingredient is bioactive alkali [77]. Modern pharmacological studies have shown that corydalis yanhusuo can improve the learning and memory ability of chronic cerebral hypoperfusion rats by alleviating neuron injury and increasing the expression of vascular endothelial growth factor [80]. However, it was reported that the total alkaloids of *Corydalis yanhusuo* (473.36 mg/kg) could cause liver injury, muscle tremor and renal hemorrhage in mice [81].

*Glycyrrhiza uralensis* fisch has complex ingredients, such as glycyrrhizic acid, glycyrrhetinic acid, flavonoids and other components, that have anti-inflammatory and neuroprotective effects [82, 83]. Studies have shown that glycyrrhizin can regulate a variety of anti-apoptotic and proapoptotic factors and exert anti-inflammatory effects by inhibiting the phosphorylation of HMGB1 through the ERK signaling pathway [84]. Glycyrrhizic acid can inhibit the aggregation of β-amyloid, scavenge free radicals, and reduce the expression of NO, TNF-α, IL-1β, Caspase3 and BAX, thereby inhibiting neuronal apoptosis and playing a neuroprotective role [85]. However, studies have found that glycyrrhizic acid and glycyrrhetinic acid have pseudaldosteronoid effects, which can cause hypertension, edema and other adverse reactions [86].

*Uncaria rhynchophylla* has a variety of pharmacological effects on the central nervous system, such as cerebral ischemia and hypoxia, neurodegenerative diseases and other neuroprotective effects [87]. Uncarine, one of the main components of *Uncaria rhynchophylla*, inhibits the neurotoxicity induced by soluble Aβ1-42 by inhibiting the overactivation of extrasynaptic NMDA receptors.
to find important MCI-related targets by searching and screening multiple databases. On this basis, we matched potential ingredients and herbs using the TCMSP platform. We further discussed and analyzed the core components, herbs and related mechanisms of TCM in the treatment of MCI by constructing a target-component-herb network. The results of this study can effectively and systematically screen herbal and compound components for the treatment of MCI and provide a reference for further experimental research, thereby reducing the economic cost of drug development and research investigating the treatment of MCI.

Data Availability

Supporting data for the results of this study are included in the article and supplementary Materials.

Conflicts of Interest

All authors declare that there is no conflict of interest in this article.

Authors’ Contributions

Zhen-Yun Han conceived and designed the study. Ze Chang and Yu-Chun Wang, with equal contribution, performed this study. Ze Chang processed the data and wrote the manuscript. Yu-Chun Wang collected data and revised manuscripts. Dang-Fen Tian, Wen-Yue Hu and Zhen-Yi Wang assisted in data collection, collation and analysis. Gan-Lu Liu, Hua-Ping Ma, Yu-Li Hu and Bin Wu analyzed the data and participated in the production of the graph.

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Supplementary Materials

Figure 7 data: Heatmap of the molecular docking results.

(Supplementary Materials)

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