

Research Progress of Traditional Chinese Medicine Targeting Endothelial Cell Ferroptosis for the Intervention of Atherosclerosis

Yan Cao¹, Yukai Zhao¹, Minglang Zhang¹, Haibo Yang¹, Peng Lei^{1,2,*}

¹*The First Clinical Medical College, Shaanxi University of Chinese Medicine, Xianyang, 712046, Shaanxi, China*

²*Shaanxi Provincial People's Hospital, Xi'an, 710000, Shaanxi, China*

**Corresponding author*

Keywords: Atherosclerosis; Ferroptosis; Vascular Endothelial Cells; Lipid Peroxidation; Traditional Chinese Medicine

Abstract: Atherosclerosis (AS) is a chronic vascular disorder characterized by lipid metabolism disturbance, chronic inflammation and vascular endothelial dysfunction, which acts as a critical pathological basis for the occurrence and progression of diverse cardiovascular-cerebrovascular diseases. Ferroptosis, an iron-dependent regulated cell death, is closely associated with iron metabolic dysregulation, lipid peroxidation and oxidative stress, and has been recognized as an important mechanism involved in AS progression. Ferroptosis in vascular endothelial cells can accelerate AS progression by promoting reactive oxygen species (ROS) generation, aggravating lipid peroxidative injury and destroying vascular homeostasis. Existing studies demonstrate that active components and formulas of Traditional Chinese Medicine (TCM) can relieve ferroptosis-related damage of vascular endothelial cells via regulating iron homeostasis, enhancing the System Xc⁻/glutathione (GSH)/glutathione peroxidase 4 (GPX4) antioxidant defense system, reducing lipid peroxidation and alleviating oxidative stress, so as to exert anti-atherosclerotic effects. This review summarizes the mechanism of ferroptosis and its role in AS, and discusses research advances of TCM-derived bioactive compounds and formulas targeting endothelial ferroptosis for AS intervention, aiming to provide theoretical basis and novel research perspectives for TCM prevention and treatment of AS.

1. Introduction

With social development and growing population aging, cardiovascular diseases (CVDs) [1] have become the leading cause of death among residents in both urban and rural areas of China. Atherosclerosis (AS) [2] serves as the pathological basis for multiple cardiovascular and cerebrovascular diseases. It is a chronic inflammatory disease characterized by lipid deposition, fibrosis and calcification in the walls of large- and medium-sized arteries. So far, multiple theories have been proposed to interpret the pathological mechanisms of AS [3], including lipid infiltration, thrombosis, smooth muscle cell proliferation, inflammation and endothelial injury hypotheses. With

advances in clinical and basic research, regulating immune-inflammatory responses, protecting vascular endothelium and improving lipid metabolism have become vital strategies for the prevention and treatment of AS.

Accumulating evidence confirms that ferroptosis participates in the initiation and progression of AS and its complications. Three typical features, namely lipid oxidation, massive cell death and iron deposition, can be observed within human atherosclerotic plaques [4]. Via multiple pathways including oxidative stress, inflammation and ferroptosis, excess iron aggravates endothelial dysfunction, accelerates smooth-muscle calcification and triggers macrophage foam-cell formation. Iron overload further activates ferroptosis, leading to plaque destabilization and disease progression [5].

Traditional Chinese medicine (TCM) is featured by multi-component, multi-target and holistic regulatory properties. Numerous recent studies have demonstrated that TCM-derived active compounds and formulas can mitigate ferroptosis-related injuries in vascular endothelial cells by modulating iron metabolism, enhancing anti-oxidative defense capacity and alleviating lipid peroxidation damage, so as to exert anti-atherosclerotic effects. This review summarizes the pathogenesis of ferroptosis and its role in AS, and elaborates research advances of TCM monomers and formulas targeting vascular endothelial cell ferroptosis for AS intervention, so as to provide theoretical references and novel research perspectives for AS prevention and treatment by TCM.

2. Overview of ferroptosis

In 2012, Dixon et al. [6] firstly proposed ferroptosis as a novel form of programmed cell death, which is triggered by intracellular abnormal iron accumulation-mediated lipid peroxidation and ultimately results in cell death. Distinct from apoptosis, pyroptosis, necrosis and other programmed cell death patterns, ferroptosis occurs when intracellular anti-oxidative metabolic systems are imbalanced. Excess free Fe^{2+} accumulates and triggers the Fenton reaction to generate cytotoxic reactive oxygen species (ROS) and lipid peroxides. Excessive ROS induces lipid peroxidation of polyunsaturated fatty acids (PUFAs) on cell membranes and consequently gives rise to ferroptosis. The main morphological manifestations of ferroptosis include loss of plasma membrane integrity, swelling of cytoplasm and organelles, as well as mitochondria-specific changes such as shrunken volume, increased membrane density, reduced or vanished mitochondrial cristae and ruptured outer membranes, while the nucleus remains morphologically unchanged [7].

2.1. Disturbed iron metabolism

Homeostatic iron metabolism lays the foundation for stable intracellular biochemical environment. Iron participates in diverse in-vivo metabolic reactions mainly in two redox states: Fe^{2+} and Fe^{3+} [8]. Under physiological conditions, intracellular iron ion concentration is strictly regulated. Once iron homeostasis is disrupted, excessive iron, especially highly reactive Fe^{2+} , accumulates inside cells, promotes ROS production and elevates oxidative stress levels [9]. Extracellular Fe^{3+} binds to transferrin and enters endosomes via transferrin receptor 1 (TFR1)-mediated endocytosis. Within endosomes, Fe^{3+} is reduced to Fe^{2+} , which is then released into cytosol through divalent metal transporter 1 (DMT1) and joins the metabolically active intracellular free iron pool, namely the labile iron pool (LIP). Part of intracellular iron is stored by ferritin, and surplus iron is exported out of cells via ferroportin (FPN) to maintain dynamic iron equilibrium. Increased iron uptake, impaired iron storage or blocked iron efflux can raise Fe^{2+} levels in LIP. Excessive Fe^{2+} catalyzes the Fenton reaction to produce cytotoxic ROS and accumulates lipid peroxides (LPO). Progressive lipid peroxidation destroys the structural and functional integrity of cell membranes and facilitates ferroptosis onset [10]. Therefore, iron is an essential prerequisite for ferroptosis. Its aberrant

accumulation contributes to ferroptosis progression by amplifying oxidative stress and lipid peroxidation. Dysregulated cellular iron homeostasis and subsequent iron-dependent oxidative injury are key regulatory links in the initiation and progression of ferroptosis.

2.2. Lipid peroxidation

Disordered lipid metabolism acts as a core regulatory link of ferroptosis [11], which is driven by accumulation of lipid peroxidation products. The core pathogenic mechanism lies in oxidative reactions between PUFAs and phosphatidylethanolamine (PE), generating abundant LPO, disrupting cellular structural homeostasis and accelerating ferroptosis. PUFAs within organelle membrane phospholipids serve as major substrates for lipid peroxidation and constitute critical lipid prerequisites for ferroptosis initiation. Acyl-CoA synthetase long-chain family member 4 (ACSL4), lysophosphatidylcholine acyltransferase 3 (LPCAT3) and lipoxygenases (LOXs) are pivotal molecules governing LPO generation. ACSL4, a member of long-chain acyl-CoA synthetase family, participates in fundamental fatty-acid metabolism. LPCAT3 is an acyltransferase involved in membrane phospholipid remodeling. During ferroptosis, ACSL4 and LPCAT3 jointly activate free PUFAs. On one hand, they promote the conversion from lysophosphatidylcholine to lecithin; on the other hand, they participate in biosynthesis of oxidized membrane phospholipids [12,13].

2.3. Imbalanced antioxidative systems

Ferroptosis is a form of programmed cell death tightly correlated with intracellular redox disequilibrium [14], and its occurrence is closely related to impaired cellular antioxidative defense capacity. System Xc⁻, reduced glutathione (GSH) and glutathione peroxidase 4 (GPX4) constitute a vital intracellular amino-acid-related antioxidative defense system. Composed of two subunits, solute carrier family 3 member 2 (SLC3A2) and solute carrier family 7 member 11 (SLC7A11) [15], System Xc⁻ locates predominantly on cell membranes and mediates cystine uptake from extracellular space into cells. Intracellular cystine is reduced into cysteine [16], which provides essential substrates for GSH synthesis and sustains cellular redox homeostasis. On this basis, GPX4 uses GSH as reducing agent and converts cytotoxic lipid hydroperoxides (LOOH) into relatively stable lipid alcohols (LOH). Meanwhile, GSH is oxidized into oxidized glutathione (GSSG) [17], thereby suppressing lipid peroxidation and consequent cellular damage. Inhibition of System Xc⁻-mediated cystine uptake, decreased intracellular GSH content or impaired GPX4 function weakens cellular capacity to eliminate lipid peroxides, which further accumulate intracellularly and accelerate ferroptosis. Existing research has demonstrated that the System Xc⁻/GSH/GPX4 signaling axis exerts crucial functions in regulating cellular amino-acid metabolism and antioxidative homeostasis. Functional disturbance of this pathway may represent one of the key factors driving ferroptosis development [18].

2.4. Endothelial cell ferroptosis and atherosclerosis

AS is a vascular disorder featured by disturbed lipid metabolism and impaired vascular endothelial function [19]. Lipid deposition, endothelial injury, disrupted oxidative stress, inflammation and immune dysregulation are major pathogenic triggers. Ferroptosis is highly correlated with AS progression. Elevated levels of free iron (especially Fe²⁺) within vascular endothelial cells, smooth muscle cells and macrophages facilitate ROS generation and induce lipid peroxidation, thus initiating ferroptosis [20]. Once triggered, ferroptosis amplifies local inflammatory responses, accelerates foam-cell formation, breaks vascular wall physiological homeostasis and ultimately increases atherosclerotic plaque vulnerability.

Endothelial dysfunction is the initiating event of AS [21]. This pathological alteration activates inflammatory cytokines and triggers abnormal lipid deposition, which further promotes the occurrence and progression of AS. Mounting evidence validates that ferroptosis serves as a critical mechanism modulating physiological functions of endothelial cells. In Bai et al.'s research [22], oxidized low-density lipoprotein (ox-LDL) was applied to stimulate mouse aortic endothelial cells. Ox-LDL treatment induced lipid peroxidation and ferroptosis-related injuries. After intervention with ferroptosis inhibitor ferrostatin-1 (Fer-1), lipid peroxidation level and cell death rate were markedly reduced, indicating that ferroptosis mediates ox-LDL-triggered vascular endothelial cell injury.

Iron overload provokes massive ROS production and activates cyclooxygenase pathways to induce endothelial dysfunction and accelerate AS progression in ApoE^{-/-} mice [23], which may be associated with imbalance between vasodilators and vasoconstrictors secreted by endothelial cells. Xiao et al. [24] also confirmed that iron overload gives rise to ROS accumulation and lipid peroxidation in endothelial cells. SLC7A11 inhibitor Erastin suppresses GPX4 activity, up-regulates ACSL4 expression, induces endothelial ferroptosis and exacerbates atherosclerosis. Therefore, targeted modulation of endothelial cell ferroptosis is expected to become a promising therapeutic target for AS prevention and treatment.

3. Traditional Chinese medicine regulating endothelial cell ferroptosis against atherosclerosis

3.1. TCM monomers

3.1.1. Tanshinone IIA

Tanshinone IIA can alleviate vascular endothelial injury, scavenge accumulated ROS and block endothelial ferroptosis so as to exert anti-atherosclerotic effects. As a core active monomer isolated from *Salvia miltiorrhiza*, tanshinone IIA has demonstrated cardiovascular protective effects in experimental studies. He et al. [25] reported that tanshinone IIA activates the nuclear factor erythroid 2-related factor 2 (Nrf2) antioxidative pathway, up-regulates ferritin heavy chain polypeptide 1 (FTH1), elevates intracellular GSH concentration and enhances GPX4 activity. Consequently, it reduces free iron overload, lowers ROS and lipid peroxide levels and alleviates ferroptotic injuries induced by Erastin and RAS-selective lethal small molecule 3 (RSL3) in human coronary artery endothelial cells.

3.1.2. Icariin

Icariin, one of the principal bioactive components from *Epimedium* [26], possesses anti-inflammatory, antioxidative and cardiovascular-protective properties. In vitro experiments established injury models by stimulating human umbilical vein endothelial cells with ox-LDL. Ox-LDL stimulation led to increased intracellular ROS, free iron accumulation, down-regulated GPX4 and FTH1 expression, as well as up-regulated TFR1 expression, ultimately inducing ferroptosis in vascular endothelial cells. Icariin intervention restored cell viability, stabilized mitochondrial membrane potential and improved mitophagy. In vivo, AS models were constructed in high-fat-diet-fed ApoE^{-/-} mice. Icariin decreased serum total cholesterol (TC), triglyceride (TG), interleukin-6 (IL-6) and tumor necrosis factor- α (TNF- α), mitigated aortic plaque formation and collagen deposition. It up-regulated protective proteins including transcription factor EB (TFEB), GPX4 and FTH1, reduced accumulation of ROS and lipid peroxidation products, inhibited endothelial ferroptosis and ameliorated atherosclerotic lesions [27].

3.1.3. Curcumin

Curcumin can promote blood circulation, resolve stasis and reduce lipids. Modern pharmacological researches have verified its antioxidative, endothelium-protective and other cardiovascular-protective bioactivities [28]. Wang et al. [29] built AS models in high-fat-diet-fed ApoE^{-/-} mice for intervention experiments. Curcumin activated the Nrf2/GPX4/heme oxygenase-1 (HO-1) signaling pathway, increased aortic expression of Nrf2 and HO-1 proteins, ameliorated lipid disorders, mitigated aortic collagen deposition and atherosclerotic plaque formation. It suppressed oxidative stress and endothelial ferroptosis and thereby retarded AS progression.

3.1.4. Polygonum cuspidatum

As a traditional TCM herb for activating blood circulation and removing blood stasis, Polygonum cuspidatum exerts antioxidative, anti-inflammatory and vascular-protective effects according to modern studies [30]. Zhao et al. [31] established in vitro foam-cell models by treating human umbilical vein endothelial cells with ox-LDL. Polygonum cuspidatum-containing serum elevated expression levels of superoxide dismutase (SOD), GSH, Nrf2, HO-1 and GPX4, and reduced levels of Fe²⁺, malondialdehyde (MDA) and lipid ROS. It ameliorated mitochondrial damage and ferroptosis-related phenotypes. These findings suggest that Polygonum cuspidatum-containing serum may relieve vascular endothelial cell ferroptosis by activating Nrf2/HO-1 signaling and improving oxidative stress status.

3.2. TCM compound formulas

3.2.1. Danxia Tiaoban Decoction

Chen et al. [32] constructed in vitro injury models by treating human umbilical vein endothelial cells with ox-LDL and administered different concentrations of Danxia Tiaoban Decoction-containing serum for intervention. Danxia Tiaoban Decoction improved endothelial cell viability in a dose-dependent manner, decreased intracellular Fe²⁺ concentration and lipid ROS levels, and alleviated ferroptosis-associated mitochondrial morphological damage. It is indicated that Danxia Tiaoban Decoction exerts vascular-protective effects by inhibiting iron overload and lipid peroxidation so as to mitigate ox-LDL-induced ferroptotic injuries in vascular endothelial cells.

3.2.2. Erchen Decoction and Taohong Siwu Decoction

Erchen Decoction can dry dampness, invigorate the spleen, resolve phlegm and regulate qi; Taohong Siwu Decoction functions to nourish and promote blood circulation. He et al. [33] simultaneously built atherosclerosis models in high-fat-diet-fed ApoE^{-/-} mice and ox-LDL-damaged EA.hy926 endothelial cell models in vitro. Intervention with Erchen Decoction and Taohong Siwu Decoction elevated SOD and GSH levels, down-regulated MDA and ROS contents, and suppressed mRNA and protein expression of p53 in the aorta and endothelial cells. Meanwhile, it up-regulated protein and gene expression of SLC7A11, GPX4 and FTH1, and inhibited the elevation of cyclooxygenase-2 (COX-2) and NADPH oxidase 1 (NOX1). These findings demonstrate that Erchen Decoction and Taohong Siwu Decoction alleviates oxidative stress and ferroptotic injuries in vascular endothelial cells and exerts anti-atherosclerotic effects by modulating the p53/SLC7A11 signaling pathway.

3.2.3. Xiaoxianxiong Decoction

Xiaoxianxiong Decoction has pharmacological effects of clearing heat, resolving phlegm,

broadening chest and dissipating masses. Lu et al. [34] revealed that Xiaoxianxiong Decoction increased mRNA and protein levels of growth arrest-specific 6 (GAS6), receptor tyrosine kinase AXL, SLC7A11 and GPX4. It reduced intracellular accumulation of Fe^{2+} , ROS and MDA, enhanced activities of SOD, total glutathione peroxidase (GPx) and glutathione reductase (GR), relieved lipid peroxidation injuries, ameliorated ferroptosis-related alterations in vascular endothelial cells, and improved lipid disorders as well as aortic plaque formation.

3.2.4. Xueguan Ruanhua Pills

Derived from modified Baohe Pills, Xueguan Ruanhua Pills act to promote digestion, resolve phlegm, calm liver, suppress yang, activate blood circulation and remove stasis. Sun et al. [35] established AS models in high-fat-diet-fed ApoE^{-/-} mice to explore its therapeutic effects and underlying mechanisms against AS and endothelial ferroptosis. Xueguan Ruanhua Pills reduced serum TG, TC, low-density lipoprotein-cholesterol (LDL-C), Fe^{2+} and MDA, and increased high-density lipoprotein-cholesterol (HDL-C), SOD and GSH. It up-regulated protein expression of Nrf2, xCT, SLC7A11, GPX4, FTH1 and ferritin light chain (FTL), and improved typical mitochondrial damages caused by ferroptosis. Combined application of Nrf2 inhibitor ML385 reversed the protective effects of Xueguan Ruanhua Pills. These results suggest that Xueguan Ruanhua Pills activate the Nrf2/xCT/GPX4 signaling axis, enhance antioxidative capacity and intracellular iron-storage ability, suppress lipid peroxidation and iron overload, and consequently inhibit vascular endothelial ferroptosis.

4. Discussion

Atherosclerosis is a complex disease jointly driven by abnormal lipid metabolism, chronic inflammatory responses and vascular endothelial dysfunction. In recent years, ferroptosis, an iron-dependent regulated cell death mode, has been recognized as an important participant in AS pathogenesis. As key components maintaining vascular homeostasis, vascular endothelial cells undergo injury at the early stage of AS. Disturbed iron metabolism, free iron accumulation, aggravated lipid peroxidation and impaired antioxidative defense systems can trigger ferroptosis in vascular endothelial cells. In turn, ferroptosis amplifies oxidative stress and inflammatory responses, forms a vicious cycle and accelerates AS progression.

Current researches have illustrated that TCM-derived active ingredients and formulas can modulate ferroptosis-related processes via multiple targets and pathways, which provides novel ideas for targeted therapy of AS with TCM. Compared with single-component chemical agents, TCM presents unique strengths of multi-target and holistic regulation, which can complement existing anti-atherosclerotic therapeutic regimens. Nevertheless, the exact targets and upstream-downstream regulatory networks of various TCM monomers and compounds remain incompletely elucidated. In-vivo and in-vitro experimental conditions cannot fully recapitulate human pathological status, and relevant clinical studies are still scarce. Most existing studies focus on phenotypic observation, lacking deep exploration of upstream regulatory axes. Further ferroptosis-specific intervention experiments are required to verify findings and identify precise targets of TCM in regulating ferroptosis. Multi-center clinical trials should be carried out to translate basic experimental outcomes into clinical application, so as to lay solid theoretical and clinical foundations for TCM prevention and treatment of atherosclerosis.

References

[1] Hu S S. Report on cardiovascular health and diseases in China: an updated summary. *Chinese Circulation Journal*. 2026;41(6):527-563.

- [2] Peter L. The changing landscape of atherosclerosis. *Nature*. 2021;592(7855):524-533.
- [3] Soehnlein O, Libby P. Targeting inflammation in atherosclerosis-from experimental insights to the clinic. *Nature Reviews Drug Discovery*. 2021;20(8):589-610.
- [4] Jinson S, Zhang Z, Lancaster G I, Murphy A J, Morgan P K. Iron, lipid peroxidation, and ferroptosis play pathogenic roles in atherosclerosis. *Cardiovascular Research*. 2025;121(1):44-61.
- [5] Gao Y, Wang B, Hu M, Ma Y, Zheng B. The role of iron in atherosclerosis and its association with related diseases. *Current Atherosclerosis Reports*. 2024;27(1):1.
- [6] Dixon S J, Lemberg K M, Lamprecht M R, et al. Ferroptosis: an iron-dependent form of nonapoptotic cell death. *Cell*. 2012;149(5):1060-1072.
- [7] Geng H J, Zhang P, Wang G Y, et al. Research progress of ferroptosis. *Chemistry of Life*. 2021;41(11):2376-2382.
- [8] Lee J, Roh J L. Ferroptosis: iron release mechanisms in the bioenergetic process. *Cancer Metastasis Reviews*. 2025;44(1):36.
- [9] Jansová H, Šimůnek T. Cardioprotective potential of iron chelators and prochelators. *Current Medicinal Chemistry*. 2019;26(2):288-301.
- [10] Zhang Y, Ren X, Wang Y, et al. Targeting ferroptosis by polydopamine nanoparticles protects heart against ischemia/reperfusion injury. *ACS Applied Materials & Interfaces*. 2021;13(45):53671-53682.
- [11] Bersuker K, Hendricks J M, Li Z, et al. The CoQ oxidoreductase FSP1 acts parallel to GPX4 to inhibit ferroptosis. *Nature*. 2019;575(7784):688-692.
- [12] Sha W, Hu F, Xi Y, et al. Mechanism of ferroptosis and its role in type 2 diabetes mellitus. *Journal of Diabetes Research*. 2021;2021:9999612.
- [13] Tang Y, Zhou J, Hooi S C, et al. Fatty acid activation in carcinogenesis and cancer development: essential roles of long-chain acyl-CoA synthetases. *Oncology Letters*. 2018;16(2):1390-1396.
- [14] Kuang F, Liu J, Tang D, et al. Oxidative damage and antioxidant defense in ferroptosis. *Frontiers in Cell and Developmental Biology*. 2020;8:586578.
- [15] Jiang X, Stockwell B R, Conrad M. Ferroptosis: mechanisms, biology and role in disease. *Nature Reviews Molecular Cell Biology*. 2021;22(4):266-282.
- [16] Lin C H, Lin P P, Lin C Y. Decreased mRNA expression for the two subunits of system xc-, SLC3A2 and SLC7A11, in WBC in patients with schizophrenia: evidence in support of the hypo-glutamatergic hypothesis of schizophrenia. *Journal of Psychiatric Research*. 2016;72:58-63.
- [17] Gao M, Monian P, Quadri N, et al. Glutaminolysis and transferrin regulate ferroptosis. *Molecular Cell*. 2015;59(2):298-308.
- [18] Guo D, Cai S, Deng L, et al. Ferroptosis in pulmonary disease and lung cancer: molecular mechanisms, crosstalk regulation, and therapeutic strategies. *MedComm*. 2025;6(3):e70116.
- [19] Alwi I. Targeting inflammation and immune system in acute myocardial infarction. *Acta Medica Indonesiana*. 2019;51(4):287-289.
- [20] Wang Y Q, Zhao Y J, Ye T, et al. Ferroptosis signaling and regulators in atherosclerosis. *Frontiers in Cell and Developmental Biology*. 2021;9:809457.
- [21] Li H X, Cao Z Q, Wang L L, et al. Macrophage subsets and death are responsible for atherosclerotic plaque formation. *Frontiers in Immunology*. 2022;13:843712.
- [22] Bai T, Li M, Liu Y, Qiao Z, Wang Z. Inhibition of ferroptosis alleviates atherosclerosis through attenuating lipid peroxidation and endothelial dysfunction in mouse aortic endothelial cell. *Free Radical Biology and Medicine*. 2020;160:92-102.
- [23] Marques V B, Leal M A S, Mageski J G A, et al. Chronic iron overload intensifies atherosclerosis in apolipoprotein E deficient mice: role of oxidative stress and endothelial dysfunction. *Life Sciences*. 2019;233:116702.
- [24] Xiao F J, Zhang D, Wu Y, et al. miRNA-17-92 protects endothelial cells from erastin-induced ferroptosis through targeting the A20-ACSL4 axis. *Biochemical and Biophysical Research Communications*. 2019;515(3):448-454.
- [25] He L, Liu Y Y, Wang K, et al. Tanshinone IIA protects human coronary artery endothelial cells from ferroptosis by activating the NRF2 pathway. *Biochemical and Biophysical Research Communications*. 2021;575:1-7.
- [26] Hu Y, Liu K, Yan M, et al. Effects and mechanisms of icariin on atherosclerosis. *International Journal of Clinical and Experimental Medicine*. 2015;8(3):3585-3589.
- [27] Wang X, Zhang M, Mao C, et al. Icariin alleviates ferroptosis-related atherosclerosis by promoting autophagy in ox-LDL-induced vascular endothelial cell injury and atherosclerotic mice. *Phytotherapy Research*. 2023;37(9):3951-3963.
- [28] Wasim R, Azmi S, Ahmad A. Integrating traditional chinese medicine and modern pharmacology: the role of Jiang Huang (curcumin) in cardiovascular health. *Pharmacological Research-Modern Chinese Medicine*. 2025;17:100706.
- [29] Wang S, Zhao W, He F, et al. Investigating the mechanism of curcumin in inhibiting ferroptosis against atherosclerosis in mice based on the Nrf2/GPX4/HO-1 signaling pathway. *Lishizhen Medicine and Materia Medica Research*. 2026;37(13):2449-2455.

- [30] Ye G Y, Jiang X, Wang Z X. Research progress in anti-atherosclerosis mechanism of polydatin. *Medical Recapitulate*. 2022;28(7):1302-1307.
- [31] Zhao M H, Liu T, Fan C W, et al. Exploration on the intervention effect of *Polygonum cuspidatum*-containing serum on ferroptosis of vascular endothelial cells based on Nrf2/HO-1 pathway. *Journal of Chinese Medicinal Materials*. 2023;46(11):2831-2836.
- [32] Chen Z T, Chen H, Zhang H, et al. Study on the inhibitory effect of Danxia Tiaoban Decoction on ox-LDL-induced ferroptosis in human umbilical vein endothelial cells. *Global Traditional Chinese Medicine*. 2026;19(2):260-266.
- [33] He X Y, Wang J Y, Song N, et al. Effects and mechanism of Erchen Decoction and Taohong Siwu Decoction on the regulation of p53/SLC7A11 mediated oxidative damage and ferroptosis on atherosclerosis. *China Journal of Traditional Chinese Medicine and Pharmacy*. 2020;35(5):2344-2348.
- [34] Lu C X, Jin Y H, Liu Y, et al. Xiaoxianxiong Decoction alleviates atherosclerosis by activating GAS6/AXL to inhibit ferroptosis in endothelial cells. *Acta Pharmaceutica Sinica*. 2026;61(5):1654-1662.
- [35] Sun M Y, Qin H W, Li Y J, et al. Xueguan Ruanhua Pills improve atherosclerosis by inhibiting ferroptosis through the Nrf2/xCT/GPX4 pathway. *Journal of Beijing University of Traditional Chinese Medicine*. 2024;47(3):383-393.