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Review on the Treatment of Cerebral Ischemia-Reperfusion Injury by Traditional Chinese Medicine

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Abstract: This study aims to investigate the clinical effects and mechanisms of traditional Chinese medicine (TCM) in treating cerebral ischemia-reperfusion injury. Through a systematic review and analysis of relevant literature, the study evaluates the effects of TCM on nerve function recovery, regulation of oxidative stress responses, and its combination with Western medicine. Findings reveal that Chinese medicinal formulations, such as Danshen decoction and Naoxintong, significantly improve NIHSS scores, reduce ischemic lesion areas, and lower oxidative stress marker levels in patients. These formulations exhibit unique advantages in modulating oxidative stress and inflammatory responses, and their integration with Western medicine enhances therapeutic efficacy while reducing adverse reactions. The effectiveness of TCM prescriptions offers a novel clinical approach for managing cerebral ischemia-reperfusion injury and promotes the advancement of integrated Chinese-Western treatment strategies. Further research is required to elucidate the precise mechanisms of TCM formulations to facilitate their broader clinical application.

Keywords: Traditional Chinese medicine prescription; Cerebral ischemia-reperfusion injury; Oxidative stress

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1. Introduction

1.1. Research background

Cerebral ischemia-reperfusion injury is a complex pathological process commonly observed during stroke, resuscitation following cardiac arrest, and certain surgical procedures. In ischemic conditions, brain tissue experiences oxygen and energy deprivation due to reduced blood flow. Paradoxically, the restoration of blood flow can trigger detrimental reactions such as oxidative stress, inflammatory responses, and apoptosis. These processes exacerbate brain cell damage and may lead to dysfunction and long-term neurological impairment.

According to the guidelines from the American Heart Association (AHA) and the American Stroke Association, the management of acute ischemic stroke includes thrombolytic therapy and mechanical thrombolysis.

However, these treatments have limitations, including variable efficacy and risks of complications. Consequently, exploring alternative therapeutic approaches, particularly the application of traditional Chinese medicine (TCM), has become a vital research focus.

The theoretical framework of TCM emphasizes holistic regulation and the balance of qi, blood, and Yin-Yang, offering unique perspectives for preventing and treating cerebral ischemia-reperfusion injury. Recent studies have demonstrated the efficacy of TCM formulas, such as Danshen decoction and Naoxintong, in improving neurological function and modulating oxidative stress responses. For instance, a systematic review published in Frontiers in Neurology highlighted the therapeutic potential of TCM in managing acute ischemic stroke.

Literature reviews have also detailed the pathological mechanisms of cerebral ischemia-reperfusion injury, identifying oxidative stress, inflammatory responses, and neuronal apoptosis as key contributors to nerve damage. The Chinese Guidelines for the Diagnosis and Treatment of Acute Stroke emphasize that integrating TCM with modern medicine can provide more comprehensive treatment strategies, improving patient outcomes.

From a TCM perspective, Qi deficiency and blood stasis are regarded as the primary pathogenic factors of ischemic cardiovascular and cerebrovascular diseases. This conceptualization dates back to the Qing Dynasty, when Qingren Wang proposed Qi deficiency and blood stasis as the fundamental causes of stroke. Most contemporary TCM scholars agree with this view. Key herbal components such as Astragalus and Angelica are noted for their ability to supplement Qi and nourish blood, while *Salvia miltiorrhiza*, recognized for its role in promoting blood circulation and resolving stasis, has been widely used for cerebrovascular conditions. Modern pharmacological studies have shown that tanshinones, active components of *Salvia miltiorrhiza*, exhibit significant anti-platelet aggregation effects. Guizhi (Cinnamomi Ramulus) is associated with the heart meridian and is known for its function in warming the meridians and promoting circulation, as supported by its vasodilatory properties.

Emerging evidence suggests that TCM prescriptions, such as Danshen decoction and Naoxintong, effectively enhance neurological recovery and regulate oxidative stress responses in cerebral ischemia-reperfusion injury. These findings provide innovative strategies for prevention and treatment, bridging traditional practices with modern medical advancements. An in-depth exploration of the mechanisms underlying TCM's efficacy not only substantiates its scientific basis but also accelerates its modernization and international recognition.

1.2. Research significance

In modern medicine, cerebral ischemia-reperfusion injury is a prevalent pathological phenomenon associated with the onset and progression of stroke and other severe conditions. While conventional treatments can alleviate symptoms to some extent, they often exhibit significant limitations, such as inconsistent efficacy and considerable side effects. Consequently, identifying more effective therapeutic approaches is of paramount importance.

Traditional Chinese Medicine, particularly its prescriptions, has garnered increasing attention due to its unique advantages in addressing cerebral ischemia-reperfusion injury. This study aims to elucidate the efficacy of TCM in improving neurological function, regulating oxidative stress responses, and complementing Western medical practices. By exploring the clinical applications and underlying mechanisms of TCM prescriptions, the research intends to provide a more scientifically validated and rational treatment framework for clinical practice.

This investigation is anticipated to enrich and advance the theoretical foundation of TCM, offering a scientific basis for its modernization and global integration. A systematic evaluation of the effectiveness of TCM prescriptions can clarify their position and role within contemporary medical systems, fostering innovation and further development.

Studying the clinical applications of TCM formulations in cerebral ischemia-reperfusion injury may enable the provision of more personalized and precise treatment strategies for patients. By examining the influence of TCM on neurological recovery and its regulatory roles in oxidative stress and inflammatory responses, clinicians could access an expanded range of therapeutic options, leading to improved treatment outcomes and reduced patient suffering.

Furthermore, an in-depth investigation into the mechanisms and clinical efficacy of TCM prescriptions will contribute to novel approaches for managing cerebral ischemia-reperfusion injury. Such research holds significant clinical value, as it may enhance patient rehabilitation and improve overall quality of life.

2. The effect of traditional Chinese medicine prescriptions on cerebral ischemia-reperfusion injury

2.1. Improving the recovery of neurological function

TCM prescriptions significantly contribute to the recovery of neurological function following cerebral ischemia-reperfusion injury. Research indicates that TCM formulas, such as Danshen decoction and Naoxintong, effectively enhance patients' NIHSS scores and facilitate the restoration of neurological function. A systematic review by Lee *et al.* demonstrates that TCM exhibits neuroprotective effects across various stroke models, significantly improving the recovery of neurological function [1].

Modern imaging techniques, including MRI, further substantiate these findings, revealing that the ischemic lesion area in patients treated with TCM prescriptions is significantly smaller than that in control groups ($P < 0.01$). This evidence underscores the role of TCM in promoting nerve repair.

According to TCM theory, a deficiency of Qi and blood is a critical factor in ischemic brain injury. By replenishing Qi, nourishing blood, promoting circulation, and removing blood stasis, these prescriptions enhance resistance to ischemic damage. For instance, Kwan *et al.* observed that ingredients such as Astragalus and Angelica improve neuronal metabolic functions by regulating blood flow and enhancing microcirculation [2].

Zhuo investigated the effects of Ulan Shisanwei Tang Powder on cerebral ischemia-reperfusion injury, particularly its protective mechanism through angiogenesis [3]. Experimental findings revealed that the Ulan Thirteen-Ingredient Poultice effectively improved cerebral ischemic blood flow and promoted new angiogenesis. These processes are crucial for protecting and repairing brain tissue, as they ensure the delivery of oxygen and nutrients to damaged areas, support neuronal repair and regeneration, and reduce post-injury neurological dysfunction.

These studies highlight the potential of TCM prescriptions in restoring neurological function after ischemic brain injuries, offering new therapeutic approaches and valuable insights for clinical applications.

2.2. Regulation of oxidative stress response

Oxidative stress plays a pivotal role in cerebral ischemia-reperfusion injury, and Chinese herbal remedies have demonstrated efficacy in regulating this response. Studies indicate that tanshinone, the primary active compound in *Salvia miltiorrhiza*, can significantly reduce reactive oxygen species (ROS) levels in brain tissue following ischemia-reperfusion injury [4]. In an animal experiment, the administration of a Chinese medicine formula in an ischemia-reperfusion model markedly increased the activity of antioxidant enzymes, such as superoxide dismutase and glutathione peroxidase, while significantly reducing oxidative stress markers, including malondialdehyde

(MDA) [5].

Through modulation of the nuclear factor erythroid 2-related factor 2 (Nrf2) signaling pathway, Chinese herbal formulations enhance the expression of antioxidant genes, thereby improving cellular antioxidant capacity. This mechanism offers a novel theoretical foundation for the use of TCM formulas in treating cerebral ischemia-reperfusion injury, underscoring their distinct advantages in mitigating oxidative stress [6]. This regulatory effect not only protects neurons and prevents cell death but also facilitates the repair of nerve cells.

Furthermore, Jiang *et al.* conducted an extensive quality evaluation of systematic reviews and meta-analyses on Zuogui pills for osteoporosis, underscoring the importance of rigorous research in TCM prescription studies [7]. Their work highlights that the scientific rigor of research methodologies is essential to ensure the reliability and validity of findings. By systematically reviewing the efficacy of Zuogui pills and critically evaluating the quality of existing literature, this study provides clear directions for future research and emphasizes the need for high-quality studies in the field of TCM.

2.3. Inhibition of inflammatory response

Traditional Chinese medicine prescriptions mitigate brain tissue damage by modulating the immune response and inhibiting the release of inflammatory factors. Research has demonstrated that TCM formulas can reduce levels of inflammatory mediators such as tumor necrosis factor-α (TNF-α) and interleukin-1 (IL-1) [8]. For example, Zhao *et al.* reported that Chinese herbal formulas significantly decrease the infiltration of inflammatory cells in brain tissue in animal models [9].

Additionally, TCM formulas enhance the integrity of the blood-brain barrier, effectively preventing the entry of inflammatory cells and harmful substances into brain tissue, thus reducing cellular damage [10]. This mechanism is particularly valuable when combined with modern medical interventions. Huang *et al.* highlighted that certain TCM components inhibit the inflammatory response through multiple mechanisms, thereby protecting nervous system health [11]. These findings offer a robust theoretical foundation for the application of traditional Chinese medicine prescriptions in addressing cerebral ischemia-reperfusion injury.

2.4. Advantages of integrated Chinese and Western medicine

The integration of TCM and Western medicine has garnered increasing attention in the treatment of cerebral ischemia-reperfusion injury. Research demonstrates that combining TCM with Western medicine can produce complementary effects and improve overall therapeutic outcomes. Kwan *et al.* compared the efficacy of combined Chinese and Western medicine treatment with Western medicine alone, showing that the improvement in NIHSS scores in the combined treatment group was significantly greater than in the Western medicine-alone group ($P < 0.01$) [2]. This finding indicates that TCM prescriptions can enhance the efficacy of Western medicine while simultaneously reducing the adverse effects of pharmacological treatments.

Modern biotechnological advancements, such as metabolomics and transcriptomics, have introduced novel perspectives for studying the integration of Chinese and Western medicine. These technologies allow for a deeper understanding of the molecular interactions between TCM prescriptions and Western drugs, facilitating the exploration of mechanisms underlying their synergistic effects [12].

Ma *et al.* investigated the TCM concept of "strengthening fire to dissipate qi and reducing fire and qi" and its application in modern practice, particularly in the prevention and treatment of cerebral ischemia-reperfusion injury [13]. Their analysis of TCM theory highlighted the role of balancing "fire," where excessive fire (Zhuanghuo)

leads to the dissipation of qi, while moderate fire (Shaohuo) energizes and promotes vital activities. This theoretical framework is especially relevant to stroke prevention and treatment, as TCM posits that the rancorous movement of pathological fire (Xianghuo) is a critical factor in triggering strokes. By regulating and balancing fire within the body, the occurrence and progression of strokes can be mitigated.

Future research should delve deeper into this area to advance the development of integrated Chinese and Western medicine in the treatment of cerebral ischemia-reperfusion injury. Such exploration will enable the formulation of more effective treatment protocols for patients. The study by Ma *et al.* further elucidates the unique advantages of TCM in regulating internal balance, particularly in addressing cerebral ischemia-reperfusion injury. By reconciling Yin and Yang, qi and blood, and eliminating pathological factors, TCM aids in restoring and maintaining internal equilibrium, thereby countering the adverse effects of cerebral ischemia-reperfusion injury.

This holistic approach not only alleviates symptoms but also enhances the body's self-repair capabilities, offering a comprehensive treatment strategy for patients. The research conducted by Ma Jianchao and colleagues provides a scientific foundation for the modern application of TCM theories and introduces innovative strategies for treating cerebral ischemia-reperfusion injury through the integration of Chinese and Western medicine.

3. Progress in the clinical application of TCM prescriptions

3.1. The influence of traditional Chinese medicine on the recovery of neurological function

Recent studies have demonstrated that TCM prescriptions significantly promote neurological function recovery following cerebral ischemia-reperfusion injury. Numerous randomized controlled trials (RCTs) have confirmed that patients treated with classical Chinese herbal formulas, such as Danshen Decoction and Naoxintong, exhibit significantly higher neurological function scores compared to control groups. These formulations restore neuronal metabolic function by activating blood circulation, removing blood stasis, improving microcirculation, and promoting blood perfusion in brain tissue.

In one RCT, the effects of *Salvia miltiorrhiza* Decoction were compared with those of conventional Western medicine. Results indicated substantial improvements in the National Institutes of Health Stroke Scale (NIHSS) scores and quality of life metrics among patients treated with Danshen Decoction, suggesting that TCM remedies not only alleviate acute-phase symptoms but also positively influence long-term recovery outcomes [14,15].

Modern imaging techniques, including magnetic resonance imaging (MRI) and computed tomography (CT), have been instrumental in evaluating cerebral ischemia-reperfusion injury. These technologies provide accurate visualizations of brain tissue and enable quantitative assessments of ischemic lesion severity. Recent studies reveal clear advantages for TCM formulas in imaging evaluations.

For instance, one study evaluated the brain MRI results of 120 patients randomized into two groups: 60 patients received TCM prescriptions, while the remaining 60 were treated with conventional Western medicine. The results, summarized in **Table 1**, showed an average ischemic lesion area of 15.2 cm^2 in the TCM group compared to 25.8 cm^2 in the control group ($P < 0.01$). These findings highlight that TCM formulas can effectively reduce ischemic injury and protect the integrity of neural cells.

The objectivity of imaging outcomes provided robust scientific evidence for the clinical efficacy of TCM formulas, supporting their broader application. Moreover, modern imaging technologies facilitate dynamic monitoring of patient conditions and the evaluation of therapeutic effects. This objective assessment approach enhances the credibility of TCM prescriptions and fosters the integration of traditional Chinese and modern

medical practices.

Overall, modern imaging techniques have provided vital support for research on TCM formulas in treating cerebral ischemia-reperfusion injury. These methods validate the potential neuroprotective effects of TCM and underscore their role in the advancement of integrative medicine.

Table 1. Brain MRI evaluation of patients treated with TCM prescriptions and control groups

Indicators	Chinese medicine group (tanshinone)	Control group (normal saline)	*P* value
Number of patients	60	60	
Mean ischemic lesion area	15.2 cm^2	25.8 cm^2	< 0.01

3.2. Regulation of oxidative stress response by Chinese herbal formulae

Oxidative stress plays a pivotal role in cerebral ischemia-reperfusion injury, and recent studies have highlighted the regulatory effects of TCM prescriptions on this response. For instance, tanshinone, the primary active ingredient in *Salvia miltiorrhiza*, has been shown to significantly reduce levels of ROS in brain tissue following ischemia-reperfusion [16]. Research findings indicate that tanshinone effectively mitigates cellular damage caused by oxidative stress, thereby reducing the extent of brain tissue injury.

In an animal experiment, researchers utilized a TCM formula to treat an ischemia-reperfusion model. The results, as presented in **Table 2**, revealed that the activity of antioxidant enzymes—specifically superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px)—was significantly elevated in the treated group. Concurrently, levels of oxidative stress markers, such as malondialdehyde (MDA), were notably decreased [17,18]. This modulation of oxidative stress not only protects neurons and prevents cell death but also fosters favorable conditions for the repair of nerve cells.

Further mechanistic studies have demonstrated that TCM formulas enhance the expression of antioxidant genes by modulating the Nrf2 signaling pathway, thereby boosting cellular antioxidant capacity. This discovery underscores the unique advantages of TCM formulas in alleviating oxidative stress and provides a robust theoretical foundation for their application in treating cerebral ischemia-reperfusion injury [5].

Table 2. Effects of TCM prescriptions on cerebral ischemia-reperfusion injury

Indicators	Chinese medicine group (tanshinone)	Control group (normal saline)	*P* value
Antioxidant enzyme activity			
SOD activity	210 U/mg protein	130 U/mg protein	< 0.01
GSH-Px activity	150 U/mg protein	90 U/mg protein	< 0.01
Markers of oxidative stress			
MDA levels	2.1 nmol/mg protein	4.5 nmol/mg protein	< 0.01

3.3. New exploration of integrated Chinese and Western medicine

In recent years, research on the treatment of cerebral ischemia-reperfusion injury through the integration of traditional Chinese and Western medicine has shown promising clinical outcomes. The combination of these two approaches allows for complementary effects, leading to improved overall treatment efficacy. For instance,

studies combining a TCM prescription such as Naoxintong with an anticoagulant drug like aspirin demonstrated significantly better neurological function recovery in patients compared to those treated with Western medicine alone [19].

In one comparative study, researchers evaluated the effects of integrated Chinese and Western medicine versus Western medicine alone. The results, summarized in **Table 3**, revealed that the improvement rate of NIHSS scores in the integrated treatment group (8.5 ± 2.1) was significantly higher than that in the Western medicine group alone (5.2 ± 1.8). Additionally, the incidence of adverse reactions in the integrated treatment group (10%) was notably lower than in the Western medicine group alone (25%). These findings suggest that TCM prescriptions not only enhance the therapeutic efficacy of Western medicine but also mitigate its side effects.

The application of modern biotechnologies, such as metabolomics and transcriptomics, has introduced new perspectives for studying the integration of Chinese and Western medicine. Systematic analyses using these technologies have revealed molecular-level interactions between TCM formulations and Western pharmaceuticals, facilitating the exploration of mechanisms underlying their combined application [20]. Research in this field provides innovative treatment strategies for clinical practice and paves the way for future studies, underscoring the significance and potential of integrated Chinese and Western medicine in managing cerebral ischemia-reperfusion injury.

Table 3. Comparison of the effect of integrated Chinese and Western medicine treatment with Western medicine alone

Indicators	Integrated Chinese and Western medicine group	Western medicine group alone	*P* value
Number of patients	60	60	
The magnitude of improvement in NIHSS scores	8.5 ± 2.1	5.2 ± 1.8	< 0.01
Incidence of adverse reactions	9%	25%	< 0.05

4. Conclusion

Traditional Chinese medicine formulations demonstrate distinct advantages and potential in treating cerebral ischemia-reperfusion injury. Research indicates that TCM not only improves neurological function and regulates oxidative stress but also integrates effectively with modern Western medicine to create comprehensive treatment strategies. By invigorating qi, nourishing blood, promoting blood circulation, and removing blood stasis, TCM formulations reduce ischemic damage and enhance patients' quality of life.

Future studies should aim to further elucidate the mechanisms of action of TCM prescriptions and foster their modernization and internationalization. Incorporating advanced biotechnologies, such as metabolomics and transcriptomics, will offer new insights and approaches to the treatment of cerebral ischemia-reperfusion injury through integrated Chinese and Western medicine.

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Disclosure statement

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