Salvia miltiorrhiza adjuvant therapy facilitates cardiac function recovery in patients with myocardial infarction

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Abstract: Myocardial infarction (MI), a leading cause of global mortality, often leads to heart failure and impaired quality of life. This randomized controlled trial evaluated *Salvia miltiorrhiza* (SM), a traditional Chinese herb containing bioactive compounds like tanshinone IIA and salvianolic acid A, as an adjunct therapy for acute MI. SM is known for anti-inflammatory, antioxidant, anticoagulant and microcirculatory benefits. In the study, 120 MI patients were divided into two groups: routine treatment (RT) and RT plus SM injection. After two weeks, the SM group demonstrated significantly increased left ventricular ejection fraction (LVEF) and reduced left ventricular end-systolic and end-diastolic diameters (LVESD, LVEDD) compared to RT (P<0.001). Hemodynamic parameters—cardiac output (CO), cardiac index (CI), and stroke volume (SV) also improved markedly in the SM group. Additionally, SM enhanced vascular endothelial function and lowered serum markers of myocardial injury. These findings suggest SM supplementation synergizes with conventional therapies to accelerate cardiac functional recovery and hemodynamic stabilization in MI patients. The study highlights SM's potential as a safe, effective adjuvant treatment for MI, warranting further clinical exploration.

Keywords: Myocardial infarction, *Salvia miltiorrhiza*, cardiac function, vascular endothelial function, Chinese medicine adjuvant therapy.

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INTRODUCTION

Myocardial infarction (MI) represents a severe clinical manifestation of coronary artery disease (CAD) and is a leading cause of mortality on a global scale (Pilarczyk et al., 2021). MI pathology can be classified into STsegment elevation myocardial infarction (STEMI) and non-ST-segment elevation myocardial infarction (NSTEMI), with over 3 million people experiencing STEMI annually (Grines and Mehta, 2021). In a study of 19,781 patients with coronary heart disease, MI was prevalent in 23.3% of cases (Dyrbuś et al., 2019). Myocardial infarction (MI) occurs when blood flow to the heart is blocked, resulting in ischemia and hypoxia in the myocardial region. This can lead to the death of cardiomyocytes. MI often significantly affects cardiac function, including decreased pumping capacity and changes in cardiac structure. These changes not only affect patients' quality of life but may also lead to serious complications such as heart failure (Akhtar et al., 2024). Therefore, it is of great significance to seek effective treatment to promote the recovery of cardiac function, which can improve the prognosis of MI patients.

Salvia miltiorrhiza (SM) is a commonly used ingredient in traditional Chinese medicine (TCM) (fig. 1). Its efficacy in treating cardiovascular diseases is attributed to its capacity to enhance blood circulation and eliminate blood stasis (Hu *et al.*, 2020; Yin *et al.*, 2021). SM contains several biologically active compounds, including

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tanshinone IIA, salvianolic acid A, and cryptotanshinone (fig. 2). These ingredients have demonstrated various pharmacological effects, including anti-oxidation, antianti-coagulation inflammation, and improved microcirculation (Huang et al., 2024). SM, in particular, has been found to aid in the treatment of MI by reducing myocardial cell damage and promoting the repair of damaged tissues through its antioxidant and antiinflammatory effects. This may have a positive impact on the recovery of cardiac function (Wu et al., 2021a). Nonetheless, it is important to acknowledge the potential risks and controversies surrounding the clinical use of TCM. Concerns may include variability in the quality and potency of SM preparations, potential herb-drug interactions, and the need for further rigorous scientific validation of their efficacy and safety. Despite these considerations, the integration of TCM with modern medical practices continues to be an area of interest due to its potential to complement conventional therapies.

In recent years, the use of SM as an adjuvant therapy in MI treatment has gained attention due to the rise of integrated traditional Chinese and Western medicine treatment modes. Although laboratory studies have revealed the potential benefits of SM's bioactive components on MI recovery, there is still a lack of clinical studies on the specific effects and mechanisms of SM on cardiac function recovery. Therefore, further clinical studies are needed to verify its effectiveness. The aim of this study is to investigate the impact of SM adjuvant therapy on the recuperation of cardiac function in MI patients and its potential mechanism. The study aims to

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provide more scientific and systematic evidence to support the use of SM in MI treatment and to offer more precise treatment guidance for clinicians.

MATERIALS AND METHOD

Study Design

The study was a randomized controlled trial conducted at Shanghai Changhai Hospital, aiming to evaluate the effects of SM adjuvant therapy on patients with AMI. The randomization process was performed by independent statisticians and a central randomization system was used to ensure the allocation was both random and blind. To maintain the double-blind design, all therapeutic products were uniformly packaged and marked by third parties. All result data will be collected during the study. In case of missing data, intention-to-treat analysis (ITT analysis) will be used to ensure result integrity.

Subject selection

A total of 120 patients diagnosed with AMI were selected for the study.

Inclusion criteria

(1) Clinical symptoms that meet the diagnostic criteria for acute myocardial infarction, including chest pain lasting more than 30 minutes and not relieved by nitroglycerin. The patient's electrocardiogram displays pathological Q waves, ST segment elevation or depression, and elevated levels of myocardial enzymes. The patient is experiencing their first onset. The patient has signed the informed consent.

Exclusion criteria

(1) Allergy to Danshen injection; (2) history of cardiac surgery; (3) anticoagulant, antiplatelet, or other related treatment within the past month; (4) severe lesions of organs and tissues; (5) previous myocardial infarction; and (6) occult or active bleeding of aortic dissection.

Sample size selection

The sample size of 120 patients was determined based on the expected effect size and statistical power calculations from pilot studies and previous research, ensuring adequate representation to detect significant differences in cardiac function recovery between the two study groups.

Ethical approval

The study protocol was approved by the Ethics Committee of Shanghai Changhai Hospital, Naval Medical University (Approval Number: CHH20220316). The trial was conducted in accordance with the ethical standards and principles of the Declaration of Helsinki.

Intervention method

A random number sequence was generated by a computer to randomly assign 120 patients to either the routine treatment group (RT group) or the *Salvia miltiorrhiza* group (SM group). The patients in the RT group were administered conventional thrombolytic therapy. The specific methods included routine ECG monitoring. oxygen inhalation and bed rest. Prior to thrombolysis, heparin sodium injection was diluted to 60-80 units per kilogram of body weight with normal saline, and then administered intravenously. Following this, pro-urokinase injection was administered. Intravenous injection of 10 mL of normal saline and 20mg of pro-urokinase was then given, followed by rapid intravenous drip of 90 mL of normal saline and 30mg of pro-urokinase (Yin et al., 2022). Thrombolysis was performed and patients were instructed to take enteric-coated aspirin tablets orally once a day for the remainder of their lives (75mg to 160mg per dose). Clopidogrel tablets were also used for treatment. taken orally in a single daily dose of 75mg. Patients who received stent treatment were advised to take clopidogrel for 1 year, while those who did not receive stent treatment were advised to take it for 1 month. The recommended method of treatment for atorvastatin tablets is oral administration. The conventional starting dose is 10mg once a day. After 4 weeks of treatment, the dosage may be adjusted based on the patient's condition, with a maximum daily dose of 80mg. It is important to follow the prescribed dosage for the duration of the treatment.

The criteria for evaluating the success of thrombolysis include an ST segment elevation drop of greater than 50%, the appearance of creatine kinase isoenzyme and creatine kinase peak in advance, and the disappearance of chest pain. At least two of these conditions can be considered indicative of successful thrombolysis (Li *et al.*, 2024).

The SM group received Danshen injection in addition to conventional thrombolytic therapy (fig. 3). The curative effect was analyzed. The Danshen injection, produced by Jiangsu Shenlong Pharmaceutical Co., Ltd., had specifications of 2mL per branch and batch numbers of 20200105, 20201115, 20220905 and 20230103. The injection was administered intravenously at a dose of 10mL, combined with 300mL of glucose injection, once daily for a period of 2 weeks.

Observation indexes

Cardiac function indicators

The assessment of cardiac function was conducted by evaluating parameters including the left ventricular ejection fraction (LVEF), which indicates the heart's ability to eject blood, the left ventricular end-systolic diameter (LVESD), signifying the heart's size at the end of contraction, and the left ventricular end-diastolic diameter (LVEDD), representing the heart's size at the end of relaxation. These parameters were recorded at the onset of the treatment period and again two weeks posttreatment, employing the Feynaud digital color ultrasound diagnostic device, model VINNO E10, with the serial number su mechanical injection 20172231243, for the measurements. The differences in these indexes between the two groups were compared.

Hemodynamic parameters

Vital indicators reflecting the circulatory system's performance, including the measurement of cardiac output (CO), which quantifies the heart's pumping capacity per minute, the cardiac index (CI), a normalized value of cardiac output adjusted for body surface area, and the stroke volume (SV), representing the volume of blood ejected by the heart with each beat, were evaluated prior to the initiation of treatment and again at the two-week mark post-treatment. These assessments were conducted using the Feynaud digital color ultrasound diagnostic instrument, model VINNO E10, identified by the serial number su mechanical injection 20172231243. Subsequently, the variations in the aforementioned hemodynamic parameters between the two study groups were analyzed for comparative insights.

Vascular endothelial function indicators

Venous blood samples, each 5mL in volume, were obtained from participants in both study groups at the outset of the treatment and two weeks post-intervention. Following collection, the blood specimens were subjected to centrifugation at a rate of 3500 revolutions per minute for a duration of 15 minutes to separate components. Post-centrifugation, the samples were preserved at a temperature of -80°C for subsequent analysis. Subsequently, the concentrations of endothelin-1 (ET-1), nitric oxide (NO) and the measure of flow mediated dilation (FMD) were determined utilizing the Zhongchi XL1000i coagulation analyzer.

Serum index of myocardial injury

Prior to the commencement and upon the conclusion of the treatment phase, venous blood specimens were procured from the patient cohort. Post the centrifugation process, which facilitated the separation of the serum layer, the supernatant serum was carefully collected for further analysis. This serum was then subjected to enzyme-linked immunosorbent assay (ELISA) to quantify the concentrations of serum high-sensitivity troponin (hscTn), apolipoprotein A (Apo-A), and lipoproteinassociated phospholipase A2 (Lp-PLA2). The ELISA procedure was conducted utilizing the Plumbol PORABIO automatic microplate reader for precision measurement. The operation was performed according to the kit instructions provided by Jianglai Biological Company.

STATISTICAL ANALYSIS

Data analysis was conducted utilizing SPSS software, version 27.0, with results presented as the Mean \pm Standard Deviation (SD). To ensure the appropriate application of statistical tests, we first assessed the assumptions of normality and homogeneity of variance, which are critical for the validity of our parametric comparisons. Normality was evaluated using the Shapiro-

Wilk test and all continuous variables were found to be normally distributed across groups. Homogeneity of variance was confirmed with Levene's test, indicating that the variances between groups were equivalent, thus supporting the use of independent samples t-tests for comparing means between groups. For categorical data, we depicted frequencies as percentages and employed the χ^2 test to assess differences between groups. Statistical significance was set at a p-value of less than 0.05.

RESULTS

Initial patient data comparison across both groups

The study included 120 participants divided into two groups: RT group and SM group. The RT group was composed of 60 participants, including 40 males and 20 females, aged between 37 to 71 years, with an average age of 52.18 years (SD: 6.42). The Killip classification showed 21 cases of grade II, 29 cases of grade III and 10 cases of grade IV. The SM group was made up of 37 males and 23 females, aged 31 to 65 years, averaging 51.27 years in age (SD: 6.59). The Killip classification showed grade II in 24 cases, grade III in 23 cases, and grade IV in 13 cases. There were no significant differences in the general data between the two groups (P>0.05), as shown in table 1.

Cardiac function indicator trends between baseline and post-intervention for both groups

No statistically significant difference was observed in LVEF, LVESD and LVEDD levels between the RT and SM groups prior to therapy (all P>0.05). Following a twoweek course of therapy, the LVEF of the SM group exhibited a statistically significant increase, with a higher mean value than that observed in the RT group (P<0.001). Similarly, the RT group also showed a significant improvement in LVEF compared to its baseline (P<0.05). The left ventricular end-systolic diameter (LVESD) and left ventricular end-diastolic diameter (LVEDD) of the SM group exhibited a statistically significant reduction, with values that were markedly lower than those observed in the RT group (P<0.001), and also significantly lower than their own baseline measurements (P<0.05). This is illustrated in fig. 4.

Emodynamic parameter shifts from baseline to posttreatment within both groups

No statistically significant difference was observed in the levels of CO, CI, and SV between the RT and SM groups prior to treatment (all P>0.05). Following a two-week course of treatment, the levels of CO, CI and SV in the SM group were found to be considerably higher than those observed in the RT group (P<0.001). Additionally, both the RT and SM groups showed statistically significant improvements compared to their own baseline measurements (P<0.05), as illustrated in fig. 5.



Fig. 1: SM TCM diagram, SM=Salvia miltiorrhiza

Pre-and post-treatment vascular endothelial function marker changes across both groups

Prior to the commencement of treatment, no notable discrepancies were observed in the levels of ET-1, NO, and FMD between the RT and SM groups (all P>0.05). Following a two-week course of treatment, the SM group exhibited a statistically significant reduction in ET-1 levels compared to the RT group (P<0.001). Additionally, the SM group showed significant increases in NO and FMD levels compared to the RT group (P<0.001). It is important to note that both the RT and SM groups demonstrated statistically significant improvements in these parameters compared to their own baseline measurements (P<0.05), as depicted in fig. 6.

Serum myocardial injury marker variations in both groups pre-and post-treatment

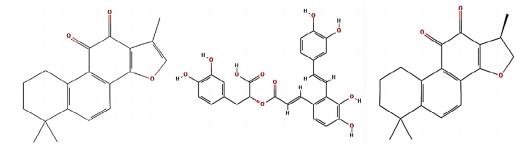
Prior to the commencement of treatment, no notable discrepancies were observed in the levels of hs-cTn, Lp-PLA2 and Apo-A between the RT and SM groups (all P > 0.05). Following a two-week course of treatment, the SM group exhibited a statistically significant reduction in hs-cTn and Lp-PLA2 levels compared to the RT group (P< 0.001). Additionally, the SM group showed significant increases in Apo-A levels compared to the RT group

(P<0.001). It is important to note that both the RT and SM groups demonstrated statistically significant improvements in these parameters compared to their own baseline measurements (P<0.05), as depicted in fig. 7.

DISCUSSION

An acute myocardial infarction, referred to as AMI, results from a lack of oxygen to the heart muscle due to the narrowing of the coronary arteries by atherosclerotic plaques. The accumulation of lipids within the arterial vessels has been demonstrated to facilitate the activation and migration of inflammatory cells, regulate the secretion of a range of inflammatory factors, and exacerbate vascular endothelial injury (Wu et al., 2021b). TCM postulates that the heart qi exerts predominant control over blood circulation, and that the optimal functionality of the veins is a prerequisite for effective heart qi-mediated blood flow. When there is a deficiency of heart qi, it fails to promote blood circulation, leading to blood stasis and blockage of the heart vein. This can cause damage to the organs and result in water retention, leading to myocardial insufficiency and energy metabolism disorder. This statement is consistent with the pathological mechanisms of vascular endothelial dysfunction, myocardial energy metabolism disorder, and ventricular remodeling in patients with myocardial infarction (Yang et al., 2023b). The aetiology of MI in TCM is thought to be attributable to deficiencies in qi and blood stasis. In order to enhance the clinical outcomes for patients, it is anticipated that the implementation of strategies such as qi tonification, water promotion, enhanced blood circulation, and the removal of blood stasis will serve to compensate for the limitations of conventional therapeutic approaches.

Following a two-week course of treatment, the SM group exhibited a notable enhancement in LVEF and a considerable reduction in LVESD and LVEDD, which were found to be significantly disparate from the RT group. After 2 weeks of treatment, the SM group showed significantly higher levels of CO, CI and SV compared to the RT group (P<0.001).



Tanshinone IIA

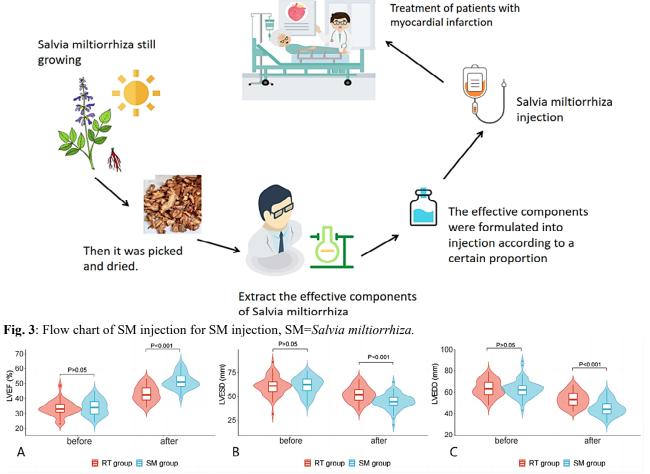
Salvianolic acid A

Cryptotanshinone

Group	Gender		1	killip classes		
	Male	Female	Age	II	III	IV
RT group	40 (66.67)	20 (33.33)	52.18±6.42	21	29	10
SM group	37 (61.67)	23 (38.33)	51.27±6.59	24	23	13
t/χ^2	$\chi^2 = 0.326$		<i>t</i> =0.771	$\chi^2 = 1.284$		
Р	0.568		0.442	0.526		

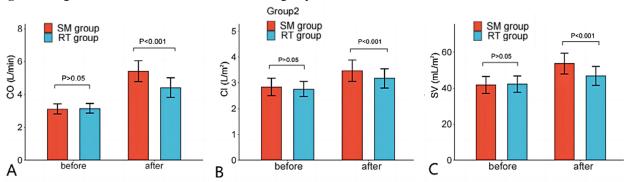
Table 1: Baseline Characteristics and Group Comparisons

Note: Routine treatment group (RT group), Salvia miltiorrhiza group (SM group)



Note: Left ventricular ejection fraction (LVEF), left ventricular end-systolic diameter (LVESD) and end-diastolic diameter (LVEDD). routine treatment group (RT group), *Salvia miltiorrhiza* group (SM group)

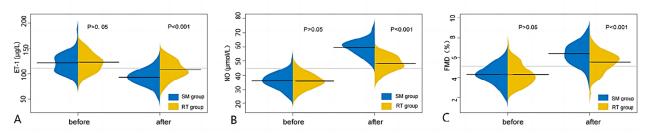
Fig. 4: Changes in cardiac function indicators in two groups before and after treatment.



Note: Cardiac output (CO), cardiac output index (CI), stroke volume (SV), routine treatment group (RT group), Salvia miltiorrhiza group (SM group)

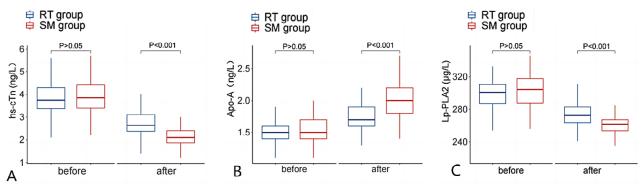
Fig. 5: Changes in hemodynamic parameters in the two groups before and after treatment.

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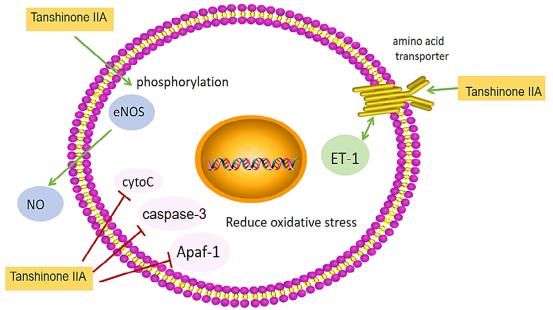
Note: endothelin (ET-1), nitric oxide (NO) and flow mediated dilation (FMD), routine treatment group (RT group), Salvia miltiorrhiza group (SM group)

Fig. 6: Changes in vascular endothelial function indicators in the two groups before and after treatment.



Note: High-sensitivity troponin (hs-cTn), apolipoprotein A (Apo-A), lipoprotein-associated phospholipase A2 (Lp-PLA2), routine treatment group (RT group), *Salvia miltiorrhiza* group (SM group).

Fig. 7: Changes in Serum myocardial injury marker before and after treatment in both groups.



Note: Endothelial Nitric Oxide Synthase (eNOS), Nitric Oxide (NO), Cytochrome C (cytoC), Caspase-3 (caspase-3), Apoptotic Protease Activating Factor 1 (Apaf-1), Endothelin-1 (ET-1)

Fig. 8: Mechanism of Tanshinone IIA protecting cardiomyocytes

This suggests that SM injection can improve ventricular diastolic and systolic function, as well as hemodynamics. SM injection is a TCM composed of effective components extracted from *Salvia miltiorrhiza*. The main component of this substance is tanshinone IIA. It has anticoagulant, antiplatelet, anti-atherosclerotic, anti-

apoptotic, and vascular smooth muscle hyperplasia inhibiting effects. Tanshinone IIA can significantly reduce clinical symptoms of myocardial infarction, decrease myocardial injury and protect cardiac function (Lian *et al.*, 2021). Previous studies have found that tanshinone IIA pretreatment significantly reduced the infarct size of rats

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with coronary heart disease after myocardial ischemiareperfusion injury and improved cardiac function (Chai et al., 2023). Tanshinone IIA ameliorated oxidative stressinduced damage, mitigated inflammatory reactions, and prevented apoptosis in cardiomyocytes of rats through modulating the activity of the phosphoinositide 3kinase/protein kinase B (PI3K/AKT) pathway. Antimvocardial ischemia therapy aims to reduce cardiomyocyte apoptosis induced by myocardial ischemia. Tanshinone IIA inhibits myocardial infarction (MI) and post-infarction heart failure by regulating the signaling pathway of cardiomyocyte mitochondrial apoptosis. In their study, Fang et al (Fang et al., 2021) demonstrated that tanshinone IIA can reduce myocardial apoptosis through the endoplasmic reticulum stress-dependent pathway and mitochondrial apoptosis signaling pathway. Additionally, they found that it can decrease myocardial infarct size and improve myocardial function in rats with myocardial ischemia. The observed effect may be attributed to the ability of tanshinone IIA to enhance the viability of damaged cardiomyocytes, decrease the expression levels of caspase-3, cytochrome C (cyto C), and apoptotic protease activating factor-1 (Apaf-1) in myocardial tissue, increase the expression of proapoptotic proteins B-cell lymphoma-2 (Bcl-2), Bak, and Bim in cardiomyocytes, and reduce the production of peroxides (Li et al., 2022).

The vascular endothelium plays a central role in MI lesions. Regulating its function has a positive effect on stabilising the MI condition, restoring normal circulatory system function and improving prognosis (Shamaki et al., 2022). ET-1 is a vasoconstrictor peptide that directly affects vasomotor and cardiovascular remodelling. During myocardial ischemia, the release of ET-1 increases, which can further aggravate myocardial injury (Brewster et al., 2020). Nitric oxide (NO) has various functions, including regulating vasodilation and inducing vascular remodeling. A low concentration of NO in blood vessels can decrease the activity of angiotensin in plasma, stimulate the differentiation and proliferation of smooth muscle cells, and exacerbate endothelial cell injury (Cyr et al., 2020). Flow-Mediated Dilation (FMD) is a non-invasive echocardiographic technique used to evaluate vascular endothelial function. FMD measures the degree of change in vascular diameter after the release of vasodilators such as NO by vascular endothelial cells under the stimulation of increased shear stress. Reports indicate that individuals suffering from heart failure exhibit endothelial dysfunction, a condition where ET-1 levels are notably elevated. Interventions that aim to decrease ET-1 levels and boost NO levels are shown to enhance endothelial function among this patient population (Zuchi et al., 2020). This study demonstrates that Danshen injection adjuvant therapy can effectively reduce ET-1 levels, increase NO and FMD levels and improve endothelial dysfunction in patients with myocardial infarction,

promoting the remission of patients' conditions. Currently, tanshinone IIA's pharmacological effects are mostly studied through in vitro experiments. Lu *et al* (Lu *et al.*, 2022) discovered that tanshinone IIA can regulate the production of nitric oxide (NO) by activating the phosphorylation of endothelial nitric oxide synthase (eNOS), and control the expression of amino acid transporters while inhibiting the expression of ET-1. Tanshinone IIA not only reduces the expression of ET-1 in vascular cells but also increases the concentration of NO by activating the transcription factor (ATF3) and promoting the phosphorylation of eNOS (Lin *et al.*, 2021) (fig. 8).

The study results indicate that after treatment, the SM group had higher serum Apo-A levels compared to the RT group. Additionally, the SM group had lower serum hscTn and Lp-PLA2 levels than the RT group. These findings suggest that SM injection can help reduce myocardial injury in AMI patients and delay the formation of atherosclerosis. Lp-PLA2 is typically secreted by inflammatory cells in coronary atherosclerosis, which can impact plaque formation and stability. Its level is positively correlated with the degree of inflammatory response in MI (Zifu et al., 2022). Apo-A can remove lipids from tissue cells, inhibit atherosclerosis formation, regulate blood fat protein secretion, and is closely related to the occurrence of cardiovascular events (Gilliland et al., 2023). Hs-cTn is a cardiac injury marker with high sensitivity and specificity. It can be used to evaluate the degree of myocardial injury and the outcome of patients with acute myocardial infarction (AMI). The level of hscTn significantly increases with the aggravation of myocardial injury (Hempel and Wyatt, 2022). Several studies have confirmed that tanshinone IIA's antiinflammatory, anticoagulant, and antithrombotic effects are related to its regulation of the Toll-like receptor 4/Nuclear transcription factor-κB (TLR/NF-κB) pathway, as well as its influence on the signaling cascade of the mitogen-activated protein kinases (MAPK) and the Nuclear Factor-kappa B (NF-KB) pathways (Ding et al., 2020; Guo et al., 2020; Jin et al., 2020). Therefore, the active ingredients in SM injection, such as tanshinone IIA, may effectively inhibit the pathological process of these MI by regulating the above pathways.

Although the study has yielded some findings, it is important to acknowledge the limitations of the study, including the relatively small sample size and the lack of multiple control groups. Further studies should aim to expand the sample size and include multiple controlled trials in order to provide a comprehensive evaluation of the efficacy and safety of SM injection treatment in combination with other therapies for patients with AMI. Additionally, further research can investigate the mechanism of action of SM injection to provide theoretical support for its clinical application. Our study underscores the beneficial effects of SM adjuvant therapy on cardiac function recovery. However, it is imperative to consider the potential adverse effects associated with SM treatment. While SM is generally well-tolerated, some patients may experience adverse reactions. Research has indicated that sodium tanshinone IIA sulfonate (STS), a water-soluble derivative of tanshinone IIA, can induce allergic reactions in approximately 30% of patients, predominantly affecting the skin and its appendages. Although the majority of adverse reactions are mild, there is a risk of lifethreatening conditions, such as anaphylactic shock (Yang et al., 2023a). Consequently, it is advisable for healthcare providers to conduct a comprehensive assessment of patients' medical history, including allergies, hepatic and renal function, and underlying diseases, prior to administration. Overall, compared to other conventional therapies, SM has demonstrated a favorable safety profile with minimal reported adverse effects. Nevertheless, the implementation of monitoring strategies is essential to promptly identify and manage any detrimental impacts. Future research should continue to monitor the long-term safety of SM treatment and explore strategies to mitigate potential risks.

Furthermore, we observed significant improvements in cardiac function following the adjuvant therapy with *Salvia miltiorrhiza* (SM). However, the potential long-term impacts of SM treatment warrant further investigation. While the short-term benefits are evident, it is essential to consider the sustainability of these long-term effects. Long-term studies are required to assess the chronic safety, the potential development of drug resistance, and the impact on patients' quality of life. It is important to note that our study has limitations, such as a relatively small sample size and a short follow-up period. Future research should focus on conducting larger, multicenter trials with extended follow-up durations to comprehensively evaluate the long-term efficacy and safety of SM treatment.

CONCLUSION

In summary, the study demonstrates that SM adjuvant therapy can markedly enhance cardiac performance in patients with MI, augment hemodynamic parameters and vascular endothelial function, and mitigate serum indicators of myocardial injury. The injection of SM helps to reduce myocardial cell injury and promote the recovery of cardiac function through its antioxidant and antiinflammatory effects. This provides an effective auxiliary means for MI treatment using Chinese medicine.

REFERENCES

Akhtar K, Khan M, Baron S, Zieroth S, Estep J, Burkhoff D, Butler J and Fudim M (2024). The spectrum of postmyocardial infarction care: From acute ischemia to heart failure. *Prog. Cardiovasc. Dis.*, 82: 15-25.

- Brewster L, Garcia V, Levy M, Stockelman K, Goulding A, DeSouza N, Greiner J, Hijmans J and DeSouza C (2020). Endothelin-1-induced endothelial microvesicles impair endothelial cell function. *J. Appl Physiol.* (1985), **128**(6): 1497-1505.
- Chai R, Ye Z, Xue W, Shi S, Wei Y, Hu Y and Wu H (2023). Tanshinone IIA inhibits cardiomyocyte pyroptosis through TLR4/NF- κ B p65 pathway after acute myocardial infarction. *Front. Cell Dev. Biol.*, **11**: 1252942.
- Cyr A, Huckaby L, Shiva S and Zuckerbraun B (2020). Nitric oxide and endothelial dysfunction. *Crit. Care Clin.*, **36**(2): 307-321.
- Ding B, Lin C, Liu Q, He Y, Ruganzu J, Jin H, Peng X, Ji S, Ma Y and Yang W (2020). Tanshinone IIA attenuates neuroinflammation via inhibiting RAGE/NF-κB signaling pathway *in vivo* and *in vitro*. J Neuroinflammation, **17**(1): 302.
- Dyrbus K, Gąsior M, Desperak P, Osadnik T, Nowak J and Banach M (2019). The prevalence and management of familial hypercholesterolemia in patients with acute coronary syndrome in the Polish tertiary centre: Results from the TERCET registry with 19,781 individuals. *Atherosclerosis*, **288**: 33-41.
- Fang Y, Duan C, Chen S, Liu Z, Jiang B, Ai W, Wang L, Xie P and Fang H (2021). Tanshinone-IIA inhibits myocardial infarct via decreasing of the mitochondrial apoptotic signaling pathway in myocardiocytes. *Int. J. Mol Med.*, **48**(2): 158.
- Gilliland T, Liu Y, Mohebi R, Miksenas H, Haidermota S, Wong M, Hu X, Cristino J, Browne A and Plutzky J (2023). Lipoprotein(a), oxidized phospholipids, and coronary artery disease severity and outcomes. *J. Am. Coll. Cardiol.*, **81**(18): 1780-1792.
- Grines C and Mehta S (2021). ST-segment elevation myocardial infarction management: Great strides but still room for improvement. *Eur. Heart J.*, **42**(44): 4550-4552.
- Guo R, Li L, Su J, Li S, Duncan SE, Liu Z and Fan G (2020). Pharmacological activity and mechanism of tanshinone IIA in related diseases. *Drug Des. Devel. Ther.*, **14**: 4735-4748.
- Hempel T and Wyatt A (2022). High sensitivity troponins. *Emerg. Med. Clin. North Am.*, **40**(4):809-821.
- Hu J, Zhao M, Hou Z and Shang J (2020). The complete chloroplast genome sequence of *Salvia miltiorrhiza*, a medicinal plant for preventing and treating vascular dementia. *Mitochondrial DNA B Resour.*, **5**(3): 2460-2462.
- Huang J, Zhang J, Sun C, Yang R, Sheng M, Hu J, Kai G, and Han B (2024). Adjuvant role of *Salvia miltiorrhiza* bunge in cancer chemotherapy: A review of its bioactive components, health-promotion effect and mechanisms. *J. Ethnopharmacol.*, **318**(Pt B): 117022.
- Jin H, Peng X, He Y, Ruganzu J and Yang W (2020). Tanshinone IIA suppresses lipopolysaccharide-induced neuroinflammatory responses through NF-κB/MAPKs

signaling pathways in human U87 astrocytoma cells. *Brain Res. Bull.*, **164**: 136-145.

- Li B, Lv J, Han S, Chen R, Hu Y, Fang J, Wang Z, Zhong W, Hu Y and Liu W (2024). Successful percutaneous coronary intervention in a congenital single right coronary artery with acute myocardial infarction: A case report and literature review. *Medicine (Baltimore)*, **103**(31): e39143.
- Li D, Yang Z, Gao S, Zhang H and Fan G (2022). Tanshinone IIA ameliorates myocardial ischemia/reperfusion injury in rats by regulation of NLRP3 inflammasome activation and Th17 cells differentiation. *Acta Cir. Bras.*, **37**(7): e370701.
- Lian B, Zeng R, Chen Y, Liao P, Guo L and Zhang M (2021). Sodium Tanshinone IIA sulfonate for acute myocardial infarction: A systematic review and Metaanalysis. J. Tradit. Chin. Med., **41**(1): 26-35.
- Lin S, He X, Zhai G, Wang C, Xue H and Lin S (2021). Prospective study of the effect of sulfotanshinone sodium combined with tirofiban on vascular endothelial function and indicators of plaque stability in elderly patients with acute coronary syndrome. J. *Clin. Pharm. Ther.*, **46**(2): 319-327.
- Lu T, Wu Y, Chen W and Hung Y (2022). Targeting oxidative stress and endothelial dysfunction using Tanshinone IIA for the treatment of tissue inflammation and fibrosis. *Oxid. Med. Cell Longev.*, **2022**: 2811789.
- Pilarczyk K, Werdan K, Russ M, Thiele H, Michels G, Boeken U and Thielmann M (2021). The German-Austrian S3 Guideline, Cardiogenic shock due to myocardial infarction: Diagnosis, monitoring, and treatment. *Thorac Cardiovasc Surg.*, **69**(8): 684-692.
- Shamaki G, Markson F, Soji-Ayoade D, Agwuegbo C, Bamgbose M and Tamunoinemi B (2022). Peripheral artery disease: A comprehensive updated review. *Curr. Probl. Cardiol.*, **47**(11): 101082.

- Wu X, Liu L, Zheng Q, Hao H, Ye H, Li P and Yang H (2021a). Protocatechuic aldehyde protects cardiomycoytes against ischemic injury via regulation of nuclear pyruvate kinase M2. Acta Pharm. Sin. B., 11(11): 3553-3566.
- Wu X, Reboll M, Korf-Klingebiel M and Wollert K (2021b). Angiogenesis after acute myocardial infarction. *Cardiovasc. Res.*, **117**(5): 1257-1273.
- Yang C, Mu Y, Li S, Zhang Y, Liu X and Li J (2023a). Tanshinone IIA: A Chinese herbal ingredient for the treatment of atherosclerosis. *Front. Pharmacol.*, 14: 1321880.
- Yang Y, Li X, Chen G, Xian Y, Zhang H, Wu Y, Yang Y, Wu J, Wang C and He S (2023b). Traditional Chinese medicine compound (Tongxinluo) and clinical outcomes of patients with acute myocardial infarction: the CTS-AMI randomized clinical trial. *JAMA*, **330**(16): 1534-1545.
- Yin X, Huang Y, Li Z, Dong J, Zou J, Tian L and Yang J (2022). Efficacy and safety of intracoronary prourokinase injection during percutaneous coronary intervention in treating ST elevation myocardial infarction patients: a systematic review and metaanalysis of randomized controlled trials. *Eur. Rev. Med. Pharmacol. Sci.*, 26(16): 5802-5813.
- Yin Z, Wang X, Yang X, Chen Y, Duan Y and Han J (2021). Salvia miltiorrhiza in anti-diabetic angiopathy. *Curr. Mol. Pharmacol.*, **14**(6): 960-974.
- Zifu T, Jiaquan L and Juan Z (2022). Effect of Qingre Jiedu Huoxue Huayu recipe on blood stasis and toxin syndrome in patients with non-ST segment elevation acute coronary syndrome, serum Lp-PLA2, TNF- α , and PIGF expression level. *Cell. Mol. Biol. (Noisy-le-grand)*, **67**(4): 121-129.
- Zuchi C, Tritto I, Carluccio E, Mattei C, Cattadori G and Ambrosio G (2020). Role of endothelial dysfunction in heart failure. *Heart Fail. Rev.*, **25**(1): 21-30.