Journal of Inflammation Research

Dovepress
Taylor & Francis Group

Open Access Full Text Article

REVIEW

Traditional Chinese Medicine Treatment for Coronary Heart Disease: Pathological Mechanisms of Modulating Cell Death Pathways

Wanying Jia[1], Jinwei Liu[1], Zhibo Zhu[2,3]

[1]Pharmacy Department, Chifeng Municipal Hospital, Chifeng City, Inner Mongolia, People's Republic of China; [2]Life Sciences and Medicine, University of Science and Technology of China, Hefei City, Anhui, People's Republic of China; [3]Nuclear Medicine Department, Chifeng Municipal Hospital, Chifeng City, Inner Mongolia, People's Republic of China

Correspondence: Zhibo Zhu, Life Sciences and Medicine, University of Science and Technology of China, Hefei City, Anhui, People's Republic of China, Email 15147349934@163.com

Abstract: Coronary heart disease (CHD) is one of the most prevalent cardiovascular pathologies, with complications significantly increasing mortality rates. The pathogenesis of CHD is complex and multidimensional, and its cellular and molecular basis remains incompletely understood. Recent studies indicate that multiple forms of cell death participate in the initiation and progression of CHD, including inflammation-driven factors (Pyroptosis- Necroptosis- Ferroptosis), context-dependent modulators (Apoptosis- Autophagy), and emerging/hypothetical mechanisms (PANoptosis- Cuproptosis- Disulfidptosis). Meanwhile, traditional Chinese medicine (TCM) is gaining increasing attention in the management of cardiovascular diseases, particularly CHD. This research summarizes the roles of multiple cell death pathways in the pathogenesis of CHD and provides a detailed review and comprehensive analysis of the mechanisms underlying existing experimental studies on TCM formulas and active components used to treat CHD. We highlight representative TCM metabolites and TCM formulas, such as resveratrol, TongMai YangXin Wan, Gualoupi Injection, etc. It concludes that TCM counteracts CHD by inhibiting various cell death pathways. Current basic research primarily focuses on signaling pathways such as PI3K/Akt, TNF, and MAPK. This work provides new insights and approaches for the treatment of CHD and further research. Finally, it identifies current challenges, including unclear compositions of TCM and insufficient validation of mechanisms, and proposes new directions for future research.

Keywords: coronary heart disease, cell death, traditional Chinese medicine/formula, cardiovascular disease, literature review

Introduction

Cell death constitutes a fundamental physiological process across all living organisms, serving diverse roles that encompass embryonic development, organ homeostasis, aging, immune function, and the modulation of autoimmunity. The Cell Death Nomenclature Committee has established a classification system for cell death that distinguishes between two primary categories: accidental cell death and regulated cell death (RCD). The basis for this classification is a multifaceted framework encompassing morphological, biochemical, and functional criteria.[1] Accidental cell death is characterized as an uncontrolled biological event precipitated by unforeseen injurious stimuli.[2] Conversely, RCD is mediated by orchestrated signaling pathways that are integral to organismal development and tissue regeneration.[3] Cardiovascular disease remains the foremost cause of mortality globally and represents a significant source of morbidity.[4] Coronary heart disease (CHD) is characterised by functional impairments and structural lesions arising from coronary artery stenosis and inadequate myocardial perfusion, which culminate in clinical manifestations such as angina pectoris, sudden cardiac death, and myocardial infarction.[5] The underlying pathology of CHD involves vascular and myocardial dysfunction driven by ischemia, hypoxia, oxidative stress, inflammation, and cell death processes.[6,7] The prevalence and mortality associated with CHD are escalating in both developed and developing nations.[8] Established risk factors include hyperlipidemia, hyperglycemia, insulin resistance, and hypertension. As a chronic inflammatory disease,

https://doi.org/10.2147/JIR.S590293
Received: 29 December 2025
Accepted: 28 March 2026
Published: 23 April 2026

the pathogenesis of CHD implicates multiple cellular mechanisms, including necroptosis, apoptosis, ferroptosis, pyroptosis, and autophagy.[9] Inflammation, the primary response of innate immunity, is considered essential in initiating and driving vascular diseases.[10] Regulated cell death pathways are drivers, amplifiers, or regulators of inflammation in CHD. Nevertheless, the precise molecular mechanisms remain incompletely elucidated, and current therapeutic strategies are subject to ongoing debate. Consequently, there is a pressing need to identify novel therapeutic targets for CHD.

Traditional Chinese medicine (TCM) and its formulations are extensively employed in clinical settings, including for cardiovascular conditions. TCM typically functions as complex mixtures of herbs, where the therapeutic benefits arise from synergistic interactions among multiple bioactive components rather than isolated compounds. Existing research has largely focused on the effects of individual components on specific pathways, potentially failing to fully capture the holistic efficacy of traditional Chinese medicine formulations. Compared to single-target chemical drugs (such as statins for lipid-lowering), traditional Chinese medicine's multi-target, multi-pathway approach aligns with the complex pathogenesis of CHD, involving oxidative stress and inflammation. TCM's holistic regulation of diverse pathways holds unique therapeutic potential, yet challenges remain in elucidating mechanisms and achieving standardization. To address this research gap, this review further examines the impact of novel cell death (PANoptosis- Cuproptosis-Disulfidptosis) on the pathogenesis of CHD, offering new therapeutic directions. It also systematically reviews Chinese herbal extracts, compound formulations, and single herbs used to treat CHD. By integrating basic and clinical research findings, this study aims to elucidate the potential role of traditional Chinese medicine in CHD management.

Mechanisms of Different Cell Death Pathways in CHD

Cell death can be classified into programmed and unprogrammed types. Programmed cell death encompasses apoptosis, pyroptosis, autophagy, ferroptosis, and other forms.

Apoptosis-Context-Dependent Modulators

Apoptosis is a form of programmed cell death precisely regulated at the genetic level, facilitating the orderly and efficient removal of damaged cells, such as those resulting from DNA damage or developmental processes.[11] While apoptosis eliminates impaired cells, excessive apoptosis can be detrimental. This process involves numerous cell-killing and phagocytic proteins and constitutes a caspase-dependent active death mechanism. It primarily engages pathway markers including Bcl-2, BAK, and Bax, which participate in multiple stages of CHD development such as atherosclerosis, myocardial ischemia/reperfusion injury, myocardial infarction, and heart failure. Apoptosis in endothelial and smooth muscle cells weakens plaque structure and promotes rupture.[12] Oxidative stress and cholesterol overload are primary triggers. Statins (simvastatin) inhibit cardiomyocyte apoptosis by reducing Bax and caspase-3 expression while increasing Bcl-2 levels, thereby improving cardiac function post-myocardial infarction.[13] The Fas/FasL pathway induces apoptosis by activating caspase-8, correlating with the severity of myocardial injury in CHD patients.[14] Patients with end-stage heart failure exhibit substantially increased myocardial apoptosis rates linked to an imbalance between Bcl-2 and Bax.[15] The process of apoptosis results in the loss of cardiomyocytes, thereby accelerating ventricular remodelling.[16] Research indicates that myocardial ischemia/reperfusion injury is associated with apoptotic cell death. This process disrupts mitochondrial membrane integrity and promotes the cytoplasmic release of pro-apoptotic factors by activating pro-apoptotic Bcl-2 modulators BAX and BAK, thereby triggering caspase-dependent cell death.[17] Liu proposed that long non-coding RNAs inhibit apoptosis and promote proliferation in human coronary artery endothelial cells by enhancing MAPK1 expression, demonstrating significant therapeutic potential for CHD.[18]

Autophagy-Context-Dependent Modulators

Autophagy is a conserved self-digestion process in eukaryotic cells that maintains cellular homeostasis through proteolysis.[19] During autophagy, LC3 is cleaved into LC3I and LC3II. The conjugation of LC3I to phosphatidylethanolamine converts it into LC3II. LC3II associates with both sides of the autophagosome membrane, promoting autophagosome elongation and closure, ultimately engulfing mitochondria to form mitophagosomes. These mitophagosomes are then transported along microtubule tracks to lysosomes for degradation.[20] Through this process, cells degrade their own components within lysosomes. Autophagy exhibits a dual role: moderate activation clears damaged organelles, whereas

excessive activation induces type II programmed cell death. Ischemic preconditioning mitigates myocardial injury by activating autophagy, while sustained ischemia triggers excessive autophagy, exacerbating cell death.[21] It has been demonstrated by a number of studies that the process of macrophage autophagy exerts a significant influence on the development of atherosclerosis by promoting cholesterol efflux, suppressing inflammation, and inhibiting apoptosis.[22] Defects in macrophage autophagy have been observed to accelerate foam cell formation, whereas enhanced autophagy has been shown to mitigate atherosclerosis.[23] Mitochondrial autophagy plays dual roles in myocardial ischemia-reperfusion injury: autophagy during ischemia is protective by clearing damaged mitochondria, but excessive activation during reperfusion may worsen cellular damage. Research shows that miR-499 reduces hypoxia/reoxygenation-induced myocardial cell injury by decreasing oxidative stress through Drp1-mediated mitochondrial autophagy.[24] The role of autophagy in CHD exhibits phase- and pathway-dependent. For example, autophagy during ischemia relies on AMPK activation to exert protective effects, whereas during reperfusion, it may exacerbate injury via Beclin 1-dependent mechanisms.[25,26] Fibroblast growth factor 21 (FGF21) has been demonstrated to play a pivotal role in a number of pathological processes, including vascular calcification, atherosclerosis and protection against myocardial ischemia-reperfusion injury. This function is thought to be achieved by inducing autophagy, thus suggesting a potential for FGF21 to be utilised as a therapeutic target.[27] Berberine alleviates myocardial injury in ischemic heart disease by modulating autophagy through mTOR and AMPK pathways.[28] Molecules such as circACR can reduce infarct size by inhibiting autophagy. Although mTORC1 inhibitors (rapamycin) can modulate autophagy levels, their clinical application requires caution.[29]

Pyroptosis-Established Inflammatory Drivers in CHD

Pyroptosis is a highly inflammatory form of cell death characterised by membrane permeabilisation, the release of cellular contents (including proinflammatory cytokines) and cell lysis. It primarily involves the release of markers such as Gasdermin D, Caspase-1, Caspase-4, IL-1β, and IL-18.[30] Pyroptosis depends on inflammasome activation, with the released IL-1β/IL-18 exacerbating inflammation. The NLRP3 inflammasome activates the enzyme caspase-1, which in turn cleaves the substrate Gasdermin D, forming membrane pores. These pores result in the pyroptosis of endothelial cells and subsequent inflammation of the plaque, thus contributing to the development of atherosclerosis.[31,32] The process of pyroptosis in endothelial cells has been demonstrated to result in the disruption of endothelial barrier function, thereby promoting lipid deposition and monocyte infiltration.[33] In the context of macrophages, the release of inflammatory factors has been shown to contribute to plaque instability and to increase the risk of myocardial infarction.[31] Finally, in smooth muscle cells, pyroptosis has been observed to accelerate fibrous cap degradation and to facilitate plaque rupture.[34] Pyroptosis is involved in the pathological processes of angina pectoris, myocardial infarction, ischemia-reperfusion injury, and heart failure. During myocardial ischemia, pyroptosis exacerbates cardiomyocyte death and inflammatory cascades, leading to ventricular remodeling.[33] Studies have demonstrated that monoclonal antibodies targeting Gasdermin D effectively suppress pyroptosis in atherosclerosis models.[35] Monoclonal antibodies targeting NLRP3 (MCC950), Caspase-1 (VX-765), or IL-1β (Canakinumab) have shown anti-atherosclerotic effects in clinical trials.[31] Additionally, IL-1β antagonists (Anakinra) and IL-18 binding proteins have entered clinical trials, with preliminary results indicating reduced inflammatory markers in patients with CHD.[31] Research indicates that certain TCM (Simiao Yong'an Decoction) reduce pyroptosis by inhibiting the NF-κB/NLRP3 pathway. The TCM theory of simultaneous treatment of heart and liver proposes regulating pyroptosis-related stasis toxins to delay the progression of atherosclerosis, thereby slowing the course of CHD.[36]

Necroptosis-Established Inflammatory Drivers in CHD

Necroptosis is a regulated form of cell death that can be activated under conditions of apoptotic insufficiency.[37] It is mediated by the RIP1-RIP3-MLKL signaling cascade[38] and is closely associated with inflammation and oxidative stress. In the process of atherosclerotic plaque formation, oxidized low-density lipoprotein has been shown to promote plaque instability by inducing necroptosis in macrophages. This, in turn, accelerates the expansion of the necrotic core and the thinning of the fibrous cap.[39] Experimental studies have demonstrated that necrostatin-1, an oral inhibitor of necroptosis, reduces plaque area by 62% and increases smooth muscle cell content, thereby enhancing plaque stability and further

lowering the incidence of CHD.[40] Following reperfusion after partial or complete acute occlusion of a sclerotic coronary artery, ischemic myocardium may experience progressive and irreversible tissue damage despite restored blood supply,[41] increasing susceptibility to myocardial infarction. RIP3 activates the CaMKII-mPTP pathway, leading to mitochondrial dysfunction and cardiomyocyte death. These findings establish CaMKII as a novel RIP3 substrate and delineate the RIP3-CaMKII-mPTP pathway for cardiomyocyte programmed necrosis, representing a promising therapeutic target for treating ischemia- and oxidative stress-induced myocardial injury and heart failure.[42] In animal models, inhibiting RIP1 or knocking out RIP3 reduces infarct size and improves left ventricular function.[43] Concurrently, inhibitors targeting RIP1/RIP3 (NEC-1) and MLKL antagonists demonstrate potential for reducing myocardial injury in experimental settings.[44] Further studies indicate that liraglutide may mitigate myocardial ischemia/reperfusion injury partly by inhibiting programmed necrosis and partly by enhancing activity in the GLP-1R/PI3K/Akt pathway.[45]

Ferroptosis-Established Inflammatory Drivers in CHD

Ferroptosis is a non-apoptotic cell death mechanism characterized by iron-dependent membrane lipid peroxidation,[46] which is associated with abnormalities in iron metabolism and ultimately leads to cell membrane disruption and cell death. The mechanisms underlying ferroptosis primarily involve dysregulation of iron metabolism, lipid peroxidation, glutathione depletion, and reduced GPX4 activity.[47] Iron overload induces mitochondrial lipid peroxidation, triggering endothelial dysfunction, promoting plaque formation, and exacerbating ischemia-reperfusion injury. Concurrently, iron overload may enhance platelet aggregation and thrombosis, increasing the risk of acute coronary events.[48,49] Fang found that ferritin H deficiency exacerbates myocardial ferroptosis via SLC7A11-mediated glutathione depletion, whereas SLC7A11 overexpression improves cardiac function by elevating glutathione levels.[50] Ferroptosis regulates macrophage polarization toward a proinflammatory phenotype, increasing plaque inflammation and oxidative stress, which leads to plaque instability.[51] Thus, targeting ferroptosis reduces macrophage lipid accumulation and necrotic core formation.[52] In animal models, ferroptosis inhibitors (Ferrostatin-1, Liproxstatin-1) reduce cardiomyocyte death by inhibiting lipid peroxidation, thereby decreasing myocardial injury.[50,53] Iron chelators (deferasirox) and low-iron diets reduce cardiac iron deposition and improve the prognosis of CHD.[54] Research found that TCM components such as paeoniflorin and tanshinone inhibit ferroptosis by regulating Nrf2/HO-1 signaling activation, demonstrating anti-atherosclerotic and cardioprotective effects in animal models.[55] Multiple epidemiological studies have established a positive correlation between elevated iron levels and the incidence and mortality of CHD. For example, a meta-analysis demonstrated that increased serum ferritin levels are significantly associated with a higher risk of cardiovascular events in the general population.[56]

PANoptosis-Emerging/Hypothetical Mechanisms

The concept of PANoptosis was first proposed by Dr. Kanneganti in 2019.[57] PANoptosis is defined as an inflammatory form of cell death regulated by the PANoptosis pathway, exhibiting key features of pyroptosis, apoptosis, and necroptosis.[58] Studies have shown that during myocardial ischemia/reperfusion injury, the expression levels of multiple molecules-including caspase-8, caspase-3, NLRP3, caspase-1, Gasdermin D, RIPK1, RIPK3, and MLKL-significantly increase over time in injured cardiac tissue, indicating that PANoptosis occurs in ischemic/reperfused hearts.[59] Additionally, ACP5 and HO-1 have been identified as potential atherosclerosis-associated genes linked to PANoptosis. These genes may contribute to atherosclerosis pathogenesis by regulating macrophage PANoptosis.[60] Further studies demonstrate that inhibiting ZBP1 expression significantly reduces the levels of PANoptosis regulatory proteins, thereby exerting a cardioprotective effect against myocardial ischemia/reperfusion injury.[61] Although bioinformatics analyses have revealed substantial associations between multiple PANoptosis-related genes and cardiovascular diseases, experimental validation remains lacking. Therefore, further experimental studies are necessary to confirm the role of PANoptosis in cardiovascular diseases.

Cuproptosis-Emerging/Hypothetical Mechanisms

Copper acts as a catalytic cofactor in various physiological processes, including energy metabolism, mitochondrial respiration, and antioxidant defense. Generally, intracellular copper levels remain relatively low. However, when copper accumulates within cells, excess copper binds to mitochondrial proteins, triggering protein toxicity stress-mediated cell

death-a phenomenon termed cuproptosis.[62] Ferrodoxin is a key regulator of cuproptosis and an upstream modulator of protein lipoylation. Yang used bioinformatics analysis and in vitro experiments to suggest that Ube2d3 further influences the progression of myocardial infarction by regulating cuproptosis.[63] Research indicates that cuproptosis-related genes may contribute to the onset and development of acute myocardial infarction via the HIF-1 signaling pathway. Nevertheless, the mechanisms underlying their involvement require further validation in human, animal, and cellular models to provide novel insights for the diagnosis, prognosis, and treatment of acute myocardial infarction.[64] In their study, Zhang utilised advanced analytical techniques, including differential and correlation analyses, to investigate the immune microenvironment in both healthy controls and patients suffering from CHD.[65] This analysis led to the identification of several cuproptosis-related genes that have the potential to serve as diagnostic biomarkers and therapeutic targets for CHD. These findings provide novel insights that could shape future scientific research in this field.

Disulfidptosis-Emerging/Hypothetical Mechanisms

In 2023, Professor Gan Boyi's research group discovered a novel mechanism of cell death induced by disulfide stress, which they named disulfidptosis. Unlike other cell death pathways, studies show that disulfidptosis cannot be inhibited by drugs commonly used to suppress cell death, nor can it be prevented by knocking out key genes involved in ferroptosis/apoptosis. However, thiol oxidants such as diamides and diethyl maleate significantly enhance this cell death pathway, hence the designation "disulfidptosis".[66] The mechanism involves elevated cysteine levels and subsequent depletion of nicotinamide adenine dinucleotide phosphate (NADPH), triggering massive intracellular accumulation of disulfide bonds.[67] SLC7A11 is a transporter responsible for moving cysteine from the extracellular to the intracellular space. Under glucose deprivation, increased SLC7A11 expression leads to substantial cysteine accumulation, which subsequently induces disulfide stress and causes cell death.[66,68] Thus, the activation of disulfidptosis likely requires three key factors: (1) high expression of SLC7A11, which imports extracellular cysteine and exports intracellular glutamate, resulting in elevated cysteine uptake and excessive intracellular cysteine accumulation, thereby causing disulfide stress in cellular metabolism;[68,69] (2) impaired glucose metabolism under glucose-deprived conditions, which prevents the generation of reduced NADPH via the pentose phosphate pathway;[70] and (3) abnormal disulfide bond formation between actin cytoskeletal proteins. Currently, research on disulfidptosis has primarily focused on cancer and neurodegenerative diseases. Fan revealed a potential association between disulfidptosis and hypertrophic cardiomyopathy, proposing a predictive model for disulfidptosis-related genes, including GYS1, MYH10, SLC3A2, and CAPZB. This model enabled the identification of novel therapeutic drugs targeting core genes through gene prediction.[71] Through bioinformatics analysis, Zhao identified four disulfide-related genes dysregulated in heart failure samples, highlighting the critical role of these genes in shaping the diversity and complexity of the heart failure immune microenvironment.[72] Bioinformatics analysis and in vitro experiments demonstrated altered expression of key disulfide-related genes MYH9, NUBPL, MYL6, MYH10, and NCKAP1 in ischemic myocardial regions, elucidating the significance of disulfide-related cell death in ischemic cardiomyopathy and underscoring the diagnostic potential of the identified core genes.[73] Findings by Wang suggest that disulfidptosis may promote the progression of type A aortic dissection by inducing immune responses and metabolic activities. This research provides new insights into the pathogenesis and identifies potential therapeutic targets for type A aortic dissection.[74] We summarize the mechanisms of different cell death pathways in CHD in Figure 1.

TCM Treats CHD by Regulating Cell Death

TCM Modulates Apoptosis to Intervene in CHD

Tanshinone IIA is a liposoluble diterpene extracted from Salvia miltiorrhiza that alleviates myocardial ischemic injury. It enhances the viability of damaged cardiomyocytes and inhibits apoptosis by increasing the expression of Bcl-2 and Bak in myocardial tissue while decreasing the expression of Cyt-c, caspase-3, and Apaf-1.[75] Tanshinonic acids A and B, active components of Salvia miltiorrhiza, exhibit significant pharmacological activities. Treatment with tanshinonic acid A reduces tunnel-positive cells and pro-apoptotic Bax following myocardial infarction. Further studies indicate that it promotes thioredoxin and inhibits c-JNK activation, thereby mitigating inflammation and apoptosis post-myocardial infarction.[76] Tanshinol B alleviates myocardial ischemia/reperfusion injury by activating PI3K/Akt signaling and inhibiting HMGB1 expression, thereby improving cardiac function and reducing infarct size.[77] Research found that

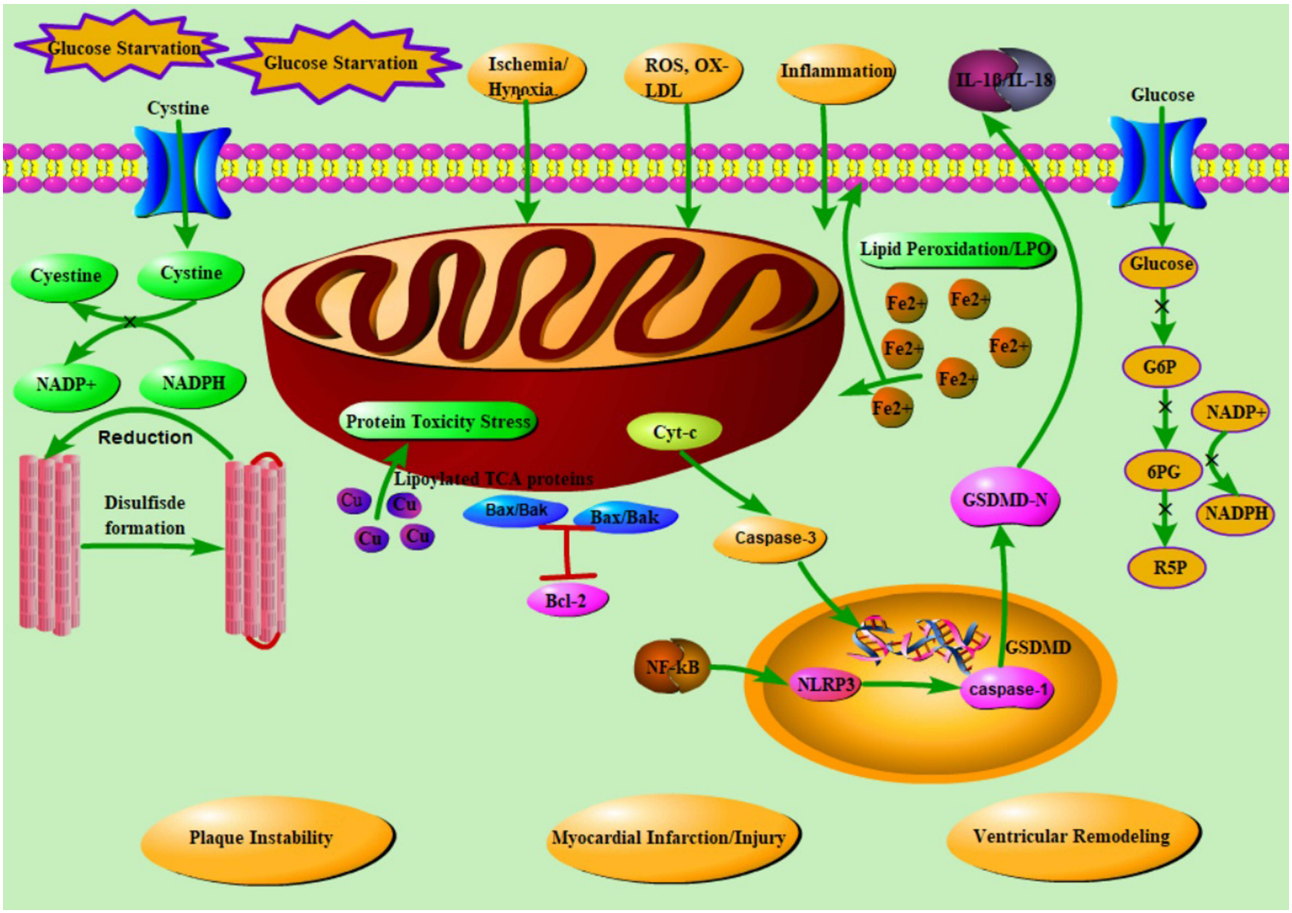

Figure 1 The Mechanisms of Different Cell Death Pathways in CHD.

Acorus tatarinowii volatile oil inhibits myocardial infarction-induced apoptosis by downregulating COX-2 and upregulating PPAR protein, thereby alleviating myocardial ischemia.[78] Tongmai Yangxin Pills are commonly used to treat CHD, arrhythmia, and chest pain. Their potential mechanism may involve enhancing eNOS activity and eNOS Ser (1177) phosphorylation levels in the myocardium, increasing Bcl-2 expression, while simultaneously reducing caspase-3 and Bax expression, thereby inhibiting myocardial cell apoptosis.[79] In the systematic review of randomized clinical trials on Tongmai Yangxin Pills, a total of nine randomized controlled trials were included. Only one study reported adverse events, while five studies reported no adverse events.[80] The beneficial effects of Rhodiola rosea injection on myocardial ischemia/reperfusion injury involve improving mitochondrial function, regulating autophagy, and inhibiting apoptosis through the AMPK/mTOR pathway. It significantly reduces cleaved caspase-3 and increases the Bcl-2/Bax ratio,[81] thereby further controlling the progression of CHD.

TCM Modulates Autophagy to Intervene in CHD

Huang's research suggests that epiberberine protects cardiomyocytes during myocardial ischemia/reperfusion by inhibiting autophagy activation, positioning it as a promising therapeutic agent for treating ischemia/reperfusion-induced cardiomyocyte injury.[82] Hesperidin reduces myocardial ischemia/reperfusion injury by inhibiting excessive autophagy, with activation of the PI3K/Akt/mTOR pathway contributing to hesperidin's inhibitory effect on excessive autophagy.[83] Qin's research demonstrated that ginsenoside Rb1 protects against myocardial ischemia/reperfusion injury by inhibiting cardiomyocyte autophagy through the PI3K/Akt/mTOR signaling pathway.[84] The Yiqi Huoxue Decoction is a prescription designed to tonify qi, strengthen the spleen, resolve stasis, and unblock collaterals. It primarily consists of herbs such as Astragalus, Fried Atractylodes, Poria, and Ligusticum. Research indicates that this formula may mitigate myocardial ischemia/reperfusion injury by targeting mitochondrial autophagy, potentially serving as a therapeutic

strategy for this condition.[85] Su Xiao Jiu Xin Wan, a frequently administered Chinese patent medicine, contains primary components such as Chuanxiong and Borneol. It has been demonstrated to alleviate autophagy-related myocardial ischemia/reperfusion injury by downregulating miR-193a-3p, enhancing ALKBH5 expression, and reducing m6A methylation. This mechanism may be attributed to its constituents Ligustilide A and synthetic Dextrorotatory Borneol.[86]

TCM Modulates Pyroptosis to Intervene in CHD

Cinnamic acid, an active phenolic compound extracted from cinnamon, exerts cardioprotective effects against myocardial ischemia/reperfusion injury by inhibiting NLRP3 inflammasome-mediated inflammation and cardiomyocyte pyroptosis.[87] Zhang et al demonstrated that resveratrol glycoside exerts anti-atherosclerotic effects by suppressing inflammation and pyroptosis through blocking the NLRP3/caspase-1 pathway and activating mTOR-mediated autophagy.[88] Chen showed that administration of Astragalus-Panax ginseng granules confers cardioprotective effects by inactivating the NF-κB/NLRP3/Gasdermin D pathway in myocardial infarction, resulting in improved cardiac function, reduced inflammatory cell infiltration and collagen deposition, and suppression of NLRP3 inflammasome activation and pyroptosis.[89] Emodin enhances in vitro cell survival and reduces in vivo myocardial infarction size by inhibiting ischemia/reperfusion-induced pyroptosis and decreasing the expression of pyroptosis-associated proteins.[90] Guizhi Tongluo Pian, an herbal formulation composed primarily of Radix Pseudostellariae, Cortex Phellodendri, Rhizoma Dioscoreae Oppositae, and Poria, has been shown to inhibit vascular inflammation and macrophage pyroptosis via the Piezo1/NLRP3 signalling pathway.[91] This has been demonstrated to result in a delay in atherosclerosis progression, thus providing a potential therapeutic target for the treatment and development of drugs for atherosclerosis. Danshen Decoction prevents cardiac injury by inhibiting activation of the TXNIP/NLRP3/caspase-1 signaling pathway, thereby reducing cardiomyocyte pyroptosis and providing a theoretical basis for treating myocardial ischemia/reperfusion injury.[92]

TCM Modulates Necroptosis to Intervene in CHD

It has been demonstrated through rigorous research that Tanshinone I has the capacity to alleviate programmed cell necrosis by inhibiting the RIP1/RIP3/MLKL pathway and activating the Akt/Nrf2 signalling pathway. This process has been shown to exert cardiovascular protective effects both in vitro and in vivo. It holds potential for development as a cardiovascular protective agent.[93] Xing showed that quercetin inhibits necrosis in ischemic/reperfused cardiomyocytes by coordinating mitochondrial quality control through the DNA-PKcs-SIRT5 axis, providing additional protection to cardiomyocytes.[94] Sugarcane leaf polysaccharides mitigate oxidative stress and necrotic apoptosis by regulating the Nrf2/HO-1 and RIP1/RIP3/MLKL signaling pathways, playing a crucial role in cardiovascular protection and holding promise for development as novel drugs for cardiovascular diseases.[95] TCM formulas possess multi-component and multi-target characteristics. Compound Danshen Droplet Pills, composed of Danshen (Salvia miltiorrhiza), Sanqi (Panax notoginseng), and Bingpian (Borneol), regulate qi and relieve pain, promote blood circulation, and remove blood stasis. They are indicated for treating blood stasis patterns. These pills inhibit RIPK3-related pathways while simultaneously modulating the AKT/GSK-3β/β-catenin pathway, suppressing epithelial-mesenchymal transition in cardiomyocytes, and reducing fibrosis and left ventricular remodeling.[96] According to the pooled results of clinical drug trials, the combination of Western medicine with compound Danshen Droplet Pills demonstrates favorable safety in the treatment of stable angina pectoris. It is characterized by minimal adverse reactions (primarily gastrointestinal) and high patient tolerability.[97] The Liqi Huoxue Droplet Pill formulation includes Miao medicinal ingredients such as Litsea lancilimba Merr. oil, Allium macrostemon Bunge, Sichuan lovage rhizome, and Borneolum Syntheticum.[98] Its mechanism involves protecting myocardial cells from ischemia-reperfusion injury by inhibiting necrotic apoptosis in rats.[99]

TCM Modulates Ferroptosis to Intervene in CHD

Naringenin is a major flavonoid found in various citrus fruits, bergamot, and tomatoes. It suppresses inflammation, lipid peroxidation, and ferroptosis induced by myocardial ischemia-reperfusion injury by activating the Nrf2/GPX4 pathway.[100] Resveratrol, the primary compound extracted from Polygonum cuspidatum, has been shown by Li to prevent myocardial ischemia/reperfusion injury by inhibiting oxidative stress and ferroptosis.[101] Gegen Qinlian Decoction is a classical prescription used to treat unexplained superficial syndrome caused by exogenous pathogenic factors. It contains chemical constituents such as flavonoids, alkaloids, saponins, phenolic acids, coumarins, and lignans.[102]

Research discovered that this decoction modulates the expression of iron-related genes, reduces lipid peroxidation levels in myocardial tissue, and upregulates GPX4 protein expression.[103] Shexiang Baoxin Wan possesses effects that promote blood circulation, relieve pain, restore yang, and expel pathogenic factors. Research indicates that Shexiang Baoxin Wan also inhibits myocardial remodeling, improves vascular endothelial function, promotes angiogenesis, reduces plaque formation, and mitigates myocardial ischemia/reperfusion injury.[104] Ye found that Shexiang Baoxin Wan reduces myocardial iron overload by modulating the miR-144-3p/SLC7A11 signaling pathway.[105] Clinical trials have revealed that adverse reactions (such as tongue numbness, gastrointestinal reactions, palpitations, and rashes) occurred less frequently in the intervention group than in the control group.[106] Other clinical studies have also demonstrated adverse reactions associated with Shexiang Baoxin Wan, including decreased blood pressure and heart rate, as well as abnormal liver and kidney function during treatment.[107] Most clinical trials on Shexiang Baoxin Wan have not identified significant adverse reactions.[108] Shengmai San has qi-tonifying, pulse-activating, yin-nourishing, and fluid-promoting effects and is commonly used clinically to treat qi-yin deficiency, palpitations, dyspnea, and spontaneous sweating with a weak pulse. Mei found that Shengmai San activates Nrf2/GPX4-mediated ferroptosis to mitigate myocardial ischemia/reperfusion injury.[109] The Shengmai preparation combined with Western medicine combination favorably impacts cardiovascular events, angina symptoms, endothelial function, platelet aggregation, and blood viscosity, with comparable safety to that of routine Western medicine.[110]

TCM Modulates PANoptosis to Intervene in CHD

PANoptosis is a recently identified form of cell death, first described in 2019, that integrates key features of pyroptosis, apoptosis, and necroptosis. Xianlinggubao Capsules, a well-known traditional Chinese herbal formula, are acclaimed for their ability to nourish yin and replenish blood, promote blood circulation and remove blood stasis, regulate the immune system, and enhance bone density.[111] Research has shown that Xianlinggubao Capsules can reverse myocardial injury following myocardial infarction by inhibiting the NLRP3/Caspase-3/RIP1-mediated PANoptotic pathways.[112] Xiao Chai Hu Decoction, a classic TCM formula, contains ingredients such as Bupleurum, Scutellaria, Pinellia, Ginseng, and Ginger. Wang proposed that Xiao Chai Hu Decoction protects against sepsis-induced cardiomyopathy by inhibiting ZBP1-triggered PANoptosis.[113] It is evident that the research conducted on PANoptosis has been predominantly focused on the domains of cancer and neurodegenerative diseases, with a paucity of investigation directed towards cardiovascular disorders. Consequently, the effects of TCM on CHD remain largely theoretical.

TCM Modulates Cuproptosis to Intervene in CHD

TCM primarily focuses on heat-clearing and toxin-eliminating therapies for cuproptosis, supplemented by diuretic treatments. In contrast, western medicine typically employs copper-chelating agents, such as ammonium tetrathiomolybdate-a small hydrophilic compound capable of highly specific copper chelation.[114] Triethylenetetramine, a chelating agent that specifically and selectively binds copper ions, has been used as a second-line treatment for Wilson's disease.[115] Copper carrier 8-hydroxyquinoline and its derivatives possess metal-chelating capabilities and exhibit broad biological applications across various disease states, ranging from neurodegenerative disorders to cancer.[116] Curcumin compounds are the primary bioactive constituents identified in the traditional Chinese herbal formula Gancao Decoction, and these components have been detected in rat liver tissue. Research has demonstrated that turmeric may also be utilized for the treatment of cuproptosis.[117] Curcumin belongs to the flavonoid class of compounds. The mechanism of action of flavonoids in treating cuproptosis may be related to their hydroxyl and double-bond structures, which enable them to form complexes with metal ions and regulate metal concentrations. Consequently, certain TCM formulations may exhibit therapeutic effects against cardiovascular diseases and cuproptosis.[118,119]

TCM Modulates Disulfidptosis to Intervene in CHD

Disulfidptosis is a newly identified form of cell death characterized by cytoskeletal disintegration triggered by the abnormal accumulation of intracellular disulfide bonds. This process is induced by disulfide stress resulting from glucose deprivation and was first described by cancer researchers.[120] TCM researchers propose that the herbal compound dragon's blood provides multi-target neurovascular protection in ischemic stroke by modulating inflammation, preserving blood-brain barrier integrity, and inhibiting disulfidptosis, highlighting its potential as a therapeutic candidate.[121]

Additionally, bioinformatics analyses have identified sulfide-related genes, which were validated in mouse models using Western blotting, RNA sequencing, and immunohistochemistry. This led to the selection of resveratrol as a core target compound for developing therapeutics against hypertrophic cardiomyopathy.[71] However, most studies on cardiovascular diseases associated with disulfidptosis remain limited to bioinformatics analyses, with minimal multi-level in vitro validation. Research on specific cardiovascular conditions, such as CHD, is even more scarce. Therefore, the precise mechanisms of disulfidptosis in CHD and the therapeutic efficacy of TCM treatments require further systematic experimental validation. We summarize the mechanisms of action of common Chinese herbs and formulas in Table 1.

Table 1 Mechanisms of Action of TCM Compound Preparations in Regulating Cell Death to Intervene in CHD

TCM/Formula	Primary Ingredients	Cellular Death Mechanisms	Mechanisms and Primary Signaling Pathways	References
Gualoupi Injection	Snakegourd Peel	Apoptosis, Autophag, Necroptosis, Ferroptosis	PI3K/Akt signaling pathway, inflammatory response, endothelial injury, alleviation of oxidative stress	[122]
TongMai YangXin Wan	Daidzin, Emodin, Isoliquiritigenin, Glycyrrhizinic Acid, Gallic Acid, Acteoside, Quercetin, Anthraquinone, Flavone glycosides and Methamphetamine	Apoptosis, Autophagy, Necroptosis, Ferroptosis, Pyroptosis	TNF signaling pathway, PI3K-Akt signaling pathway, p53 signaling pathway, MAPK signaling pathway, NOD-like receptor signaling pathway	[123]
Danshen Hawthorn Soup	Dan-Shen Root, Crataegus Pinnatifida	Apoptosis	Inflammation, oxidative stress	[124]
Xuefu Zhuyu Capsules	Peach Seed, Safflower, Red paeony root, Sichuan lovase rhizome, Immature Trifoliate-orange Fruit, Chinese Thorowax Root, Platycodon Grandiflorum, Chinese Angelica, Rehmannia Glutinosa, Twotooth Achyranthes Root, liquorice root	Apoptosis	FOXO signaling pathway, Ras signaling pathway, VEGF signaling pathway	[125]
Sanqi Danshen Tablets	Sanchi, Dan-Shen Root	Apoptosis, Autophagy, Necroptosis, Ferroptosis	PI3K/Akt signaling pathway	[126]
Eliminating dampness and resolving phlegm Decoction	Lotus Leaf, Hemp Fruit, Safflower, Mullberry Fruit, Dwarf Flowering Cherry Seed, Atractylodes, Rhizoma Atractylodis, Chinese Clematis Root, Nutgrass Galingale Rhizome, liquorice root, Chinese Angelica, Agaric, Pinellia Ternata	Apoptosis	AKT/HIF-1α and TLR4/NF-κB signaling pathway	[127]
Dan Xiong Tong Mai granule	Dan-Shen Root, Safflower, Sichuan lovase rhizome, red paeony root, Corydalis Yanhusuo, Babury Wolfberry Fruit, Tuber Fleeceflower, Nutgrass Galingale Rhizome	Ferroptosis	Regulate oxidative stress and inflammatory responses	[128]
Dan Lou Pian	Snakegourd Peel, Allium macrostemon Bunge, Lobed Kudzuvine Root, Sichuan lovase rhizome, Dan-Shen Root, red paeony root, Alisma Orientale, Milkvetch Root, Drynaria fortunei, Aromatic Turmeric Root-tuber	Apoptosis	NOD-like receptor signaling pathways and NLRP3 inflammasome	[129]
Shengxian Decoction	Milkvetch Root, Common Anemarrhena Rhizome, Chinese Thorowax Root, Platycodon Grandiflorum, Largetrifoliolious Bugbane Rhizome	Apoptosis, Autophagy, Necroptosis, Ferroptosis	PI3K/Akt signaling pathway	[130]
Qishen Yiqi Dropping Pills	Sanchi, Milkvetch Root, Dan-Shen Root	Ferroptosis	Anti-inflammatory, antioxidant, antiplatelet, and vasodilatory effects	[131]
Taohong Siwu Decoction	White Paeony Root, Chinese Angelica, Prepared Rehmannia Root, Sichuan lovase rhizome, Peach Seed, Safflower	Apoptosis	AKT1-eNOS signaling pathway	[132]
Fufang Zhenzhu Tiaozhi Capsule	Glossy Privet Fruit, Finger Citron Fruit, Atractylodes, Sanchi	Apoptosis, Autophagy, Necroptosis, Ferroptosis	PI3K/Akt signaling pathway, reduction of pro-inflammatory cytokines	[133]
Wendan Decoction	Pinellia Ternata, Bamboo Shavings, Charred Immature Bitter Orange Fruit, Tangerine Peel, Indian buead, Prepared Liquorice Root, Fresh Ginger, Common Jujube	Apoptosis, Autophagy, Necroptosis, Ferroptosis	PI3K/Akt signaling pathway	[134]
Shengmai Decoction	Red ginseng, Radix Ophiopogonis, Chinese Magnolcavine Fruit	Apoptosis, Autophagy, Necroptosis, Ferroptosis, Pyroptosis	PPAR, FoxO, and VEGF signaling pathways	[135]
Gualou Xiebai Guizhi Decoction	Aurantii Fructus Immaturus, Allium macrostemon Bunge, Cmnamomi Mmulus, Officinal magnolia bark, Snakegourd Seed	Apoptosis, Autophagy, Necroptosis, Ferroptosis, Pyroptosis	HIF-1, TNF, PI3K-Akt signaling pathways	[136]

https://doi.org/10.2147/JIR.S590293

Of note, one should bear in mind that TCM medications are usually prescribed as complex formulae, which are often further manipulated by the practitioner on a personalized basis. Moreover, most active ingredients isolated from TCM may target multiple molecules or pathways. Most basic experiments face obstacles in translating to human clinical practice. According to adverse reaction reports from multiple drug clinical trials, adverse reactions associated with TCM are predominantly linked to sudden cardiogenic death, heart failure, angina pectoris, gastrointestinal systemic adverse reactions, and skin rash. Meanwhile, the limitations of traditional Chinese medicine lie in: 1) Its diverse composition, making quantitative characterization challenging; 2) The absence of rigorous approval procedures for TCM products on the Chinese market, unlike Western pharmaceuticals, rendering their efficacy and safety unverifiable; 3) Small sample sizes in randomized controlled trials, reliance on surrogate endpoints, short patient follow-up periods, and inconsistent outcomes. Meanwhile, since emerging/hypothetical mechanisms cell death remain understudied, PANoptosis research primarily focuses on cancer, cuproptosis studies are predominantly animal-based, and disulfidptosis remains largely theoretical. Not surprisingly, we are facing immense challenges in interpreting the observed therapeutic benefits of TCMs with contemporary pharmacological approaches by pinpointing individual compounds and their molecular targets.

Conclusions

Cell death plays a crucial role in the onset and progression of CHD. The pathological mechanisms of CHD are closely linked to multiple cell death pathways, including apoptosis, autophagy, pyroptosis, necroptosis, PANoptosis, cuproptosis, and disulfidptosis. These pathways serve as important therapeutic targets by regulating processes such as atherosclerotic plaque stability, myocardial ischemia/reperfusion injury, and ventricular remodeling. Inflammasomes can induce cell death, and cell death can activate inflammasomes. Therefore, inflammation also plays a relatively central role in linking these cell death pathways to the progression of CHD. In recent years, targeted treatments for CHD using TCM and herbal formulas have yielded promising results. Despite significant achievements in treating CHD, TCM faces numerous practical limitations. For instance, clinical research often suffers from inconsistent trial designs, unreasonable efficacy assessment criteria, lack of unified diagnostic standards, insufficient sample sizes, absence of dynamic follow-up, and scarcity of multicenter, double-blind randomized controlled trials. In basic research, limitations exist in validating the success of animal model development, potentially resulting in models that fail to accurately reflect the clinical efficacy and mechanisms of TCM treatment. Most natural products discussed in this review have been evaluated only in preliminary pharmacological studies, and the molecular mechanisms underlying their anti-CHD activity remain poorly understood. Research on the mechanisms of action of TCM formulas often carries speculative elements, with many analyses relying on bioactive compounds identified in their key constituents. The reductionist approach of studying isolated compounds, while mechanistically informative, may overlook the synergies inherent in TCM formulations. Future research should integrate quantitative systems pharmacology to decode the multi-target, multi-component characteristics of TCM. Meanwhile, we are developing multi-target inhibitors by identifying cross-regulatory nodes among cell death pathways such as PANoptosis, ferroptosis, cuproptosis, and disulfidptosis. Disulfidptosis, as a newly discovered form of cell death, also represents a promising new direction for research.

Abbreviations

Bcl-2, B-cell lymphoma-2; BAK, BCL2-antagonist/killer; Bax, BCL-2-associated X protein; Fas/FasL, Factor associated suicide/Factor associated suicide ligand; MAPK1, Mitogen-Activated Protein Kinase 1; LC3, Light Chain 3; AMPK, Adenosine 5'-monophosphate (AMP)-activated protein kinase; mTOR, Mammalian Target of Rapamycin; mTORC1, Mechanistic target of rapamycin complex 1; IL-1β, Interleukin-1beta; IL-18, Interleukin 18; NLRP3, NOD-, LRR-, and pyrin domain-containing protein 3; NF-κB, Nuclear Factor kappa-light-chain-enhancer of activated B cells; RIP1-RIP3-MLKL, Receptor-interacting protein 1-Receptor-interacting protein 3-Mixed lineage kinase domain-like; CaMKII, Calcium Calmodulin Dependent Protein Kinase II; mPTP, mitochondrial permeability transition pore; GLP-1R, Glucagon-like peptide-1 receptor; PI3K, Phosphoinositide 3-Kinase; Akt, Protein Kinase B; GPX4, Glutathione Peroxidase 4; SLC7A11, Solute Carrier Family 7 Member 11; Nrf2, Nuclearfactor erythroidderived 2-like 2; HO-1, Heme Oxygenase-1; ACP5, Acid phosphatase 5; ZBP1, Z-DNA binding protein 1; HIF-1, Hypoxia inducible factor-1; GYS1, Glycogen synthase 1; MYH10, Myosin heavy chain 10; SLC3A2, Solute Carrier Family 3 Member 2; CAPZB, Capping Actin Protein of Muscle Z-Line

Subunit Beta; MYH9, Myosin heavy chain 9; NUBPL, NUBP iron-sulfur cluster assembly factor; MYL6, Myosin heavy chain 6; NCKAP1, NCK associated protein 1; Cyt-c, Cytochrome C; Apaf-1, Apoptotic peptidase activating factor 1; c-JNK, c-Jun N-terminal kinase; HMGB1, High Mobility Group Box 1 Protein; COX-2, Cyclooxygenase-2; PPAR, Peroxisome proliferators-activated receptors; eNOS, Endothelial Nitric Oxide Synthase; ALKBH5, AlkB Homolog 5, RNA Demethylase; TXNIP, Thioredoxin Interacting Protein; GSK-3β, Glycogen synthase kinase 3 beta.

Data Sharing Statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

Acknowledgments

All figures were edited using the Pathway Builder Tool 2.0 software. We would like to express our sincere gratitude to the online scientific illustration software Pathway Builder Tool.

Author Contributions

Wanying Jia: Conceptualization, Data curation, Formal analysis, Methodology, Resources, Software, Writing – original draft; Jinwei Liu: Investigation, Validation, Visualization, Software, Writing – original draft; Zhibo Zhu: Project administration, Software, Supervision, Funding acquisition, Writing – review and editing. All authors gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

ZB Z is supported by the Natural Science Foundation of Inner Mongolia Province (2023LHMS08056), the Inner Mongolia Public Hospital Research Consortium Fund Project (2023GLLH0303) and the Open Fund Projects of the Laboratory at the Affiliated Hospital of Inner Mongolia Medical University (2023NYFYSYS002).

Disclosure

The author(s) report no conflicts of interest in this work.

References

1. Tong X, Tang R, Xiao M. et al. Targeting cell death pathways for cancer therapy: recent developments in necroptosis, pyroptosis, ferroptosis, and cuproptosis research. *J Hematol Oncol*. 2022;15(1):174. doi:10.1186/s13045-022-01392-3
2. Peng F, Liao M, Qin R, et al. Regulated cell death (RCD) in cancer: key pathways and targeted therapies. *Signal Transduct Target Ther*. 2022;7(1):286. doi:10.1038/s41392-022-01110-y
3. Koren E, Fuchs Y. Modes of Regulated Cell Death in Cancer. *Cancer Discov*. 2021;11(2):245–265. doi:10.1158/2159-8290.CD-20-0789
4. Roth GA, Mensah GA, Johnson CO, et al. Global Burden of Cardiovascular Diseases and Risk Factors, 1990–2019: update From the GBD 2019 Study. *J Am Coll Cardiol*. 2020;76(25):2982–3021. doi:10.1016/j.jacc.2020.11.010
5. Stone PH, Libby P, Boden WE. Fundamental Pathobiology of Coronary Atherosclerosis and Clinical Implications for Chronic Ischemic Heart Disease Management-The Plaque Hypothesis: a Narrative Review. *JAMA Cardiol*. 2023;8(2):192–201. doi:10.1001/jamacardio.2022.3926
6. Khosravi M, Poursaleh A, Ghasempour G, Farhad S, Najafi M. The effects of oxidative stress on the development of atherosclerosis. *Biol Chem*. 2019;400(6):711–732. doi:10.1515/hsz-2018-0397
7. Wang S, Cheng Z, Chen X. Promotion of PTEN on apoptosis through PI3K/Akt signal in vascular smooth muscle cells of mice model of coronary heart disease. *J Cell Biochem*. 2019;120(9):14636–14644. doi:10.1002/jcb.28725
8. Li T, Shi W, Wang G, Jiang Y. Prevalence and risk factors of frailty in older patients with coronary heart disease: a systematic review and meta-analysis. *Arch Gerontol Geriatr*. 2025;130:105721. doi:10.1016/j.archger.2024.105721
9. Zheng D, Liu J, Piao H, Zhu Z, Wei R, Liu K. ROS-triggered endothelial cell death mechanisms: focus on pyroptosis, parthanatos, and ferroptosis. *Front Immunol*. 2022;13:1039241. doi:10.3389/fimmu.2022.1039241
10. Zheng Y, Gardner SE, Clarke MCH. Cell death, damage-associated molecular patterns, and sterile inflammation in cardiovascular disease. *Arterioscler Thromb Vasc Biol*. 2011;31(12):2781–2786. doi:10.1161/ATVBAHA.111.224907
11. Fuchs Y, Steller H. Programmed cell death in animal development and disease. *Cell*. 2011;147(4):742–758. doi:10.1016/j.cell.2011.10.033
12. Yan RN, Li JS, Fu Y. Tissue factor pathway inhibitor regulates cell apoptosis and coronary heart disease. *J Clin Pathol Med*. 2021;41(05):1140–1145.
13. Luo KQ, Long HB, Xu BC. Reduced apoptosis after acute myocardial infarction by simvastatin. *Cell Biochem Biophys*. 2015;71(2):735–740. doi:10.1007/s12013-014-0257-1

14. Zhang YQ, Wang YB, Song SK. Research progress on Fas system-induced apoptosis and coronary atherosclerotic heart disease. *Int J Intern Med*. 2008;2008(4):205–208.
15. Qi B, Cao L, Wang L, Zhou J. Study on apoptosis and expression of P53, bcl-2, Bax in cardiac myocytys of congestive heart failure induced by ventricular pacing. *J Tongji Med Univ*. 2001;21(3):202–205. doi:10.1007/BF02886429
16. Li N, Xia N, He J, et al. Amphiregulin improves ventricular remodeling after myocardial infarction by modulating autophagy and apoptosis. *FASEB J*. 2024;38(4):e23488. doi:10.1096/fj.202302385R
17. Wu MY, Yiang GT, Liao WT, et al. Current Mechanistic Concepts in Ischemia and Reperfusion Injury. *Cell Physiol Biochem*. 2018;46 (4):1650–1667. doi:10.1159/000489241
18. Liu H, Ma XF, Dong N, Wang GN, Qi MX, Tan JK. LncRNA PVT1 inhibits endothelial cells apoptosis in coronary heart disease through regulating MAPK1 expression via miR-532-3p. *Acta Cardiol*. 2024;79(3):295–303. doi:10.1080/00015385.2023.2209448
19. Yamamoto H, Matsui T. Molecular Mechanisms of Macroautophagy, Microautophagy, and Chaperone-Mediated Autophagy. *J Nippon Med Sch*. 2024;91(1):2–9. doi:10.1272/jnms.JNMS.2024_91-102
20. Vargas JNS, Wang C, Bunker E, et al. Spatiotemporal Control of ULK1 Activation by NDP52 and TBK1 during Selective Autophagy. *Mol Cell*. 2019;74(2):347–362e6. doi:10.1016/j.molcel.2019.02.010
21. Guo YT, Liu Y, Liu WX. Research Progress on Programmed Cell Death in Myocardial Infarction. *J Clin Pathol*. 2022;42(02):441–448.
22. Sergin I, Razani B. Self-eating in the plaque: what macrophage autophagy reveals about atherosclerosis. *Trends Endocrinol Metab*. 2014;25 (5):225–234. doi:10.1016/j.tem.2014.03.010
23. Chen JP, Peng YT, Liu J, Wei YY, Wang LF. Research Progress on the Relationship Between Macrophage Autophagy and Atherosclerosis. *J Gannan Med Univ*. 2023;43(05):435–441.
24. Wu J, Nie ZQ, Yin WL. miR-499 protects hypoxic/reoxygenated cardiomyocytes through Drp1-mediated mitochondrial autophagy. *J Pract Med*. 2023;39(17):2196–2203.
25. Zhou B, Leng Y, Lei SQ, Xia ZY. AMPK activation restores ischemic post-conditioning cardioprotection in STZ-induced type 1 diabetic rats: role of autophagy. *Mol Med Rep*. 2017;16(3):3648–3656. doi:10.3892/mmr.2017.7033
26. Takagi H, Matsui Y, Hirotani S, Sakoda H, Asano T, Sadoshima J. AMPK mediates autophagy during myocardial ischemia in vivo. *Autophagy*. 2007;3(4):405–407. doi:10.4161/auto.4281
27. Li YK, He SY, Wang Z, Shi YC, Liu JH. Fibroblast growth factor 21 exerts protective effects in cardiovascular diseases by inducing autophagy. *Acta Physiol*. 2022;74(04):633–638. doi:10.13294/j.aps.2022.0061
28. Ai F, Chen M, Yu B, et al. Berberine regulates proliferation, collagen synthesis and cytokine secretion of cardiac fibroblasts via AMPK-mTOR-p70S6K signaling pathway. *Int J Clin Exp Pathol*. 2015;8(10):12509–12516.
29. Dong Y, Zhu S, Feng LL, Liu YM, Li J, Wang J. Research Progress on the Regulatory Mechanisms and Treatment of Coronary Heart Disease-Related Circular RNAs. *J Heart*. 2019;31(05):581–587.
30. Panganiban RA, Nadeau KC, Lu Q. Pyroptosis, gasdermins and allergic diseases. *Allergy*. 2024;79(9):2380–2395. doi:10.1111/all.16236
31. Liu C, Gao JL, Wang J. Research progress on the molecular mechanism of cell pyroptosis in coronary heart disease and its new drug targets. *Med Rev*. 2021;27(02):246–252.
32. Jiang Y, Ge W, Zhao Y, et al. LINC00926 promotes pyroptosis of hypoxia-induced human umbilical vein vascular endothelial cells by recruiting ELAVL1. *Nan Fang Yi Ke Da Xue Xue Bao*. 2023;43(5):807–814. doi:10.12122/j.issn.1673-4254.2023.05.17
33. Qiu Y, Meng L, Xing Y, et al. The Role of Pyroptosis in Coronary Heart Disease. *Anatol J Cardiol*. 2024;28(7):318–328. doi:10.14744/AnatolJCardiol.2024.4001
34. Qiu YY, Liu HX, Yu ZJ, Peng F. Research progress on cell pyroptosis in atherosclerosis. *Modern Chin Doctor*. 2024;62(18):115–119.
35. Huang SN, Cai HW. Progress in the Relationship Between Pyroptosis and Atherosclerosis. *Chin J Comparative Med*. 2024;34(01):146–150.
36. Wang SJ, Yang K, Yao WQ, Han X. Exploring the impact of interfering with cell pyroptosis on coronary heart disease based on the principle of "treating both the heart and liver". *J Traditional Chin Med*. 2023;38(02):233–237. doi:10.16368/j.issn.1674-8999.2023.02.040
37. Degterev A, Huang Z, Boyce M, et al. Chemical inhibitor of nonapoptotic cell death with therapeutic potential for ischemic brain injury. *Nat Chem Biol*. 2005;1(2):112–119. doi:10.1038/nchembio711
38. Sun S, Kang PF. Research progress on the involvement of cell programmed necrosis in the pathogenesis of coronary heart disease. *J Hainan Med Univ*. 2020;26(07):556–560. doi:10.13210/j.cnki.jhmu.20200210.008
39. Karunakaran D, Geoffrion M, Wei L, et al. Targeting macrophage necroptosis for therapeutic and diagnostic interventions in atherosclerosis. *Sci Adv*. 2016;2(7):e1600224. doi:10.1126/sciadv.1600224
40. Leeper NJ. The role of necroptosis in atherosclerotic disease. *JACC Basic Transl Sci*. 2016;1(6):548–550. doi:10.1016/j.jacbts.2016.08.002
41. Krzywonos-Zawadzka A, Franczak A, Sawicki G, Wozniak M, Bil-Lula I. Multidrug prevention or therapy of ischemia-reperfusion injury of the heart-Mini-review. *Environ Toxicol Pharmacol*. 2017;55:55–59. doi:10.1016/j.etap.2017.08.004
42. Zhang T, Zhang Y, Cui M, et al. CaMKII is a RIP3 substrate mediating ischemia- and oxidative stress-induced myocardial necroptosis. *Nat Med*. 2016;22(2):175–182. doi:10.1038/nm.4017
43. Oerlemans MI, Liu J, Arslan F, et al. Inhibition of RIP1-dependent necrosis prevents adverse cardiac remodeling after myocardial ischemia-reperfusion in vivo. *Basic Res Cardiol*. 2012;107(4):270. doi:10.1007/s00395-012-0270-8
44. Zhu P, Hu S, Jin Q, et al. Ripk3 promotes ER stress-induced necroptosis in cardiac IR injury: a mechanism involving calcium overload/XO/ROS/mPTP pathway. *Redox Biol*. 2018;16:157–168. doi:10.1016/j.redox.2018.02.019
45. Zhou G, Wu H, Yang J, et al. Liraglutide Attenuates Myocardial Ischemia/Reperfusion Injury Through the Inhibition of Necroptosis by Activating GLP-1R/PI3K/Akt Pathway. *Cardiovasc Toxicol*. 2023;23(3–4):161–175. doi:10.1007/s12012-023-09789-3
46. Dixon SJ, Olzmann JA. The cell biology of ferroptosis. *Nat Rev Mol Cell Biol*. 2024;25(6):424–442. doi:10.1038/s41580-024-00703-5
47. Liu Y, Yu Z, Lu Y, Liu Y, Chen L, Li J. Progress in the study of the mechanism of ferroptosis in coronary heart disease and clinical intervention strategies. *Front Cardiovasc Med*. 2025;12:1545231. doi:10.3389/fcvm.2025.1545231
48. Vinchi F, Porto G, Simmelbauer A, et al. Atherosclerosis is aggravated by iron overload and ameliorated by dietary and pharmacological iron restriction. *Eur Heart J*. 2020;41(28):2681–2695. doi:10.1093/eurheartj/ehz112
49. Xu S, Ilyas I, Little PJ, et al. Endothelial Dysfunction in Atherosclerotic Cardiovascular Diseases and Beyond: from Mechanism to Pharmacotherapies. *Pharmacol Rev*. 2021;73(3):924–967. doi:10.1124/pharmrev.120.000096

50. Fang X, Cai Z, Wang H, et al. Loss of Cardiac Ferritin H Facilitates Cardiomyopathy via Slc7a11-Mediated Ferroptosis. *Circ Res*. 2020;127(4):486–501. doi:10.1161/CIRCRESAHA.120.316509
51. Liu RN, Wang D, Wang DX. Latest research progress on ferroptosis as a therapeutic target for atherosclerosis. *J Clin Cardiol*. 2024;40(04):335–340. doi:10.13201/j.issn.1001-1439.2024.04.016
52. Han T, Li Y, Li C, Zhang CY, Wang CX, Zhang Y. Occurrence and Regulatory Mechanisms of Ferroptosis and Research Progress on Atherosclerosis. *J Heart*. 2024;36(01):71–76+80.
53. Fang X, Wang H, Han D, et al. Ferroptosis as a target for protection against cardiomyopathy. *Proc Natl Acad Sci U S A*. 2019;116(7):2672–2680. doi:10.1073/pnas.1821022116
54. Fang X, Ardehali H, Min J, Wang F. The molecular and metabolic landscape of iron and ferroptosis in cardiovascular disease. *Nat Rev Cardiol*. 2023;20(1):7–23. doi:10.1038/s41569-022-00735-4
55. Li H, Song F, Duan LR, et al. Paeonol and danshensu combination attenuates apoptosis in myocardial infarcted rats by inhibiting oxidative stress: roles of Nrf2/HO-1 and PI3K/Akt pathway. *Sci Rep*. 2016;6:23693. doi:10.1038/srep23693
56. Gill D, Del Greco MF, Walker AP, Srai SKS, Laffan MA, Minelli C. The Effect of Iron Status on Risk of Coronary Artery Disease: a Mendelian Randomization Study-Brief Report. *Arterioscler Thromb Vasc Biol*. 2017;37(9):1788–1792. doi:10.1161/ATVBAHA.117.309757
57. Malireddi RKS, Kesavardhana S, Kanneganti TD. ZBP1 and TAK1: master Regulators of NLRP3 Inflammasome/Pyroptosis, Apoptosis, and Necroptosis (PAN-optosis). *Front Cell Infect Microbiol*. 2019;9:406. doi:10.3389/fcimb.2019.00406
58. Samir P, Malireddi RKS, Kanneganti TD. The PANoptosome: a Deadly Protein Complex Driving Pyroptosis, Apoptosis, and Necroptosis (PANoptosis). *Front Cell Infect Microbiol*. 2020;10:238. doi:10.3389/fcimb.2020.00238
59. Li PB, Bai JQ, Jiang WX, Li HH, Li CM. The mechanosensitive Piezo1 channel exacerbates myocardial ischaemia/reperfusion injury by activating caspase-8-mediated PANoptosis. *Int Immunopharmacol*. 2024;139:112664. doi:10.1016/j.intimp.2024.112664
60. Chen H, Xie X, Xiao H, et al. A Pilot Study About the Role of PANoptosis-Based Genes in Atherosclerosis Development. *J Inflamm Res*. 2023;16:6283–6299. doi:10.2147/JIR.S442260
61. Cui B, Qi Z, Liu W, Zhang G, Lin D. ZBP1-mediated PANoptosis: a possible novel mechanism underlying the therapeutic effects of penehyclidine hydrochloride on myocardial ischemia-reperfusion injury. *Int Immunopharmacol*. 2024;137:112373. doi:10.1016/j.intimp.2024.112373
62. Tsvetkov P, Coy S, Petrova B, et al. Copper induces cell death by targeting lipoylated TCA cycle proteins. *Science*. 2022;375(6586):1254–1261. doi:10.1126/science.abf0529
63. Yang M, Wang Y, He L, Shi X, Huang S. Comprehensive bioinformatics analysis reveals the role of cuproptosis-related gene Ube2d3 in myocardial infarction. *Front Immunol*. 2024;15:1353111. doi:10.3389/fimmu.2024.1353111
64. Liu Z, Wang L, Xing Q, et al. Identification of GLS as a cuproptosis-related diagnosis gene in acute myocardial infarction. *Front Cardiovasc Med*. 2022;9:1016081. doi:10.3389/fcvm.2022.1016081
65. Zhang B, He M. Identification of Potential Biomarkers for Coronary Artery Disease Based on Cuproptosis. *Cardiovasc Ther*. 2023;2023:5996144. doi:10.1155/2023/5996144
66. Liu X, Nie L, Zhang Y, et al. Actin cytoskeleton vulnerability to disulfide stress mediates disulfidptosis. *Nat Cell Biol*. 2023;25(3):404–414. doi:10.1038/s41556-023-01091-2
67. Zheng T, Liu Q, Xing F, Zeng C, Wang W. Disulfidptosis: a new form of programmed cell death. *J Exp Clin Cancer Res*. 2023;42(1):137. doi:10.1186/s13046-023-02712-2
68. Machesky LM. Deadly actin collapse by disulfidptosis. *Nat Cell Biol*. 2023;25(3):375–376. doi:10.1038/s41556-023-01100-4
69. Koppula P, Zhuang L, Gan B. Cystine transporter SLC7A11/xCT in cancer: ferroptosis, nutrient dependency, and cancer therapy. *Protein Cell*. 2021;12(8):599–620. doi:10.1007/s13238-020-00789-5
70. Xia N, Guo X, Guo Q, et al. Metabolic flexibilities and vulnerabilities in the pentose phosphate pathway of the zoonotic pathogen *Toxoplasma gondii*. *PLoS Pathog*. 2022;18(9):e1010864. doi:10.1371/journal.ppat.1010864
71. Fan H, Tan X, Xu S, et al. Identification and validation of differentially expressed disulfidptosis-related genes in hypertrophic cardiomyopathy. *Mol Med*. 2024;30(1):249. doi:10.1186/s10020-024-01024-1
72. Zhao L, Zhang J, Song Q, Dai C, Qin Y, Li A. Comprehensive analysis of disulfidptosis-related genes and the immune microenvironment in heart failure. *Front Cell Dev Biol*. 2024;12:1516898. doi:10.3389/fcell.2024.1516898
73. Tan X, Xu S, Zeng Y, et al. A Novel Disulfidptosis-Related Diagnostic Gene Signature and Differential Expression Validation in Ischaemic Cardiomyopathy. *J Cell Mol Med*. 2025;29(5):e70475. doi:10.1111/jcmm.70475
74. Wang D, Wang C, Liu H, et al. Integrated bioinformatic analysis of immune infiltration and disulfidptosis related gene subgroups in type A aortic dissection. *Sci Rep*. 2025;15(1):13719. doi:10.1038/s41598-025-98149-y
75. Wu P, Du Y, Xu Z, et al. Protective effects of sodium tanshinone IIA sulfonate on cardiac function after myocardial infarction in mice. *Am J Transl Res*. 2019;11(1):351–360.
76. Zhou R, Gao J, Xiang C, et al. Salvianolic acid A attenuated myocardial infarction-induced apoptosis and inflammation by activating Trx. *Naunyn Schmiedebergs Arch Pharmacol*. 2020;393(6):991–1002. doi:10.1007/s00210-019-01766-4
77. Liu H, Liu W, Qiu H, et al. Salvianolic acid B protects against myocardial ischaemia-reperfusion injury in rats via inhibiting high mobility group box 1 protein expression through the PI3K/Akt signalling pathway. *Naunyn Schmiedebergs Arch Pharmacol*. 2020;393(8):1527–1539. doi:10.1007/s00210-019-01755-7
78. Zang ZZ, Chen LM, Liu Y, et al. Uncovering the Protective Mechanism of the Volatile Oil of Acorus tatarinowii against Acute Myocardial Ischemia Injury Using Network Pharmacology and Experimental Validation. *Evid Based Complement Alternat Med*. 2021;2021:6630795. doi:10.1155/2021/6630795
79. Chen R, Chen T, Wang T, et al. Tongmai Yangxin pill reduces myocardial no-reflow by regulating apoptosis and activating PI3K/Akt/eNOS pathway. *J Ethnopharmacol*. 2020;261:113069. doi:10.1016/j.jep.2020.113069
80. Pang WT, Zhang JH, Zhai JB, et al. Tongmai Yangxin Pills in treatment for angina pectoris of coronary heart disease: a systematic review of randomized clinical trails. *Zhongguo Zhong Yao Za Zhi*. 2019;44(11):2390–2396. doi:10.19540/j.cnki.cjcmm.20190305.005
81. Zhao J, Zhang J, Liu Q, et al. Hongjingtian injection protects against myocardial ischemia reperfusion-induced apoptosis by blocking ROS induced autophagic- flux. *Biomed Pharmacother*. 2021;135:111205. doi:10.1016/j.biopha.2020.111205

82. Huang Z, Han Z, Ye B, et al. Berberine alleviates cardiac ischemia/reperfusion injury by inhibiting excessive autophagy in cardiomyocytes. *Eur J Pharmacol*. 2015;762:1–10. doi:10.1016/j.ejphar.2015.05.028
83. Li X, Hu X, Wang J, et al. Inhibition of autophagy via activation of PI3K/Akt/mTOR pathway contributes to the protection of hesperidin against myocardial ischemia/reperfusion injury. *Int J Mol Med*. 2018;42(4):1917–1924. doi:10.3892/ijmm.2018.3794
84. Qin GW, Lu P, Peng L, Jiang W. Ginsenoside Rb1 Inhibits Cardiomyocyte Autophagy via PI3K/Akt/mTOR Signaling Pathway and Reduces Myocardial Ischemia/Reperfusion Injury. *Am J Chin Med*. 2021;49(8):1913–1927. doi:10.1142/S0192415X21500907
85. Chen M, Zhong G, Liu M, et al. Integrating network analysis and experimental validation to reveal the mitophagy-associated mechanism of Yiqi Huoxue (YQHX) prescription in the treatment of myocardial ischemia/reperfusion injury. *Pharmacol Res*. 2023;189:106682. doi:10.1016/j.phrs.2023.106682
86. Wang D, Wang D, Jin Q, Wang X. Suxiao Jiuxin Pill alleviates myocardial ischemia/reperfusion-induced autophagy via miR-193a-3p/ALKBH5 pathway. *Phytomedicine*. 2024;125:155359. doi:10.1016/j.phymed.2024.155359
87. Luan F, Rao Z, Peng L, et al. Cinnamic acid preserves against myocardial ischemia/reperfusion injury via suppression of NLRP3/Caspase-1/GSDMD signaling pathway. *Phytomedicine*. 2022;100:154047. doi:10.1016/j.phymed.2022.154047
88. Zhang X, Wang Z, Li X, et al. Polydatin protects against atherosclerosis by activating autophagy and inhibiting pyroptosis mediated by the NLRP3 inflammasome. *J Ethnopharmacol*. 2023;309:116304. doi:10.1016/j.jep.2023.116304
89. Chen X, Li Y, Li J, et al. Qishen granule (QSG) exerts cardioprotective effects by inhibiting NLRP3 inflammasome and pyroptosis in myocardial infarction rats. *J Ethnopharmacol*. 2022;285:114841. doi:10.1016/j.jep.2021.114841
90. Liu Y, Zhang J, Zhang D, Yu P, Zhang J, Yu S. Research Progress on the Role of Pyroptosis in Myocardial Ischemia-Reperfusion Injury. *Cells*. 2022;11(20):3271. doi:10.3390/cells11203271
91. Pan X, Xu H, Ding Z, et al. Guizhitongluo Tablet inhibits atherosclerosis and foam cell formation through regulating Piezo1/NLRP3 mediated macrophage pyroptosis. *Phytomedicine*. 2024;132:155827. doi:10.1016/j.phymed.2024.155827
92. Chen M, Wang R, Liao L, et al. DanShen Decoction targets miR-93-5p to provide protection against MI/RI by regulating the TXNIP/NLRP3/Caspase-1 signaling pathway. *Phytomedicine*. 2024;135:156225. doi:10.1016/j.phymed.2024.156225
93. Zhuo Y, Yuan R, Chen X, et al. Tanshinone I exerts cardiovascular protective effects in vivo and in vitro through inhibiting necroptosis via Akt/Nrf2 signaling pathway. *Chin Med*. 2021;16(1):48. doi:10.1186/s13020-021-00458-7
94. Chang X, Zhang Q, Huang Y, et al. Quercetin inhibits necroptosis in cardiomyocytes after ischemia-reperfusion via DNA-PKcs-SIRT5-orchestrated mitochondrial quality control. *Phytother Res*. 2024;38(5):2496–2517. doi:10.1002/ptr.8177
95. Sun K, Yuan R, He J, et al. Sugarcane leaf polysaccharide exerts a therapeutic effect on cardiovascular diseases through necroptosis. *Heliyon*. 2023;9(11):e21889. doi:10.1016/j.heliyon.2023.e21889
96. Yang Y, Feng K, Yuan L, et al. Compound Danshen Dripping Pill inhibits hypercholesterolemia/atherosclerosis-induced heart failure in ApoE and LDLR dual deficient mice via multiple mechanisms. *Acta Pharm Sin B*. 2023;13(3):1036–1052. doi:10.1016/j.apsb.2022.11.012
97. Liu XF, Zhu XX. Advances of clinical trials on compound Danshen dripping pills for stable angina pectoris: a perspective. *Medicine*. 2025;104(16):e42175. doi:10.1097/MD.0000000000042175
98. Sun G, Zhou Q. Clinical efficacy of Liqi Huoxue Dropping Pill in treating coronary heart disease with angina pectoris. *J Clin Rational Drug Use*. 2016;9(03):141–142. doi:10.15887/j.cnki.13-1389/r.2016.03.073
99. Chen Y, Mo L, Liu X. Liqi Huoxue Dripping Pill protects ischemia and reperfusion-induced myocardial injury through mechanism involving inhibition of necroptosis in rat. *Pak J Pharm Sci*. 2025;38(1):109–118.
100. Xu S, Wu B, Zhong B, et al. Naringenin alleviates myocardial ischemia/reperfusion injury by regulating the nuclear factor-erythroid factor 2-related factor 2 (Nrf2)/System xc-/glutathione peroxidase 4 (GPX4) axis to inhibit ferroptosis. *Bioengineered*. 2021;12(2):10924–10934. doi:10.1080/21655979.2021.1995994
101. Li T, Tan Y, Ouyang S, He J, Liu L. Resveratrol protects against myocardial ischemia-reperfusion injury via attenuating ferroptosis. *Gene*. 2022;808:145968. doi:10.1016/j.gene.2021.145968
102. Li Q, Cui Y, Xu B, et al. Main active components of Jiawei Gegen Qinlian decoction protects against ulcerative colitis under different dietary environments in a gut microbiota-dependent manner. *Pharmacol Res*. 2021;170:105694. doi:10.1016/j.phrs.2021.105694
103. Yu JY, Lin YH, Zhou FH, et al. The effect of Gegenqinlian Decoction on cardiac diastolic function in diabetic mice with damp-heat syndrome. *Chin J Trad Chin Med*. 2022;47(10):2705–2711. doi:10.19540/j.cnki.cjcmm.20211201.401
104. Lu L, Sun X, Chen C, Qin Y, Guo X. Shexiang Baoxin Pill, Derived From the Traditional Chinese Medicine, Provides Protective Roles Against Cardiovascular Diseases. *Front Pharmacol*. 2018;9:1161. doi:10.3389/fphar.2018.01161
105. Ye J, Li LY, Xi X, Wang X, Tai JQ, Liu ZJ. Study on the mechanism of Shexiang Baoxin Pill in alleviating cardiomyocyte ferroptosis based on the miR-144-3p/SLC7A11 pathway. *Chin J Integrat Tradit Western Med*. 2022;42(11):1335–1340.
106. Wu C, Wang G, Sun Z. Effect of Shexiang Baoxin pills combined with nicorandil in the treatment of patients with coronary slow flow angina. *Shanghai Pharmaceuticals*. 2019;40(19):26–28,43. doi:10.3969/j.issn.1006-1533.2019.19.009
107. Wen J, Ma X, Zhang L, et al. Therapeutic efficacy and safety of Shexiang Baoxin Pill combined with trimetazidine in elderly patients with heart failure secondary to ischaemic cardiomyopathy: a systematic review and meta-analysis. *Medicine*. 2018;97(51):e13580. doi:10.1097/MD.0000000000013580
108. Wang H. Observation on the Curative Effect of Shexiang Baoxin Pill on Heart Syndrome X. *Chin J Disabil*. 2015;2015(2):152–152,153. doi:10.13214/j.cnki.cjotadm.2015.02.112
109. Ouyang Y, Tang L, Hu S, et al. Shengmai san-derived compound prescriptions: a review on chemical constituents, pharmacokinetic studies, quality control, and pharmacological properties. *Phytomedicine*. 2022;107:154433. doi:10.1016/j.phymed.2022.154433
110. Li Y, Li D, Jin X, Yang S, Zhao R, Wu M. Efficacy and Safety of Shengmai Preparation Combined with Western Medicine for Coronary Heart Disease: a Systematic Review and Meta-Analysis. *Am J Chin Med*. 2022;50(1):133–159. doi:10.1142/S0192415X22500057
111. He L, Xu C, Wang Z, et al. Identification of naturally occurring inhibitors in Xian-Ling-Gu-Bao capsule against the glucuronidation of estrogens. *Front Pharmacol*. 2022;13:935685. doi:10.3389/fphar.2022.935685
112. Wu X, Wei J, Zhang W, et al. Targeting the PANoptosis signaling pathway for myocardial protection: therapeutic potential of Xian Ling Gu Bao capsule. *Front Pharmacol*. 2024;15:1391511. doi:10.3389/fphar.2024.1391511

113. Wang Y, Fu X, Shang Z, et al. In vivo and in vitro study on the regulatory mechanism of XiaoChaiHu decoction on PANoptosis in sepsis-induced cardiomyopathy. *J Ethnopharmacol*. 2025;336:118740. doi:10.1016/j.jep.2024.118740
114. Chen X, Cai Q, Liang R, et al. Copper homeostasis and copper-induced cell death in the pathogenesis of cardiovascular disease and therapeutic strategies. *Cell Death Dis*. 2023;14(2):105. doi:10.1038/s41419-023-05639-w
115. Cooper GJ. Therapeutic potential of copper chelation with triethylenetetramine in managing diabetes mellitus and Alzheimer's disease. *Drugs*. 2011;71(10):1281–1320. doi:10.2165/11591370-000000000-00000
116. Gupta R, Luxami V, Paul K. Insights of 8-hydroxyquinolines: a novel target in medicinal chemistry. *Bioorg Chem*. 2021;108:104633. doi:10.1016/j.bioorg.2021.104633
117. Maghool F, Emami MH, Alipour R, et al. Rescue effect of curcumin against copper toxicity. *J Trace Elem Med Biol*. 2023;78:127153. doi:10.1016/j.jtemb.2023.127153
118. Jomova K, Cvik M, Lauro P, et al. The role of redox active copper(II) on antioxidant properties of the flavonoid baicalein: DNA protection under Cu(II)-Fenton reaction and Cu(II)-ascorbate system conditions. *J Inorg Biochem*. 2023;245:112244. doi:10.1016/j.jinorgbio.2023.112244
119. Yanjuan L, Shuangyou D, Ying W, et al. The Research Progress: cuproptosis and Copper Metabolism in Regulating Cardiovascular Diseases. *J Cardiovasc Pharmacol*. 2025;85(2):89–96. doi:10.1097/FJC.0000000000001653
120. Chang J, Liu D, Xiao Y, et al. Disulfidptosis: a new target for central nervous system disease therapy. *Front Neurosci*. 2025;19:1514253. doi:10.3389/fnins.2025.1514253
121. Xu C, Hang H, Li W, et al. Dragon's Blood Modulates Disulfidptosis-Related Genes to Alleviate Ischemic Brain Injury in Mice. *Neurochem Res*. 2025;50(3):185. doi:10.1007/s11064-025-04428-5
122. Yuan Z, Zhou HD, Zhou TT, Hu YX. Clinical observation of the treatment of coronary heart disease with Trichosanthis Pericarpium injection combined with angiotensin II receptor blockers. *Chin Emerg Med Tadit Chin Med*. 2025;34(05):867–869.
123. Zhang Y, Li CH, Yan YZ, et al. Network pharmacology to unveil the blood components and mechanisms of Tongmai Yangxin Pills in treating elderly coronary heart disease. *Front Cardiovasc Med*. 2025;12:1475546. doi:10.3389/fcvm.2025.1475546
124. Feng T, Xu Q, Yu Z, et al. Exploring the underlying mechanisms of Danshen-Shanzha Decoction on coronary heart disease: an integrated analysis combining pharmacoinformatics and experimental validation. *J Ethnopharmacol*. 2025;337(Pt 1):118779. doi:10.1016/j.jep.2024.118779
125. Qian H, Chen BB, Zhang M, et al. Network pharmacology and molecular docking approach to explore the potential mechanisms of Xuefu Zhuyu Capsule in coronary heart disease. *Medicine*. 2025;104(1):e41154. doi:10.1097/MD.0000000000041154
126. Zhao M, Feng L, Li W. Network Pharmacology and Experimental Verification: sanQi-DanShen Treats Coronary Heart Disease by Inhibiting the PI3K/AKT Signaling Pathway. *Drug Des Devel Ther*. 2024;18:4529–4550. doi:10.2147/DDDT.S480248
127. Yin C, Lan T, Wu Y, et al. Integrating Network Pharmacology and Experimental Validation to Investigate the Mechanism of Qushi Huatan Decoction Against Coronary Heart Disease. *Drug Des Devel Ther*. 2024;18:4033–4049. doi:10.2147/DDDT.S463054
128. Ye J, Yang R, Li L, Zhong S, Jiang R, Hu Z. Molecular mechanism of Danxiong Tongmai Granules in treatment of coronary heart disease. *Aging*. 2024;16(10):8843–8865. doi:10.18632/aging.205845
129. Gao S, He Y, Liu Y, et al. Dan-Lou tablets reduce inflammatory response by inhibiting the activation of NLRP3 inflammasome for coronary heart disease. *Phytomedicine*. 2024;131:155773. doi:10.1016/j.phymed.2024.155773
130. Zhou HM, Yue SJ, Wang WX, et al. Exploring the effective compounds and potential mechanisms of Shengxian Decoction against coronary heart disease by UPLC-Q-TOF/MS and network pharmacology analysis. *Heliyon*. 2024;10(8):e29558. doi:10.1016/j.heliyon.2024.e29558
131. Man Q, Chen S, Li X. Efficacy and safety of Qishen Yiqi dropping pills combined with modern medicine for coronary heart disease with ischemic heart failure: a systematic review and meta-analysis. *Medicine*. 2024;103(44):e39927. doi:10.1097/MD.0000000000039927
132. Wang X, Wang T, Wang Y, et al. Research progress on classical traditional Chinese medicine Taohong Siwu decoction in the treatment of coronary heart disease. *Biomed Pharmacother*. 2022;152:113249. doi:10.1016/j.biopha.2022.113249
133. Song L, Zhang D, Guo C, et al. The traditional Chinese medicine formula Fufang-Zhenzhu-Tiaozhi protects myocardia from injury in diabetic minipigs with coronary heart disease. *Biomed Pharmacother*. 2021;137:111343. doi:10.1016/j.biopha.2021.111343
134. Lin P, Hu L, Huang Q, et al. Pharmacokinetics integrated with network pharmacology to clarify effective components and mechanism of Wendan decoction for the intervention of coronary heart disease. *J Ethnopharmacol*. 2023;314:116669. doi:10.1016/j.jep.2023.116669
135. Jiang Y, He Q, Zhang T, Xiang W, Long Z, Wu S. Exploring the mechanism of Shengmai Yin for coronary heart disease based on systematic pharmacology and chemoinformatics. *Biosci Rep*. 2020;40(6):1. doi:10.1042/BSR20200286
136. Teng C, Wang Y, Pang S, Wei X, Liu X. Study on the mechanism of Gualou Xiebai Guizhi decoction (GLXBGZD) in the treatment of coronary heart disease based on network pharmacology. *Medicine*. 2022;101(29):e29490. doi:10.1097/MD.0000000000029490