



Review

Pharmacodynamic advantages and characteristics of traditional Chinese medicine in prevention and treatment of ischemic stroke

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ABSTRACT

Ischemic stroke (IS) is a severe cerebrovascular disease with a high incidence, mortality, and disability rate. The first-line treatment for IS is the use of recombinant tissue plasminogen activator (r-tPA). Regrettably, numerous patients encounter delays in treatment due to the narrow therapeutic window and the associated risk of hemorrhage. Traditional Chinese medicine (TCM) has exhibited distinct advantages in preventing and treating IS. TCM enhances cerebral microcirculation, alleviates neurological disorders, regulates energy metabolism, mitigates inflammation, reduces oxidative stress injuries, and inhibits apoptosis, thereby mitigating brain damage and preventing IS recurrence. This article summarizes the etiology, pathogenesis, therapeutic strategies, and relationship with modern biology of IS from the perspective of TCM, describes the advantages of TCM in the treatment of IS, and further reviews the pharmacodynamic characteristics and advantages of TCM in the acute and recovery phases of IS as well as in post-stroke complications. Additionally, it offers valuable insights and references for the clinical application of TCM in IS prevention and treatment, as well as for the development of novel drugs.

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1. Introduction

Stroke is the second most frequent cause of death in human disease, and ischemic stroke (IS) is the most common type, caused by a blood clot blocking the middle cerebral artery resulting in inadequate blood supply to the brain (Benjamin et al., 2019). With the rapid growth and aging of the population, the incidence of IS increases dramatically with age, which has a significant impact on the affected families and society as a whole. The primary objective of IS treatment is the prompt restoration of blood flow to the ischemic area. However, in some cases, reestablishing blood flow after ischemia can worsen tissue injury and dysfunction, known as cerebral ischemia–reperfusion injury (CIRI). Thrombolytic therapy and thrombectomy during the acute phase of IS represent the most effective means to restore blood flow to the ischemic region (Zhang et al., 2020). Recombinant fibrinogen activator (r-tPA) is the only drug approved by the Food and Drug Administration (FDA) for IS treatment. However, this drug has a limited time window and a single target, potentially resulting in severe adverse effects like cerebral hemorrhage and neurotoxicity, and benefits only a highly restricted population (Dibajnia & Morshead, 2013; Dirnagl & Endres, 2014). Furthermore, research indicates that r-tPA treatment beyond the prescribed time frame exacerbates the blood–brain barrier disruption 24 h post-stroke and may be linked to complications such as cerebral edema and hemorrhagic transformation (Kelly et al., 2012). Consequently, there is an urgent need to develop novel strategies for IS patient treatment.

IS is a complex process that includes various aspects such as excitatory amino acid toxicity, cellular calcium overload, free radical damage, inflammatory response, and apoptosis (Zhu et al., 2022). Traditional Chinese medicine (TCM) formulas, known for their multi-component–multi-target–multi-pathway integration, have been widely used for treating cerebrovascular diseases for thousands of years (Tang, Yi, Lu, Chen, & Liu, 2022; L.Y. Wang et al., 2021; P. Wang et al., 2021; Y.F. Wang et al., 2021; D.D. Zhang et al., 2022; J. Zhang, Yu, Guo, Shen, & Feng, 2022; J.H. Zhang, Xu, Liu, & Li, 2022; Wang, Li, Zhong, Liang, & Liu, 2021; Zhang, Fan, Guo, & Song, 2022). As one of the TCM predominant diseases publicized by the National Administration of Traditional Chinese Medicine (NATCM), TCM exhibits unique advantages and holds promising potential in the prevention and treatment of stroke (Kong et al., 2021; Long et al., 2021). Research has demonstrated that TCM has distinct benefits in ameliorating neurological deficits in IS patients, preventing IS recurrence, managing stroke complications, and enhancing overall quality of life (Wang et al., 2021; Zhu et al., 2022). Moreover, TCM can be tailored to individ-

ual patient conditions to craft personalized treatment plans. Therefore, this article summarizes the etiology, pathogenesis, therapeutic strategies, and relationship with modern biology of IS in the perspective of TCM, describes the advantages of TCM in the treatment of IS, and further reviews the pharmacodynamic characteristics and advantages of Chinese medicine preparations (clinically validated Chinese medicine preparations) and acupuncture in the acute and recovery phases of IS as well as in post-stroke complications. Furthermore, it provides clues and references for the clinical application of TCM in the prevention and treatment of IS and the research and development of new drugs.

2. Etiology, pathogenesis and treatment of IS in TCM

TCM has accumulated rich clinical experience in treating IS over thousands of years of clinical practice. In TCM theory, the clinical symptoms of IS belong to the category of “stroke”. TCM scholars have believed that the etiology and pathogenesis of IS are caused by healthy-*qi* deficiency, diet, emotion, fatigue, and internal injuries, which cause *qi* and blood rebellions, resulting in wind, fire, phlegm, and blood stasis disturbing the upper orifices and leading to damaging brain collaterals (Zhang et al., 2022). Some researchers believe that the core pathogenesis of IS involves “loss of nourishment of the veins and channels, stasis blocking the veins and channels” (Lai et al., 2021). Other scholars believe that “toxin damaging brain collaterals” serving as the core mechanism of IS, and toxic evils such as heat, stasis, and phlegm produced after the onset of IS will further damage the cerebral collaterals and aggravate the condition of IS (Jian et al., 2015). According to the Chinese medicine’s understanding of the etiology and pathogenesis of IS, “eliminating phlegm and dredging collaterals”, “benefiting *qi*, promoting blood circulation, and removing blood stasis”, “clearing heat and toxin”, “calming liver and dispelling wind”, “opening orifices and awakening brain”, and “invigorating spleen and tonifying kidney” are the basic treatments for this disease (Yu et al., 2021) (Fig. 1).

3. Relationship between IS pathogenesis and modern biology

The pathogenesis of IS is complex, involving microcirculatory disorders, platelet function abnormalities, coagulation function abnormalities, hemodynamic changes, oxidative stress damage, organism metabolic abnormalities, inflammatory response, and other critical pathological aspects (Zhu et al., 2022). Using advanced science and technology, modern medicine has found that

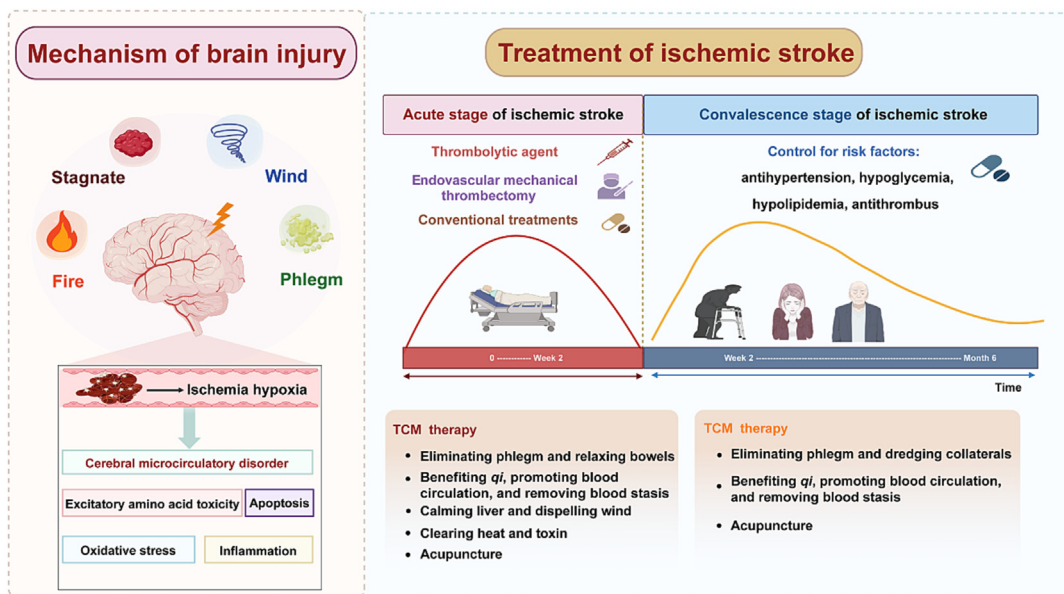


Fig. 1. Interventional role of TCM in preventing and treating ischemic stroke at different stages.

the changes in platelet aggregation and adhesion, thrombosis, coagulation and fibrinolytic system, microcirculation, blood rheology, and other current biological indexes in the pathogenesis of IS can be attributed to the micro-indicators of “stasis blocking the veins and collaterals” (Chi et al., 2023; Li & Chen, 2012). The ischemic cascade of IS triggered by inflammatory reactions, oxidative stress damage, and metabolic abnormalities can be attributed to the micro-indicators of “toxin evils”, which damages the permeability and integrity of the cerebrovascular, thus further exacerbating IS (Chi et al., 2023; Sun et al., 2022).

4. Advantages of TCM in treatment of IS

IS is a highly prevalent disease, and intravenous thrombolysis is the mainstay of therapy in the acute phase of IS (within two weeks of onset). However, this therapy still has the disadvantages, such as a narrower therapeutic time window, numerous contraindications, and the risk of hemorrhagic transformation after treatment. After active clinical treatment in the acute phase, the survival chances of IS patients were significantly improved. However, as IS transitions into the convalescence phase (within two weeks to six months of onset), many residual neurological deficit problems, such as limb movement disorders, speech dysfunction, hemiparesis, etc., seriously affect patients' physical and mental health and quality of life. Notably, Western medicine still lacks effective treatment for remodeling neurological function during the convalescence phase of IS. In addition, post-stroke complications are a tricky area of clinical care, with approximately one-third of stroke patients experiencing post-stroke complications such as depression and cognitive deficits (Skajaa et al., 2022). For stroke survivors, post-stroke complications directly affected the prognosis of stroke patients and were significantly associated with disability and mortality (Ayerbe et al., 2013). Currently, Western medicine has limited treatment methods for stroke complications, and the side effects of drugs are significant, which are not favorable for long-term use by IS patients. Besides addressing IS and its complications, secondary prevention of stroke has become a public health issue that cannot be ignored. Studies have shown that the risk of recurrence after one year in patients with a first stroke is 11.1%, while the risk of recurrence after five years increases to 26.4% (Mohan et al., 2011). In addition, recurrent stroke tends to result

in severe neurologic deficits and significantly higher mortality rates than initial stroke. Researchers have shown that timely implementation of secondary prevention effectively mitigates the risk of recurrence, disability, and mortality among stroke patients (Zhou et al., 2023). Antiplatelet, antihypertensive and lipid-lowering drugs are the traditional secondary prevention strategies for IS used in Western medicine, but long-term use carries bleeding risks and adverse effects (Wei et al., 2021). Given these considerations, timely diagnosis, rational treatment, and effective prevention strategies are essential to improve IS patients' survival rates and prognoses.

TCM has many advantages in preventing and treating IS as well as improving IS complications through multi-targets and multiple pathways. Personalized treatment is the shared advantage of TCM in preventing and treating IS in the acute and recovery phases. Chinese medicine has the principle of “syndrome differentiation and treatment”, through the clinical experience of Chinese medicine combined with clinical indicators, based on different stages and types of the disease, the flexible use of Chinese medicinal preparations and acupuncture is conducted in clinic to improve the condition of IS patients. Clinical and animal experiments have shown that Chinese medicine can effectively regulate cerebral blood flow, inhibit neuroinflammation and neuronal apoptosis, and reduce neurological deficits through Chinese medicinal preparations and acupuncture, which can improve the survival rate and recovery of IS patients (Lu et al., 2016; Sun et al., 2023; Zhu et al., 2022). The advantages of TCM in the acute phase of IS are mainly manifested in: (1) Early treatment: For acute IS patients who are not eligible for vascular thrombolytic therapy, early intervention with TCM prescriptions and acupuncture can improve the clinical efficacy (Chen et al., 2011). (2) Combination therapy: The combination of Chinese medicinal preparations and Western medical treatment can complement and compensate for the shortcomings of Western medical treatment for better treatment of patients. Numerous clinical studies have shown that for patients in the acute phase of IS, combining TCM therapy with Western medical treatment (thrombolysis, antiplatelet, etc.) can improve the treatment and recanalization rates of IS and reduce the risk of bleeding (Chen et al., 2020; Gong et al., 2019). The advantages of TCM in the recovery phase of IS are summarized as follows: (1) Post-stroke complications treatment: Studies have demonstrated that TCM and

Table 1
TCM formulas and preparations intervene in acute stage of IS.

Therapeutics	Names	Active ingredients/Composition of formulas	Outcomes	Efficacy	References
Eliminating phlegm and relaxing bowels	Huatan Tongfu Decoction	<i>Trichosanthis Fructus</i> ; <i>Spatholobi Caulis</i> ; <i>Salviae Miltiorrhizae Radix et Rhizoma</i> ; <i>Scutellariae Radix</i> ; <i>Acori Tatarinowii Rhizoma</i> ; <i>Gardeniae Fructus</i> ; <i>Arisaema Cum Bile</i> ; <i>Persicae Semen</i> ; <i>Rhei Radix et Rhizoma</i> ; <i>Natrii Sulfas</i>	The overall effective rate of the treatment group was 95.99 %, and the overall effective rate of the control group was 77.60 %, which was a significant difference between the two groups.	It inhibits inflammatory reaction and vasoconstriction, protects nerve function and vascular endothelial function, reduces plasma viscosity, restores blood circulation, improves clinical symptoms and neurological deficits, and enhances patients' ability to live an active life.	Shao, 2021; Song & Song, 2022; L.Y. Wang et al., 2021; P. Wang et al., 2021; Y.F. Wang et al., 2021; Wang, Li, Zhong, Liang, & Liu, 2021; Zhu & Hu, 2021
	Xinglou Chengqi Decoction	<i>Trichosanthis Fructus</i> ; <i>Arisaema Cum Bile</i> ; <i>Rhei Radix et Rhizoma</i> ; <i>Natrii Sulfas</i> ; <i>Notopterygii Rhizoma et Radix</i>	The overall effective rate of the treatment group was 97.92 %, and the overall effective rate of the control group was 81.25 %, which was a significant difference between the two groups.	It inhibits the inflammatory response, protects neurons, improves hemodynamics and blood rheology, regulates intestinal flora and the gut-brain axis, and improves patients' Chinese medicine symptoms and neurological deficits.	Liu et al., 2022; Zhen, 2017; Zheng et al., 2023
Benefiting qi, promoting blood circulation, and removing blood stasis	Buyang Huanwu Decoction	<i>Astragali Radix</i> ; <i>Angelicae Sinensis Radix</i> ; <i>Paeoniae Radix Rubra</i> ; <i>Pheretima</i> ; <i>Chuanxiong Rhizoma</i> ; <i>Persicae Semen</i> ; <i>Carthami Flos</i>	The overall effective rate of the treatment group was 92.00 %, and the overall effective rate of the control group was 68.00 %, which was a significant difference between the two groups.	It improves nerve function, reduces neuronal damage, inhibits neuroinflammation, improves hippocampal metabolic pathways, regulates intestinal flora, and improves the patient's Chinese medicine evidence and neurological deficits.	Xin, 2020; Wang & Xiao, 2017; Xin, 2020; Wan et al., 2021; Wang et al., 2016; Wang & Wang, 2023; Tang et al., 2022
	Dengzhan Xixin Injection	Total caffeoyl quinic acid ester and scutellarin	The overall effective rate of the treatment group was 95.24 %, and the overall effective rate of the control group was 80.95 %, which was a significant difference between the two groups.	It improves microcirculation and blood rheology, regulates oxidative stress, protects vascular endothelium and nerve cells, and improves neurological deficits and activities of daily living in IS patients.	Liao et al., 2020; Yang et al., 2021; Yang et al., 2018
Calming liver and dispelling wind	Xiaoxuming Decoction	<i>Ephedrae Herba</i> ; <i>Stephaniae Tetrandrae Radix</i> ; <i>Codonopsis Radix</i> ; <i>Scutellariae Radix</i> ; <i>Zingiberis Rhizoma Recens</i> ; <i>Cinnamomi Ramulus</i> ; <i>Glycyrrhizae Radix et Rhizoma</i> ; <i>Paeoniae Radix Rubra</i> ; <i>Aconiti Lateralis Radix Praeparata</i> ; <i>Chuanxiong Rhizoma</i> ; <i>Armeniacae Semen Amarum</i> ; <i>Saposhnikovia Radix</i>	The overall effective rate of the treatment group was 86.67 %, and the overall effective rate of the control group was 71.11 %, which was a significant difference between the two groups.	It improves cerebral blood flow, reduces cerebral edema, regulates oxidative stress, inhibits inflammatory response and apoptosis, improves patients' neurological deficits, and enhances patients' ability to perform activities of daily living.	Chen et al., 2021; Huang et al., 2021; Wu et al., 2021
	Tianma Gouteng Yin Formula	<i>Gastrodiae Rhizoma</i> ; <i>Uncariae Ramulus Cum Uncis</i> ; <i>Leonuri Herba</i> ; <i>Taxilli Herba</i> ; <i>Gardeniae Fructus</i> ; <i>Scutellariae Radix</i> ; <i>Haliotidis Concha</i> ; <i>Eucommiae Cortex</i> ; <i>Cyathulae Radix</i> ; <i>Poria</i> ; <i>Polygoni Multiflori Caulis</i>	The overall effective rate of the treatment group was 94.44 %, and the overall effective rate of the control group was 75.00 %, which was a significant difference between the two groups.	It improves cerebral blood flow dynamics, reduces oxidative stress damage and inflammatory damage, regulates immune function, protects vascular endothelial function, improves symptoms of neurological deficits in IS patients, and promotes neurological function recovery.	Fang, Jiang, & Ge, 2023; Lu, Sun, & Ma, 2021; Zhong, Zheng, & Ye, 2022; Ding, Guo, Liu, Ding, & Chen, 2020
Clearing heat and toxin	Angong Niu Huang Pill	<i>Bovis Calculus</i> ; Concentrated <i>Bubalus bubalis</i> Powder; <i>Moschus</i> ; <i>Margarita</i> ; <i>Cinnabaris</i> ; <i>Realgar</i> ; <i>Coptidis Rhizoma</i> ; <i>Scutellariae Radix</i> ; <i>Gardeniae Fructus</i> ; <i>Curcumae Radix</i> ; <i>Borneolum</i>	The overall effective rate of the treatment group was 94.12 %, and the overall effective rate of the control group was 85.29 %, which was a significant difference between the two groups.	It improves coagulation function and consciousness disorder, reduces cerebral edema, inhibits inflammatory response, and promotes neurological function recovery.	Li et al., 2019; Lin et al., 2020; Liu & Cai, 2020; Wang et al., 2022
	Xingnaojing Injection	<i>Moschus</i> ; <i>Gardeniae Fructus</i> ; <i>Curcumae Radix</i> ; <i>Borneolum</i>	The overall effective rate of the treatment group was 97.50 %, and the overall effective rate of the control group was 80.00 %, which was a significant difference between the two groups.	It improves their blood rheology, hemodynamics, inflammatory factor levels, and level of impaired consciousness and protects neurological functions.	Ba, 2023; Lyu, Zhang, Zhang, Shao, & Yang, 2022; L.Y. Wang et al., 2021; P. Wang et al., 2021; Y.F. Wang et al., 2021; J.N. Wu et al., 2021; Z.Q. Wu et al., 2021; Wang, Li, Zhong, Liang, & Liu, 2021

acupuncture have significant efficacy and advantages in treating post-stroke complications, which can alleviate the complications and improve the symptoms of neurological deficits to a certain extent (Fang et al., 2022; Yang et al., 2022). (2) Secondary prevention: In recent years, clinical studies have shown that Chinese herbal preparations can reduce the recurrence rate of IS and prevent secondary stroke (Yang et al., 2018). Simultaneously, acupuncture can modulate multiple targets of multiple risk factors for IS (hypertension, hypercholesterolemia, diabetes, etc.) and intervene in IS recurrence (Zhou et al., 2023). In addition, acupuncture has simple and inexpensive advantages in treating IS. Compared with other therapeutic strategies for IS, acupuncture does not require surgical procedures or medication administration, and is characterized by simplicity, inexpensiveness, and good patient compliance. Clinical trials and meta-analysis results have demonstrated the effectiveness of acupuncture in improving balance function, reducing spasticity, increasing muscle strength after stroke, and enhancing overall health (Chavez et al., 2017). Acupuncture improves the effectiveness and speed of rehabilitative care for IS patients, it also significantly reduces healthcare costs and should be used more widely in the community and hospitals (Wu et al., 2010).

5. Intervention of TCM in acute stage of IS

The acute phase of IS is the critical stage in the rapid transformation of IS syndrome, and early treatment (for patients who are not eligible for thrombolytic therapy) and combination therapy (TCM combined with pharmacologic thrombolytic therapy) with TCM in this stage can effectively improve the prognosis of IS patients in this stage. Chinese researchers have explored the evidence patterns of the acute phase of IS and found that “phlegm heat and viscera excess”, “qi deficiency and blood stasis”, and “wind and fire disturbing upward” were the main symptoms of the acute stage of IS (Song et al., 2023; Song et al., 2017; Yang et al., 2022). Moreover, the toxic evils produced after the occurrence of IS are involved in the development of stroke disease, which leads to the death of cerebral neurons and further aggravates brain damage (Zhang & Zhang, 2008). Therefore, for the acute stage of IS, “eliminating phlegm and relaxing bowels”, “benefiting qi, promoting blood circulation, and removing blood stasis”, “calming liver and dispelling wind”, and “clearing heat and toxin” are often used as the primary treatments (Table 1).

5.1. Eliminating phlegm and relaxing bowels

5.1.1. Huatan Tongfu Decoction

Huatan Tongfu Decoction (HTTFD) is a typical Chinese medicine formula for IS with effects of eliminating phlegm and relaxing bowels (Wang et al., 1986). In recent years, studies have confirmed that the therapeutic effect of HTTFD on patients with IS in the acute stage was remarkable (overall effective rate: 95.99%), and it could effectively alleviate the clinical symptoms and neurological impairment of the patients, which is suitable for clinical popularization and use (Wang et al., 2021; Zhu & Hu, 2021). The application of HTTFD could reduce the levels of central nerve-specific protein (S100- β), neuron-specific enolase (NSE), thromboxane B2 (TXB2), C-reactive protein (CRP), tumor necrosis factor-alpha (TNF- α), and interleukin-6 (IL-6) in acute IS patients, which suggests that HTTFD can improve the neurological function and vascular endothelial function impairment for the treatment of acute IS (Wang, 2023). Song et al. found that HTTFD was effective in treating IS patients, inhibiting inflammation and vasoconstriction, protecting neurological and endothelial functions, reducing plasma viscosity, restoring blood circulation, and improving the ability of patients' daily life activities (Shao, 2021; Song & Song,

2022). Clinical trials have confirmed that HTTFD combined with r-tPA intravenous thrombolytic therapy can significantly improve National Institute of Health Stroke Scale (NIHSS) and Fugl-Meyer assessment (FMA) scores and promote recovery in IS patients. (Huang et al., 2022). In addition, HTTFD combined with Angong Niu Huang Pill can enhance the therapeutic effect of stroke patients (Shui, 2018). These findings suggest that HTTFD can effectively protect ischemic brain tissue.

5.1.2. Xinglou Chengqi Decoction

Academician Wang created Xinglou Chengqi Decoction (XLCQD) based on Da Cheng Qi Tang to treat IS patients with symptoms of phlegm-heat and visceral solidity (manifestation: abdominal distension, constipation, bad breath, and dry throat) (Wang et al., 2021). Clinical trials found that the application of XLCQD can reduce the levels of serum NSE and TNF- α in patients with IS, which suggests that XLCQD can reduce neuronal cell damage, inhibit inflammatory responses, and protect brain cells. (Liu et al., 2022; Zhen, 2017). In addition, the combination of XLCQD and butylphthalide improved blood rheology and oxidative stress levels in IS patients, as demonstrated by significantly increasing the levels of glutathione peroxidase (GSH-Px), superoxide dismutase (SOD), and cerebral arterial mean blood velocity, and decreasing the levels of whole blood high shear viscosity, plasma viscosity, whole blood low shear viscosity, malondialdehyde (MDA), and resistance index (RI) (Zheng et al., 2023). By analyzing and summarizing the literature in recent years, Liu et al. found that the mechanism of XLCQD in treating IS may have the following effects: inhibiting inflammatory response, protecting neurons, improving blood rheology and hemodynamics, regulating intestinal flora and brain-gut axis (Liu et al., 2022). The results of animal experiments showed that XLCQD could regulate the CREB-BDNF pathway and protect ischemic brain tissue in middle cerebral artery occlusion (MCAO) rats (Liu, Yu, Xu, & Tong, 2021).

5.2. Benefiting qi, promoting blood circulation, and removing blood stasis

5.2.1. Buyang Huanwu Decoction

Buyang Huanwu Decoction (BYHWD) is a formula based on the pathogenesis of “qi deficiency and blood stasis”, recorded in Correction on the Errors of Medical Works (Xin, 2020). It has the efficacy of tonifying qi, promoting blood circulation, and dredging collaterals. Clinical trials have shown that BYHWD can significantly improve the neurological deficits in the acute stage of IS, and improve the clinical efficacy of the acute stage of IS patients with Qi deficiency and blood stasis (Wang & Xiao, 2017; Xin, 2020). The animal experimental results show that BYHWD has the effect of improving cerebral blood flow, reducing calcium overload, inhibiting inflammatory response, inhibiting neural apoptosis and anti-hypoxia, improving microcirculation, and antithrombotic (Wan et al., 2021; Wang et al., 2016). Wang et al. observed the effect of BYHWD combined with thrombolytic injection in treating acute ischemic stroke, and the cerebral blood flow, NIHSS score, and total effective rate of patients in the combined treatment group were better than those in the conventional treatment group (Wang & Wang, 2023). Moreover, compared with the conventional treatment group, the combination treatment significantly improved the oxidative stress (GSH-Px and MDA) and inflammation (hs-CRP, TNF- α , and IL-6) level in patients. Some scholars used metabolomics to study the therapeutic effect of BYHWD on the MCAO rat model, and the study showed that BYHWD could effectively improve neural function (NIHSS score), reduce neuronal damage (nissl bodies in survival neurons), inhibit the neuroinflammation (microglia activation), improve the hippocampal metabolism pathway (e.g., purine metabolism, glutamatergic synapses,

and arginine biosynthesis), and regulate the intestinal bacterial flora (Tang et al., 2022).

5.2.2. Dengzhan Xixin Injection

Dengzhan Xixin Injection (DZXXI) is extracted from *Erigeron breviscapus* Hand.-Mazz., the main active ingredients are total caffeoyl quinic acid ester and scutellarin, which effectively activate blood circulation and remove blood stasis (Li et al., 2017). Researchers have observed the therapeutic effects of DZXXI on IS patients, and found that after two weeks of treatment with DZXXI, the Chinese medicine symptoms, markers of vascular endothelial damage (LPA and Hcy), inflammatory response (MCP-1), and blood rheology indexes (plasma viscosity, whole blood high shear viscosity, and whole blood low shear viscosity) of IS patients were significantly improved (Li et al., 2017; Tian, Chen, & Chen, 2020). Relevant studies have shown that combining antithrombotic therapy with DZXXI improved IS patients' self-care ability and neurological deficits in the acute stage of the disease better than antithrombotic therapy alone (Zhao & Wang, 2021). Modern pharmacological studies have shown that DZXXI can improve microcirculation and blood rheology (whole blood viscosity, platelet adhesion, and fibrinogen), regulate oxidative stress (SOD, MDA, and NO), and protect vascular endothelium and nerve cells (endothelin-1, matrix metalloproteinase-3, and NSE) in treating IS (Liao, 2021; Liao et al., 2020; Yang et al., 2021). In addition, the 4:6 combination of Huangqi Injection and DZXXI can improve the neurological deficits, reduce oxidative stress, and shrink the infarcted area in a rat model of cerebral ischemia/reperfusion injury, and the combination of the two drugs has a better therapeutic effect than that of the single use (Tian et al., 2019).

5.3. Calming liver and dispelling wind

5.3.1. Xiaoxuming Decoction

Xiaoxuming Decoction (XXMD) has the therapeutic efficacy of supporting the right and dispelling the wind. It is mainly used clinically for treating patients with acute cerebral infarction (overall effectiveness rate: 86.67%), which can improve neurological function (Barthel Index and NIHSS scores) in IS patients, decrease inflammation and lipid peroxidation and protect the brain by lowering serum MCP-1 and SOD levels and elevating BDNF levels (Li et al., 2020). Huang et al. evaluated the efficacy and safety of XXMD in treating IS through the Meta system in clinical trials, and the results showed that the clinical efficacy of XXMD in treating acute cerebral infarction was better than that of conventional treatment in Western medicine, with no severe adverse reactions and mild, and better safety (Huang et al., 2021). Animal studies have found that XXMD can significantly improve neurological deficits, reduce the volume rate of cerebral infarction and increase the number of nidus in the cerebral cortex's parietal cortex, effectively restoring neurological function and repairing brain tissues to improve cerebral ischemia/reperfusion injury (Chen et al., 2021). Furthermore, compared with Taohong Siwu Decoction, rats using XXMD in the early stage of IS had lower mortality and better neurological function scores, confirming that XXMD is more suitable for application in the acute stage of IS (Chen et al., 2021). Wu et al. investigated the potential mechanism of XXMD for the treatment of IS through a network pharmacology approach and found that the active ingredients (such as quercetin, luteolin, and kaempferol) acted on the key targets (such as AKT1, IL-6, and MAPK3) to affect the pathways related to oxidative stress, apoptosis, and inflammatory response for the treatment of IS (Wu et al., 2021).

5.3.2. Tianma Gouteng Yin formula

Tianma Gouteng Yin Formula (TGYF) has the efficacy of calming the liver and dispelling the wind, clearing heat and activating

blood, tonifying spleen and kidney, and playing an essential role in treating cerebrovascular diseases (Nie, 2019). Clinical trial data show that TGYF has a significant therapeutic effect on patients with acute cerebral ischemia with wind and fire disturbing type (overall effectiveness rate: 94.44%), which helps alleviate the patients' clinical symptoms, improve the neurological deficits, and increase the overall clinical efficiency with fewer adverse reactions (Fang et al., 2023; Lu et al., 2021). The results of a large number of studies show that the Chinese medicine acupuncture combined with TGYF treatment of acute cerebral infarction has significant clinical efficacy, can significantly improve the vascular endothelial function (NO and endothelin-1), cerebral vascular reserve function (pulsatility index and cerebrovascular reserve), neurological function (NIHSS and BI scores), platelet activation (platelet CD62P and CD63), inflammatory response (IL-6 and hs-CRP), and is worthy of clinical promotion (J. Wang, Shi, & Wang, 2022; W.G. Wang et al., 2022; Zhong, Zheng, & Ye, 2022; Ding, Guo, Liu, Ding, & Chen, 2020). Modern pharmacological studies have found that TGYF can reduce oxidative stress after IS and thus promote the recovery of neurological function, and its mechanism may be through the regulation of the Nrf2/HO-1 signaling pathway (Wang et al., 2021). Literature suggests that TGYF may inhibit the activation of the NMDAR/ERK signaling pathway, improve the tissue lesions of cerebral ischemia/reperfusion rats, maintain intracellular calcium homeostasis, and reduce neurological damage (Zhang et al., 2022).

5.4. Clearing heat and toxin

5.4.1. Angong Niu Huang Pill

Angong Niu Huang Pill (AGNHP) is an essential drug for first aid in Chinese medicine, which has the effect of clearing heat, removing toxins, opening the orifices, and awakening the brain. It is especially suitable for patients with acute cerebral infarction with impaired consciousness. Consciousness disorder is one of the severe complications of cerebral infarction, and actively restoring patients' consciousness can reduce the occurrence of sequelae such as aspiration and lung infection (Lin et al., 2020). Clinical trials have shown that AGNHP can effectively improve neurological deficits, consciousness, and coagulation function in patients with acute cerebral infarction (overall effectiveness rate: 94.12%), and no significant adverse effects have been observed during the treatment (Lin et al., 2020; Liu & Cai, 2020; Wang et al., 2022). Modern pharmacological studies have shown that administering AGNHP to rats with acute CIRI significantly improve their neurological function scores, reduce the volume of cerebral infarction, improve blood rheology indexes, and reduce brain tissue edema, which protective effects may be related to the inhibition of the expression of MMP9 and AQP4 (Li et al., 2019; Liu et al., 2011).

5.4.2. Xingnaojing Injection

Xingnaojing Injection (XNJI) is a kind of TCM injection commonly used to treat acute cerebrovascular diseases in clinical practice (Tian et al., 2021). The results of clinical trials show that XNJI is effective in treating acute IS (overall effectiveness rate: 97.50%), which can effectively improve cerebral edema, neurological function, inflammatory response, blood rheology, hemodynamics, and has high safety, so it is worth promoting (Ba, 2023; L.Y. Wang et al., 2021; P. Wang et al., 2021; Y.F. Wang et al., 2021; Wang, Li, Zhong, Liang, & Liu, 2021). The treatment of XNJI combined with alteplase can significantly improve the intracranial blood flow velocity, inflammatory factor level, and neurological function score of IS patients, and promote the recovery of patients' neurological function (Lyu et al., 2022). According to modern pharmacological studies, XNJI has a brain-protective effect on rats with cerebral ischemic coma, and its mechanism is related to the up-regulation

Table 2
TCM formulas and preparations intervene in convalescence stage of IS.

Therapeutics	Names	Active ingredients/Composition of formulas	Outcomes	Efficacy	References
Benefiting qi, promoting blood circulation, and removing blood stasis	Buyang Huanwu Decoction	<i>Astragalus Radix</i> ; <i>Angelica Sinensis Radix</i> ; <i>Paeoniae Radix Rubra</i> ; <i>Pheretima</i> ; <i>Chuanxiong Rhizoma</i> ; <i>Persicac Semen</i> ; <i>Carthami Flos</i>	The overall effective rate of the treatment group was 96.00 %, and the overall effective rate of the control group was 80.00 %, which was a significant difference between the two groups. The overall effective rate of the treatment group was 93.33 %, and the overall effective rate of the control group was 80.00 %, which was a significant difference between the two groups.	It improves blood flow and oxygen supply in the cerebral ischemic area, protects neurons, dilates blood vessels, inhibits inflammatory response, promotes neurological function recovery of IS patients, and reduces the recurrence of IS. It regulates oxidative stress and intracellular calcium concentration, inhibits inflammatory response and platelet aggregation, promotes vascular nerve regeneration and blood flow restoration in cerebral ischemic areas, promotes neurological function recovery in patients with IS, and improves motor and language function in patients.	Huang, 2022; Zhao et al., 2023; Qu, 2023; Wang et al., 2019; Yu, 2013
	Salvianolic Acids for Injection	Multiple salvia polyphenolic acids			Li et al., 2022; Liu et al., 2017; Ma et al., 2021
Eliminating phlegm and dredging collaterals	Dengzhan Shengmai Capsule	<i>Erigeronis Herba</i> ; <i>Ginseng Radix et Rhizoma</i> ; <i>Schisandrae Chinensis Fructus</i> ; <i>Ophiopogonis Radix</i>	The overall effective rate of the treatment group was 92.90 %, and the overall effective rate of the control group was 78.00 %, which was a significant difference between the two groups.	It is anti-platelet aggregation, regulates blood lipids, scavenges oxygen free radicals, promotes fibrinolytic activity, improves neurological deficits in IS patients, reduces recurrence of IS, and improves patients' quality of life.	Kong & Gu, 2017; Li et al., 2021; Zhong et al., 2023
	Tongluo Huatan Capsule	<i>Ursi Felle Pulvis</i> ; <i>Gastrodiae Rhizoma</i> ; <i>Notoginseng Radix et Rhizoma</i> ; <i>Salviae Miltiorrhizae Radix et Rhizoma</i> ; <i>Bambusae Concretio Silicea</i> ; <i>Rhei Radix et Rhizoma</i>	The overall effective rate of the treatment group was 84.70 %, and the overall effective rate of the control group was 71.43 %, which was a significant difference between the two groups.	It inhibits apoptosis and inflammatory response of neuronal cells in the ischemic penumbra, promotes nerve regeneration, repairs the function and metabolism of neurons in the ischemic brain area, and improves the Chinese medicine evidence and neurological deficits in IS patients.	He, Su, Lai, Fan, & Zhou, 2019; Li et al., 2023; Su & Fan, 2013; D.D. Zhang et al., 2022; J. Zhang, Yu, Guo, Shen, & Feng, 2022; J.H. Zhang, Xu, Liu, & Li, 2022; Zhang, Fan, Guo, & Song, 2022

of PI3K/Akt-mediated phosphorylation of cAMP-responsive element binding protein (CREB), regulation of neurotransmitters and protection of hippocampal tissues (Xin et al., 2019). In addition, the research scholars used GC-MS integrated with network pharmacology and molecular docking technology to predict that geniposide, curdione and neocurdione might be the key active ingredients of XNJI for the treatment of cerebral ischemia, which provides a more scientific and practical reference basis for its quality control study (Wu et al., 2021).

6. Intervention of TCM in convalescence stage of IS

The convalescence stage of IS is a critical time for the recovery of limb function and reconstruction of neurological function of patients (Xu et al., 2023). TCM intervention can effectively reduce the rate of disability and recurrence of IS in this phase. Clinical studies conducted in recent years have confirmed that TCM has a neuroprotective effect on the convalescence period of IS, which can improve patients' neurological deficits and limb dyskinesias, reduce IS recurrence rates, and improve quality of life. Chinese researchers have adopted an innovative approach, combining a latent structure with an association rule network, to investigate TCM syndromes prevalent during the convalescence phase of IS. Their findings have spotlighted that “qi deficiency and blood stasis” and “wind-phlegm blocking collateral” were the primary syndromes, and the syndromes gradually shifted from the “excess syndromes” to the “syndrome of deficiency and excess” (Song et al., 2023; Zhu et al., 2022). Consequently, the treatment of IS recovery should be based on the efficacy of TCM to “benefiting qi, promoting blood circulation, and removing blood stasis” and “eliminating phlegm and dredging collaterals” (Table 2).

6.1. Benefiting qi, promoting blood circulation, and removing blood stasis

6.1.1. Buyang Huanwu Decoction

BYHWD has significant efficacy in treating patients in the convalescence phase of IS. BYHWD with additions and subtractions, could significantly improve the patients' neurological function, daily living ability, and quality of life scores, with an overall effective rate of 96% (Huang, 2022). In addition, researchers have used serum metabolomics technology to find that BYHWD affects the organism's energy metabolism and improves neurological function by regulating fat metabolism and phospholipid metabolism in the body to treat IS (Zhao et al., 2023). Acupuncture combined with BYHWD can increase cerebral arterial hemodynamics in patients recovering from ischemic stroke, protect neurons, dilate blood vessels, and inhibit inflammatory responses (Qu, 2023; Wang et al., 2019). At the same time, BYHWD has particular efficacy in the secondary prevention of IS recovery patients. Clinical results showed that compared with the patients in the basic treatment group, the recurrence rate of IS decreased and the ability of daily life activities improved in patients treated with basic treatment combined with BYHWD (Yu, 2013).

6.1.2. Salvianolic acids for Injection

Salvianolic Acids for Injection (SAFI) is a Chinese medicine preparation composed of multiple salvia polyphenolic acids used in patients in the recovery stage of IS (Xia et al., 2021). Clinically SAFI can improve the blood supply to the ischemic site and improve oxidative stress, thus improving patients' motor, speech, and exercise functions (Liu et al., 2017). In addition, SAFI can promote the recovery of neurological function by reducing homocysteine and anti-atherosclerosis (Li et al., 2022). Modern pharmacological studies have shown that SAFI has pharmacologi-

cal effects such as anti-inflammatory, anti-oxidative stress, neurotrophic, regenerative, and protection of cerebral neurovascular units, which can significantly improve the neurological function damage of IS patients, restore their daily life behaviors, and improve the prognosis and quality of survival (Ma et al., 2021; L. Wang et al., 2023). Scholars demonstrated that SAFI can reduce neuronal apoptosis *in vivo* and *in vitro* models by using the MCAO/R rat model and the oxygen-glucose deprivation/reoxygenation (OGD/R) cell model, and its neuroprotective mechanism was probably the modulation of microglia phenotypes (switching from M1 to M2 phenotype), and the inhibition of NLRP3 inflammasome/pyroptosis axis in microglia (Ma et al., 2021).

6.1.3. Dengzhan Shengmai Capsule

Dengzhan Shengmai Capsule (DZSMC) is a proprietary Chinese medicine, which has the efficacy of benefiting *qi*, nourishing *yin*, and activating blood circulation, is often used in treating IS during the convalescence period (Wei et al., 2011). Clinical studies have shown that intravenous thrombolytic therapy (alteplase) combined with DZSMC can improve blood viscosity, plasma fibrinogen, and neurological scores in patients with IS, promote local microcirculation, and reduce the potential for neurological damage and disability (Kong & Gu, 2017; Zhong et al., 2023). A randomized controlled trial confirmed that, compared with placebo, DZSMC was superior to placebo in improving the quality of life and reducing the recurrence rate of patients in the recovery phase of IS, and there were no serious adverse events (Yang et al., 2018). Modern pharmacological studies have proved that DZSMC can play the roles of antiplatelet aggregation, regulation of blood lipids, scavenging of oxygen free radicals, and promoting fibrinolytic activity (Li et al., 2021). Using single-cell RNA sequencing, Cao et al. found that DZSMC has an essential role in inflammation and apoptosis, while Vimentin (VIM) and interferon induced transmembrane protein 3 (IFITM3) are vital targets of DZSMC for treating IS (Cao et al., 2023).

6.2. Eliminating phlegm and dredging collaterals

Tongluo Huatan Capsule (TLHTC) was created based on the theory of “toxin damaging brain collaterals”, which believes that after stroke, pathological products such as phlegm, heat, and stasis accumulate in the brain, causing further damage to the brain and

that “eliminating phlegm and dredging collaterals” should be the main treatment (Zhang et al., 2022). In the phase IV clinical study, after four weeks of administration of TLHTC, patients with phlegm and stasis obstruction in the recovery stage of IS manifested a decrease in NIHSS scores, modified Rankin scores, and Chinese medicine symptom scores compared to the pre-treatment period, indicating that TLHTC can improve neurological function in patients with cerebral infarction in the recovery stage (Zhang et al., 2022). Complementary to these clinical results, preclinical animal experiments have provided additional insights into TLHTC’s efficacy. Animal experiments demonstrated that TLHTC could improve the microenvironment of the cortical area after IS injury, restore neurological dysfunction, and rescue the apoptosis of neurons in the ischemic penumbra (He et al., 2019; Su & Fan, 2013).

7. Intervention of TCM in post-stroke complications

Stroke survivors frequently experience complications, which directly impact the prognosis of stroke patients. The underlying mechanism behind post-stroke complications is intricate, and relying solely on single-target therapies often yields suboptimal results. Western medical treatments often control or change the patient’s basic disease and are supplemented with drugs to treat complications (Dubois et al., 2012; Fang et al., 2022). TCM has significant advantages in treating stroke complications, which can improve IS neurological function and complications (depression and cognitive impairment) through multi-target and multi-pathway as well as with few side effects (Fig. 2 and Table 3).

7.1. Post-stroke depression

Post-stroke depression (PSD) is one of the most common complications of stroke, with patients displaying neuropsychiatric symptoms such as depression, anxiety, and loss of interest (Li et al., 2023). The presence of anxiety and depression also seriously impacts patients’ quality of life, mental health, and functional recovery. Studies have shown that PSD occurs in more than half of stroke survivors (Ayerbe et al., 2013). Western medicine often uses antidepressants (5-hydroxytryptamine and 5-hydroxytryptamine reuptake inhibitors) to treat PSD. However, these antidepressants have limitations such as slow onset of action, prolonged duration of treatment, and many adverse effects

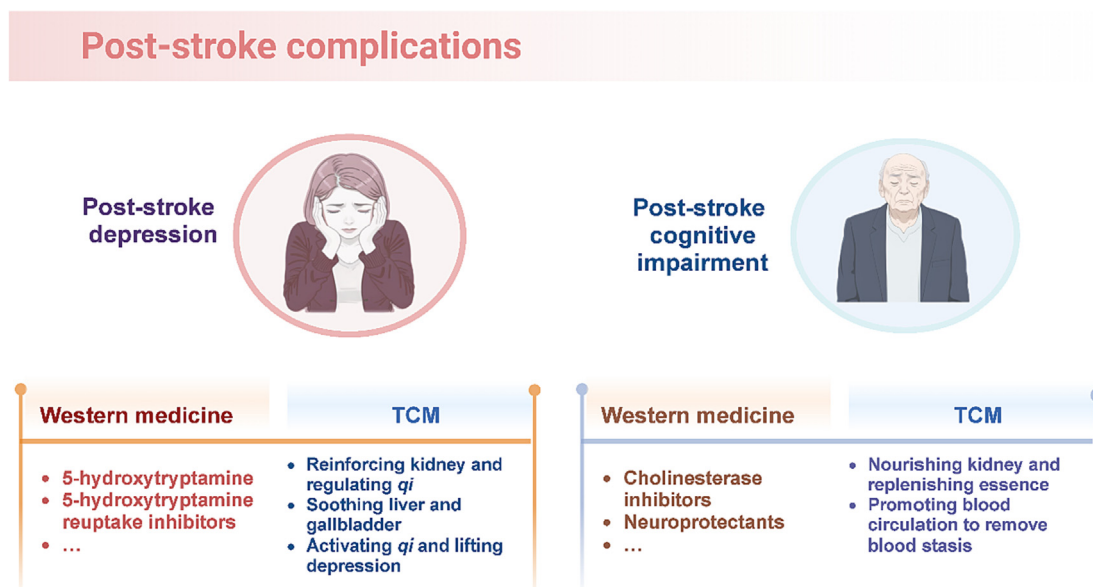


Fig. 2. Role of TCM in prevention and treatment of stroke complications.

Table 3
Role of TCM formulas and preparations in treatment of post-stroke complications.

Complication	Names	Composition of formulas	Outcomes	Efficacy	References
Post-stroke depression	Chaihu Jia Longgu Muli Decoction	<i>Bupleuri Radix</i> ; <i>Os Draconis</i> ; <i>Ostreae Concha</i> ; <i>Pinelliae Rhizoma</i> ; <i>Poria</i> ; <i>Codonopsis Radix</i> ; <i>Scutellariae Radix</i> ; <i>Cinnamomi Ramulus</i> ; <i>Rhei Radix et Rhizoma</i> ; <i>Jujubae Fructus</i> ; <i>Zingiberis Rhizoma Recens</i>	The overall effective rate of the treatment group was 94.12 %, and the overall effective rate of the control group was 78.43 %, which was a significant difference between the two groups.	It regulates the expression of neurotransmitters and their receptors, regulates the hypothalamic–pituitary–adrenal axis, protects neuronal cells, improves the immune status of the body, reduces the secretion of inflammatory factors, improves the patients' Chinese medicine symptoms and neurological functions, and reduces the degree of depression.	Lu, 2022; Wu et al., 2022; J. Zhang et al., 2022; Zhang et al., 2022; Zhang et al., 2015
	Yinao Jieyu Recipe	<i>Acanthopanax Senticosus Radix et Rhizoma Seu Caulis</i> ; <i>Schisandrae Chinesis Fructus</i> ; <i>Curcumae Radix</i> ; <i>Bupleuri Radix</i> ; <i>Gardeniae Fructus</i>	The overall effective rate of the treatment group was 98.67 %, and the overall effective rate of the control group was 80.00 %, which was a significant difference between the two groups.	It protects neuronal function in the hippocampus and prefrontal cortex, regulates glutamate levels in the brain, promotes hippocampal glial cell proliferation, and relieves depressed mood and depression-associated somatic symptoms.	Du et al., 2021; Pei et al., 2008; Qu et al., 2019; Wang et al., 2012; Zhao et al., 2016
Post-stroke cognitive impairment	Compound Congrong Yizhi Capsules	<i>Nelumbinis Folium</i> ; <i>Rhapontica Radix</i> ; <i>Cistranches Herba</i> ; <i>Polygoni Multiflori Radix</i> ; <i>Pheretima</i>	The overall effective rate of the treatment group was 85.10 %, and the overall effective rate of the control group was 81.80 %, which was a significant difference between the two groups.	The effect of increasing blood flow to brain tissue, decreasing blood viscosity, improving energy load, and thus improving cognitive functioning.	Liu et al., 2023; Sun et al., 2010; Wang et al., 2023; Zhang & Zhang, 2020
	Compound Danshen tablet	<i>Salviae Miltiorrhizae Radix et Rhizoma</i> ; <i>Notoginseng Radix et Rhizoma</i> ; <i>Borneolum</i>	The overall effective rate of the treatment group was 85.90 %, and the overall effective rate of the control group was 70.30 %, which was a significant difference between the two groups.	It enhances the function of the central cholinergic nervous system to secrete Ach, increases the release of monoamine neurotransmitter 5-HT in the hippocampus and hypothalamus, reduces lipid peroxidation damage in brain tissue, inhibits inflammatory response and promotes angiogenesis, thus improving the effect of cognitive function.	Liang et al., 2019; Wang et al., 2016; Weng, 2011; Zhang, 2020; Zhang et al., 2015

(Lu, 2022). In TCM, PSD is categorized under the category of “stroke” combined with “depression”, and the pathogenesis of PSD is based on “kidney essence deficiency” and “liver qi stagnation” (Zhang et al., 2023). Therefore, the clinical treatment of PSD should be based on “reinforcing kidney and regulating qi” and “soothing liver and gallbladder”, and “activating qi and lifting depression”.

7.1.1. Chaihu Jia Longgu Muli Decoction

Chaihu Jia Longgu Muli Decoction (CLMD) is a classic formula for depression, which can be used to treat depression, insomnia, anxiety, and other mental disorders (Jia et al., 2023). The results of clinical trials have confirmed that CLMD has improved the neurological function, depressive state, blood levels of monoamines and amino acid neurotransmitters in PSD patients, and the improvement effect is better than that of Western medicine treatment alone (Lu, 2022; J. Zhang et al., 2022; Zhang et al., 2022). In addition, Jia et al. found that CLMD has a synergistic effect when combined with antidepressants, which can enhance the efficacy of antidepressants and reduce their adverse effects, making it a practical choice for treating depression (Jia et al., 2023). Some scholars observed the pharmacodynamic effect of CLMD on depressed rats in animal experiments and confirmed that the antidepressant mechanism of CLMD is mainly manifested in the following ways: protecting neurons in the hippocampus, increasing the expression of hippocampus DARD2 and 5-HT2AR, and regulating the level of serum inflammatory factors (Wu et al., 2022).

7.1.2. Yinao Jieyu Recipe

Yinao Jieyu Recipe (YNJYR) has the efficacy of “reinforcing kidney and regulating qi” and “soothing liver and lifting depression”, which is satisfactory in basic research and clinical treatment of depressive disorders (Wang et al., 2012). Clinical trials have confirmed that YNJYR is effective in treating depression of “kidney deficiency and liver depression” pattern and PSD, which is worth promoting in clinical application (Du et al., 2021; Pei et al., 2008; Qu et al., 2019). By using magnetic resonance spectroscopy to observe the interventional effect of YNJYR on PSD rats, it was found that YNJYR could protect the neuronal function of the hippocampus and anterior cortex, regulate the level of glutamate in the brain, and promote the proliferation of hippocampal glial cells (Zhao et al., 2016). Researchers administered YNJYR for four weeks to intervene in the PSD rats and found that YNJYR significantly improved the expression levels of BDNF in the hippocampus, hypothalamus, and amygdaloid nucleus of rats, which may be a potential mechanism for the treatment of PSD with YNJYR (Li et al., 2015).

7.2. Post-stroke cognitive impairment

Post-stroke cognitive impairment (PSCI) is a subtype of vascular cognitive impairment, which refers to the cognitive dysfunction that occurs in post-stroke patients, mainly manifested as a decline in attention, memory, comprehension, and executive function, seriously affecting the patient's daily life (Wang et al., 2016). Currently, no drug can cure PSCI, and the treatment of Western medicine is mainly through controlling or changing the patient's underlying disease and supplemented with drugs (cholinesterase inhibitors and neuroprotectants) to improve the cognitive dysfunction of the patient (Dubois et al., 2012). According to TCM, PSCI belongs to the category of “stroke” combined with “dementia and amnesia”. Moreover, “deficiency of kidney essence and qi” is the basis of its pathology, and blood stasis is the key to its pathogenesis, so “nourishing kidney and replenishing essence” and “promoting blood circulation to remove blood stasis” are the main treatments (Wang et al., 2016).

7.2.1. Compound Congrong Yizhi Capsule

Compound Congrong Yizhi Capsule (CCYC) is approved by National Medical Products Administration (NMPA) of China for the treatment of vascular dementia, which has the efficacy of “benefiting kidney and nourishing liver”, “activating blood circulation to eliminate turbid”, and “strengthening brain and increasing intelligence”. Clinical studies have found that CCYC can improve the MoCA, MMSE, and CDT scores and improve the cognitive function of Alzheimer’s patients (Zhang & Zhang, 2020). In addition, clinical trials have confirmed that CCYC combined with Galantamine Hydrobromide Tablets can significantly improve the memory and cognitive function of patients with PSCI and improve clinical efficacy and safety (Wang et al., 2023). The results of animal experiments showed that CCYC down-regulated the expression of myristoylated alanine-rich C-kinase substrate (MARCKS) in the hippocampus of rats and improved the learning and memory ability of demented rats (Sun et al., 2010). Liu et al. used network pharmacology to predict the mechanism of CCYC in treating vascular dementia. Moreover, the active ingredients, such as imipramine, glycyrrhizin and isorhamnetin, may regulate the signaling pathways by regulating the expression of several molecules, such as amyloid precursor protein (APP), phosphatidylinositol-3-kinase catalytic subunit α (PIK3CA), and tyrosine protein kinase SRC, thus improving the cognitive disorders (Liu et al., 2023).

7.2.2. Compound Danshen tablet

Compound Danshen Tablet (CDT) comprises three traditional Chinese medicines: Danshen (*Salviae Miltiorrhizae Radix et Rhizome*), Sanqi (*Notoginseng Radix et Rhizome*) and Tianranbingpian (*Borneolum*), mainly used for treating coronary heart disease and angina pectoris. In recent years, with the deepening of research and understanding, it has been found that CDT can protect the nerve function of IS rats and promote neovascularization around the infarction, which has a new use in the prevention and treatment of cerebrovascular diseases (Zhang, 2020). Some scholars have found that CDT positively treats dementia through clinical and animal experimental studies (Wang et al., 2016; Weng, 2011; Zhang et al., 2015). CDT can improve the cognitive learning and memory ability of demented rats. Furthermore, its mechanism of action may be realized by enhancing the function of acetylcholine secretion of the central cholinergic nervous system, increasing the release of monoamine neurotransmitter 5-HT in the hippocampus and hypothalamus, reducing the damage of lipid peroxidation in brain tissues, inhibiting inflammatory damage reaction and promoting angiogenesis, etc. Researchers compared the effects of CDT and its disassembled formula on demented rats and found that CDT was better than the single formula group in antioxidant damage, vascular regulation, promotion of angiogenesis, and promotion of neurotransmitter release; the Danshen extract group was better than the Sanqi group in antioxidant damage, vasoconstriction regulation, promotion of angiogenesis, and anti-inflammation, etc.; and the Sanqi group was slightly better than the Danshen extract group in the promotion of neurotransmitter release. Therefore, in the CDT, Danshen extract is the monarch drug, and Sanqi supplements the monarch drug in treating dementia (Liang et al., 2019).

8. Discussion and perspectives

IS is a severe cerebrovascular disease with high mortality and disability rates, and effective and timely treatment is crucial for favorable patient outcomes. Nevertheless, the current treatment strategy for IS lacks a multi-target and multi-pathway approach, which may contribute to the unsatisfactory therapeutic effect of IS in recent years. As a treasure of traditional Chinese culture,

TCM emphasizes “syndrome differentiation and treatment” and “preventive treatment of disease”, and has accumulated rich experience in the prevention and treatment of IS (Zhou et al., 2023). In this paper, we analyze the etiology and pathogenesis of IS and review the advantages and characteristics of TCM in preventing and treating IS at different stages and post-stroke complications. We discuss their efficacy and mechanisms of action. The advantages of TCM in preventing and treating IS can be summarized as follows: individualized treatment, early treatment, combination therapy, post-stroke complications treatment, secondary prevention, and simple and inexpensive therapy. Overall, TCM provides a comprehensive and holistic approach to the prevention and treatment of IS, addressing different stages of the disease and post-stroke complications. Its individualized treatment plans, combination therapies, and multi-target approach contribute to its advantages in improving patient outcomes.

Although TCM has demonstrated remarkable efficacy in the treatment of IS, there are still some challenges that need to be addressed. Firstly, existing clinical studies often have small sample sizes, limiting their ability to fully confirm the effectiveness and safety of TCM in treating IS. Larger-scale clinical trials are needed to provide more robust evidence. Secondly, the mechanism of action of TCM in treating IS is not well understood. There is a lack of clear linkage between clinical observations and experimental studies. To address this, it is crucial to combine clinical and experimental research methods. Utilizing approaches such as multi-omics, network pharmacology, and molecular biology can help to unravel the mechanisms of action of TCM in treating IS. To gain a comprehensive understanding of its mechanisms and optimize its role, more in-depth studies that harmoniously combine clinical and experimental approaches should be conducted. In summary, the treatment of IS with TCM still faces challenges, but with advancements in science and technology, there is a promising future for the application of TCM in IS treatment.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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