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Exploring the Mechanisms of Traditional Chinese Medicine Intervention in Ischemic Stroke: A CiteSpace-Based Bibliometric Study and Visualized Analysis

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Abstract

Purpose: This study aims to analyze the research hotspots and emerging trends in the application of Traditional Chinese Medicine (TCM) for the intervention of Ischemic Stroke (IS) utilizing CiteSpace.
Method: A comprehensive search was conducted for pertinent publications within the Science Citation Index Expanded (SCI-Expanded) of the Web of Science Core Collection, covering the period from its inception to May 5, 2025 AD. CiteSpace was employed to generate a network map, facilitating the identification of leading authors, institutions, countries, keywords, co-cited authors, journals, references, and prevailing research trends.
Result: A comprehensive search yielded 1,929 pertinent articles from the SCI-Expanded database. Gao Ying and Wang Lei emerged as the most prolific authors in the SCI-Expanded database, with their publications appearing in various prominent journals. Long Enze and Wang Yi were identified as the authors with the highest citation counts. Leading institutions in this domain include Beijing University of Chinese Medicine and the China Academy of Chinese Medical Sciences, with China being recognized as a dominant contributor to the field. The most frequently cited authors and references predominantly address the epidemiology and characteristics of IS. The top ten keywords, characterized by high frequency and median centrality, include activation, neural regeneration, ischemic stroke, cerebral infarction, Alzheimer's disease, rats, oxidative stress, reperfusion injury, cerebral ischemia, and blood-brain barrier. Notably, the keyword "cell death" exhibited the highest citation burst rate, while "molecular docking", "network pharmacology", and "cognitive impairment" have emerged as significant research frontiers.
Conclusion: This bibliometric analysis identified cell death, cognitive impairment, and brain–gut interactions as major research hotspots in TCM intervention for IS. Future studies should move beyond conventional network pharmacology and molecular docking toward integrating spatial transcriptomics, AI-driven drug discovery, and subtype-specific regulatory cell death research, while establishing a dynamic "TCM syndrome–microbiota–metabolite–brain target" framework to support precise brain–gut co-treatment strategies for IS.

Keywords: Traditional Chinese medicine; Ischemic stroke; bibliometric analysis; Visual Analysis; Cite Space

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1. Introduction

Stroke ranks as the second leading cause of mortality globally, with the burden of post-stroke disability increasing more rapidly in low- and middle-income countries compared to high-income nations. IS is a significant medical condition that can lead to cerebral infarction, characterized by the death of brain tissue and focal neuronal damage. According to the World Stroke Organization's Global Stroke Fact Sheet 2025, the worldwide economic burden of stroke exceeds $890 billion, equivalent to 0.66% of the global GDP. Between 1990 and 2021, there was a marked increase in the global stroke burden, evidenced by a 70.0% rise in new stroke cases, a 44.0% increase in stroke-related deaths, an 86.0% escalation in stroke prevalence, and a 32.0% growth in disability-adjusted life years (DALYs). The majority of this burden, accounting for 87.0% of stroke-related deaths and 89.0% of DALYs, is concentrated in low- and lower-middle-income countries (LMICs). Strokes attributable to metabolic, environmental, and behavioral risks constitute 69.0%, 37.0%, and 35.0% of all stroke cases, respectively.

TCM is recognized as playing a vital role in the management of IS. In particular, the enhancement of neurological function in IS and the reduction of recurrence rates associated with conventional IS therapies are notable [1,2]. The use of the thrombolytic agent Tissue Plasminogen Activator (TPA) has been shown to significantly improve neurological scores and reduce infarction volume following thrombolysis, while also mitigating cerebral hemorrhage and blood-brain barrier injury [3]. A randomized clinical trial involving 2,007 patients with Acute Ischemic Stroke (AIS) demonstrated that those who received Tongxinluo [4], in addition to standard treatment within 72 hours of symptom onset, achieved better functional outcomes compared to the placebo group. TCM offers advantages such as abundant resources [5], effective therapeutic outcomes [6], and minimal side effects [7], positioning it as a promising candidate for the treatment of cerebral ischemia-reperfusion injury (CI/RI) [8].

Consequently, several authoritative guidelines have been issued regarding the application of TCM in the treatment of IS, including the Hong Kong Evidence-Based TCM Clinical Practice Guidelines for Stroke [9], the evaluation of Clinical Practice Guidelines for the management of IS in TCM, and the evaluation of research and evaluation tools through a systematic review [10]. Additionally, the development plan for the core outcome set for IS in TCM clinical trials [11] and the Chinese TCM Patient Stroke Registry (CASES-TCM), which involves multiple institutions and outlines the basic principles and design of a prospective, multicenter, and observational study [12], have contributed to this body of work. Furthermore, a systematic review and meta-analysis on the use of TCM for treating cognitive impairment following stroke [13] have been conducted.

In the context of TCM, ischemic stroke is categorized under "stroke", "epilepsy" or "falling attack". As articulated in "The Inner Classic - Chapter on Regulating the Meridians", it is stated: "When blood and qi travel together upward, it becomes a major collapse", indicating that the occurrence of ischemic stroke is intricately linked to the dynamics of blood and qi [14]. Meanwhile, acupuncture has been employed in the treatment of strokes since ancient times, with the earliest documentation of stroke symptoms and corresponding acupoints found in the seminal Chinese medical text, "The Yellow Emperor's Inner Classic" [15]. Additionally, the differentiation of syndromes and treatment modalities for stroke are elaborated in "Comprehensive Achievements of Acupuncture" [16].

In light of the rapid advancements in science and technology, contemporary research into the anti-ischemic stroke effects of TCM predominantly emphasizes its antioxidant, anti-apoptotic, anti-inflammatory, pro-angiogenic, and pro-neurogenic properties [17]. Despite these advancements, the primary research trends and emerging areas within this domain remain inadequately defined. Future research should prioritize the exploration of signal transduction pathways [18], pyroptosis [19], and the brain-gut axis [20].

Cite Space is a Java-based application that analyzes and visualizes the hotspots of scientific literature and research frontiers in a certain discipline or knowledge field within a certain period through metrology, co-occurrence analysis and cluster analysis [21]. This study analyzed the research hotspots and frontiers of TCM on IS through Cite Space, which is helpful for us to better understand the therapeutic and preventive effects of TCM on IS.

2. Method

2.1. Search strategy

The articles in the core collection of Web of Science, Science Citation Index Expanded (SCI-Expanded) were retrieved from its establishment to May 28, 2025. The detailed retrieval strategy is outlined in Table 1.

2.2. Inclusion and exclusion criteria

The inclusion criteria for the SCI-Expanded database are as follows: peer-reviewed original articles or reviews focusing on the intervention of ischemic stroke with Traditional Chinese Medicine. The exclusion criteria include: 1) meeting abstracts or errata documents; 2) unpublished articles; 3) duplicate publications; and 4) unrelated articles.

The rationale behind this inclusion strategy is that original research provides the most recent experimental data and discoveries, which are fundamental to the advancement of knowledge in the field. In contrast, review articles offer systematic summaries and evaluations of the field, highlighting existing consensus, controversies, and theoretical frameworks. The integration of both types of literature allows for a more comprehensive and multi-dimensional exploration of research hotspots and knowledge structures. At the same time, including reviews also helps to identify high-impact literature and key researchers.

The retrieved articles were exported in plain text format, each file containing complete records and references, and named "download_XXX.txt". These files were subsequently imported into CiteSpace, version 6.2.R4 Advanced Edition, for further analysis.

In constructing the visual knowledge graph, we adhered to the primary procedural steps of CiteSpace, including merging and mapping as outlined in reference [21]. To ensure the reproducibility of the analysis, key parameters in CiteSpace were configured as follows: the time slicing was set to intervals of one year, and the threshold criterion involved extracting the top 50 data points with the highest citation or occurrence frequency within each time slice (Top N = 50). Additionally, a selection criterion of K = 15 was applied, selecting the top 15 high-frequency nodes in each slice. The Cosine algorithm was employed to calculate connection strength, with the analysis scope confined to within the slices. Concurrently, to streamline the network and emphasize the core structure, the Pathfinder algorithm was utilized to prune the merged network, thereby optimizing the network structure and highlighting key paths and turning points.

The fundamental concepts underpinning CiteSpace encompass burst detection, betweenness centrality, and heterogeneous networks, all of which facilitate the timely visualization of research status, emerging trends, and research frontiers [21]. In the various maps, nodes symbolize authors, institutions, countries, or keywords, respectively. The size of a node reflects its frequency of occurrence or citation frequency, while the color of a node denotes either the frequency of occurrence or the year of citation. Additionally, nodes highlighted in purple signify a high degree of centrality and are typically considered as indicators of significant hotspots or pivotal turning points within a given field.

3. Result

3.1. The distribution of articles classified by publication year

Following the removal of 132 invalid records from the SCI-Expanded database, a total of 1,929 records were obtained. As illustrated in Figure 1, there has been an overall increase in the number of published articles, although some fluctuations are evident, with numbers ranging from 84 to 219. The period from 2023 to 2024 witnessed the most significant increase in related publications, with an increment of 56, suggesting a growing interest among researchers in this field.

Similarly, a total of 2,016 records were retrieved from the CNKI and core databases. As depicted in Figure 8, there is a general upward trend in the number of published articles, albeit with certain fluctuations, ranging from 61 to 117. The most notable increase occurred between 2021 and 2022, with an addition of 18 publications, further indicating an increasing focus on this area by the research community.

3.2. Co-Authorship, Co-Institution, Co-Country

We conducted an analysis of the publications using a one-year time interval, focusing on the top 50 entities with the highest citation or occurrence frequency within each interval. The node display mode was set to ”tree ring history”. The lines connecting the nodes represent collaborative relationships, with the color of each line indicating the year of initial collaboration.

The SCI-Expanded merged cooperative network comprises 575 nodes and 838 links, from which we have chosen to visualize only the largest connected component (refer to Figure 2). Similarly, the CNKI merged cooperative network consists of 608 nodes and 827 links, with visualization limited to the largest connected component (refer to Figure 2). The co-author network highlights prolific authors and their collaborative interactions. The most prolific author identified is Gao Ying, with a total of 20 publications, followed by Wang Lei with 17 publications. Despite the presence of numerous authors contributing related articles, there is minimal collaboration among them. Additionally, the authors' centrality is relatively low, suggesting a need for more extensive and high-quality collaborations in future research endeavors.

Generally speaking, Silhouette values are commonly employed to assess the effectiveness of clustering. A silhouette value exceeding 0.7 suggests that the clustering is both efficient and reliable. In this study, the log-likelihood ratio method was utilized to generate 11 clusters within the SCI-Expanded database, all of which exhibited silhouette values greater than 0.9. Similarly, 10 clusters were derived from the CNKI database using the same method, with each cluster also attaining silhouette values above 0.9.

The analysis of SCI-Expanded primarily highlighted topics such as the Brain Heart Formula Capsule, clinical trials, acute cerebral infarction, cognition, cerebral ischemia-reperfusion injury, stellate ganglion, cohort studies, nerve regeneration, antioxidants, the Rosaceae family, and Chinese herbal medicine (refer to Figure 2). In contrast, the CNKI database emphasized areas including cerebral infarction, rats, stroke, traditional Chinese medicine constitution, electroacupuncture, cerebral ischemia, and real-world applications of traditional Chinese medicine (refer to Figure 2).

Figure 3 presents the network diagram of the merged cooperative institutions within the SCI-Expanded database, comprising 275 nodes and 437 links. The leading five institutions in terms of publication output are Beijing University of Chinese Medicine with 144 articles, China Academy of Chinese Medical Sciences with 137 articles, the Ministry of Education - China with 120 articles, Capital Medical University with 82 articles, and Guangzhou University of Chinese Medicine with 72 articles. In contrast, Figure 3 illustrates the network diagram of the merged cooperative institutions within the CNKI database, which consists of 422 nodes and 246 links. The leading five institutions in terms of publication output are Tianjin University of Traditional Chinese Medicine (51 articles); Tianjin University of Traditional Chinese Medicine First Affiliated Hospital (45 articles); Henan University of Traditional Chinese Medicine (42 articles); Henan University of Traditional Chinese Medicine First Affiliated Hospital (38 articles); and the Chinese Academy of Chinese Medical Sciences Institute of Clinical Basic Medicine of Traditional Chinese Medicine (38 articles).

The integrated cooperative country network comprises 65 nodes and 143 links. The People's Republic of China is the most prolific country, contributing 1,701 articles, followed by the United States with 118 articles, South Korea with 75 articles, Singapore with 36 articles, and Japan with 33 articles. With the exception of Singapore, the centrality of the median degree in the other countries exceeds 0.1, underscoring the substantial contributions of these nations to this field (refer to Figure 3).

3.3. Co-cited by the author and the journal

Figure 4 illustrates the co-citation network of authors and journals. The author with the highest number of citations is LONGA EZ, cited 315 times, followed by WANG Y with 277 citations, ZHANG Y with 214 citations, FEIGIN VL with 203 citations, and WANG J with 193 citations. Additionally, WANG L, LI Y, LIU Y, ZHANG L, and LI J are contributors to High School Psychology (Figure 4).

The journal with the highest citation count is STROKE, with 1,229 citations, followed by the Journal of Ethnopharmacology (J ETHNOPHARMACOL) with 1,093 citations, Brain Research (BRAIN RES) with 736 citations, PLOS ONE with 727 citations, and Evidence-Based Complementary and Alternative Medicine (EVID-BASED COMPL ALT) with 693 citations (Figure 4). Moreover, both LANCET and the Journal of Neurochemistry (J NEUROCHEM) exhibit high frequencies and midpoints, underscoring their significant roles in this field (Table 3).

3.4. Key words co-citation and clustering

In general, references that are co-cited most frequently tend to exhibit the most significant citation bursts. Keyword co-citation and clustering provide high-level summaries of the literature. Keywords with high frequency and intensity often indicate the research hotspots within a given field. In our analysis, we examined publications using a one-year time slice and identified the top 30 entries with the highest citation or occurrence frequency within each slice. The resulting co-occurring keyword network comprises 442 nodes and 694 links. Table 4 lists the top 10 keywords characterized by high frequency and centrality.
Using the logarithmic likelihood ratio, we generated 10 clusters, which include topics such as activation, neural regeneration, ischemic stroke, cerebral infarction, Alzheimer's disease, rats, oxidative stress, reperfusion injury, cerebral ischemia, and the blood-brain barrier, as illustrated in Figure 7.

3.5. Keywords: With Citation burst

Figure 8 illustrates the top 30 keywords exhibiting citation bursts. The blue line represents the temporal interval, while the red line denotes the period during which the keywords experienced a surge in citations [30]. The emergence of the highly prominent keyword "cell death" in 2002 underscores the critical importance of cell death in the context of IS. In 2022, the most recent keywords to experience a citation surge were "molecular docking", "network pharmacology" and "cognitive impairment".

4. Discussion

4.1. Summary of the investigation results

Ultimately, in SCI-Expanded a total of 1,929 relevant articles were retrieved. In recent years, there has been a notable increase in research focused on the application of Chinese herbal medicine for the intervention in ischemic stroke (IS), leading to the establishment of a prolific group of authors, prominently including Gao Ying and Wang Lei. China has emerged as a leading nation in this area of research, with numerous studies being published by Chinese universities. The most frequently cited authors and references predominantly address the epidemiology and characteristics of IS. The top ten keywords, characterized by both high frequency and high median centrality, include activation, neural regeneration, ischemic stroke, cerebral infarction, Alzheimer's disease, rats, oxidative stress, reperfusion injury, cerebral ischemia, and blood-brain barrier. Notably, the keyword "cell death" holds the highest citation burst rate, while "molecular docking," "network pharmacology," and "cognitive impairment" are identified as emerging research frontiers.
A comprehensive search on CNKI identified a total of 2,016 pertinent articles. In recent years, there has been a notable increase in scholarly interest regarding the effects of traditional Chinese medicine interventions on ischemic stroke. This burgeoning field of research has led to the emergence of a cohort of prolific authors, prominently led by Xie Yanming. Numerous Chinese universities have contributed significantly to this body of literature. The ten most frequently occurring and centrally positioned keywords include "cerebral infarction", "acupuncture", "cerebral ischemia", "cerebral embolism", "traditional Chinese medicine", "rats", "acupuncture therapy", "electroacupuncture" and "review". Additionally, the terms "gut microbiota", "inflammation", "signal pathways" and "neurofunction" have been identified as emerging focal points within this research domain.
Significant disparities exist in the high-frequency keywords between the SCI-Expanded and CNKI databases. The prevalent terms in SCI-Expanded, such as "Cell Death", "Oxidative Stress" and "Molecular Docking", predominantly concentrate on the cutting-edge research areas of molecular and cellular mechanisms, as well as modern pharmacology. This focus reflects the international academic community's emphasis on understanding the intricate mechanisms of diseases and employing contemporary research methodologies, such as cell experiments, animal models, and molecular pathways, which are widely recognized within the Western scientific paradigm.
Conversely, the high-frequency terms in CNKI, including "Acupuncture", "Electroacupuncture" and "TCM", underscore a greater focus on traditional Chinese medical therapies, clinical interventions, and holistic syndrome differentiation. This divergence is primarily attributed to two factors: firstly, the differing research foci, with international research being more inclined towards the exploration of mechanisms, while domestic research prioritizes clinical practice and the application of traditional therapies. The second factor pertains to Language and Database Bias. Chinese databases tend to focus on the collection of research related to local traditional medicine, whereas English databases predominantly encompass basic and mechanistic research. This divergence complementarily illuminates the distinct dimensions of TCM intervention within Information Systems research.
The disparities observed between the keywords in the SCI-Expanded and CNKI databases should not be construed as data deviations; rather, they represent the intrinsic differences in perspectives and methodologies between traditional Chinese and Western medical research. The SCI-Expanded database exemplifies the deductive reasoning model of "from mechanism to application", while the CNKI database reflects the traditional research trajectory of "from clinical to mechanism". Together, these approaches are complementary and collectively contribute to the body of research on traditional Chinese medicine.

4.2. Research hotspots of Chinese tradition medicine Intervention in IS

4.2.1. Cell death

Apoptosis may be associated with the imbalance of yin and yang, while autophagy might correspond to the impaired function of the spleen in transportation and transformation, and necrosis may be linked to heat toxins, fire pathogens, or blood stasis. The cell death pathway represents a critical pathological mechanism in IS, encompassing endogenous and exogenous apoptosis, necroptosis, autophagy, ferroptosis, parthanatos, phagocyte apoptosis, and pyroptosis [31]. Notably, the inhibition of apoptosis has been shown to mitigate brain ischemia/reperfusion (I/R) injury, thereby reducing the extent of cerebral infarction and enhancing the treatment of IS [32]. Numerous studies have demonstrated that various active ingredients and compounds in TCM exert anti-cell death and neuroprotective effects by modulating key signaling pathways.

For instance, the TCM formulation Buyang Huanwu Decoction has been found to decrease the protein levels of pan-Kla and H3K18la, as well as the transcriptional activity of Apaf-1, thus inhibiting apoptosis [33]. Additionally, baicalein, derived from the TCM Scutellaria extract, has been shown to upregulate the expression of p-PI3K, p-AKT, and Bcl-2 proteins, while concurrently decreasing the levels of apoptotic markers Bax and cleaved caspase-3. This modulation activates the PI3K/AKT signaling pathway, a crucial pro-survival mechanism, thereby influencing cell death and enhancing neuroprotection [34]. Recent research has also indicated a correlation between ferroptosis and endoplasmic reticulum (ER) stress. ER stress, through the generation of NADPH oxidase 4 and other factors, is activated, resulting in cell death [35]. Furthermore, ferroptosis is associated with the inhibition of the Nrf2 pathway. Astragaloside IV (AST IV), an active component in the TCM Astragalus membranaceus, has been found to modulate the Nrf2 pathway, thereby mitigating neuronal death. AST IV effectively prevents ischemic reperfusion injury and significantly reduces its impact on brain cells [36, 37].

4.2.2. Oxidative stress

Oxative stress arises from an imbalance between the generation and elimination of reactive oxygen species (ROS). Traditional Chinese medicine concepts, such as the ”imbalance of yin and yang” [38], ”insufficiency of vital energy” [39], and ”heat pathogen/toxic heat” [40], are notably linked to oxidative stress. Empirical evidence indicates that ROS is implicated in brain damage associated with IS. An elevated ROS level disrupts the antioxidant defense system, leading to oxidative stress and subsequent tissue damage [41]. Furthermore, mitochondrial dysfunction can contribute to the onset of oxidative stress. In IS, abnormal mitochondrial membrane potential and excessive reactive oxygen species (ROS) production are commonly observed, leading to neuronal damage [42].

Oxidative stress plays a significant role in thrombosis formation. The generation of ROS is associated with increased platelet activation, resulting in platelet aggregation and subsequent thrombosis, which may contribute to the onset of IS [43]. In TCM, Salvia miltiorrhiza has been shown to mitigate ROS production by inhibiting oxidase activity, reducing superoxide generation, preventing the oxidative modification of low-density lipoprotein (LDL), and ameliorating mitochondrial oxidative stress. Additionally, it can attenuate the effects of ischemia/reperfusion (I/R) injury [44, 45].

4.2.3. Inflammation

The immune response constitutes a significant pathological mechanism in IS. The inflammatory mediators generated during this process disseminate throughout the body, potentially transforming the physiological state into an ”inflammatory environment”. Among the key representatives of adaptive immune cells are CD4, CD25, and Foxp3 regulatory T (Treg) cells, which play a crucial role in suppressing inflammatory responses and maintaining immune homeostasis. Furthermore, a growing body of research suggests that Treg cells may facilitate the repair of neuronal cells and offer neuroprotection [46].

Additionally, recent years have witnessed increasing scholarly attention on the microbiota-gut-brain axis and its impact on stroke. This axis primarily modulates the immune system and compromises the integrity of the blood-brain barrier (BBB) by influencing gut microbiota and associated metabolites, thereby precipitating inflammatory [47, 48] responses. Empirical studies have demonstrated that the integration of the Traditional Chinese Medicine formula, Tanhuo Decoction, with standard treatment protocols significantly reduces the prevalence of lipopolysaccharide (LPS)-producing bacteria and enhances the diversity of the intestinal microbiota, in comparison to the control group receiving only anticoagulation, lipid-lowering, and blood circulation improvement therapies. This finding suggests a novel approach for stroke treatment [49]. Based on the results of Cite Space, we summarized the research hotspots of Chinese herbal medicine intervention in IS (Tables 5 and 6).

4.3. The purpose and shortcomings of the research

This study represents the inaugural application of CiteSpace analysis to examine the advancements in research on TCM interventions for IS, thereby offering a trajectory for future investigations. Subsequent research endeavors should prioritize exploring cell death mechanisms [78], the brain-gut axis [79–81], and signal transduction pathways [18]. Concurrently, emphasis should be placed on clinical studies of IS utilizing distinctive TCM approaches [82] and on deepening the understanding of TCM theoretical frameworks [83].

The current body of research is notably constrained, lacking a comprehensive exploration of TCM treatments for IS [82], with TCM-related theories remaining underdeveloped [83], and the signal transduction pathways associated with TCM interventions for ischemic stroke not yet fully elucidated [18]. Consequently, future research should concentrate on addressing these gaps.

4.4. New Advances and Prospects of Traditional Chinese Medicine in the Intervention of Ischemic Stroke

From the perspective of citation burst analysis, the most recent keywords that experienced significant citation bursts in 2022 include ”molecular docking,” ”network pharmacology,” and ”cognitive impairment.” Molecular docking and network pharmacology have emerged as prominent topics in the realm of TCM for the treatment of IS, likely due to their strong alignment with the network regulatory approach and holistic perspective inherent in TCM. This trend is linked to developments such as the expansion of TCM-related databases. Nonetheless, future research in this domain should prioritize areas such as the application of deep learning techniques to TCM-related data to enhance docking precision and the development of specialized databases for TCM. The active constituents of Gynostemma pentaphyllum (including Ruvoside_qt, quercetin, 3’-methylformaldehyde, spinasterol, and CLR) have been analyzed through molecular docking, demonstrating potential in IS treatment by modulating various pathways [84].

Furthermore, early cognitive impairment in Chinese patients with AIS is correlated with an increased risk of disability and diminished activities of daily living (ADL) [85]. Irrespective of the identified risk factors, short-term vitamin D deficiency in the acute phase of IS has been linked to an increased incidence of cognitive impairment within one month [86]. In the acute stage of IS, interleukin-6 (IL-6), S100B, and matrix metalloproteinase-9 (MMP-9) are commonly recognized biomarkers present in peripheral blood [87].

Xu M et al. conducted a comprehensive review on the impact of TCM on IS, focusing particularly on the nomenclature, families, drug components, traditional applications, phytochemical properties, and pharmacological activities of frequently used Chinese patent medicines

and TCMs [88]. The nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) family consists of transcription factors that play a complex and critical role in regulating immune responses and inflammation [89]. The NF-κB signaling cascade is an inflammatory pathway activated by numerous cytokines and inflammatory signals, which increase post-IS, positioning it as a central hub of inflammation following a stroke [90]. Empirical evidence has demonstrated that miR-671-5p agomir mitigates neuroinflammation by inhibiting NF-κB expression in both in vitro and in vivo models of IS. Furthermore, miR-671-5p emerges as a viable therapeutic target for reducing neuroinflammation in IS patients [91]. These methodologies offer novel insights into the potential interventional role of TCM in IS.

Given the diverse characteristics of Chinese herbal medicines, future research should undertake comprehensive investigations into the interactions among various Chinese herbal medicines, with a focus on elucidating the mechanisms of IS, particularly through the brain-gut axis, signal transduction pathways, and pyroptosis. In comparison to other studies, our research, utilizing CiteSpace, provides a visual representation of research hotspots and emerging frontiers. Nonetheless, this study is subject to certain limitations. Due to the constraints of the CiteSpace software, our analysis is confined to studies indexed in the Science Citation Index Expanded (SCI-Expanded) and published in English. Consequently, the data may not be entirely comprehensive. Further research is warranted to include articles published in other languages and indexed in different databases.

5. Conclusion

This study employed CiteSpace to examine the research hotspots and frontiers concerning the intervention of TCM in IS. The findings indicate that cell death, molecular docking, network pharmacology, and cognitive impairment are prominent research areas related to the mechanisms of TCM in addressing IS. It should be noted that network pharmacology and molecular docking have been widely applied in TCM research for over a decade and are now considered standard and routine tools; thus, describing them as “emerging trends” in the context of 2025/2026 does not accurately reflect the true frontiers of the field. Current cutting-edge research is moving toward integrating these established methods with advanced techniques such as spatial transcriptomics, AI-driven drug discovery beyond simple molecular docking, and the study of regulatory cell death in specific IS subtypes.

According to the Huangdi Neijing, the spleen and stomach are foundational to the body’s postnatal constitution, and there is a meridian-based connection between the intestines and the brain. Relevant studies suggest a significant association between gut microbiota and IS. Consequently, future research should aim to establish a “dynamic map of TCM syndromes – microbiota – metabolites – brain targets” to facilitate precise brain-gut co-treatment strategies. In addition, further studies are needed to explore the interactions among various mechanisms and to elucidate the relationship between IS and TCM, particularly via the brain-gut axis, signal transduction pathways, and pyroptosis.

Author Contributions

Ruizhe Jiang: Conceptualization, Methodology, Writing–Original Draft. Qifei Fu: Software, Visualization. Jinyang Li: Investigation, Resources, Project administration. Zijian Li: Methodology, Formal analysis, Writing–Review & Editing. Yiyun Luo: Software, Visualization. Songsong Tan: Writing–Original Draft. Chunyang Wang: Writing–Original Draft. Xiaozhen Ma: Methodology, Writing–Editing.

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Data Availability

Data available on request.

Ethics Statement

Not applicable.

Conflict of Interest

The authors declare that there are no conflicts of interest related to the publication of this manuscript. No financial, personal, or professional relationships with individuals or organizations have influenced the research, authorship, or publication of this work. All authors have reviewed the manuscript and approved its submission in its current form.

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Figures and Tables

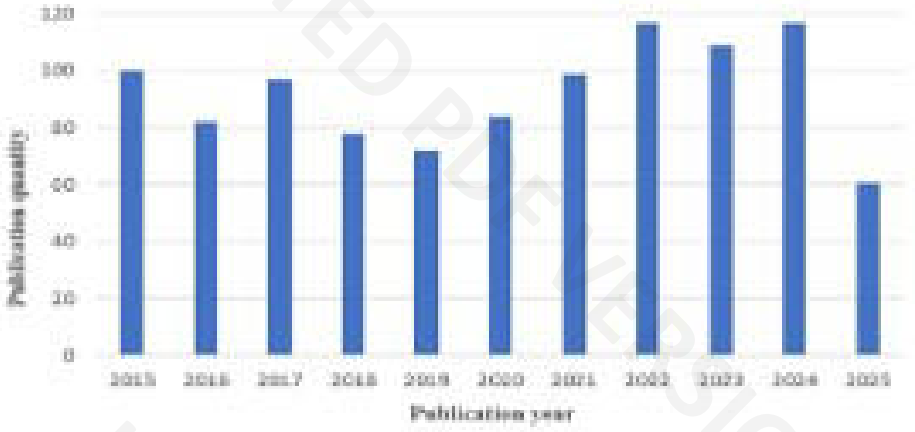


Figure 1. Annual trend of publication. (SCI-Expend)

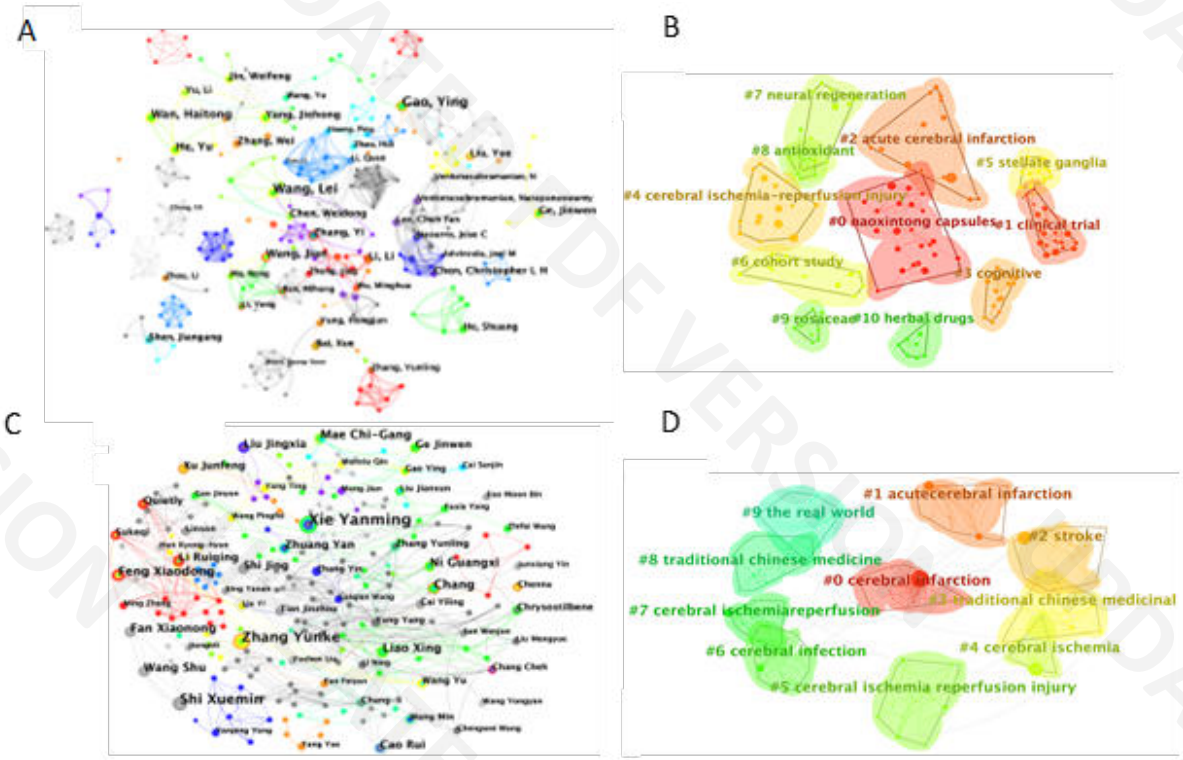


Figure 2. The network of co-author and the network of co-author. A: SCI-Expanded, The network of co-author; B: SCI-Expanded, The network of co-authorship; C: CNKI, The network of co-author; D: CNKI, The network of co-authorship

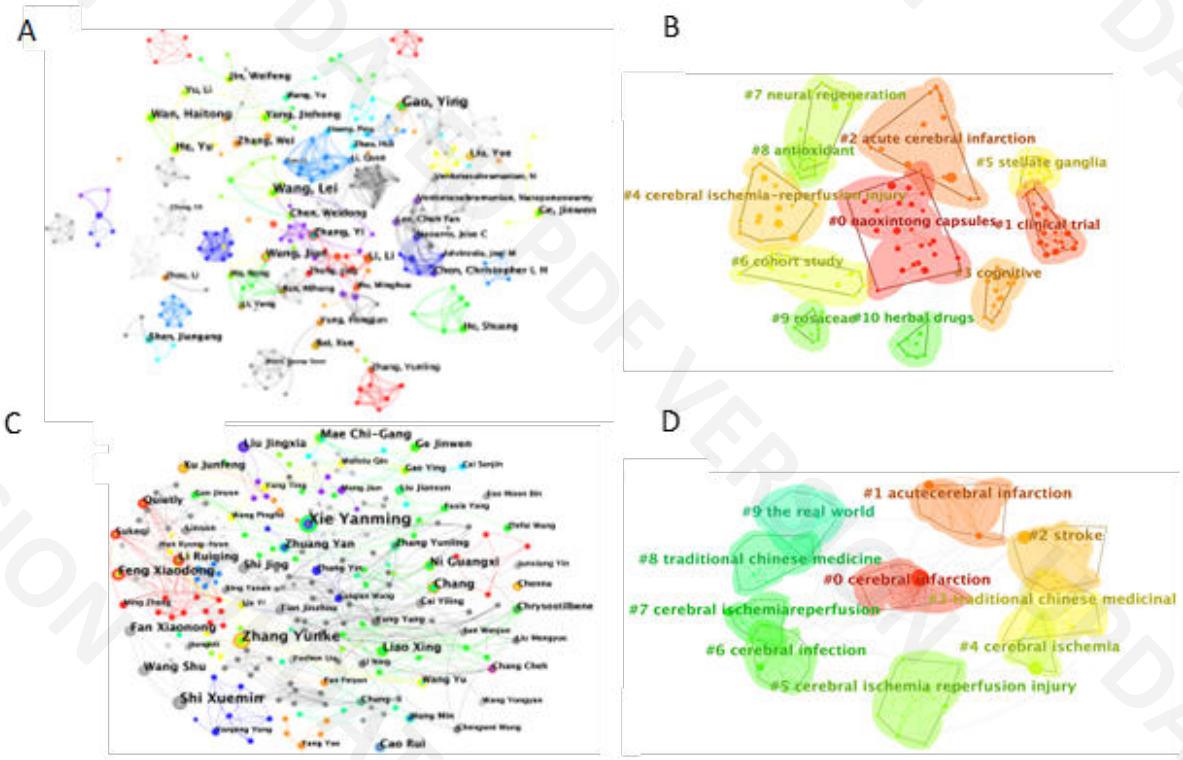


Figure 3. The network of co-institution and the network of co-country. A: SCI-Expanded, The network of co-institution; B: SCI-Expanded, The network of co-country; C: CNKI, The network of co-institution

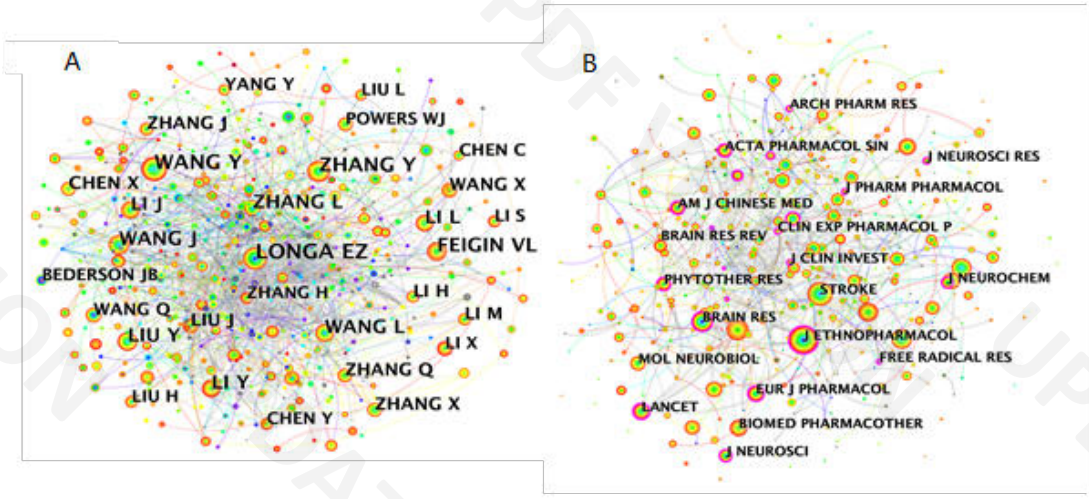


Figure 4. Co-cited by the author and the journal. A: The network of author co-citation; B: The network of journal co-citation

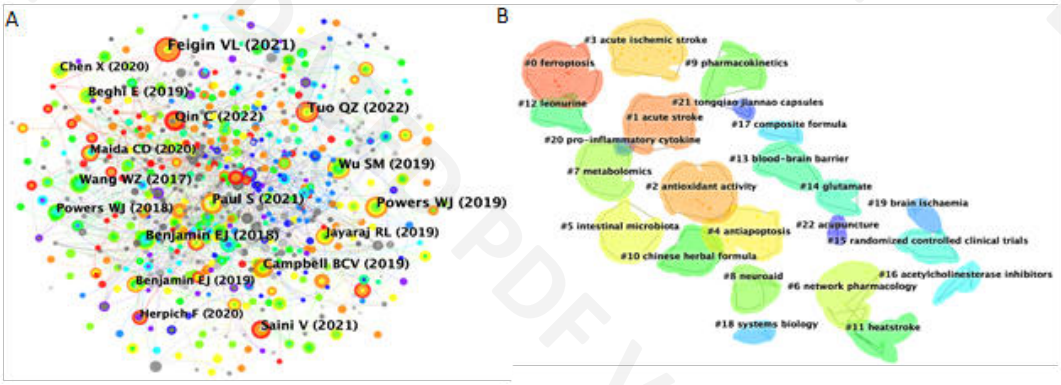


Figure 5. The network of co-cited references and the network of co-cited references clusters. A: The network of co-cited references. B: The network of co-cited references clusters

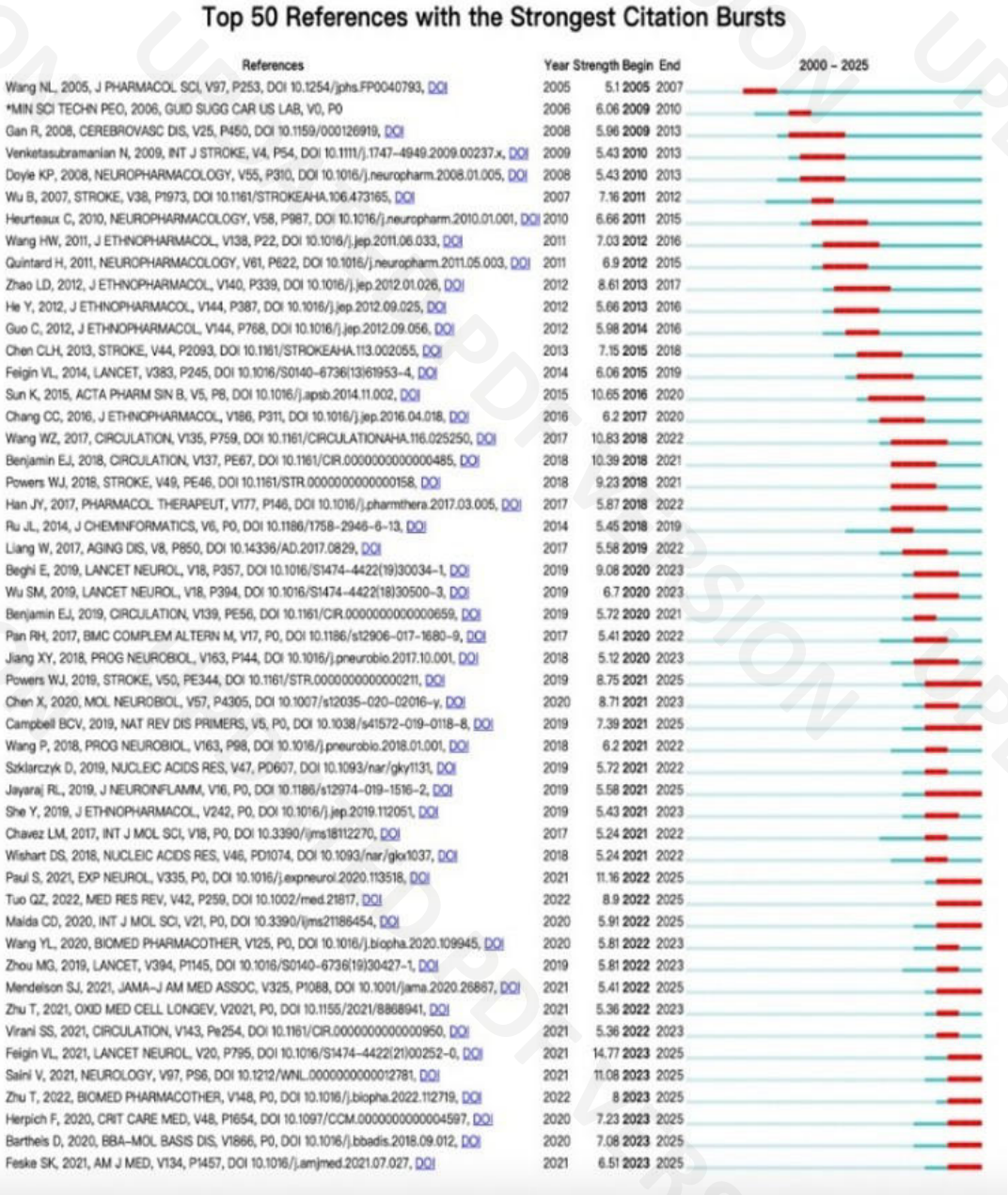


Figure 6. The top 50 references with the strongest citation explosion, which indicates the emerging trends or growing interest in this field.

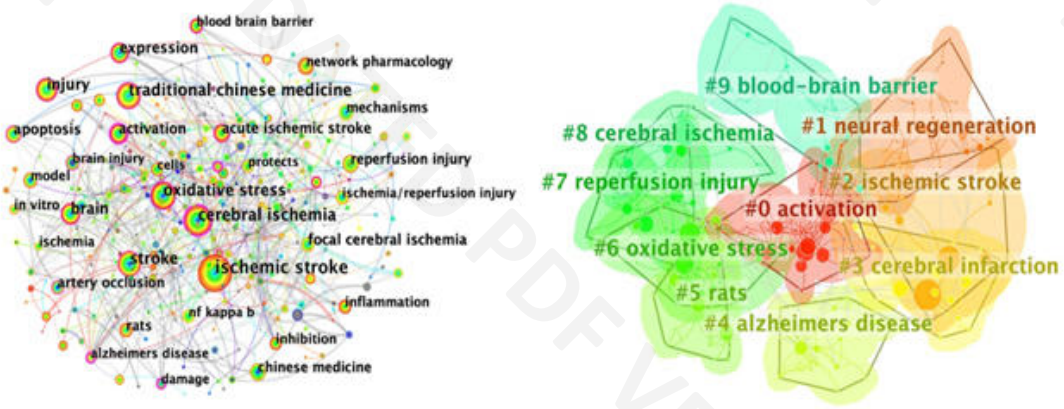


Figure 7. The network of co-occurring keywords and the network of co-occurring keywords clusters. A: The network of co-occurring keywords; B: The network of co-occurring keywords clusters

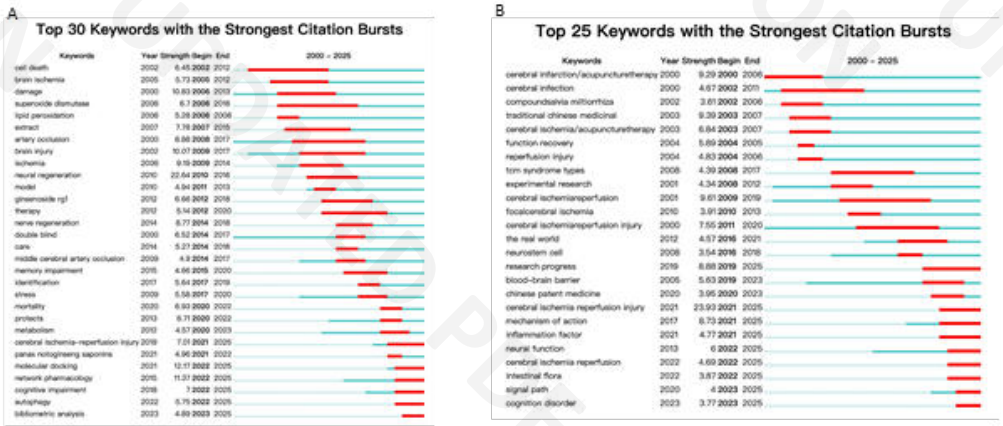


Figure 8. Keywords highlighted analysis. A: SCI-Expend; B: CNKI

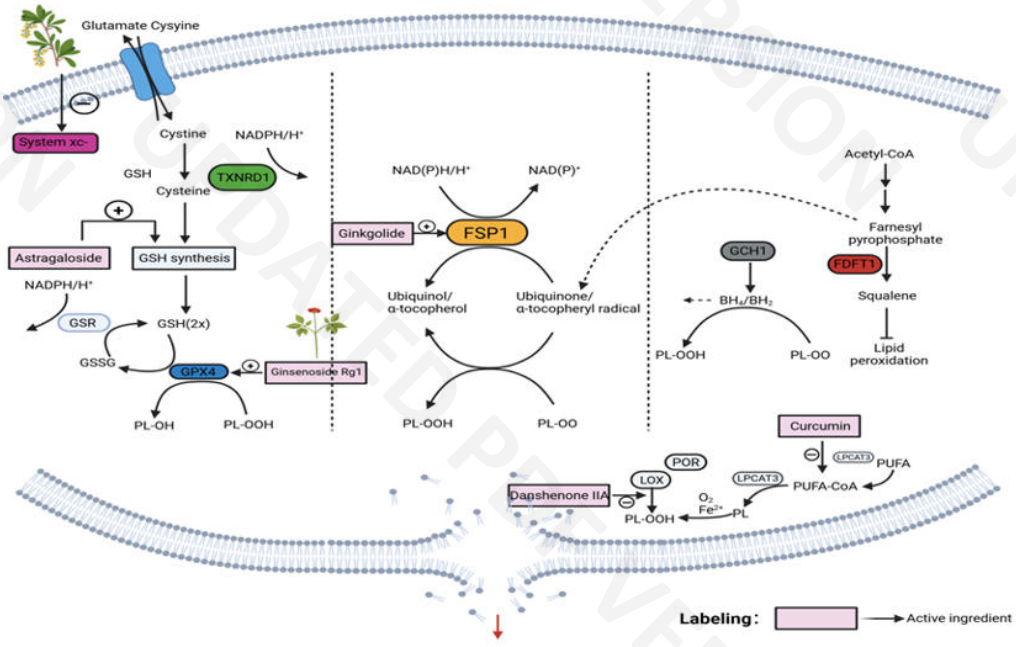


Figure 9. This shows the mechanism diagram of Chinese herbal medicine intervening in ischemic stroke by regulating ferroptosis

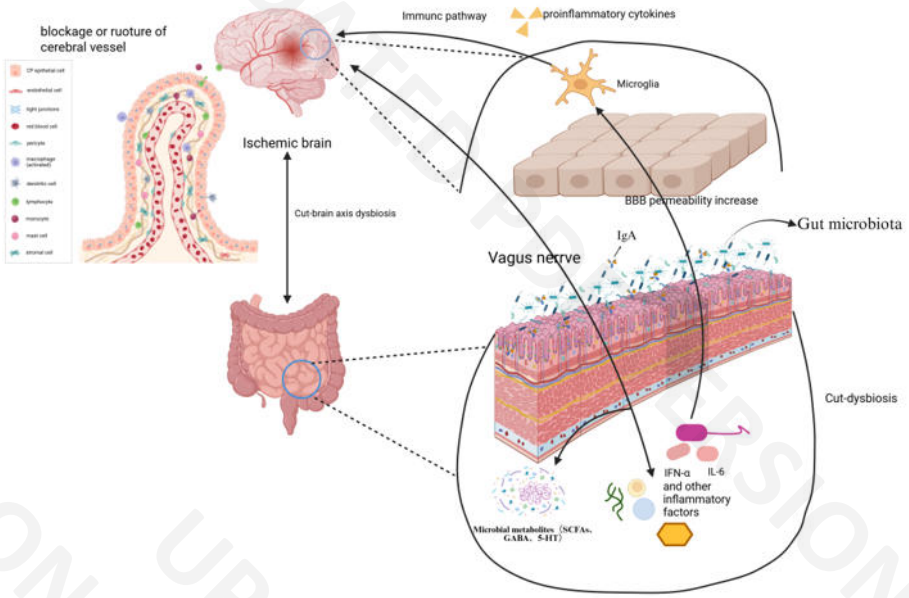


Figure 10. Relationship between the brain-gut axis and ischemic stroke

Table 1. Search strategy (SCI-Expanded)

Set	Search query
#1	TS = (Traditional Chinese Medicine* OR TCM* OR Chinese herbal medicine* OR acupuncture* OR herbal formula* OR Chinese medicine* OR herbal extract* OR tuina*)
#2	TS = (Ischemic stroke* OR cerebral ischemia* OR brain ischemia* OR acute ischemic stroke* OR cerebrovascular accident* OR CVA*)
#3	(#2) AND (#1)

Table 2. Search strategy (CNKI)

Set	Search query
#1	SU = (Ischemic stroke OR cerebral infarction OR cerebral embolism OR cerebral ischemia)
#2	SU = (Traditional Chinese Medicine OR Traditional Chinese Medicine Practitioner OR Chinese Herbal Medicine OR Traditional Medicine OR Traditional Chinese Medical Therapy OR Treatment by Traditional Chinese Medicine OR Formula OR Decoction OR Compound Formula OR Chinese Patent Medicine OR Acupuncture OR Needling Therapy OR Fire-Acupuncture OR Massage OR Manipulation OR Syndrome Differentiation and Treatment OR Syndrome)
#3	(#2) AND (#1)

Table 3. Top five Cited Journals (SCI-Expanded)

Rank	Frequency	Cited journal	IF	Centrality	Cited journal	IF
1	1229	STROKE	8.3	0.3	LANCET	168.9
2	1093	J ETHNOPHARMACOL	5.4	0.18	J NEUROCHEM	4.4
3	736	BRAIN RES	3	0.17	ARCH PHARM RES	4.1
4	727	PLOS ONE	3.7	0.21	FREE RADICAL RES	3.3
5	693	EVID-BASED COMPL ALT	2.6	0.12	AM J PHYSIOL-REG I	3.2

Table 4. The top 10 keywords in terms of frequency and centrality

Rank	Frequency	Keywords	Centrality	Keywords
1	454	ischemic stroke	0.21	cerebral ischemia
2	361	cerebral ischemia	0.2	brain
3	313	traditional chinese medicine	0.16	expression
4	275	oxidative stress	0.38	activation
5	254	stroke	0.17	artery occlusion
6	228	injury	0.37	alzheimers disease
7	209	brain	0.11	blood brain barrier
8	186	expression	0.21	damage
9	161	activation	0.25	cell death
10	146	focal cerebral ischemia	0.18	cerebral infarction

Table 5. Active Substances and Biological Effects of Common Traditional Chinese Medicine

Traditional Chinese medicine	The active ingredient or formulation	Biological effect	Mechanism of action	Model	References
Salvia miltiorrhiza	Tanshinone I, salvianolic acid A	NeuN-positive neurons↑ PI3K↑ β-catenin proteins↑ p-PDK1/PDK1↑ p-AKT/AKT↑ p-GSK3β/GSK3β proteins↑ Wnt-3↑ A beta↓	Induced in vivo, activation of PI3K/AKT signaling pathway and protect the surviving neuronal cells, promote neurogenesis, platelet aggregation was inhibited, infarct size was reduced	MCAO	[30,50]
Ginkgo biloba	Ginkgo biloba extract (EGb)	Neurobehavioral scores↓ infarct volume↓ inflammatory cytokines↓ The proportion of Treg cells↑ HIF-1α↓ HK2↓ Autophagic activity of Beclin1↓ LC3-II↓	Inhibition of the HIF-1α/HK2 signaling pathway and promoting autophagy/lysosomal signaling in penumbra neurons can promote Treg cell differentiation and improve stroke.	MCAO rats	[51,52]
Panax Notoginseng Saponins	Notoginsenoside R1 (NG-R1) ginsenoside Rb1 Rd Rg1 Re	Ischemic brain and colo: TLR4↓ MyD88↓ NF-κB↓	Inhibition of TLR4 signaling pathway, enhanced microbiota dysregulation, inhibition of astrocyte activation, promotes the transfer of astrocyte mitochondria to neurons, Inhibition of oxidation and neuroinflammation.	MCAO/R	[53,54]
Chuanxiong	TMP	Nrf2/HO-1↑ HMGB1/TLR4↓ AKT↓ ERK↓ TNF-α↓ IL-1β↓ MCP-1↓ CD11b↓ ICAM-1↓ iNOS↓	Activates free radical scavenging, the inhibition of Ca^{2+} overload, the maintenance of mitochondrial function, inhibition of TLR-4/NF-κB signaling pathway.	MCAO rats	[55,56]
gastrodia elata	Gastrodin	DCX/BrdU double positive cells↑ TNF-α↓ IL-1β↓ Cyclooxygenase-2↓ iNOS↓ MDA↓ HO-1↓ SOD1↓ Zn^{2+}↓	Inhibition of apoptosis, Zn^{2+} toxicity, inflammation and oxidative damage, promoting neurogenesis after injury.	MCAO	[57–59]
Scutellaria	Baicalin (BA)	MMP-9↓ ROS↓ Drp-1↓ MFN2↑	Inhibition of apoptosis, enhanced mitophagy, inhibition of ferroptosis and alleviation of brain damage.	MCAO rats	[60–62]
puerarin	Puerarin, isoflavone	Plasma S-100B protein↑ NSE↑	Promote cerebral angiogenesis, reduce the apoptosis of brain neurons after hypoxia.	Patients with ischemic stroke	[63]

Table 6. Common Traditional Chinese Medicine Prescriptions and Their Biological Effects

Traditional Chinese medicine	Composition	Model	Biological effect	Mechanism of action	References
Buyang huanwu decoction	Astragalus membranaceus, Angelica sinensis root, Red Peony Root, Earthworm (with soil removed), Ligusticum chuanxiong, Safflower, peach kernel.	Rat MCAO model	MCAO rat brain tissue or OGD/R cells: cAMP↑, PKA↑, p-Creb1 protein↑, MDA↓, Fe^{2+}↓ GSH↑ SOD↑	The cAMP/PKA/CREB signaling pathway was activated, the expression of downstream proteins such as BDNF, Syt1, Syn1 and Psd95 was regulated, the synaptic plasticity of damaged neuronal cells was improved, and the transmission efficiency was enhanced. Inhibition of ferroptosis via the Nrf2/GPX4 pathway protects the nerves.	[64, 65]
Xuefu Zhuyu decoction	Peach kernels, safflower, Angelica sinensis, Rehmannia glutinosa, Achyranthes bidentata, Ligusticum chuanxiong, Platycodon grandiflorum, red peony root, Aurantii fructus, licorice, Bupleurum	C57BL/6 mice, tMCAO surgery, sTBI rats	Co-localization of AQP4 with its anchor protein, α-muscular dystrophic proteoglycan, β-muscular dystrophic proteoglycan and Agrin↑ Hippocampal BDNF and TrkB↑	Regulate the function of the lymphatic system, enhance AQP4 polarization on the surface of astrocytes, and alleviate early neurological deficits after ischemic stroke/ downregulation of the rno-miR-191a-5p/BDNF axis, activation of BDNF-TrkB signaling, promote hippocampal synaptic remodeling and improve cognition.	[66, 67]
Sanhua decoction	Rheum palmatum L. [Polygonaceae], Citrus × aurantium L. [Rutaceae], Magnolia officinalis Rehder & E.H.Wilson [Magnoliaceae], and Hansenia weberbaueriana (Fedde ex H.Wolff) Pimenov & Kljuykov [Apiaceae]	Network pharmacology technology	p-PI3k↑ p-Akt↑ p-CREB1↑ TNF-α↓ IL-6↓ Na^{+}-K^{+}-and Ca^{2+}-ATPase↑	Regulate the PI3K/Akt/CREB1 and TNF pathways to alleviate ischemic brain injury, inhibition of degradation of the blood-brain barrier, scavenging oxygen free radicals, and potential involvement of the microbiota-brain-gut axis.	[68, 69]
Taohong Siwu Decoction	Angelica sinensis, Rehmannia glutinosa, Ligusticum chuanxiong, Paeonia lactiflora, Peach kernel, Safflower	MCAO/R rats, Gene set enrichment analysis	MMP-9↓ TNF-α↓ IL-6↓ CD31↑ Ang1↑ PDGFB↑ PDGFR-β	By inhibiting the CCL2/CCR2 axis, mediating the polarization of macrophages, reducing inflammatory damage and protecting the blood-brain barrier, activation of the glycolytic pathway, and promoting vascular maturation.	[70, 71]
Tongqiao Huoxue Decoction	Moschus, Rhizoma Chuanxiong, Radix Paeoniae Rubra, Semen Persicae, Flos Carthami, Fistular Onion, Chinese date, Rhizoma Zingiberis Recens, Huangjiu	MCAO/R rats	TNF-α↓ IL-6↓ Lp-PLA2↓ Protein microtube-associated protein 1 light chain 3↓ Beclin1 protein microtube-associated protein 1 light chain 3↓ Beclin1↓ NF-κB↓	Regulate the AGE-RAGE signaling pathway, fluid shear stress and atherosclerosis, IL-17 signaling pathway, TNF signaling pathway, reduce the autophagy ability of cells, and alleviate cell apoptosis, blockade of NF-kappa B signaling pathway and downregulation of PTGS2, improve neurological dysfunction.	[72, 73]
Gualou Guizhi decoction	Kirilowii, cinnamon twig, Paeony, ginger, fried licorice, jujube	MCAO/R rats	cortex and striatum of MCAO group: Ca^{2+}↓, MAP-2↑, NeuN↑, MDA↓, SOD↑, GSH-PX↑, CAT↑	Inhibition of astrocyte over-activation, control of neuronal apoptosis, and anti-intracellular calcium overload in cortical and striatal neurons of MCAO rats	[75]
Angong Niuhuang Wan	Beijing Tong Ren Tang Chinese Medicine Company Limited (Hong Kong, China)	C57BL/6 mice, MCAO surgery	CD11b (microglia and MoDMs), B220 (B cells), CD4 (CD4 T cells), CD8a (CD8 T cells), CD44 (CD4 Tem and CD8 Tem cells), CD25 (Tregs), CD11c (cDCs), and CD49b (NK cells)↑, IκBα, p-PLCg2 and p-S6↓, LPO↓, Fe^{2+}↓	Mitigated monocyte-derived macrophage infiltration in the brain, distinguishing its effects from those of microglia. Potential to temper the post-ischemic inflammatory response. Modulated fundamental immune cell dynamics. Targeted modulation of the signaling pathways, revealing a remarked inhibition of key markers like IκBα, indicating potential suppression of inflammatory responses in ischemic brain injuries, by targeting the PPARγ/AKT/GPX4 pathway, the ferroptosis of IS and HS is alleviated	[76, 77]