



# Bibliometric analysis of traditional Chinese medicine in the prevention and treatment of Alzheimer's disease (2015-2024)

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## Highlights

- Summarize the latest research advances in Alzheimer's disease, including its pathogenesis, physiological biomarkers, and therapeutic strategies.
- Analyze the publication trends and current landscape of research on traditional Chinese medicine for Alzheimer's disease prevention and treatment using both quantitative and qualitative bibliometric methods.
- Summarize the therapeutic effects of traditional Chinese medicine and the discovery of novel treatment targets and pathways.
- Develop novel perioperative neurocognitive disorder therapies from Alzheimer's TCM research.

## Abstract

**Objective:** Alzheimer's disease (AD), the most common form of dementia, poses a significant global public health challenge. This study aimed to systematically assess the research landscape of traditional Chinese medicine (TCM) in the prevention and treatment of AD using bibliometric methods, with particular emphasis on its distinctive mechanisms and recent progress in clinical translation. **Methods:** Publications on TCM for AD prevention and treatment from 2015 to 2024 were retrieved from the Web of Science Core Collection. Key bibliometric indicators, including authorship, keywords, journals, countries, institutions, and references, were extracted and analyzed. **Results:** A total of 705 publications from 35 countries and 835 institutions were included. Among the top 10 contributing countries, 60% were located in Asia, while the rest were from North America, Europe, and Oceania. China led the field with 654 publications, accounting for 86.6% of the total output. The Journal of Ethnopharmacology emerged as the most influential journal based on citation count (848 citations). Keyword analysis highlighted molecular docking, neuroinflammation, and oxidative stress as key research hotspots. **Conclusion:** This bibliometric analysis offers valuable insights into global trends and research priorities regarding TCM in AD treatment. The findings provide a theoretical basis for promoting the clinical application of TCM and support the advancement of integrated efforts across industry, academia, and research sectors. The study also demonstrates enormous potential for cross-integration with perioperative medicine. Such integration is crucial for enhancing the role of TCM in the prevention and management of AD.

**Keywords:** Traditional Chinese medicine, Alzheimer's disease, bibliometrics, senile dementia

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## Introduction

Alzheimer's disease (AD) is a neurodegenerative disorder characterized by insidious onset and progressive decline, primarily manifested as cognitive impairments in language, memory, executive function, judgment, and other domains [1-3]. According to the World Health Organization, an estimated 55 million individuals worldwide were living with AD in 2023. With the global population aging, this number is projected to reach 139 million by 2050, placing a substantial burden on patients, families, and healthcare systems [4]. Although the pathogenesis of AD remains unclear, prevailing hypotheses include the amyloid-beta (A $\beta$ ) cascade and tau protein hyperphosphorylation theories [5]. Additional contributing factors involve cholinergic neuronal degeneration, neuroinflammation caused by aberrant immune responses, and oxidative stress [6]. Current first-line treatments—such as cholinesterase inhibitors (rivastigmine, galantamine, donepezil) and N-methyl-D-aspartate receptor antagonists (memantine)—primarily act on the neurotransmitter system. While these drugs can temporarily improve symptoms, they do not prevent disease progression. Notably, under the “accelerated approval” pathway, the U.S. Food and Drug Administration approved two A $\beta$ -targeted monoclonal antibodies: aducanumab in 2021 and lecanemab in 2023. Clinical trial data suggest that these agents can significantly slow cognitive decline in patients with early-stage AD [7-9]. However, their overall clinical benefit remains limited. In this context, the development of novel therapeutic strategies emphasizing multi-target and multi-mechanism approaches is gaining momentum.

With advances in science and technology and the deepening of research, the mechanisms underlying the therapeutic effects of TCM have been increasingly elucidated, contributing to its growing integration into modern healthcare systems [10-12]. TCM has demonstrated notable advantages in holistic regulation, reduced side effects, prevention-oriented care, multi-target therapeutic effects, chronic disease management, and modulation of inflammatory and immune responses. Furthermore, its emphasis on individualized treatment and systemic approaches has shown unique efficacy in managing chronic and complex diseases [13-16]. In recent years, an increasing number of researchers have investigated the application of TCM in the treatment of AD, resulting in significant progress and promising breakthroughs.

Bibliometrics is a research methodology that

combines quantitative and qualitative analyses to evaluate the academic output and developmental status of specific research fields. By analyzing publication data, it provides detailed insights across multiple dimensions—such as authors, keywords, journals, countries, institutions, and references—thereby revealing research patterns, hotspots, and emerging trends within a discipline [17, 18]. Commonly used bibliometric tools include CiteSpace, VOSviewer, the “bibliometrix” package in R, and HistCite [19]. These tools facilitate the visualization of analytical results, allowing researchers to gain an intuitive understanding of the structure, evolution, and dynamics of a given research domain. In recent years, bibliometric studies related to AD have proliferated, addressing topics such as the comorbidity between AD and depression, as well as the application of biomarkers [20-24]. However, to date, no bibliometric analysis has specifically focused on the role of TCM in the prevention and treatment of AD. To fill this gap, the present study conducts a comprehensive bibliometric analysis of publications on TCM for AD from 2015 to 2024. The study aims to identify key contributors, map the current research landscape, and explore future trends and developmental prospects in this field.

## Methods

### Search strategy

The Web of Science Core Collection (<https://www.webofscience.com/wos/woscc/basic-search>) was selected as the data source for this study due to its comprehensive coverage of peer-reviewed journals. Search terms were determined based on the Medical Subject Headings database and included: “Chinese medicine”, “Chinese herbal medicine”, “Chinese medicine prescription”, “Chinese patent medicine”, “Alzheimer's disease” and “senile dementia”. The following search strategy was applied: ((TS=(“Chinese medicine”) OR TS=(“Chinese herbal medicine”)) OR TS=(“Chinese medicine prescription”) OR TS=(“Chinese patent medicine”))) AND ((TS=(“Alzheimer's disease”) OR TS=(“senile dementia”))). The search was conducted within the titles, abstracts, and keywords of eligible articles. Given the study's focus on the pharmacological effects of traditional Chinese medicine—specifically herbal prescriptions, medicinal plants, and their active compounds—acupuncture-related terms were excluded from the search strategy. Only original research articles published in English between January 2015 and December 2024 were included. Non-English publications, conference

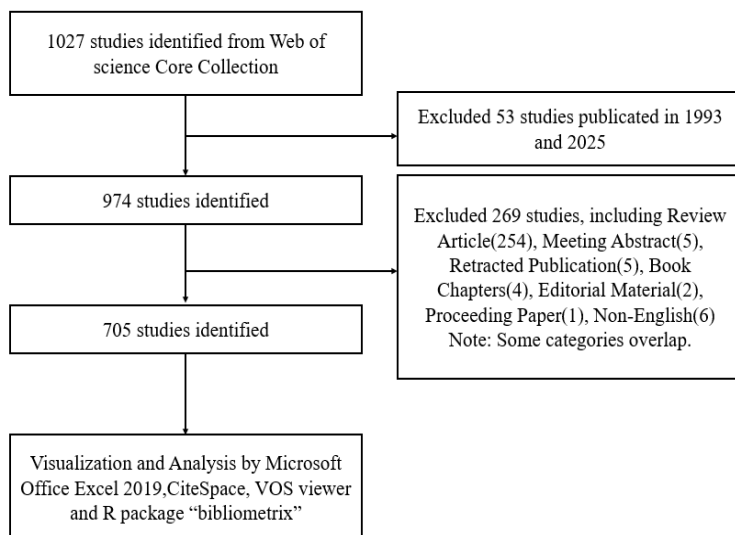


Figure 1. Flowchart of publication screening.

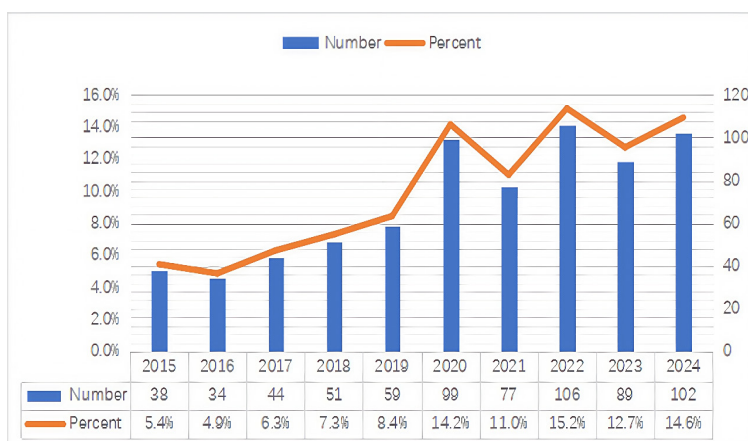


Figure 2. Annual publication output.

abstracts, book chapters, and retracted papers were excluded from the analysis. The detailed screening process is illustrated in Figure 1.

### Data Analysis

A range of specialized tools was employed for bibliometric analysis and data processing. VOSviewer (version 1.6.18), a widely used and efficient bibliometric analysis software, was utilized to extract key information from a large volume of publications. It is commonly applied to construct collaboration networks, co-citation networks, and keyword co-occurrence networks. In this study, VOSviewer was used to analyze countries and institutions, journals and co-cited journals, authors and co-cited authors, as well as keyword co-occurrence patterns. In the visual maps generated by VOSviewer, each node represents an item (e.g., country, institution, author, journal, or keyword), with node size corresponding to its frequency of occurrence. Links between nodes indicate associations

such as collaboration or co-citation. The thickness of the lines reflects the strength of these relationships, and different colors distinguish between clusters or thematic groups [25].

CiteSpace (version 6.1.R1), developed by Professor Chaomei Chen, was employed primarily for citation burst analysis to identify influential references within the dataset [26].

Additionally, the R package “bibliometrix” (version 3.2.1; website: <https://www.bibliometrix.org/>) was used for thematic evolution analysis and to map global research distributions. Microsoft Excel 2019 was applied for quantitative analysis to ensure the accuracy and completeness of the dataset [27].

### Results

#### Quantitative analysis of publications

A total of 705 studies related to the prevention and treatment of AD using TCM were identified over the past decade. Based on annual publication volume, the time frame was divided into two phases: Phase I (January 2015 to December 2019) and Phase II (January 2020 to December 2024). As illustrated in Figure 2, during Phase I, the average annual number of publications was approximately 45.2, with a relatively slow growth rate, indicating the early developmental stage of this research field. Notably, the year 2019 to 2020 marked the most significant annual increase in publication volume, rising from 59 to 99 articles—a year-on-year growth rate of 168%. In Phase II, the average annual publication output increased to 94.6, which is 2.1 times higher than that of Phase I. This trend reflects the growing academic attention and rapid advancement of research on TCM in the context of AD prevention and treatment.

#### Country and institutional analysis

A total of 705 publications were retrieved, originating from 35 countries and 835 institutions. The top ten contributing countries were predominantly located in Asia (n=6) (Table 1),



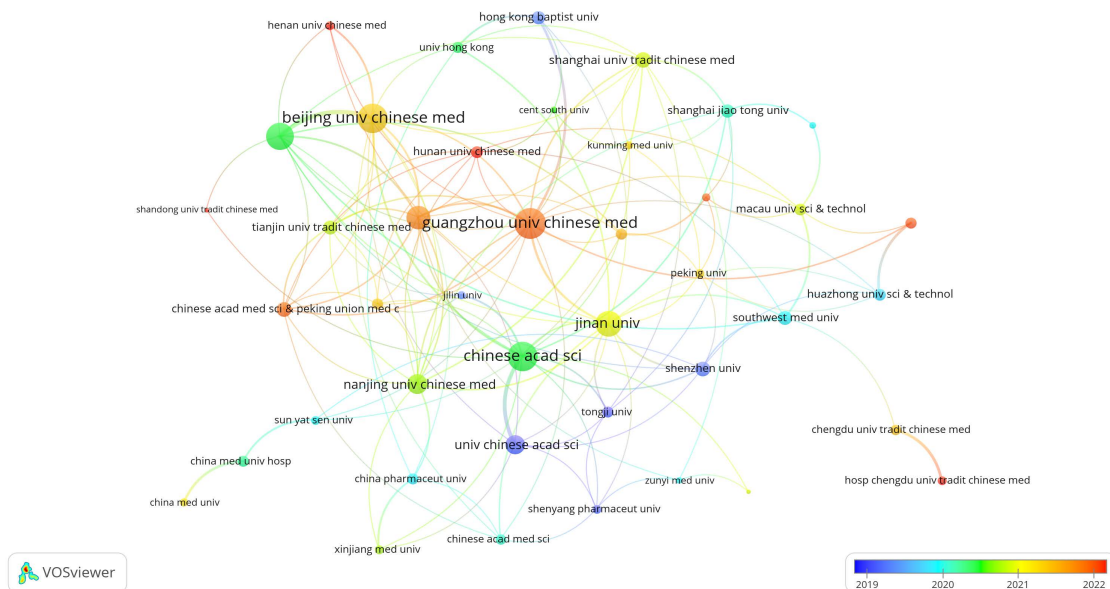


Figure 4. Institutional collaboration network.

Table 2. Top 15 journals and co-cited journals

Rank	Journal	Count	IF	Q	Co-cited Journal	Co-citation	IF	Q
1	Journal of Ethnopharmacology	67 (9.5%)	4.8	Q1	Journal of Ethnopharmacology	848	4.8	Q1
2	Frontiers in Pharmacology	52 (7.4%)	4.4	Q1	Journal of Alzheimer’s Disease	657	3.4	Q2
3	Evidence-based Complementary and Alternative Medicine	32 (4.5%)	2.7	Q3	PLOS ONE	484	2.9	Q1
4	Phytomedicine	18 (2.6%)	6.7	Q1	Nucleic Acids Research	428	16.6	Q1
5	Biomedicine & Pharmacotherapy	14 (2.0%)	6.9	Q1	Evidence-Based Complementary And Alternative Medicine	410	2.7	Q3
6	Chinese Journal of integrative medicine	14 (2.0%)	2.2	Q2	Alzheimer’s dement	409	13	Q1
7	Frontiers in aging neuroscience	14 (2.0%)	4.1	Q2	Frontiers In Pharmacology	406	4.4	Q1
8	Molecules	13 (1.8%)	4.2	Q2	International Journal of Molecular Sciences	406	4.9	Q1
9	American journal of chinese medicine	11 (1.6%)	4.8	Q1	Journal of Neuroscience	399	4.4	Q1
10	International journal of molecular sciences	10 (1.4%)	4.9	Q1	Scientific Reports	365	3.8	Q1
11	Journal of alzheimers disease	10 (1.4%)	3.4	Q2	Molecules	349	4.2	Q2
12	Neural regeneration research	10 (1.4%)	5.9	Q1	Proceedings of The National Academy of Sciences of The United States of America	341	9.4	Q1
13	Food & Function	9 (1.3%)	5.1	Q1	Nature	334	50.5	Q1
14	Bmc complementary medicine and therapies	8 (1.1%)	3.3	Q1	Journal of Biological Chemistry	333	4.2	Q2
15	Current alzheimer research	8 (1.1%)	1.8	Q4	Neurobiology of Aging	320	3.7	Q2

Note: Q, quartile; IF, impact factor.

the China Academy of Chinese Medical Sciences. Notably, Heilongjiang University of Chinese Medicine, despite its relatively high publication count, exhibited limited collaborative engagement with other institutions.

**Journals and co-cited journals**

Research on the prevention and treatment of AD using TCM has been published across 235





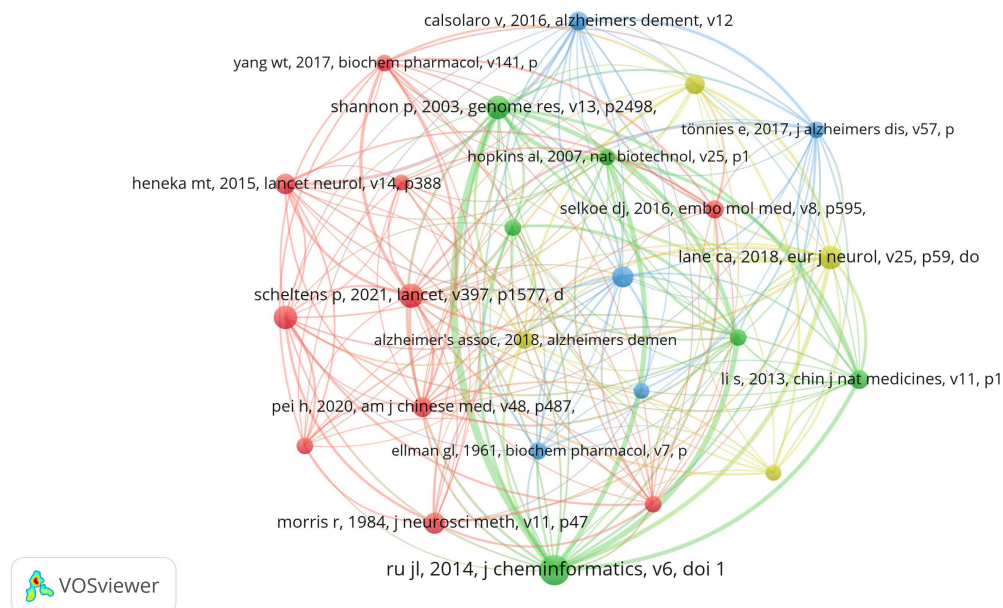


Figure 7. Visualization of co-cited references.

### Top 10 References with the Strongest Citation Bursts

References	Year	Strength	Begin	End	2015 - 2024
Scheltens P, 2016, LANCET, V388, P505, DOI 10.1016/S0140-6736(15)01124-1, DOI	2016	5.56	2017	2020	
Heneka MT, 2015, LANCET NEUROL, V14, P388, DOI 10.1016/S1474-4422(15)70016-5, DOI	2015	4.67	2018	2020	
Ru JL, 2014, J CHEMINFORMATICS, V6, P0, DOI 10.1186/1758-2946-6-13, DOI	2014	3.95	2018	2019	
Kumar A, 2015, PHARMACOL REP, V67, P195, DOI 10.1016/j.pharep.2014.09.004, DOI	2015	3.81	2018	2020	
Alzheimers Assoc, 2018, ALZHEIMERS DEMENT, V14, P367, DOI 10.1016/j.jalz.2018.02.001, DOI	2018	3.73	2018	2020	
Selkoe DJ, 2016, EMBO MOL MED, V8, P595, DOI 10.15252/emmm.201606210, DOI	2016	5.83	2019	2020	
Yang WT, 2017, BIOCHEM PHARMACOL, V141, P143, DOI 10.1016/j.bcp.2017.07.002, DOI	2017	3.87	2019	2020	
Jarrell JT, 2018, MOLECULES, V23, P0, DOI 10.3390/molecules23051143, DOI	2018	4.7	2021	2022	
Lopez JAS, 2019, HAND CLINIC, V167, P231, DOI 10.1016/B978-0-12-804766-8.00013-3, DOI	2019	4.34	2022	2024	
Pei H, 2020, AM J CHINESE MED, V48, P487, DOI 10.1142/S0192415X20500251, DOI	2020	4.14	2022	2024	

Figure 8. Top 10 references with strong citation bursts.

Table 4. Top 10 co-cited references

Rank	Co-cited reference	Citations
1	Ru JL, 2014, J Cheminformatics, v6 (28)	65
2	Scheltens P, 2021, Lancet, v397, p1577	39
3	Lane CA, 2018, Eur J Neurol, v25, p59	37
4	Shannon P, 2003, Genome Res, v13, p2498	37
5	Vorhees CV, 2006, Nat Protoc, v1, p848	37
6	Morris R, 1984, J Neurosci Meth, v11, p47	31
7	Hardy J, 2002, Science, v297, p353	30
8	Heneka MT, 2015, Lancet Neurol, v14, p388	29
9	Pei H, 2020, Am J Chinese Med, v48, p487	25
10	Scheltens P, 2016, Lancet, v388, p505	25

central nervous system-specific autoantibodies. Lastly, the impaired clearance mechanism of cell membrane-associated DNA described in the study, particularly the dysfunction of the 30 kDa membrane receptor, may provide a conceptual reference for analogous autoimmune phenomena in observed AD, such as impaired  $\beta$ -amyloid protein clearance.

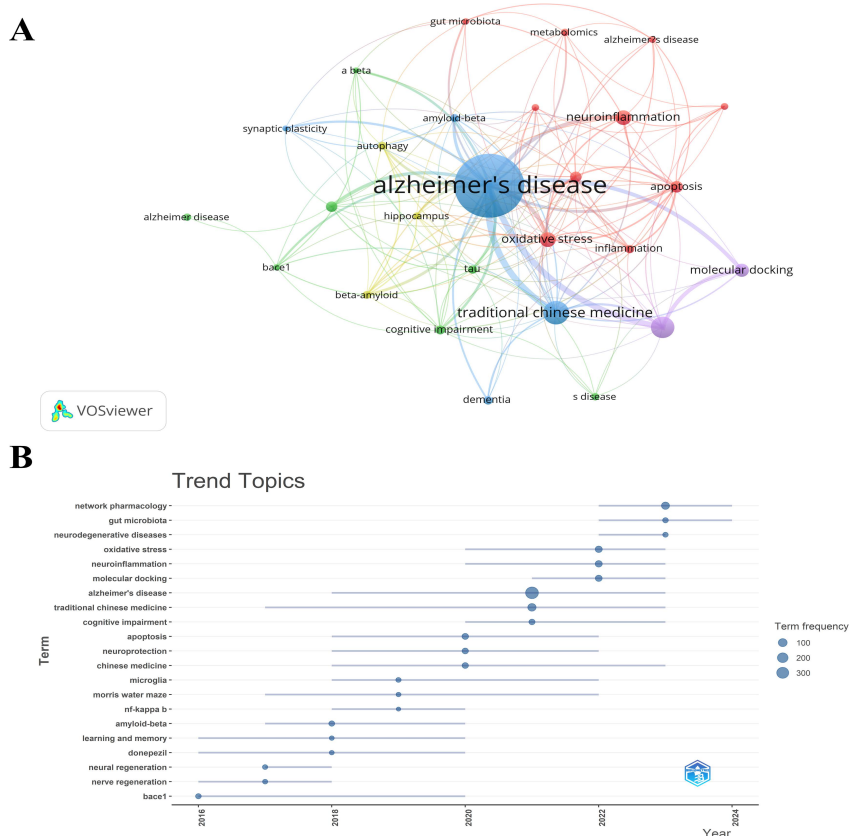
#### References with citation bursts

References with citation bursts are those that have been frequently within a specific time-frame, indicating emerging or transient scholarly interest. In this study, ten references demonstrated strong citation bursts, as identified using CiteSpace software (Figure 8). In the visualization, red bars represent periods of high ci-

**Table 5. Main research content of the top 10 references with strong citation bursts**

Rank	Strength	Main research content
1	5.56	Overview of major developments in Alzheimer’s disease research [28].
2	4.67	Characterization of the neuroinflammatory landscape in Alzheimer’s disease [29].
3	3.95	Use of the TCMSP database to construct drug-target and drug-disease networks, facilitating the development of novel herb-based therapeutics [30].
4	3.81	Exploration of various pathophysiological mechanisms underlying Alzheimer’s disease [31].
5	3.73	Assessment of the public health impact of Alzheimer’s disease [32].
6	5.83	Summary of three decades of key findings supporting the amyloid hypothesis, along with discussion of alternative perspectives and challenges [33].
7	3.87	Evaluation of the efficacy and safety of Chinese herbal medicine for Alzheimer’s disease, with exploration of its role in promoting neurogenesis [34].
8	4.7	Investigation into the potential of traditional Chinese medicine in treating Alzheimer’s disease through network pharmacology approaches [35].
9	4.43	Review of recent advances in Alzheimer’s disease research [36].
10	4.14	Demonstration of the effectiveness of traditional Chinese herbs in improving cognitive dysfunction [37].

Note: TCMSP, Traditional Chinese Medicine Systems Pharmacology Database and Analysis Platform.



**Figure 9. Hotspots and Frontiers.** (A) Visualization of keyword cluster analysis; (B) Trend topic analysis.

tation burst intensity. The earliest citation burst occurred in 2017, and the most recent in 2024. The reference with the strongest citation burst (strength=5.83) is “The amyloid hypothesis of Alzheimer’s disease at 25 years” by Selkoe et al., with a burst period from 2019 to 2020. The second strongest burst (strength= 5.56) is associated with “Alzheimer’s disease”, published in The Lancet by Philip S et al., spanning the period from 2017 to 2020. Overall, the burst

strength of these ten references ranged from 3.73 to 5.83, with durations varying between 2 and 4 years. **Table 5** provides a summary of the key research content of these references, listed in the same order as shown in **Figure 8** [28-37].

**Hotspots and frontiers**

Keyword co-occurrence analysis enables the rapid identification of research hotspots within

**Table 6. Top 20 keywords**

Rank	Keyword	Count	Rank	Keyword	Count
1	Alzheimer's disease	361	11	Dementia	17
2	Traditional Chinese medicine	78	12	Tau	17
3	Network pharmacology	68	13	Inflammation	16
4	Oxidative stress	39	14	Amyloid-beta	15
5	Neuroinflammation	38	15	Autophagy	15
6	Molecular docking	32	16	Beta-amyloid	15
7	Apoptosis	27	17	Alzheimer disease	14
8	Chinese medicine	23	18	Metabolomics	14
9	Neuroprotection	23	19	Senile disease	13
10	Cognitive impairment	18	20	Acetylcholinesterase	12

a specific field. **Table 6** presents the top 20 high-frequency keywords in studies on the prevention and treatment of AD using TCM. Among these, “Alzheimer’s disease”, “traditional Chinese medicine” and “network pharmacology” appear more than 60 times, highlighting the primary research directions in this area. Keywords with at least 10 occurrences were selected for cluster analysis using VOSviewer (**Figure 9A**). In the visualization, thicker lines indicate stronger connections between keywords.

As shown in **Figure 9A**, four major clusters were identified. The blue cluster includes keywords such as “Alzheimer’s disease”, “traditional Chinese medicine”, “dementia”, “synaptic plasticity” and “amyloid-beta”. The red cluster features keywords such as “neuroinflammation”, “oxidative stress”, “apoptosis”, “metabolomics” and “acetylcholinesterase”. The purple cluster includes “network pharmacology” and “molecular docking”. The green cluster contains terms such as “Chinese medicine”, “cognitive impairment”, “amyotrophic lateral sclerosis” and “tau protein.”

Trend topic analysis (**Figure 9B**) indicates that from 2015 to 2020, research primarily focused on neurocognitive aspects, with keywords such as “neuroregeneration”, “learning and memory”, “neuroprotection”, “amyloid-beta”, “nuclear factor kappa B”, “Morris water maze” and “microglia.” After 2020, scholars increasingly explored TCM-based interventions for AD using techniques such as network pharmacology and molecular docking. Representative keywords during this period include “traditional Chinese medicine”, “Alzheimer’s disease”, “molecular docking”, “neuroinflammation”, “oxidative stress”, “neurodegenerative diseases”, “gut microbiota” and “network pharmacology.”

Recent advancements in systems biology and computational tools have facilitated the emergence of innovative approaches—such as net-

work pharmacology and molecular docking—for deciphering the multi-target mechanisms of TCM against AD. Moving beyond the single-target paradigm, these strategies construct comprehensive “component-target-pathway” networks that systematically elucidate the synergistic effects of TCM compounds [38,39]. This integrated research framework—combining bioinformatics, computational chemistry, and experimental validation—has not only revealed the molecular mechanisms underlying classical TCM formulations (e.g., Huanglian Jiedu Decoction and Danggui Shaoyao San) in modulating neuroinflammation, oxidative stress, and synaptic plasticity, but has also provided a theoretical foundation and direction for the development of novel TCM-based anti-AD drugs. Furthermore, the frequent appearance of neuroinflammation and oxidative stress as keywords suggests that these remain central research hotspots in the treatment of AD.

## Discussion

Between 2015 and 2019, research on the prevention and treatment of AD using TCM remained in the exploratory stage, with an average annual publication output of 45.2 articles. However, from 2020 to 2024, the field witnessed a substantial surge in activity, with the average annual number of publications rising to 94.6—representing an impressive 109% increase. This rapid growth indicates that TCM-based AD research has entered a phase of accelerated development and is gradually becoming a focus of international scientific attention. The significant expansion of this research area has been closely aligned with China’s strategic initiatives for TCM development. In particular, the 14th Five-Year Plan for the Development of Traditional Chinese Medicine, issued by the General Office of the State Council in 2022, explicitly called for a substantial enhancement of TCM healthcare service capacity and the establishment of a high-quality development pol-

icy framework by 2025. Driven by strong policy support, the unique advantages of TCM in the prevention and treatment of AD have been fully harnessed, resulting in notable advancements in both research scale and quality.

These advancements have laid a solid foundation for the innovative development of TCM in the field of neurodegenerative diseases. Currently, TCM-based research on AD is rapidly transitioning from basic investigation to clinical translation, highlighting its promising prospects for future development.

The systematic advancement of modernization strategies for TCM has played a pivotal role in shaping an international framework for scientific cooperation. In building a high-level TCM system for the preservation and innovation of TCM, China has implemented a series of comprehensive measures. Notably, a specialized national program for the inheritance of ancient TCM literature has been carried out, resulting in the development of a traditional knowledge database encompassing 32,000 volumes of classical texts. In addition, the strategic establishment of 30 national TCM inheritance and innovation centers, along with 15 interdisciplinary national key laboratories, has contributed to the construction of a complete research and innovation chain.

Notably, this systematic infrastructure development has laid a strong foundation for international collaboration. Statistical evidence indicates that the majority of co-authored publications in TCM-based neurodegenerative disease research are jointly produced by institutions in China and the United States. Moreover, collaborative publications involving Australia, the United Kingdom, India, and Japan have shown a steady upward trend.

In terms of institutional cooperation networks, a stable collaborative cluster-resembling an academic community-has emerged, centered around Beijing University of Chinese Medicine and the China Academy of Chinese Medical Sciences, with more than 40% of their publications involving international collaboration. However, comparative analysis reveals that although Heilongjiang University of Chinese Medicine ranks among the top institutions with an annual output of 27 publications, its international collaboration rate remains at only 12%. This “high-output-low-collaboration” model may hinder the sustained improvement of research quality.

This phenomenon underscores the need to establish more open and inclusive academic

cooperation mechanisms to promote positive interactions between cultural dissemination and technological innovation. Such efforts are essential for advancing the strategic objective outlined in the 14th Five-Year Plan for the Development of Traditional Chinese Medicine-namely, to significantly enhance the international influence of TCM.

With regard to research on TCM for AD, the *Journal of Ethnopharmacology* [IF=4.8, quartile (Q) 1] has published the highest number of articles, indicating its prominence as a leading journal in this research domain. Among the publishing journals, *Biomedicine & Pharmacotherapy* (IF=6.9, Q1) holds the highest impact factor, followed by *Phytomedicine* (IF =6.7, Q1). In terms of co-cited journals, the majority are high-impact Q1 journals, reflecting the academic influence and credibility of the research in this field. An analysis of current clinical research on TCM for the prevention and treatment of AD reveals a clear imbalance between basic and clinical studies. While significant advancements have been achieved in basic research-with 83.2% of publications focused on mechanistic exploration-clinical translation remains relatively limited.

At present, clinical studies account for fewer than 5% of total publications, and rigorously designed trials are even scarcer. According to data from the Chinese Clinical Trial Registry, several representative clinical trials investigating TCM interventions for AD have been registered. These include: (1) A study of *Polygonum cuspidatum* Yizhi Granules for mild cognitive impairment due to AD (ChiCTR2400081422); (2) A randomized, double-blind, placebo-controlled trial of Zhinao Capsule for mild-to-moderate AD (ChiCTR2200066501); (3) A clinical observation of Nourishing Blood Oral Liquid on cognitive function in AD patients with Qi-blood deficiency type (ChiCTR2400087425) (<https://www.chictr.org.cn/question.html>). Notably, the *Polygonum cuspidatum* Yizhi Granules study represents an innovative integration of modern neuroscience theories and technologies with TCM therapeutic principles. By employing high-quality randomized controlled trial methodology, this study systematically evaluates the efficacy of the intervention for mild cognitive impairment due to AD, potentially offering novel therapeutic strategies. It exemplifies the modernization of TCM research for mild cognitive impairment due to AD, wherein the combined advantages of integrative medicine are being harnessed to establish a clinical diagnosis and treatment framework with distinct Chinese characteristics. Such efforts are expected to

yield more effective and internationally recognized treatment protocols.

From the perspective of authorship, Fang JS, Bi KS, Song FR, and Li H contributed a substantial number of publications, with an average of 9.75 articles per author. Further analysis and discussion were conducted based on the works of these most prolific scholars.

Fang et al. have employed systems pharmacology and network pharmacology approaches to investigate the mechanisms of action of various TCM formulations and their active components in the treatment of AD [40, 41]. In 2021, they screened cytochrome P450 3A4 inhibitors from the Bushen Yizhi Formula to enhance the bioavailability of osthole [42]. In the same year, they explored the ability of medicarpin to alleviate scopolamine-induced memory impairment using systems pharmacology methods [43]. Subsequently, by integrating proteomics and metabolomics, they elucidated the molecular mechanisms underlying the effects of Danggui Shaoyao San in amyloid precursor protein/presenilin-1 mice, and identified TCM-derived active compounds that target endoplasmic reticulum stress through network analysis [44]. In 2023, they conducted a comprehensive systems pharmacological evaluation using multi-network models and preliminarily identified the effective material basis and potential molecular mechanisms of kidney-tonifying TCMs for the prevention and treatment of AD via endophenotype network analysis [45]. Additionally, Fang et al. assessed the predictive capacity of the Target Knowledge Graph knowledge graph to identify potential protein targets for AD and to uncover diseases potentially associated with the metallodeubiquitinase COP9 signalosome subunit 5, validating the predictions through literature-based evidence [46]. Although these research findings have not yet to be translated into clinical applications, the exploratory nature of this body of work is highly representative. The research trajectory from 2017 to 2023 reflects the evolving landscape of TCM-based research—progressing from compound identification and mechanistic elucidation to the investigation of systemic regulatory mechanisms.

In terms of co-cited authors, Dennis JS (citation count=79) is the most frequently cited, followed by Ru JL (citation count=65) and Scheltens P (citation count=64). In 2016, Dennis JS reviewed the amyloid hypothesis, emphasizing the central role of A $\beta$  in the early pathogenesis of AD and identifying abnormal A $\beta$  accumulation as a key hallmark of the disease [33]. An

earlier study elucidated the tripeptide cleavage mechanism of  $\gamma$ -secretase in A $\beta$  production, thereby explaining A $\beta$  formation at the molecular level and offering a theoretical foundation for the development of  $\gamma$ -secretase-targeted therapies [47]. Subsequent research demonstrated that large soluble A $\beta$  oligomers possess lower neuroactivity, whereas smaller oligomers exhibit higher neurotoxicity, indicating that both the morphology and size of A $\beta$  oligomers significantly influence their toxic potential. This finding provided a novel perspective on the pathological mechanisms of A $\beta$  [48]. In 2019, clinical trial outcomes of aducanumab—a monoclonal antibody targeting A $\beta$ —were reported, underscoring the need to refine AD treatment strategies and integrate anti-amyloid therapies with other modalities [49]. Collectively, these studies advanced the understanding of A $\beta$ 's role in AD and laid a solid scientific foundation for future diagnostic and therapeutic strategies. The amyloid cascade hypothesis was systematically re-evaluated, with emphasis on abnormal A $\beta$  deposition as an early pathological indicator of AD. A $\beta$  oligomers were proposed as the primary neurotoxic species, providing a rationale for A $\beta$ -targeted drug development. Clinically, A $\beta$ -positron emission tomography imaging and cerebrospinal fluid A $\beta$ 42 detection have been established as early diagnostic criteria for AD, thereby facilitating the development of anti-A $\beta$  monoclonal antibodies such as aducanumab and lecanemab.

Co-cited references refer to publications that are simultaneously cited by multiple independent articles and are therefore considered to represent the theoretical or knowledge foundation of a particular research field. Below is a brief summary of the five most frequently co-cited references.

Ru et al. introduced the Traditional Chinese Medicine Systems Pharmacology Database and Analysis Platform, which encompasses all herbal medicines listed in the Chinese Pharmacopoeia and nearly 30,000 extracted compounds [30]. The platform provides 12 key absorption, distribution, metabolism, and excretion-related properties for drug screening and evaluation, along with information on drug targets and associated diseases for each active compound. In addition, it can automatically construct compound-target and target-disease networks, enabling users to visualize and analyze the mechanisms of drug action. Overall, the platform is designed to promote the development of herbal medicine and facilitate the integration of modern and traditional medicine to advance drug discovery and development.

Scheltens et al. summarized major advances in the field of AD over the past five years, covering clinical signs and symptoms, incidence and mortality rates, causative and risk genes, pathophysiological features, and biomarkers [29]. In 2017, Lane et al. reviewed the clinical manifestations of AD and current treatment strategies, providing an overview of the prevailing understanding of AD epidemiology, genetics, pathology, and pathogenesis [50]. Their work highlighted the extended preclinical phase of AD and its implications for novel therapeutic strategies aimed at shifting the focus from treatment to prevention. Shannon et al. explored molecular, clinical, and neuropathological networks related to viral activity, aligning with the hypothesis that viral processes may underlie general characteristics of AD [51]. By constructing multi-scale virome networks associated with late-onset AD and integrating genomic, transcriptomic, proteomic, and histopathological data from four brain regions of postmortem human tissues, they identified regulatory relationships between viral abundance and amyloid precursor protein metabolic regulators. Collectively, these three publications provided systematic reviews of research progress in AD. However, due to their relatively early publication dates, the current study does not include in-depth interpretation or critical analysis of their findings.

Vorhees et al. systematically introduced the Morris Water Maze, a widely used spatial learning test for rodents [52]. In this paradigm, animals use distal environmental cues to navigate from various starting points within an open swimming arena to locate a submerged escape platform. Key experimental metrics such as escape latency and platform crossing frequency are employed to assess spatial cognitive function. Recognized as a “behavioral cornerstone” in AD research, Morris Water Maze has yielded robust phenotypic data for elucidating pathological mechanisms and facilitating drug screening. Moreover, through continuous technological innovations, the test has driven paradigm shifts in AD research—advancing from phenomenological observation to mechanistic exploration, and from single-target interventions to systemic therapeutic strategies. This methodological approach is considered to hold significant promise for broader applications in the study of neurological disorders.

In addition to references with citation bursts, keyword analysis serves as an effective tool for identifying the distribution and evolution of research hotspots related to the prevention and

treatment of AD using TCM. Beyond general terms such as “Alzheimer’s disease”, “traditional Chinese medicine” and “Chinese herbs”. **Table 6** highlights several frequently occurring keywords, including “network pharmacology”, “oxidative stress”, “neuroinflammation”, “molecular docking” and “apoptosis”. Based on keyword clustering and trending topic analysis (**Figure 9**), the current research on TCM-based prevention and treatment of AD is primarily concentrated in the following thematic aspects.

Firstly, the potential etiology and pathophysiological characteristics of AD have been a major focus. The etiology of AD is multifactorial, involving genetic, environmental, metabolic, and immune components. Based on the cited literature, research has primarily concentrated on key pathogenic mechanisms such as A $\beta$  deposition, abnormal phosphorylation of tau protein, neuroinflammation, oxidative stress, and synaptic dysfunction. These pathological processes result in substantial neuronal loss in the hippocampus and cerebral cortex, ultimately leading to brain atrophy and progressive cognitive decline, which may advance to severe dementia. Secondly, the docking of target molecules and the discovery of novel pathways are central themes [53, 54]. Network pharmacology elucidates the multi-target mechanisms of therapeutic agents by constructing drug-target-disease interaction networks, while molecular docking simulates the binding patterns between drug molecules and target proteins to predict their interactions and affinities. Together, these approaches offer substantial advantages in drug discovery, mechanistic research, and the advancement of personalized medicine.

### Strengths and limitations

This study presents several notable strengths. First, it is the first to conduct a systematic bibliometric analysis of research on AD involving TCM, offering scholars comprehensive guidance for identifying and focusing on relevant literature. Second, three bibliometric tools were employed concurrently—two of which, VOSviewer and CiteSpace, are widely recognized and commonly used in bibliometric research—enhancing the objectivity and reliability of the data analysis process. Third, compared to traditional narrative reviews, the bibliometric approach provides deeper insights into research hotspots and emerging frontiers.

Nonetheless, several limitations should be acknowledged. First, the data were exclusively retrieved from the Web of Science Core Collec-

tion, while other databases were not included, which may have led to the omission of relevant studies. Second, only English-language publications were considered, potentially resulting in the underrepresentation of non-English literature. Finally, publications from the year 2025 were not included in the current analysis.

## Conclusions

TCM holds substantial research value and promising application prospects in the prevention and treatment of AD. The rapid growth in publication volume reflects increasing global interest in the therapeutic potential of TCM, with China playing a leading role. However, greater international collaboration and communication among countries and institutions are still needed.

On one hand, investigations into the pathogenesis and contributing factors of AD offer critical insights for early diagnosis and intervention, while also providing a theoretical foundation for the development of novel drugs and therapeutic strategies. On the other hand, compared to conventional chemical drugs, TCM demonstrates significant advantages, including holistic regulation, multi-target efficacy, and anti-inflammatory immune modulation. Furthermore, TCM emphasizes personalized treatment and a holistic perspective, showcasing unique effectiveness in managing AD.

It is important to highlight that, beyond basic research, future efforts should focus on the clinical translation of research findings, particularly regarding the application of TCM in the prevention and treatment of AD.

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