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Network Pharmacology Analysis of Tianwang Buxin Dan on Alzheimer's Disease

Wenjing Lu

Department of Natural Sciences, Durham University, Durham, UK
Email: xblu@imech.ac.cn

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Abstract

Background: This study explores the mechanism of action of Tianwang Buxin Dan in the treatment of Alzheimer's disease (AD) by using the method of network pharmacology. **Methods**: Using traditional Chinese medicine system pharmacology database and analysis platform (TCMSP), search and screen the active ingredients of Tianwang Buxin Dan formula drugs; Search and screen the potential targets of compounds through Pubchem and Swiss Target Prediction databases; Retrieve the disease genes of Alzheimer' disease from the DisGeNet database; Obtain the intersection genes of disease genes and active ingredient targets through Venny2.0 software; Then, the STRING database and Cytoscape software were used to construct and analyze the PPI network diagram and the network diagram of prescription drug active ingredient AD target for AD targets; Perform Gene Ontology (GO) enrichment analysis and KEGG pathway enrichment analysis separately by using the DAVID system. **Results**: There are a total of 458 intersecting genes between Tianwang Buxin Dan and AD. The top 10 core targets selected from Tianwang Buxin Dan are AKT1, IL6, TP53, IL1B, EGFR, ESR1, APP, and STAT3. The active ingredients can regulate KEGG Protein phosphorylation. The positive regulation of MAPK cascade, protein autophosphorylation, positive regulation of ERK1 and ERK2 cascade, peptidyl-tyrosine phosphorylation, signal transduction, and positive regulation of cell proliferation, can respond to xenobiotic stimulus and hypoxia by acting on the aforementioned AD targets, affect biological processes such as protein hydrolysis, protein phosphorylation, estrogen response, and inhibit the production of Aβ, reduce neuronal inflammation and apoptosis, weaken the cholinesterase activity, and ultimately achieve the goal of treating AD. **Conclusions**: By using network pharmacology methods to study the active ingredients and mechanism of action of Tianwang Buxin Dan in the treatment of AD, it was revealed that Tianwang Buxin Dan has the advantages of multiple components, targets, and pathways in the treatment of AD, providing new ideas for the later experiments of Tianwang Buxin Dan.

Keywords

Tianwang Buxin Dan, AD, Network Pharmacology, Active Ingredients, Target, Pathway

1. Introduction

AD is a common neurodegenerative disease. Clinically, it is characterized by memory impairment, aphasia, agnosia and impairment of visuospatial skills, even dementia. 30% - 50% of patients with AD have some mental behavior abnormalities more or less. AD brings serious social and economic burdens. Pathogenesis is complicated by multiple factors. The specific pathogenesis is not yet clear [1]. For this kind of disease, people have proposed a variety of pathogenesis, but from the effect of clinical practice, the understanding of its pathogenesis is still very lacking, so the effect of the corresponding treatment scheme is also very limited. For example, the main antidepressants currently targeted at the "monoamine neurotransmitter hypothesis", such as serotonin reuptake inhibitors (SSRI), serotonin and norepinephrine reuptake inhibitors (SNRI), have clear pharmacological mechanisms, but have a slow onset and many adverse reactions [2]. The proportion of patients with AD based on stagnation of liver Qi and deficiency of heart and spleen is high in the point of Traditional Chinese Medicine (TCM), but it takes effect slowly during treatment, and is not generally effective for patients [3]. Therefore, how to clarify its pathogenesis and formulate a reasonable and effective treatment scheme is still the direction of in-depth research in the future. The lack of correct understanding of the pathological process of the disease is the root cause of the lack of drugs that can reverse the course of the disease. The pathogenesis and related targets of AD still need to be further explored. With the aging of the population, the continuous increase of disease cases among the elderly has also become an urgent problem that needs to be solved.

At present, there is no specific treatment for AD. Acetylcholinesterase inhibitors are commonly used in clinics. There are five drugs approved by the U.S. Food and Drug Administration (FDA) for the treatment of AD patients, namely tacrine, donepezil, kabalatin, galantamine and memantine. The first four drugs are all acetylcholinesterase inhibitors [4]-[6]. The main strategies for treating AD in TCM are "tonifying the kidney" and "regulating Qi". It has been found that "tonifying the kidney" in TCM theory has the function of nourishing nerves [7]. For a long time, the therapeutic effects of single target drugs are not very obvious. Therefore, multi target therapy and combined medication may bring new hope to the treatment of AD. Secondly, researchers mainly focus on Aβ, the toxic effects of tau protein, inflammatory factors and other pathological factors on the body before, but little attention has been paid to their physiological significance in the pathological state and their production pathway. So researchers should think more about what factors lead to the complex pathological phenomena of AD. Thirdly,

with the development of the "microorganism brain gut axis" hypothesis and peripheral inflammation hypothesis, peripheral treatment will become a new hope for the treatment of AD. For a long time, AD has been considered as a simple central nervous system disease. However, studies have confirmed that systemic inflammation and intestinal flora imbalance have also become important factors in inducing AD, suggesting that AD may be the result of the joint action of peripheral and central systems. Peripheral therapy can effectively solve the problem that drugs are difficult to penetrate the blood-brain barrier.

The advantage of TCM in the treatment of AD is to improve people's mental and emotional state, so as to alleviate or control the occurrence and development of AD patients by adjusting the Yin/Yang, Qi/blood and the deficiency/excess of viscera of humans. Traditional Chinese clinical doctors have unique views on pathogenesis and the corresponding treatments for AD.

The commonly used Western medicine drugs with either single targets or multiple targets are clinically not very effective. Compared with Western medicine drugs, natural products and TCM have obtained more prominent curative effects in the prevention and treatment of complex diseases with multiple causes because of their unique advantages of multiple components, multiple targets and multiple pathways. For example, ellagic acid (EA), a natural product, is a natural phenolic antioxidant widely found in plant tissues such as potentilla discolor, gallnut, raspberry, soft fruits and nuts (such as strawberry, cranberry, pecan) [8] [9].

Tianwang Buxin Dan has the effects of nourishing Yin, clearing heat, nourishing blood, and calming the mind and is commonly used to treat insomnia, palpitations, and recurrent oral ulcers caused by neurasthenia, coronary heart disease, schizophrenia, hyperthyroidism. It is consisted of ginseng, Poria cocos, Xuanshen, Danshen, *Platycodon grandiflorus*, Yuanzhi, *Angelica sinensis*, Wuwei, *Ophiopogon japonicus*, Tianmendong, *Phellodendron amurense*, *Ziziphus jujuba*, *Rehmannia glutinosa* [10].

Network pharmacology is a new model that analyzes the functions and mechanisms of drugs based on systems biology theory. By utilizing various bioinformatics databases, a "disease-gene-target-drug" interaction network is established, and professional software and algorithms are used to analyze and explore the relationship between drugs and diseases from a holistic perspective [11].

This study takes the active ingredients with anti AD effects in Tianwang Buxin Dan as the research object, applies the advantages of network pharmacology to establish a research method, and explores the mechanism of action of the formula' multi-component, multi-target, and multi-path treatment for AD by constructing the relationship between "formula drug-active ingredient-target-pathway", providing new ideas for the subsequent research of Tianwang Buxin Dan.

2. Data Collection and Analysis Methods

Screening of Active Ingredients in Tianwang Buxin Dan

Using the TCMSP database [12], chemical composition searches were conducted

on 13 medicinal herbs in Tianwang Buxin Dan. The oral bioavailability (OB) was ≥30%, and the drug likeness (DL) was ≥0.18 as screening criteria for active ingredients. Then we use the Pubchem database (https://pubchem.ncbi.nlm.nih.gov/) [13] to search for the Smile ID of each ingredient and use the SwissTarget Prediction database [14] (http://www.swisstargetprediction.ch/) to obtain the target genes corresponding to all chemical components of the 13 drugs mentioned above. The disease genes of Alzheimer's disease were obtained by using the DisGeNet database (https://www.disgenet.org/) [15]. By using Venny 2.1 (http://www.liuxiaoyuyuan.cn/), the intersection genes of component genes and Alzheimer's disease genes were obtained. On this basis, the software Cytoscape is used for plotting. Firstly, a formula drug gene map was drawn, followed by a formula drug gene pathway map, enrichment analysis map, and core target map. The network analysis function of the software was used to calculate network parameters and analyze interrelationships. At last, we constructed and analyzed a protein-protein interaction (PPI) network diagram of the anti Alzheimer's disease targets of Tianwang Buxin Dan by using a String database and analyzing it by using the DAVID platform and KOBAS3.0 database respectively to carry out Gene Ontology (GO) enrichment analysis (selecting BP, CC, MF) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis on the AD targets obtained above.

3. Results

3.1. Screening Results of AD Related Targets

By searching TC-MSP database, the main components and targets of various drugs were obtained as follows: 5 main components of Bai Zi Ren and main target 396; There are 8 main components of Schisandra chinensis and 707 main targets; Danshen has 65 main components and 2449 main targets; *Angelica sinensis* has 2 main components and 85 main targets; Dihuang has 2 main components and 85 main targets; There are 15 main components and 912 main targets in Poria cocos; There are 7 main components and 263 main targets in *Platycodon grandiflorum*; There are 12 main components and 574 main targets in *Ophiopogon japonicus*; There are 22 main components and 1035 main targets in ginseng; There are 9 main components and 220 main targets in sour jujube kernels; There are 9 main components and 277 main targets in Asparagus japonicus; There are 9 main components and 148 main targets in Xuanshen; Yuanzhi has 6 main components and 200 main targets.

3.2. Screening Results of Active Ingredients and Anti AD Targets

Yuanzhi and Maidong (Maimendong) were not included in the TCMSP database, so BATMAN-TCM database (http://bionet.ncpsb.org.cn/batman-tcm/) was used for querying. Perlolyrine is available http://www.swisstargetprediction.ch/. The gene cannot be found in the database, but it was found through the TCMSP database. Selection criteria are adopted as follows:

For each compositive compound, the predicted candidate targets whose scores

given by the target prediction method exceed a given cutoff "Score cutoff" (including known targets) will be considered as the potential targets, and will be presented and further analyzed. The "Score cutoff" is set as 20%.

The significantly enriched Gene Ontology functional terms, KEGG biological pathways and OMIM/TTD diseases among the potential targets of the query TCM are analyzed. During the enrichment analyses, we only consider the predicted candidate targets (including known targets) with scores no smaller than 20 as set above. P-value after Benjamini-Hochberg multiple testing correction (Adjusted P-value) is set as 0.05.

The items with Probability ≤0 were deleted when organizing the main component target. No targets were found for the 7, 9 (11)-dehydroferulic acid methyl ester of Poria cocos, the 2-o-methyl-3-O-β-D-glucopyranosyl platycogenate of Platycogenate Platycogenate, the dimethyl 2-o-methyl-3-O-a-D-glucopyranosyl platycogenate and Arobinin of Platycogenate Platycogenate, the zizypsine of *Ziziphus jujuba*, and the malkangnin of *Panax ginseng*.

3.3. Analysis of the Results

All target genes corresponding to the components were imported into Venny 2.1 along with AD disease genes, resulting in a total of 458 intersecting genes. Then we used Cytoscape to draw a formula drug intersection gene network diagram, as shown in Figure 1.

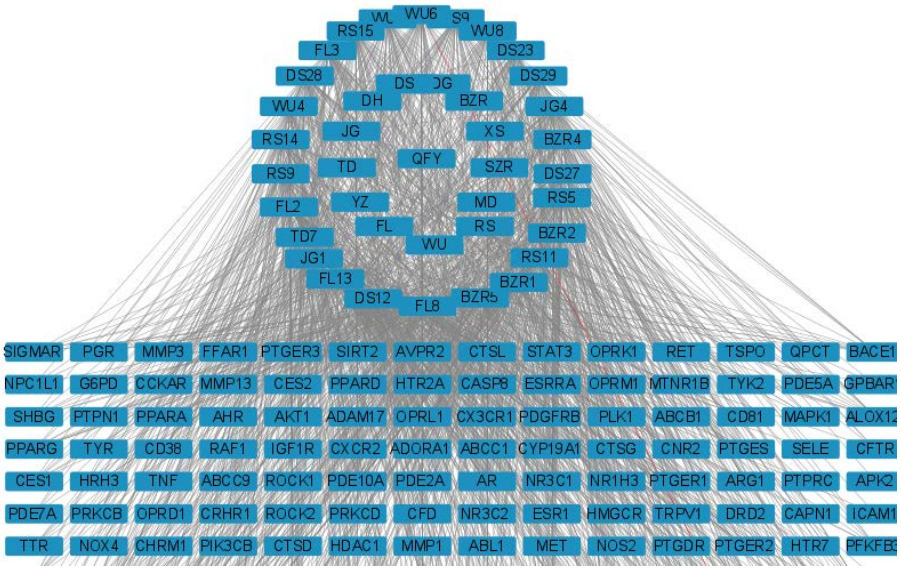

Figure 1. Diagram of drug composition-intersection gene-drug network.

The core targets were obtained by analyzing the 458 intersecting genes using the String database. Among them, the following settings were given (Figure 2): Cleanliness threshold: 0.0010241916194529829; Betweenness threshold: 538.241228070184; Degree under threshold: 82.54385964912281. The top 10 core targets selected are:

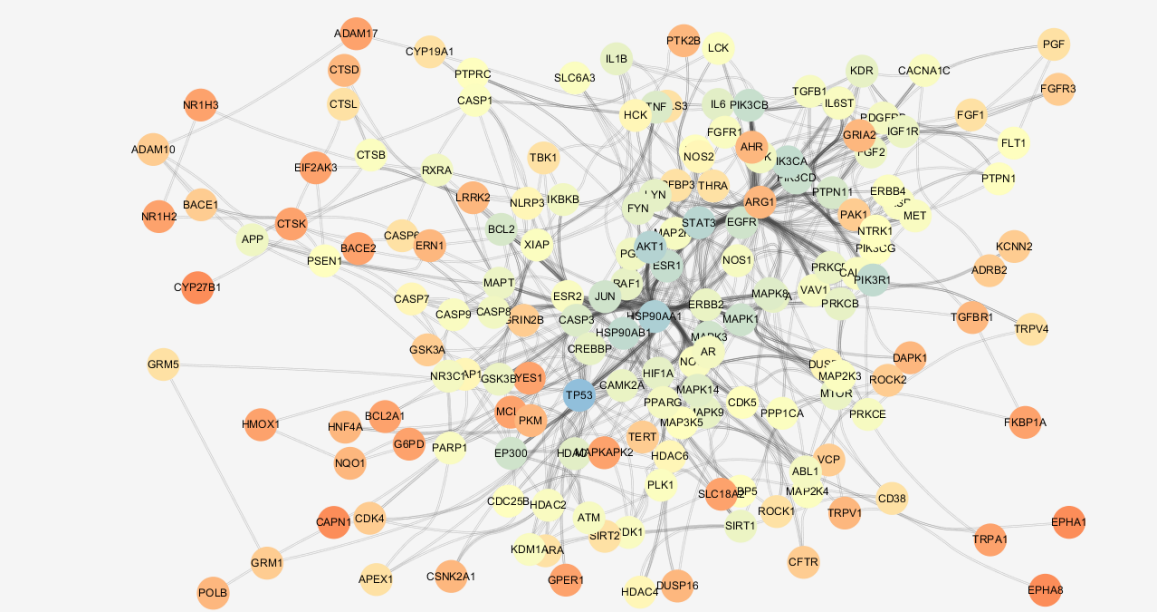

Figure 2. Core target map.

AKT1: AKT1 plays an important role in cellular signaling and is a target for many drugs and biomarkers.

IL-6: IL-6 is a 26KD peptide with a wide range of biological effects, mainly including: ① Regulating the growth and differentiation of B cells. ② Enhancing the killing effect of CTL and NK cells. ③ Stimulating the proliferation and differentiation of hematopoietic stem cells. ④ Promoting the synthesis of acute phase proteins in liver cells.

TP53: It is a gene on chromosome 17 that encodes a tumor suppressor protein containing transcriptional activation, DNA binding, and oligomeric domains.

IL1B: It generally refers to IL-1 β and can usually play an auxiliary role in controlling blood sugar in the treatment of type 2 diabetes. It is also an inflammatory factor that plays an important role in the human immune response.

EGFR: EGFR is widely distributed on the surface of mammalian epithelial cells, fibroblasts, glial cells, keratinocytes, and other cells. The EGFR signaling pathway plays an important role in physiological processes such as cell growth, proliferation, and differentiation.

ESR1: This gene encodes the estrogen receptor, a ligand-activated transcription factor composed of several domains that are important for hormone binding, DNA binding, and transcriptional activation. This protein is located in the nucleus and can form homodimers or heterodimers with estrogen receptor 2. Estrogen and its receptors are crucial for sexual development and reproductive function, but also play important roles in other tissues such as bone. Estrogen receptors are also involved in pathological processes including breast cancer, endometrial cancer and osteoporosis. The use of alternative promoters and alternative splicing has resulted in dozens of transcriptional variations, but the full-length nature of many of these variations has not yet been determined.

APP: The APP gene can encode the precursor protein of β-amyloid protein, which is considered to be the main cause of Alzheimer's disease.

STAT3: Signal transducer and activator of transcription factor 3 (STAT3) is a transcription factor involved in multiple biological functions, which can transmit extracellular signals to the nucleus and activate the transcription of target genes. Abnormal activation of STAT3 can induce tumor development and promote tumor progression, making it an attractive anti-cancer target.

When adopting the threshold 0.9 and three clusters, the results are as follows: number of nodes: 457; number of edges:1181; average node degree: 5.17; avg. local clustering coefficient: 0.436; expected number of edges: 409; PPI enrichment p-value < 1.0e−16.

3.4. Enrichment Analysis

DAVID database (Database for Annotation Visualization and Integrated Discovery) is a comprehensive bioinformatics tool mainly used for gene function enrichment analysis and gene ID conversion. It integrates biological data and analysis tools to provide systematic and comprehensive biological function annotation information for large-scale gene or protein lists, helping users extract biological information from them. By integrating annotation resources and visualization tools, it significantly simplifies the complexity of gene function analysis and is suitable for multi-level needs from basic research to clinical association analysis.

Enrichment analysis is a method used to analyze high-throughput experimental data, typically used to understand the degree of enrichment of gene sets or other biological entities in terms of their functions, pathways, or specific biological processes under given experimental conditions. The goal of enrichment analysis is to determine whether genes or other entities observed in experiments are concentrated in specific functions or pathways, in order to infer whether these functions or pathways are significantly enriched under experimental conditions. KEGG enrichment analysis focuses on examining whether genes/metabolites in gene sets are enriched in specific pathways. In this section, we will use the DAVID database and KEGG enrichment analysis to analyze the information on core gene pathways.

Insert the intersecting genes into the David database [16] to select *Homo sapies*, office-gene-symbol gene list, and after the screening, 456 genes were detected. KEGG enrichment analysis of the top 20 targets is as follows (**Figure 3**):

Protein phosphorylation is an important post-translational modification (PTM) of proteins, which regulates the function and activity of proteins by adding phosphate groups to their amino acid residues. The main mechanism of phosphorylation modification is the enzymatic transfer of ATP phosphate groups to specific amino acids in proteins, typically occurring on serine (Ser), threonine (Thr), and tyrosine (Tyr). **Phosphorylation means the activity and function of proteins can be controlled by adding or removing phosphate groups on proteins.** Protein phosphorylation means key regulatory mechanisms controlling multiple cellular responses. **Positive regulation of MAPK cascade** is to regulate

the cascade reaction of mitogen activated protein kinase (MAPK) through specific mechanisms. **Protein autophosphorylation** is a protein modification process in which proteins phosphorylate their own tyrosine residues through enzymatic reactions. **Positive regulation of cell migration is to influence cell migration through positive regulation. Negative regulation of cell population proliferation is to inhibit cell proliferation. This function plays an important role in maintaining tissue homeostasis and preventing tumor occurrence. Positive regulation of ERK1 and ERK2 cascade** mainly involves various biological processes such as cell proliferation and differentiation. **Cellular response to xenobiotic stimulus** means the response of cells to external chemical stimuli. It refers to the mechanism by which an organism responds to non self generated chemicals (*i.e.* exogenous chemicals, abbreviated as "exogenous substances"). This reaction mechanism plays a crucial role in the organism, helping it resist the effects of harmful substances and protect its own health. **Signal transduction** refers to the process in which external signals (such as light, antigens, hormones, etc.) act on cell surface receptors, causing changes in the concentration of intracellular messengers, until the genes required for cellular physiological responses begin to be expressed and various biological effects are formed. **Positive regulation of cell population proliferation** refers to promoting the process of cell population proliferation through a positive regulatory mechanism. This function is mainly achieved by influencing regulatory factors of the cell cycle, growth factors, cell signaling pathways, etc. Specifically, the positive regulation of cell population proliferation involves the action of multiple molecules and signaling pathways. **Positive regulation of gene expression** refers to the process of promoting gene expression through positive regulatory mechanisms. Gene expression regulation is an important component of life activities, which determines which genes are expressed when and where, thereby controlling the physiological functions of cells and the developmental processes of organisms. **Inflammatory response** is an immune response process initiated by multiple cells and mediators in the body's tissue cells after recognizing pathogen associated molecular patterns (PAMPs) or injury associated molecular patterns (DAMPs) through pattern recognition receptors (PRRs). It is the body's defense response to damaging factors. **Positive regulation of protein phosphorylation** is to promote protein phosphorylation through specific enzymes or signaling pathways. **Negative regulation of apoptotic process** mainly includes inhibiting the occurrence and development of cell apoptosis, thereby protecting cells from programmed cell death, such as negative regulation of cell growth by inhibiting cell proliferation and division, maintaining cell homeostasis, and preventing tumor occurrence caused by excessive proliferation; tumor suppression by preventing abnormal cell proliferation and reducing the risk of tumor formation; playing an important role in the process of signal transduction, especially in the Ras MAPK pathway, and may be involved in a wide range of signal transduction processes, particularly in embryonic development and adult tissues. **Positive regulation of cell migration** refers to the

process of promoting cell migration through certain mechanisms or molecular signals. Cell migration plays an important role in the development, tissue repair, and immune response of organisms. **Proteolysis**: **The main function of Proteolysis is protein hydrolysis, which breaks down proteins into smaller peptides or amino acids through the action of enzymes. Positive regulation of transcription by RNA polymerase II** involves mediated transcription, which is a highly regulated multi-step process that is responsible for producing all mRNA. The main functions include transcription initiation, pausing and extending, regulation etc. **Positive regulation of DNA templated transcription** influences the transcription process of DNA templates through positive regulatory factors, such as transcription factors. Transcription factors bind to specific sequences on DNA (known as promoter regions), initiating or enhancing the transcription process of genes, thereby producing mRNA and guiding protein synthesis. This regulatory mechanism plays an important role in cell growth, differentiation, metabolism, and response to environmental changes. **Negative regulation of cell population proliferation** mainly has the following functions: participation in the G protein coupled receptor signaling pathway: this regulatory mechanism participates in the G protein coupled receptor signaling pathway and affects the signal transduction process inside the cell. Participate in circadian rhythm: It has a regulatory effect on the circadian rhythm of organisms, affecting the stability and accuracy of the biological clock. Negative regulation of cell population proliferation: During the process of cell proliferation, it plays a negative regulatory role, inhibiting excessive cell proliferation and maintaining the balance of cell numbers. This regulatory mechanism plays an important role in various physiological processes of organisms, helping to maintain normal cell growth and differentiation, and

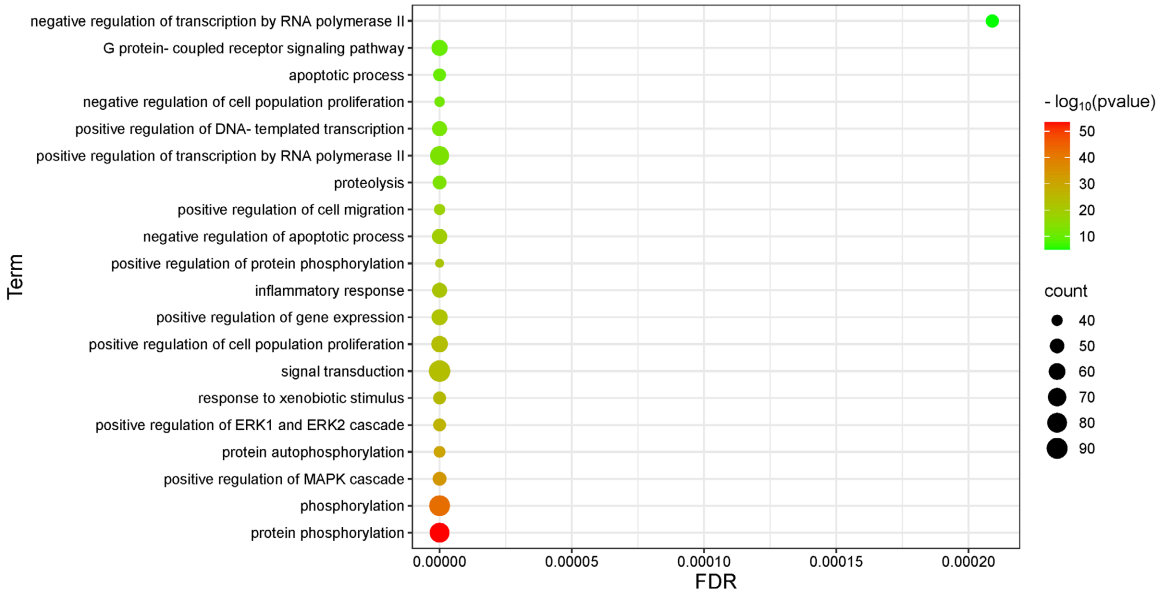

Figure 3. KEGG enrichment analysis of the top 20 targets.

preventing the occurrence and development of tumors. **Apoptotic process** is used to eliminate aging cells or lymphocytes that have not participated in immune responses. It has multiple important biological functions in organisms, such as cell removal during development: helps to remove excess or no longer needed cells during embryonic development; helps maintain tissue homeostasis by clearing aging or damaged cells in adult individuals; helps regulate the survival and death of immune cells, maintaining the balance of the immune system in the immune system. **G protein-coupled receptor signaling pathway** can convert extracellular signals into intracellular responses, thereby regulating cellular physiological activities by using G protein as a signal transduction molecule. **Negative regulation of transcription by RNA polymerase II** (RNA Pol II) can mainly regulate the elongation process of gene transcription through various negative elongation factors and pause mechanisms. After transcription initiation, RNA Pol II undergoes a proximal pause and extension phase of the promoter, in which negative regulatory factors play a critical role.

4. Discussion

We now analyze the function of each TCM in Tian Wang Bu Xin Dan on AD. Ginsenosides in ginseng can promote blood circulation in brain, increase connections between neurons, and improve memory. Ginsenoside triol compounds have anti-inflammatory and antioxidant effects, which can protect nerve cells from damage and improve cognitive function. Some components have the effect of inhibiting the deposition of β-amyloid protein and excessive phosphorylation of tau protein, both of which are pathological features of neurodegenerative diseases such as AD. Therefore, ginseng can help delay the development process of these diseases; The saponins in ginseng can stimulate the body to produce interferon, enhance the activity of natural killer cells, and strengthen the body's immune system. There are 282 intersecting genes between ginseng and AD, with the top 10 being ACE, APP, GSK3B, MAPT, PSEN1, PLAU, BACE1, INSR, IGF1R, and MPO [17].

Poria cocos has antioxidant, anti-aging, immune enhancing, and brain cell activity improving effects, as well as sedative effects, which are effective in treating neurasthenia. There are 146 intersecting genes with AD, with the top 10 being ACE, GSK3B, BACE1, IL1B, BCL2, EPHA1, ESR1, IL6, ACHE, and PPARG.

Scrophularia has good effects on clearing heat, cooling blood, detoxifying and dispersing lumps. It mainly acts on symptoms such as restlessness, thirst, yin deficiency, hot flashes, and insomnia. There are 58 intersecting genes with AD, with the top 10 being CYP2D6, ESR1, ACHE, PPARG, BCHE, F2, NOS2, PTGS2, LRRK2, and CYP19A1.

Danshen can promote blood circulation and remove blood stasis, and has a certain improvement effect on dementia. Tanshinone can be used for the prevention and treatment of AD. There are 317 intersecting genes with AD. Among which the top 10 are APP, ADAM10, GSK3B, BACE1, IL1B, INSR, BCL2, CASP3,

IGF1R, and MPO.

Platycodon grandiflorum has various pharmacological effects such as expectorant, cough suppressant, antibacterial, anti-inflammatory, immune enhancing, sedative, etc. It can improve metabolic syndrome by interacting with gut microbiota. There are 102 intersecting genes with AD, with the top 10 being APP, GSK3B, BACE1, IGF1R, MPO, ESR1, MAOB, ACHE, BCHE, and F2.

Yuanzhi is very important for treating insomnia, frequent dreams, palpitations, and forgetfulness, and preventing memory decline. Zhiyuanzhi and the monomeric compound Yuanzhi saponin B have certain therapeutic effects on AD [18] [19] and have 120 intersecting genes with AD. The first 10 genes being BACE1, CYP2D6, ESR1, ACHE, PPARG, BCHE, VEGFA, F2, MAPK14, NOS2.

Danggui can nourish blood and regulate meridians, promote blood circulation and relieve pain, moisten the intestines and promote bowel movements. It can be used to treat blood deficiency, intestinal dryness and constipation [20] [21]. There are 34 intersecting genes with AD, among. The top 10 are ESR1, ACHE, PPARG, BCHE, NOS2, CYP19A1, ESR2, NR3C1, PPARA, SLC6A4.

Schisandra chinensis has anti arteriosclerosis and other effects, and has good therapeutic effects on AD [22]. There are a total of 159 genes that intersect with AD, among which the top 10 are ADAM10, GSK3B, PSEN1, BACE1, GF1R, NOS3, PPARG, TNF, F2, MAPK14.

Ophiopogon japonicus can relieve restlessness, calm the heart, enhance intelligence and tonify deficiency, and is commonly used in the treatment of Alzheimer's disease. There are 122 intersecting genes with AD. The top 10 are GSK3B, INSR, BCL2, CHRNA7, ESR1, MAOB, CDK5, MAPK14, NOS2, PTGS1.

Tianmendong can tonify the kidneys, generate fluids, enhance intelligence, and calm the mind. There are 116 intersecting genes with AD. The top 10 are APP, GSK3B, MAPT, BACE1, INSR, IGF1R, MPO, NOS3, ESR1, MAOB.

The behavioral improvement effect of Baiziren glycoside on AD model rats. There are 99 common genes with AD, among which the top 10 are ACE, PSEN1, BACE1, ESR1, IL6, ACHE, PPARG, BCHE, MAPK14, NOS2.

Suanzaoren has various health benefits such as calming the nerves, anti anxiety, anti depression, lowering blood sugar, anti Alzheimer's disease, and enhancing the immune system. It shares 98 intersecting genes with AD. The top 10 are ACE, GSK3B, ESR1, ACHE, PPARG, BCHE, MME, NOS2, PTGS2, PTGS1.

Raw rehmannia glutinos [23] have 34 intersecting genes with AD, among which the first 10 are ESR1, ACHE, PPARG, BCHE, NOS2, CYP19A1, ESR2, NR3C1, PPARA, SLC6A4.

The top 20 genes at the intersection of prescriptions and AD, ranked by degree, closeness, and betweenness, are DS27, RS9, DS28, FL3, DS29, FL8, BZR1, JG1, RS11, DS12, WU4, FL2, RS15.

5. Conclusions

The mechanism of action of Tianwang Buxin Dan in the treatment of AD was

analyzed by using the tools: TCMSP, Pubchem, Swiss Target Prediction databases, DisGeNet database, Venny 2.0 software, STRING database, Cytoscape software and Devid database. The main conclusions are as follows:

There are a total of 458 intersecting genes between Tianwang Buxin Dan and AD. The top 10 core targets selected from Tianwang Buxin Dan are AKT1, IL6, TP53, IL1B, EGFR, ESR1, APP, and STAT3. The active ingredients regulate KEGG protein phosphorylation, phosphorylation, positive regulation of MAPK cascade, protein autophosphorylation, positive regulation of ERK1 and ERK2 cascade, peptidyl tyrosine phosphorylation, signal transduction, positive regulation of cell proliferation, response to xenobiotic stimulation, response to hypoxia and other signaling pathways by acting on the aforementioned AD targets, affecting biological processes such as protein hydrolysis, protein phosphorylation, estrogen response, inhibiting the production of Aβ, reducing neuronal inflammation and neuronal apoptosis, weakening cholinesterase activity, and ultimately achieving the goal of treating AD. This article studies the active ingredients and mechanism of action of Tianwang Buxin Dan in the treatment of AD through network pharmacology methods, revealing the advantages of Tianwang Buxin Dan in the treatment of AD with multiple components, targets, and pathways, providing new ideas for the later experiments of Tianwang Buxin Dan. This paper only provides silico data. Further work will do some experiments to certify these conclusions.

Availability of Data and Materials

The data supporting the conclusions of this article are included within the article and other related information are available from the author on reasonable request.

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Author Contributions

All the work is performed by Wenjing includes collecting data, analysis, creating figures, preparing the original draft of the manuscript and approving the final manuscript.

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Availability of Data and Materials

The datasets used or analyzed throughout this study are available from the corresponding author upon reasonable request.

Ethics Declarations

Ethics approval and consent to participate are Not applicable.

Consent for Publication

The manuscript is approved by all authors for publication.

Author Details

Department of Natural Science, Durham University, DH1 3LE, UK.

Conflicts of Interest

The author declares no competing financial interests.

References

[1] Selkoe, D.J. and Hardy, J. (2016) The Amyloid Hypothesis of Alzheimer's Disease at 25 Years. *EMBO Molecular Medicine*, **8**, 595-608. https://doi.org/10.15252/emmm.201606210

[2] Talegawkar, S.A., Bandinelli, S., Bandeen-Roche, K., Chen, P., Milaneschi, Y., Tanaka, T., *et al.* (2012) A Higher Adherence to a Mediterranean-Style Diet Is Inversely Associated with the Development of Frailty in Community-Dwelling Elderly Men and Women. *The Journal of Nutrition*, **142**, 2161-2166. https://doi.org/10.3945/jn.112.165498

[3] Su, X., Zhao, S., Zhao, T. and Yue, X. (2021) New Advances in Understanding of Pathogenesis of Alzheimer' Disease. *China Journal of Clinicians* (*Electronic Edition*), **15**, 224-228.

[4] Zan, Z. and Wang, Y. (2021) Research Progress in the Clinic Treatment of Alzheimer' Disease. *Journal of Modern Medicine & Health*, **37**, 2240-2243, 2248.

[5] Prince, M., Bryce, R., Albanese, E., Wimo, A., Ribeiro, W. and Ferri, C.P. (2013) The Global Prevalence of Dementia: A Systematic Review and Metaanalysis. *Alzheimer's & Dementia*, **9**, 63-75.e2. https://doi.org/10.1016/j.jalz.2012.11.007

[6] Hase, T., Shishido, S., Yamamoto, S., Yamashita, R., Nukima, H., Taira, S., *et al.* (2019) Rosmarinic Acid Suppresses Alzheimer's Disease Development by Reducing Amyloid β Aggregation by Increasing Monoamine Secretion. *Scientific Reports*, **9**, Article No. 8711. https://doi.org/10.1038/s41598-019-45168-1

[7] Wang, J., Chen, S. and Gao, X. (2021) Research Progress of Alzheimer' Disease Targets and Related Drugs. *Pharmaceutical Biotechnology*, **28**, 323-330.

[8] Bae, S., Lee, E., Lee, J.H., Park, I., Lee, S., Hahn, H.J., *et al.* (2013) Oridonin Protects Hacat Keratinocytes against Hydrogen Peroxide-Induced Oxidative Stress by Altering Microrna Expression. *International Journal of Molecular Medicine*, **33**, 185-193. https://doi.org/10.3892/ijmm.2013.1561

[9] Tohda, C., Urano, T., Umezaki, M., Nemere, I. and Kuboyama, T. (2012) Diosgenin Is an Exogenous Activator of 1,25D_3-MARRS/Pdia3/ERp57 and Improves Alzheimer's Disease Pathologies in 5XFAD Mice. *Scientific Reports*, **2**, Article No. 535. https://doi.org/10.1038/srep00535

[10] Zhao, X., Li, N., Du, C., Zhang, S., Li, W. and Wang, Q. (2018) Intervention Effect on Alzheimer' Disease in Mice by Tianwang Buxin Dan Combined with Rosemary Essential Oil. *Acta Chinese Medcine*, **33**, 611-615.

[11] Liu, Z. and Sun, X. (2012) Network Pharmacology: New Opportunity for the Modernization of Traditional Chinese Medicine. *Acta Pharmaceutica Sinica*, **47**, 696-703.

[12] Ru, J., Li, P., Wang, J., Zhou, W., Li, B., Huang, C., *et al*. (2014) TCMSP: A Database of Systems Pharmacology for Drug Discovery from Herbal Medicines. *Journal of Cheminformatics*, **6**, Article No. 13. https://doi.org/10.1186/1758-2946-6-13

[13] Kim, S., Chen, J., Cheng, T., Gindulyte, A., He, J., He, S., *et al*. (2023) PubChem 2023 Update. *Nucleic Acids Research*, **51**, D1373-D1380. https://doi.org/10.1093/nar/gkac956

[14] Daina, A., Michielin, O. and Zoete, V. (2019) Swisstargetprediction: Updated Data and New Features for Efficient Prediction of Protein Targets of Small Molecules. *Nucleic Acids Research*, **47**, W357-W364. https://doi.org/10.1093/nar/gkz382

[15] Piñero, J., Bravo, À., Queralt-Rosinach, N., Gutiérrez-Sacristán, A., Deu-Pons, J., Centeno, E., *et al*. (2017) Disgenet: A Comprehensive Platform Integrating Information on Human Disease-Associated Genes and Variants. *Nucleic Acids Research*, **45**, D833-D839. https://doi.org/10.1093/nar/gkw943

[16] Sherman, B.T., Panzade, G., Imamichi, T. and Chang, W. (2024) DAVID Ortholog: An Integrative Tool to Enhance Functional Analysis through Orthologs. *Bioinformatics*, **40**, btae615. https://doi.org/10.1093/bioinformatics/btae615

[17] Du, X. and Chen, B. (2018) Research Progress on the Anti Alzheimer' Disease Effects of Three Types of Ginsenoside Monomers. *West China Journal of Pharmaceutical Sciences*, **33**, 323-327.

[18] Li, X., Cui, J., Yu, Y., Li, W., Hou, Y., Wang, X., *et al*. (2016) Traditional Chinese Nootropic Medicine *Radix Polygalae* and Its Active Constituent Onjisaponin B Reduce β-Amyloid Production and Improve Cognitive Impairments. *PLOS ONE*, **11**, e0151147. https://doi.org/10.1371/journal.pone.0151147

[19] Li, X., Chen, S., Chen, W., Song, J. and Zhang, Y. (2022) Research Progress on Chemical Constituents of Polygala Tenuifolia and Prevention and Treatment of Alzheimer's Disease. *Chinese Pharmaceutical Journal*, **57**, 15-23.

[20] Zhi, L. (2018) Study on the Effect and Mechanism of the Blood Components of Danggui-Shaoyao-San on Alzheimer' Disease. Thesis for Master Degree, Guang-Zhou University of Chinese Medicine.

[21] Yin, X. and Wu, Q. (2022) Bioinformatic and Network Pharmacological Analyses on *Angelica sinensis*-Ligusticum Chuanxiong Drug Pair in the Treatment of Alzheimer' Disease. *Chinese Traditional Patent Medicine*, **44**, 72-77.

[22] Wu, L., Du, Y., Gao, Y., Jia, L. and Su, Y. (2022) Research Progress on Active Components and Mechanism Against Alzheimer' Disease of Schisandra Chinensis. *Research and Practice on Chinese Medicines*, **5**, 97-102.

[23] Han, R., Ma, T., Zhang, Z., Gao, K., Gao, J., Tang, X., Wen, B. and Yan, Y. (2018) Experimental Research Progress of Dihuang Yinzi in the Treatment of Alzheimer' Disease. *Clinical Journal of Chinese Medicine*, **24**, 124-130.