Evidence Mapping Analysis of Clinical Studies on Chinese Patent Medicine for Alzheimer's Disease: A Postprint

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Abstract

Background: Alzheimer's disease (AD) is a complex neurodegenerative disease that imposes a heavy burden on patients and their families. In recent years, clinical studies on traditional Chinese medicine preparations for AD treatment have been increasing continuously, yet the evidence base remains unclear. Objective: To analyze the evidence profile of clinical studies on traditional Chinese medicine preparations for Alzheimer's disease in the past 5 years. Methods: Literature on traditional Chinese medicine preparations for AD treatment published between January 2019 and December 2024 was retrieved from 8 Chinese and English databases (CNKI, Wanfang Data Knowledge Service Platform, VIP, Chinese Biomedical Literature Service System, PubMed, Web of Science, Cochrane Library, and Embase), with evidence distribution characteristics presented in a combination of text and figures/tables. Results: A total of 82 clinical trials, 30 systematic reviews/Meta-analyses, 9 network Meta-analyses, 7 guidelines/expert consensuses/pathways, 1 overview of systematic reviews, and 1 health technology assessment were included. In recent years, research interest in traditional Chinese medicine preparations for AD has shown a fluctuating declining trend. Clinical research and evaluation focused on 21 traditional Chinese medicine preparations, with the highest attention given to oral preparations Compound Congrong Yizhi Capsule and Compound Haishe Capsule, while the main injectable preparation was Ginkgo biloba extract. Clinical studies were primarily single-center, small-scale randomized controlled trials with generally low literature quality. Regarding outcome measure selection, the focus was mainly on cognitive function indicators, surrogate outcome indicators, and quality of life indicators, lacking characteristics of TCM syndrome differentiation and treatment, with non-standardized selection and measurement of indicators. The overall quality of systematic reviews/Meta-analyses was low, and the methodological quality as well as the formulation and reporting standardization of clinical practice guidelines and expert consensuses require fur-

ther improvement. Conclusion: Some single-center, small-sample clinical studies on traditional Chinese medicine preparations for AD treatment have been conducted. Future research should incorporate the characteristics of clinical diagnosis and treatment practice of traditional Chinese medicine for AD to further conduct multi-center, large-sample, high-quality clinical studies, in order to generate high-quality clinical evidence and provide relevant references for traditional Chinese medicine preparations in AD treatment.

Full Text

Evidence Mapping Analysis of Clinical Studies on Treatment of Alzheimer's Disease with Chinese Patent Medicines

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Abstract

Background Alzheimer's disease (AD) is a complex neurodegenerative disease that imposes heavy burdens on patients and their families. Clinical studies on Chinese patent medicines for AD have been increasing in recent years, but the supporting evidence remains unclear. **Objective** To analyze the clinical research evidence on Chinese patent medicines for AD from the past five years. **Methods** We systematically searched eight Chinese and English databases (CNKI, Wanfang, VIP, SinoMed, PubMed, Web of Science, Cochrane Library, and Embase) for literature on Chinese patent medicines for AD published between January 2019 and December 2024, presenting evidence distribution characteristics through combined text and graphical displays. **Results** A total of 130 articles were included: 82 clinical trials, 30 systematic reviews/Meta-analyses, 9 network Meta-analyses, 7 guidelines/consensus statements/clinical pathways, 1 overview of systematic reviews, and 1 health technology assessment. Attention to Chinese patent medicines for AD has shown a fluctuating downward trend, with clinical research and evaluation focusing on 21 Chinese patent medicines. Compound Congrong Yizhi Capsule and Compound Haishe Capsule received the most attention among oral preparations, while Ginkgo biloba extract dominated injectable formulations. Clinical studies consisted primarily of single-center, small-scale randomized controlled trials with generally low literature quality. Outcome measures focused mainly on cognitive function indicators, surrogate endpoints, and quality of life metrics, lacking characteristics of

Traditional Chinese Medicine (TCM) syndrome differentiation and treatment, with non-standardized selection and measurement methods. The overall quality of systematic reviews/Meta-analyses was low, and the methodological quality, formulation, and reporting standardization of clinical practice guidelines and expert consensus require further improvement. **Conclusion** Some single-center, small-sample clinical studies on Chinese patent medicines for AD have been conducted. Future research should incorporate the characteristics of AD clinical diagnosis and treatment with Chinese medicines to conduct multi-center, large-sample, high-quality clinical studies, thereby generating high-quality clinical evidence to provide relevant references for Chinese patent medicine treatment of AD.

Keywords Alzheimer's disease; Chinese patent medicines; Clinical studies; Methodology; Evidence mapping

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Alzheimer's disease (AD) is a neurodegenerative disorder characterized by progressive decline in cognitive memory function and daily living abilities [1]. The number of AD patients worldwide is projected to reach 150 million by 2050 [2]. Statistics from 2023 indicate that China currently has approximately 9.83 million AD patients, with annual treatment costs expected to reach $1.88718 trillion by 2050 [3-4]. The U.S. Food and Drug Administration (FDA) has approved acetylcholinesterase inhibitors including donepezil, galantamine, and rivastigmine, N-methyl-D-aspartate receptor antagonists such as memantine, and two anti-A monoclonal antibodies (aducanumab and lecanemab) for AD treatment [5]. However, these medications exhibit limited symptomatic improvement, significant adverse reactions, and restricted applicability for some drugs [6-7], which affect patients' quality of life and impose heavy economic burdens on families.

Based on holistic concepts and syndrome differentiation and treatment, Traditional Chinese Medicine has gradually demonstrated unique efficacy and potential for AD treatment. Chinese herbal compound formulations offer advantages through multiple components, pathways, and targets, providing new insights for AD prevention and treatment [8]. Chinese patent medicines, in particular, offer greater patient acceptance due to their convenience, portability, and fewer adverse stimuli. Although clinical studies on Chinese patent medicines for AD have been increasing, the overall evidence landscape remains unclear. This study systematically obtained relevant clinical research on Chinese patent medicines for AD and presented the results through evidence mapping to analyze the current state of research evidence and limitations in this field, aiming to provide potential research directions and references for future studies and drug development.

Methods

1.1 Literature Search

We searched eight Chinese and English databases (CNKI, Wanfang Data Knowledge Service Platform, VIP, SinoMed, PubMed, Web of Science, Cochrane Library, and Embase) for clinical research literature on Chinese patent medicines for AD from January 2019 to December 2024. We conducted searches using a combination of subject headings and free-text terms. Chinese search terms included "Alzheimer's disease," "senile dementia," "dementia," and commercial/common names of Chinese patent medicines. English search terms included "traditional Chinese medicine," "herbal medicine," "Alzheimer disease," along with frequently appearing Chinese patent medicine names from search results.

1.2 Inclusion Criteria

1.2.1 Study types: We included randomized controlled trials, non-randomized controlled trials, single-group clinical trials, cohort studies, systematic reviews (systematic overviews)/Meta-analyses, overviews of systematic reviews, guidelines, expert consensus statements, clinical pathways, and health technology assessment literature.

1.2.2 Study population: We included AD patients without specific limitations on age, sex, or disease duration.

1.2.3 Interventions: The experimental group received Chinese patent medicines alone or combined with conventional Western medicine, while control groups included blank controls, conventional Western medicine treatment, or placebo controls.

1.3 Exclusion Criteria

1.3.1 Study types: Animal studies, cell experiments, literature reviews, and experience-based discussions.

1.3.2 Experimental interventions: Literature using hospital preparations or self-made Chinese medicines, or traditional Chinese herbal formulas.

1.3.3 Other exclusions: Conference abstracts, clinical trial protocols only, duplicate publications, and literature with unavailable full text.

1.4 Literature Screening and Data Extraction

Two researchers independently screened literature and conducted cross-checking. Discrepancies were resolved through discussion with a third party. We used Noteexpress 3.8 software to remove duplicate records from database searches, then excluded irrelevant literature through title and abstract screening, and finally determined included articles through full-text reading. We extracted relevant information using a pre-designed standardized literature information form that

included author, publication year, study type, sample size, experimental group interventions, control measures, and outcome indicators [9].

1.5 Literature Quality Evaluation

We used the Cochrane Handbook-recommended Risk of Bias tool to evaluate included randomized controlled trials, rating each of seven items as "high risk," "unclear risk," or "low risk." We used the MINORS scale based on 12 items (total score 24 points) to evaluate non-randomized interventional clinical trials, with each item scored 0-2 points based on whether reporting information was adequate: 0-13 points indicated low quality, 14-18 points moderate quality, and 19-24 points high quality [10]. We used the AMSTAR-2 scale with 16 items to evaluate methodological quality of systematic reviews/Meta-analyses, rating each as "yes," "partial yes," or "no," with items 2, 4, 7, 9, 11, 13, and 15 identified as critical items, and quality grades determined based on item characteristics and compliance numbers [11]. Additionally, we used PRISMA reporting standards for network Meta-analysis [12], AGREE-China tool [13], JBI 2016 evaluation tool [14], and HTA reporting standards (2007 version) [15] to evaluate quality of included network Meta-analyses, guidelines, expert consensus statements, and health technology assessment literature.

1.6 Analysis Methods

We conducted descriptive analysis of important study information using a combination of text and charts, with evidence distribution presented using bubble charts.

Results

2.1 Literature Screening

The initial search yielded 7,695 articles. After applying inclusion and exclusion criteria, 130 articles were finally included, comprising 82 clinical trials (including 76 randomized controlled trials and 6 non-randomized controlled trials), 30 systematic reviews/Meta-analyses, 9 network Meta-analyses, 7 guidelines/consensus statements/pathways, 1 overview of systematic reviews, and 1 health technology assessment. The specific screening process is shown in Figure 1

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2.2 Publication Status

Over the past five years, publications on Chinese patent medicines for AD have shown a fluctuating downward trend, with higher numbers in 2020, 2021, and 2023, and fewer in 2024. The overall number of publications is relatively small, likely related to the preliminary research stage of Chinese medicines for AD,

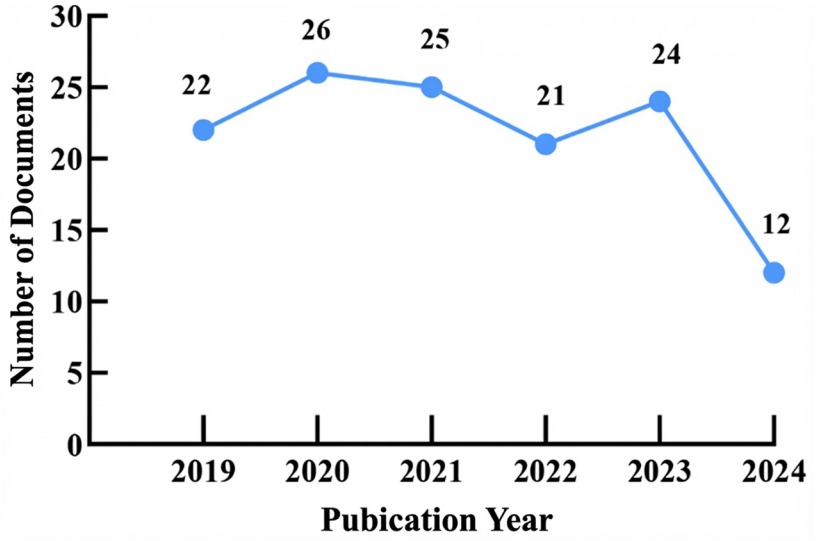

Figure 1: Figure 1

the limited number of marketed Chinese patent medicines for AD, and potential delays in database indexing. The publication trend is shown in Figure 2

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2.3 Clinical Trial Characteristics

2.3.1 Distribution of Chinese patent medicines: Among 82 clinical trial articles, 21 Chinese patent medicines were used for AD treatment (counted as 85 instances), comprising mainly oral preparations and injectable formulations. Oral preparations were dominated by Compound Congrong Yizhi Capsule (18.82%) and Compound Haishe Capsule (14.12%), while injectables were mainly Ginkgo biloba extract (10.59%), as shown in Table 1 . By reviewing drug instruction manuals, we found that none of the Chinese patent medicines had AD indications, though Compound Congrong Yizhi Capsule, Compound Haishe Capsule, Ginkgo biloba extract injection, Tianzhi Granules, Dengzhan Shengmai Capsule, Guilingji Capsule, Jiannao Capsule, Compound Huonaoshu Capsule, and Qinggong Shoutao Pills were directly related to dementia or included dementia in symptom descriptions. The remaining medicines including Ginkgo biloba tablets (capsules), Liuwei Dihuang pills, Haingshao Dan (capsules), Yangxue Qingnao pills (granules), Compound Danshen tablets, Jinkui Shenqi pills, Compound Huonaoshu capsules, Huangqi injection, Naoxintong capsules, Qinggong Shoutao pills, Yinxing Damo injection, Yinxing Neizhi injection, and Huatuo Zaizao pills were related to the etiology and pathogenesis of AD in Traditional Chinese Medicine.

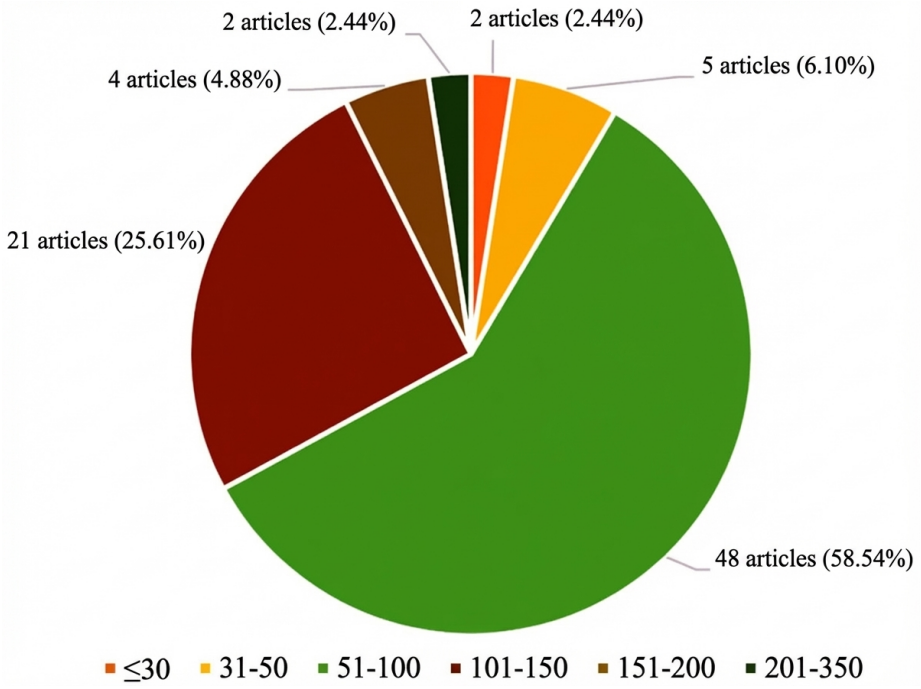

Figure 2: Figure 2

2.3.2 Sample size: The total sample size in clinical trials of Chinese patent medicines for AD ranged from 14 to 350 cases, with most (58.54%) including 51-100 cases. Smaller sample sizes were concentrated in studies with more than 150 cases (7.32%), 31-50 cases (6.10%), and fewer than 30 cases (2.44%), indicating that only a minority of clinical trials included more than 100 AD patients, as shown in Figure 3

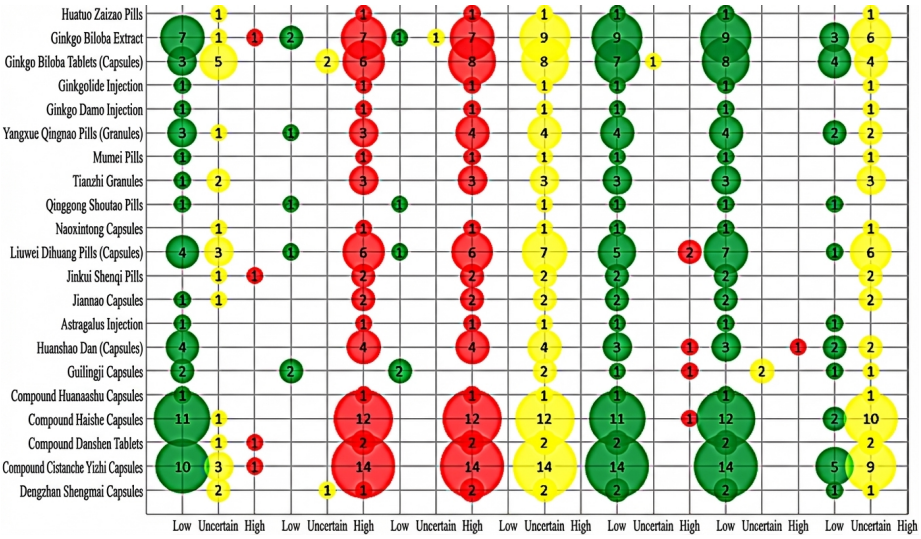

Figure 3: Figure 3

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2.3.3 Clinical trial outcome indicators: Among 82 randomized controlled trials, outcome indicators primarily evaluated efficacy and safety and could be categorized into eight domains: (1) composite endpoints including total effective rate; (2) cognitive function evaluation indicators including Mini-Mental State Examination (MMSE), Alzheimer's Disease Assessment Scale-Cognitive (ADAS-Cog), Montreal Cognitive Assessment (MoCA), Clinical Dementia Rating (CDR); (3) surrogate endpoints including -amyloid (A), Tau protein, interleukin-1 (IL-1), superoxide dismutase (SOD), Beclin-1; (4) signs and symptoms including TCM syndrome scores, TCM Syndrome Scale (CMSS), Dementia Syndrome Differentiation Scale (SDSD), clinical complications (fever, nausea, dizziness, headache), and Kidney Deficiency Syndrome Clinical Global Impression of Change (CGIC-KDS); (5) safety indicators including adverse reaction rates and adverse event rates; (6) endpoint events including AD disease progression rate and long-term clinical efficacy; (7) quality of life indicators including Alzheimer's Disease Cooperative Study Activities of Daily Living Scale (ADAS-ADL), Activities of Daily Living Scale (ADL), Barthel Index (BI); and (8) other indicators including hemorheology (vertebrobasilar artery blood flow velocity, basilar artery (BA), bilateral middle cerebral artery

(MCA) mean flow velocity (MFV), urinary AD-related neurofilament protein (AD7c-NTP), fecal gut microbiota (Firmicutes, Actinobacteria), resting-state functional magnetic resonance imaging low-frequency amplitude (ALFF)). Detailed indicator domains are shown in Figure 4

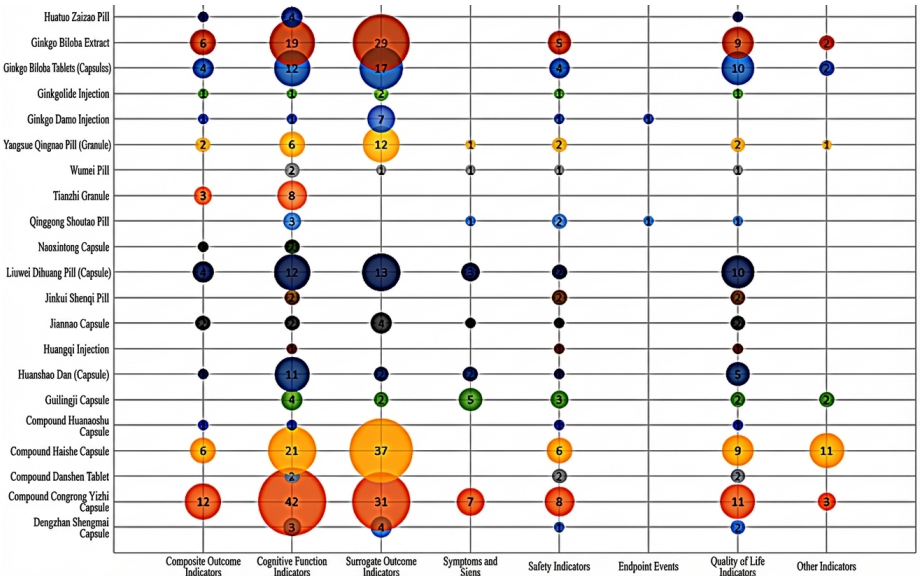

Figure 4: Figure 4

. Bubble charts revealed that cognitive function indicators, surrogate endpoints, and quality of life indicators were each used more than 50 times in clinical trials of Chinese patent medicines for AD, as shown in Figure 5

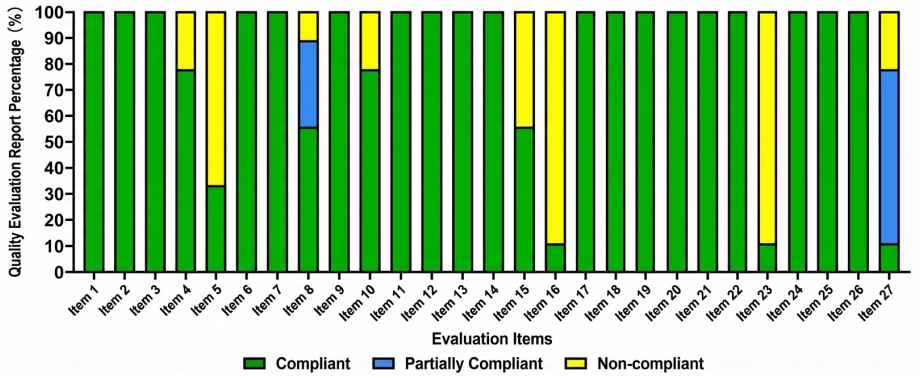

Figure 5: Figure 5

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2.3.4 Quality evaluation of clinical trial literature: Risk of bias assessment of 76 randomized controlled trials revealed generally low literature quality. Some studies had high risk of bias in random sequence generation (e.g., using admission order), reported patient dropout without describing statistical methods for handling missing data; most studies had deficiencies in blinding design and implementation, did not clearly report allocation concealment methods, and failed to report other potential sources of bias, as shown in Figure 6 [FIGURE:6]. Among six non-randomized controlled trials, three used Tianzhi Granules, two used Compound Congrong Yizhi Capsule, and one used Ginkgo biloba capsule for AD treatment, with quality evaluation scores of 14-17 points (moderate quality). Unreported items mainly involved prospective data collection, objectivity of outcome evaluation, reporting of follow-up duration, and pre-sample size calculation, as shown in Table 2 .

2.4 Systematic Reviews/Meta-analyses and Network Meta-analyses

The 30 included systematic reviews/Meta-analyses and 9 network Meta-analyses reported the efficacy and safety of Chinese patent medicines (including injections) for treating or participating in AD treatment. Network Meta-analyses reported Chinese patent medicines for AD including Compound Congrong Yizhi Capsule, Ginkgo biloba extract, Compound Haishe Capsule, Tianzhi Granules, Compound Danshen tablets (pills), Hongjingtian Capsule, Yangxue Qingnao Granules, Yinxing Tongzhi Dripping Pills, Liuwei Dihuang pills (tablets), Huatuo Zaizao pills, Naoxueshu Oral Liquid, and Dengzhan Shengmai Capsule. Network Meta-analysis results indicated that Chinese patent medicines combined with Western medicine—specifically Compound Haishe Capsule, Dengzhan Shengmai Capsule, Compound Congrong Yizhi Capsule, and Ginkgo biloba preparations—may have better therapeutic effects in promoting cognitive function improvement and enhancing quality of life. Ranking of evaluation indicators and treatment measures from five network Meta-analyses [16-20] is shown in Table 3 .

Four other network Meta-analyses involved Chinese patent medicines as follows: Xiong Fanjie [21] reported clinical outcomes of Chinese patent medicines for AD, including clinical effective rate [13 interventions, 3rd: acupuncture + Chinese patent medicine + bile + AChEIs; 6th: Chinese patent medicine + AChEIs; 7th: Chinese patent medicine), ADL scores (10 interventions, 2nd: acupuncture + Chinese patent medicine + AChEIs; 7th: Chinese patent medicine), and MMSE scores (13 interventions, 3rd: acupuncture + Chinese patent medicine + AChEIs; 4th: Chinese patent medicine + AChEIs), but did not specify the Chinese patent medicine names. Bai Yuru [22] only mentioned that one included study used Compound Danshen tablets combined with electroacupuncture for AD patients [23]. This study included 86 AD patients comparing electroacupuncture plus Compound Danshen tablets versus Compound Danshen tablets alone, showing that electroacupuncture combined with Compound Danshen tablets was superior in improving MMSE, HDS-R, and ADL scores. ZHANG [24] re-

ported clinical outcomes of different drug doses (including Ginkgo biloba extract) for AD, including MMSE scores (13 interventions, 6th: EGb761 160 mg), ADAS-Cog scores (15 interventions, 14th: EGb761 240 mg), ADL scores (14 interventions, 10th: EGb761 240 mg + donepezil 10 mg; 13th: EGb761 240 mg), NPI (10 interventions, 1st: EGb761 240 mg; 2nd: EGb761 240 mg + donepezil 10 mg), adverse reactions (14 interventions, 1st: EGb761 240 mg; 5th: EGb761 240 mg + donepezil 10 mg), and acceptability (15 interventions, 1st: EGb761 240 mg; 3rd: EGb761 160 mg; 8th: EGb761 240 mg + donepezil 10 mg). THANCHAROEN [25] reported clinical outcomes of different drugs (including Ginkgo biloba extract) for AD, including cognitive function outcomes (7 interventions, 5th: EGb761), functional outcomes (7 interventions, 5th: EGb761), behavioral symptom outcomes (7 interventions, 1st: EGb761), clinical overall improvement outcomes (7 interventions, 4th: EGb761), and adverse reaction outcomes (7 interventions, 5th: EGb761).

Using AMSTAR-2 scale to evaluate methodological quality of 30 systematic reviews/Meta-analyses revealed low quality overall, with 8 rated as low quality and 22 as critically low quality. Analysis of specific items showed that all included systematic reviews/Meta-analyses failed to report reasons for included study types, did not provide lists of excluded literature with reasons, and most did not report funding sources of included studies. More than half failed to report pre-designed protocols, dual independent searching, and did not assess the potential impact of included studies' risk of bias on systematic review/Meta-analysis results. Therefore, methodological quality of systematic reviews/Meta-analyses on Chinese patent medicines for AD requires further improvement, as shown in Figure 7 [FIGURE:7]. Evaluation of reporting quality of included network Meta-analyses revealed that more than half failed to register study protocols and did not report pre-planned sensitivity or subgroup analyses. More than half reported funding sources but did not describe their role in the study, as shown in Figure 8 [FIGURE:8]. Additionally, all literature failed to use GRADE evaluation to assess certainty of evidence from network Meta-analyses.

2.5 Guidelines/Consensus/Pathways and Quality Evaluation

Seven guidelines/consensus statements/pathways recommended Chinese patent medicines for AD, including six from China and one from Singapore. Five recommended Ginkgo biloba extract and its preparations, three recommended Compound Congrong Yizhi Capsule, two recommended Tianzhi Granules, and one each recommended Cistanche glycoside capsules, Qinggong Shoutao pills, Compound Haishe Capsule, Compound Danshen tablets, and Liuwei Dihuang pills. Quality evaluation of two guidelines yielded scores of 67 and 71.5 points, indicating strong recommendation potential. Unreported content mainly included whether external expert review was conducted before publication, guideline update plans, safety of recommended protocols, and consideration of health economics issues. Evaluation of expert consensus showed reliable formulation

and authenticity, but all failed to explicitly identify inconsistencies with previous consensus statements. Furthermore, methodological development of guidelines/consensus requires improvement, as only two guidelines reported literature search strategies and screening methods, three did not specify whether conflicts of interest existed in guideline/consensus development, and six did not clarify sponsor involvement or its impact on recommendation formation, thus affecting quality and scientific evaluation of AD clinical guidelines to some extent.

2.6 Health Technology Assessment/Overview of Systematic Reviews

One rapid health technology assessment [33] analyzed the efficacy, safety, and economic evidence of Ginkgo biloba extract for AD. The study included nine studies (eight systematic reviews and one pharmacoeconomic study), concluding that Ginkgo biloba extract could improve cognitive function, ADL scores, clinical global impression of change, and quality of life for AD patients and caregivers to some extent, though efficacy was not definitive. Regarding safety, adverse reaction rates of Ginkgo biloba extract showed no statistical difference from placebo. Economically, Ginkgo biloba extract demonstrated cost-effectiveness advantages and could indirectly save patient care costs. Quality evaluation of the health technology assessment literature revealed high reporting quality, but lacked explicit statements on specific participant roles, conflict of interest declarations, and whether external peer review was conducted, as shown in Table 4 .

One overview of systematic reviews [34] reported on systematic reviews of Chinese herbal medicine (including Ginkgo biloba extract) for AD. The study included 12 systematic reviews comprising 163 randomized controlled trials, showing that compared with donepezil alone, Chinese medicine combined with donepezil significantly improved MMSE, ADAS-Cog, CDR scores, and total effective rate, with similar efficacy for Chinese medicine alone. Both Chinese medicine alone or combined with donepezil had lower adverse reaction rates than donepezil alone, though GRADE evidence levels were all low or very low.

Discussion

This study systematically organized and analyzed literature on Chinese patent medicines for AD from the past five years using evidence mapping, further analyzing the evidence landscape and current research status. Overall, research attention on Chinese patent medicines for AD has shown a fluctuating downward trend, with most studies being single-center, small-sample randomized controlled trials. The 21 Chinese patent medicines reported were mainly oral preparations and injections, with oral preparations having the most literature reports.

Comprehensive analysis of included clinical trials revealed three main research deficiencies: (1) Insufficient focus on syndrome differentiation and treatment for AD, with only about 24.35% of clinical trials explicitly reporting TCM syn-

drome types (mainly including kidney deficiency and blood stasis syndrome, liver-kidney deficiency with phlegm-blood stasis obstruction syndrome, marrow sea insufficiency syndrome, spleen-kidney deficiency syndrome, yin deficiency syndrome, and kidney deficiency marrow reduction syndrome), while 73.17% of studies did not include TCM syndrome differentiation-based efficacy evaluation indicators (such as TCM syndrome scores), mostly using researcher-designed, non-standardized TCM syndrome efficacy evaluation indicators. (2) Among outcome indicators, cognitive function indicators, surrogate endpoints, and functional indicators were most frequently used, but variations in types, quantities, and measurement methods of cognitive function indicators across studies could introduce heterogeneity, affecting reliability, accuracy, and evaluation of high-quality clinical evidence. Meanwhile, total effective rate as a composite endpoint was vaguely defined, highly subjective, and lacked standardized evaluation criteria, making it difficult to objectively reflect intervention characteristics of Chinese medicines [35]. We recommend developing a core outcome set for AD treatment following standard development procedures to create evaluation tools that accurately reflect Chinese medicine treatment characteristics. (3) Quality of clinical trial literature on Chinese patent medicines for AD requires improvement, particularly in random sequence generation, allocation concealment, and blinding implementation, as well as addressing missing data impact on results. As the gold standard for evaluating therapeutic efficacy, randomized controlled trials in this study lacked rigorous design and implementation, potentially affecting evidence authenticity and reliability.

Quality evaluation of systematic reviews/Meta-analyses revealed that all included studies were rated as low or critically low quality. Future research should focus on: (1) Developing protocols before conducting systematic reviews and describing protocol registration in articles; (2) Explicitly stating included literature types and rationale; (3) Conducting comprehensive literature searches including grey literature to minimize publication bias; (4) Using dual independent data extraction and verification; (5) Providing lists of excluded literature with reasons; (6) Reporting funding sources of included studies; (7) Analyzing heterogeneity and publication bias; and (8) Declaring all potential conflicts of interest.

Over the past five years, two clinical practice guidelines, three expert consensus statements, one diagnostic standard, and one TCM clinical pathway were published, with only three explicitly reporting TCM syndrome differentiation for AD. This may relate to current usage of Chinese patent medicines and status of herbal extracts for AD. Future development should integrate evidence profiles with patient preferences to formulate targeted recommendations. Recommended Chinese patent medicines in guidelines/consensus all involved off-label use, which should be employed cautiously in clinical practice to reduce medication risks. However, under the current “three-combination” evidence framework for Chinese medicine registration and evaluation, accumulating real-world evidence can provide clues for developing modified new drugs with new indications for marketed Chinese medicines [36, 37].

This study is the first to use evidence mapping to analyze literature on Chinese patent medicines for AD from the past five years, visually demonstrating the evidence and research status. However, limitations include: (1) Failure to search clinical trial registration platforms, other grey literature, and non-English literature, with analysis limited to published years and relatively small evidence volume; (2) Although searches included other study types such as single-group clinical trials, cohort studies, and case-control studies, no such literature was found, suggesting relatively narrow evidence scope; (3) Methodological and reporting quality of included systematic reviews/Meta-analyses and network Meta-analyses was evaluated, but evidence grading was not further assessed.

Conclusion

This study systematically reviewed clinical research on Chinese patent medicines for AD, analyzing relevant evidence and research status. Future clinical study design and implementation should follow a "patient-centered" concept, conducting clinical studies that align with characteristics and advantages of Chinese medicine AD treatment practice. Clinical trial design should be strengthened, particularly regarding prospective trial registration, random sequence generation, random allocation concealment, blinding implementation (such as double-blind, double-dummy design), patient compliance, data attrition, and data analysis, with strict adherence to CONSORT reporting guidelines. A core outcome set for Chinese patent medicines treating AD should be developed to formulate evaluation tools that accurately reflect Chinese medicine therapeutic characteristics, explore efficacy evaluation indicators for TCM syndrome differentiation, and particularly focus on timing and methods of outcome measurement to more precisely identify clinical advantages and characteristics, further highlighting clinical value. Future evidence mapping studies should continuously improve research processes and result analysis to provide higher quality and graded Chinese medicine evidence for AD treatment. Additionally, development and standardization of TCM diagnosis and treatment expert consensus, clinical practice guidelines, and health technology assessment for AD should be further strengthened.

Author Contributions: LI Hao conceived and designed the study and discussed research ideas with TAN Libo. TAN Libo developed the overall research plan and conducted literature searches. TAN Libo and LIU Nanyang performed literature screening, data extraction, data organization, and analysis. TAN Libo drafted the manuscript. LIU Nanyang participated in manuscript revision. LI Hao revised and approved the final version, taking overall responsibility and supervision. All authors confirmed the final manuscript.

Conflict of Interest: The authors declare no conflicts of interest.

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