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Research Progress on Traditional Chinese Medicine Regulating the NLRP3/Caspase-1 Signaling Pathway in the Treatment of Coronary Heart Disease

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Abstract: Coronary Heart Disease (CHD) is a cardiovascular disease with a high global prevalence. Its pathophysiological mechanisms are complex, with inflammatory responses and pyroptosis mediated by the NLRP3/Caspase-1 signaling pathway serving as critical factors driving CHD progression. Upon activation, the NLRP3 inflammasome recruits and activates Caspase-1, which subsequently induces the cleavage of GSDMD and the maturation and release of inflammatory cytokines. This process triggers pyroptosis and exacerbates myocardial injury.Traditional Chinese Medicine (TCM), characterized by its holistic regulatory advantages of multi-component, multi-target, and multi-pathway action, has demonstrated unique potential in the prevention and treatment of CHD. This paper aims to elucidate the role of the NLRP3/Caspase-1 pathway in the pathological progression of CHD and systematically reviews the research progress of TCM monomers and compound formulas in intervening with CHD by regulating this signaling pathway. The goal is to provide a theoretical basis and new perspectives for the modernization and clinical application of TCM research.

1. Introduction

Coronary heart disease (CHD) is a form of ischemic heart disease characterized by coronary atherosclerosis. This pathological process results in luminal stenosis or obstruction, subsequently leading to myocardial ischemia, hypoxia, and necrosis[1]. According to Global Burden of Disease (GBD) data [2], the global prevalence of CHD has reached approximately 240 million, making it the leading cause of cardiovascular mortality. In China, with the accelerated aging population and lifestyle changes, the incidence of CHD continues to rise. Statistics from the "China Cardiovascular Health and Disease Report 2024" [3] show that between 2020 and 2022, the CHD prevalence rate among residents aged 18 and above in China was 758 per 100,000, posing a serious threat to national health and quality of life. Currently, Western medicine primarily treats CHD with antiplatelet agents, anticoagulants, and percutaneous coronary intervention [4-5]. Although effective, long-term use may lead to adverse reactions, resulting in suboptimal long-term outcomes for some patients. Therefore, research on the pathogenesis and effective prevention and treatment of CHD

has become urgent. CHD falls under the categories of "chest obstruction" and "heart pain" in Traditional Chinese Medicine (TCM), with its pathogenesis characterized by "deficiency root and excess manifestation" —i.e., imbalance of qi, blood, yin, and yang as the root cause, and phlegm-turbidity, blood stasis, and cold coagulation as the manifestations [6]. TCM treatment of CHD is based on holistic concepts and syndrome differentiation, employing methods such as replenishing qi and activating blood circulation, resolving phlegm and unblocking collaterals, and warming yang to dispel cold to improve clinical symptoms, delay disease progression, and enhance quality of life.

Studies have confirmed [7-10] that inflammatory responses permeate the entire process of CHD pathogenesis and development, serving as a core driver of atherosclerosis formation and plaque instability. Among these mechanisms, the signaling pathway mediated by nucleotide-binding oligomeric domain-like receptor protein 3 (NLRP3) and caspase-1 plays a pivotal role in the pathophysiological progression of CHD, acting as the primary regulatory pathway for the maturation and release of pro-inflammatory factors [11]. Consequently, intervention targeting the NLRP3/Caspase-1 signaling pathway has emerged as a cutting-edge strategy for CHD prevention and treatment. Various active monomers and compound formulations in traditional Chinese medicine can effectively delay the pathological progression of CHD by modulating this pathway.

2. Overview of NLRP3/Caspase-1

The NLRP3/Caspase-1 signaling pathway, as a critical component of the innate immune defense system, centers on the assembly and activation of NLRP3 inflammasomes. An NLRP3 inflammasome is a multi-protein supramolecular complex composed of the cytoplasmic pattern recognition receptor NLRP3, apoptosis-related speckled protein (ASC), and effector protein pro-caspase-1 [12]. Under physiological conditions, this pathway rapidly initiates and amplifies inflammatory responses upon detecting various danger signals both inside and outside cells, thereby exerting immune surveillance functions to eliminate pathogens and damaged cells. However, its dysregulated activation resulting from homeostatic imbalance serves as a core pathological driver for multiple chronic inflammatory diseases, including chronic heart disease (CHD) [13].

The NLRP3 protein, as a cytoplasmic pattern recognition receptor, typically requires two steps for activation: "priming" and "activation." Priming signals are mediated by Toll-like receptors (TLRs) that recognize pathogen-associated molecular patterns (PAMPs) or damage-associated molecular patterns (DAMPs), subsequently activating the NF-κB pathway. This induces upregulation of NLRP3 protein and pro-interleukin-1β (pro-IL-1β) transcription and expression, laying the material foundation for the assembly of inflammatory bodies. Agonistic signals, triggered by danger signals such as ATP, lipopolysaccharide (LPS), reactive oxygen species (ROS), and intracellular potassium ion efflux, induce conformational changes and oligomerization of NLRP3 protein [14-16]. Oligomeric NLRP3 recruits the adaptor protein ASC via its N-terminal pyrrolidine domain (PYD). ASC then recruits the effector protein pro-Caspase-1 through its C-terminal cysteine-asparaginase recruitment domain (CARD), ultimately forming the NLRP3 inflammatory body complex [17]. Upon assembly, pro-Caspase-1 undergoes self-cleavage to convert into the biologically active mature Caspase-1. Activated Caspase-1 cleaves pro-IL-1 β and pro-interleukin-18 (pro-IL-18), converting them into biologically active pro-inflammatory cytokines IL-1β and IL-18, which are secreted extracellularly to trigger the inflammatory response [12]. In addition, activated Caspase-1 can cleave the Gasdermin D (GSDMD) protein, releasing its N-terminal fragment (GSDMD-N). This fragment translocates to the cell membrane and forms

pores, leading to changes in osmotic pressure, cellular swelling, and ultimately pyroptosis [15-16]. Pyroptosis is a type of inflammatory programmed cell death that occurs accompanied by the release of large amounts of pro-inflammatory factors, further amplifying the inflammatory cascade.

In recent years, research on the NLRP3/Caspase-1 signaling pathway has been extended to various disease models, demonstrating its critical role in multiple inflammation-related disorders including osteoarthritis [18-20], neuroinflammation [21-22], lung injury [23], intestinal inflammation [24-25], rheumatoid arthritis [26], sepsis [27], atherosclerosis [28-30], and myocardial infarction [31-34]. These studies further confirm the universality and significance of the NLRP3/Caspase-1 pathway in inflammation-mediated diseases, providing a systematic reference framework for understanding its specific regulatory mechanisms in coronary heart disease (CHD) and developing traditional Chinese medicine intervention strategies.

3. Role of NLRP3/Caspase-1 Signaling Pathway in Coronary Heart Disease

3.1 Endothelial Dysfunction

Vascular endothelial cells, as the innermost layer of the vascular wall, serve as a barrier for maintaining vascular homeostasis. Endothelial dysfunction is the primary step in the pathogenesis of atherosclerosis, manifesting as increased vascular permeability, upregulated expression of adhesion molecules, enhanced release of pro-inflammatory factors, and impaired vasodilatory function [35]. Activation of the NLRP3/Caspase-1 signaling pathway is a critical mechanism underlying endothelial dysfunction. In coronary heart disease (CHD), oxidative low-density lipoprotein (ox-LDL), endotoxin (LPS), and reactive oxygen species (ROS) can activate NLRP3 inflammasomes in endothelial cells, inducing Caspase-1 activation. Studies have demonstrated [36] that ox-LDL can induce pyroptosis in endothelial cells by activating the NLRP3/Caspase-1 pathway, exacerbating endothelial injury and inflammatory responses. Endothelial pyroptosis leads to cell membrane rupture, releasing damage-associated molecular patterns (DAMPs) and pro-inflammatory cytokines, thereby creating a vicious cycle that continuously impairs endothelial barrier function. Additionally, luteolin inhibits the NLRP3/Caspase-1 signaling pathway to ameliorate LPS+ATP-induced endothelial inflammatory responses and pyroptosis, further confirming the central role of this pathway in endothelial dysfunction [37]. Ubiquitin-specific protease 14 (USP14) stabilizes NLRP3 protein expression through deubiquitination, promoting CHD-induced endothelial pyroptosis [38], providing novel insights into the regulatory mechanisms of endothelial pyroptosis. Therefore, these studies have emphasized the central role of the NLRP3/Caspase-1 pathway in endothelial cell dysfunction, where its activation can lead to endothelial cell inflammation, injury, and pyroptosis, thereby promoting the occurrence and progression of atherosclerosis. Consequently, targeted inhibition of the NLRP3/Caspase-1 pathway holds promise as a critical strategy for protecting endothelial function and preventing or treating coronary heart disease (CHD).

3.2 Macrophage Polarization and Foam Formation

Macrophage polarization is closely associated with atherosclerosis. The M1-type pro-inflammatory macrophage-dominated inflammatory response accelerates plaque formation, whereas M2-type anti-inflammatory macrophages promote tissue repair and exhibit anti-inflammatory effects. During the pathogenesis of atherosclerosis, macrophages typically exhibit M1 polarization and phagocytose lipids to form foam cells, which are characteristic features of early atherosclerotic plaque lesions [39]. Activation of the NLRP3/Caspase-1 signaling pathway plays a critical regulatory role in M1-type macrophage polarization and foam cell formation. When

macrophages are exposed to atherosclerosis-related stimuli such as ox-LDL, cholesterol crystals, and LPS, NLRP3 inflammasomes are activated. Activated Caspase-1 not only promotes the release of pro-inflammatory cytokines IL-1β and IL-18, which further drive macrophage M1 polarization and exacerbate local inflammatory responses, but also induces macrophage pyroptosis. Macrophage pyroptosis leads to cell membrane rupture, releasing intracellular contents including lipids, DAMPs, and pro-inflammatory cytokines, which further stimulate surrounding cells and accelerate plaque progression and instability. Studies have demonstrated [40] that Qingxin Jieyu Formula inhibits NLRP3 inflammasome activation, modulates macrophage pyroptosis, and reduces the release of pro-inflammatory cytokines IL-1β and IL-18, thereby effectively exerting anti-inflammatory effects and stabilizing vulnerable atherosclerotic plaques. Furthermore, histone H3 citrullination (CitH3) released by neutrophil extracellular traps (NETs) can activate macrophage NLRP3 inflammatory bodies, promoting caspase-1-dependent pyroptosis and mature secretion of IL-1β, thereby exacerbating plaque instability. Regulation of the CitH3/NLRP3/Caspase-1 signaling axis can suppress NETs-mediated foam cell inflammation and reduce inflammatory responses within atherosclerotic plaques [28]. Additionally, cordycepin significantly inhibits macrophage pyroptosis and foam formation by negatively regulating the expression of key molecules in the NLRP3/Caspase-1/GSDMD pathway [41], effectively reducing lipid deposition and plaque burden. In summary, the NLRP3/Caspase-1 signaling pathway plays a critical role in macrophage polarization, foam cell formation, and subsequent pyroptosis, with its activation serving as a major driver of atherosclerotic progression and plaque instability. Therefore, modulating the NLRP3/Caspase-1 pathway to inhibit abnormal macrophage activation and pyroptosis represents an important strategy for the prevention and treatment of coronary heart disease.

3.3 Pyroptosis of Cells

Cell pyroptosis is a highly inflammatory form of programmed cell death characterized by cellular swelling, membrane rupture, and release of pro-inflammatory factors IL-1β and IL-18 [12,15]. In coronary heart disease (CHD), the occurrence of cell pyroptosis has been demonstrated to be closely associated with multiple pathological processes such as myocardial ischemia-reperfusion injury, atherosclerosis, and heart failure, with its core mechanism involving abnormal activation of the NLRP3/Caspase-1 signaling pathway. In myocardial ischemia-reperfusion injury (MIRI), the burst of oxygen free radicals after reperfusion, ATP release, and initiation of inflammatory responses can activate NLRP3 inflammatory bodies in cardiomyocytes and infiltrating immune cells, thereby inducing Caspase-1 activation and cell pyroptosis. Tongxinluo alleviates MIRI by inhibiting endothelial cell pyroptosis, with its mechanism involving the NLRP3/Caspase-1/GSDMD signaling pathway [32]. Jinxiangdan mitigates MIRI in rats by suppressing the NLRP3/IL-1β/Caspase-1 signaling pathway activity [42]. Lingbao Huxindan reduces myocardial injury in rats with myocardial infarction, likely through modulation of the NLRP3/Caspase-1 cell pyroptosis signaling pathway [31]. These studies collectively indicate that NLRP3/Caspase-1 pathway-mediated cell pyroptosis is the primary pathological mechanism in MIRI. In atherosclerosis, pyroptosis of macrophages, endothelial cells, and vascular smooth muscle cells significantly influences plaque formation and instability. As previously mentioned, H2S inhibits ox-LDL-induced macrophage pyroptosis through S-thiohydrogenation of Caspase-1, thereby alleviating atherosclerosis [16]. The NETs-mediated foam cell inflammation can be suppressed via the CitH3/NLRP3/Caspase-1 signaling pathway [28]. Vascular smooth muscle cells (VSMCs) are one of the primary effector cell types in atherosclerotic

plaques. After calcification, VSMCs transition from a contractile phenotype to a synthetic phenotype and are prone to pyroptosis, further promoting plaque calcification and instability [43]. Additionally, pyroptosis plays a significant role in heart failure. Pyroptosis induces myocardial injury, fibrosis, and dysfunction through the release of pro-inflammatory cytokines and cell death, exacerbating ventricular remodeling and worsening heart failure [44]. Multiple studies have confirmed [45-47] that inhibiting the activation of the NLRP3/Caspase-1 signaling pathway effectively blocks downstream inflammatory cascades, reduces cardiomyocyte pyroptotic damage, and improves cardiac function. In summary, NLRP3/Caspase-1 pathway-mediated pyroptosis is a core component in the pathophysiological processes of coronary heart disease (CHD). This mechanism contributes to and exacerbates the development of atherosclerosis, myocardial ischemia-reperfusion injury, and heart failure. Specific blockade of NLRP3/Caspase-1 pathway activation can effectively inhibit pyroptosis and related inflammatory responses, offering potential therapeutic targets and novel strategies for CHD clinical intervention.

4. Traditional Chinese Medicine Regulates NLRP3/Caspase-1 Signaling Pathway for the Treatment of Coronary Heart Disease

4.1 Monomeric Chinese Medicinal Herbs and Their Active Components

Extensive studies have confirmed that traditional Chinese medicine extracts can treat CHD through multiple pathways including anti-inflammatory, antioxidant, and anti-cytokinesis effects. Quercetin, a common flavonoid compound, was identified as the primary component in the mechanism study of Simiao Yong'an Decoction for CHD treatment. Its anti-inflammatory effects have been widely validated, with quercetin inhibiting LPS-and ATP-stimulated fibroblast pyroptosis via suppression of the NLRP3/Caspase-1/GSDMD pathway, thereby reducing inflammatory cytokine secretion [48]. In ApoE gene knockout mouse models, baicalin effectively suppressed inflammatory responses within atherosclerotic plaques and alleviated vascular endothelial injury by lowering mRNA levels of NLRP3 and Caspase-1, as well as downstream IL-1β and IL-18 secretion [49]. Network pharmacology and experimental validation studies [50] demonstrated that isorhamnetin, the active component of Astragalus-Safflower Mixture, can target NLRP3 and Caspase-1, downregulating levels of NLRP3, Caspase-1, GSDMD, and IL-1β to inhibit the NLRP3 inflammatory small body pathway, thereby exerting cardioprotective effects against CHD. Tanshinone II A inhibits nuclear translocation of the NF-κB signaling pathway, blocking the "initiation" stage of NLRP3 inflammatory small bodies. This significantly reduces protein expression of NLRP3, ASC, and Caspase-1 in rat myocardial tissue and decreases release of downstream inflammatory cytokines IL-1β and IL-18, effectively mitigating plaque instability in atherosclerosis [51]. Dihydrodanshentone has also been demonstrated to exert protective effects against myocardial ischemia-reperfusion injury, significantly ameliorating myocardial cell damage and reducing NLRP3/Caspase-1 signaling pathway activity [34]. Isotriptolide, an alkaloid extracted from Uncaria, has been found to inhibit inflammatory responses in endothelial cells and macrophages via the NF-κB/NLRP3 signaling pathway. Studies in atherosclerosis models revealed that isotriptolide reduces the expression of NLRP3, NF-κB, IL-18, and Caspase-1 while promoting cell migration, suggesting its mechanism of alleviating vascular inflammation and atherosclerosis progression by suppressing NLRP3 inflammasome activation [30]. Colchicine has also been shown to decrease NLRP3 inflammasome activation levels, thereby delaying atherosclerotic progression in coronary heart disease (CHD) [52]. Paeonol effectively inhibits NETs-mediated foam cell

inflammatory damage by modulating the CitH3/NLRP3/Caspase-1 signaling pathway, elucidating its anti-inflammatory mechanisms in atherosclerosis prevention and treatment [28]. Additionally, extracellular vesicles extracted from Trichosanthes kirilowii can inhibit NLRP3 inflammasome activation, improve vascular endothelial function, and reduce atherosclerotic plaque formation [53], providing novel therapeutic insights for coronary heart disease management.

4.2 Traditional Chinese Medicine Compound

Traditional Chinese medicine (TCM) compound prescriptions represent the primary clinical application form of TCM, characterized by multi-component composition, multi-target effects, and synergistic enhancement. Numerous TCM compound prescriptions have been found to modulate the NLRP3/Caspase-1 signaling pathway for the treatment of coronary heart disease (CHD). Danshen Zaoxin Tea, composed of Salvia miltiorrhiza and green tea, exhibits blood-activating and stasis-resolving properties and is commonly used in the prevention and treatment of coronary heart disease. Studies have demonstrated [54] that Danshen Zaoxin Tea can reduce serum levels of NLRP3, Caspase-1, and IL-1β in model mice, significantly inhibit the activation of NLRP3 inflammatory bodies, thereby improving cardiac function and emotional behavior in CHD mice with comorbid depression. Modified Wenden Decoction possesses qi-regulating, phlegm-resolving, blood-activating, and stasis-resolving effects. It can modulate the NLRP3/Caspase-1 signaling pathway, reduce protein expression of NLRP3, Caspase-1, and IL-1β in endothelial cell injury, thereby alleviating vascular inflammatory responses, inhibiting cell pyroptosis, and ameliorating the pathological state of phlegm-stasis interconnection syndrome in CHD patients [55]. Danlou Tablets are derived from the TCM prescription "Guallou Xiebai Banxia Decoction" recorded in "Jingui Yaolue". Research has confirmed that Danlou Tablets can inhibit the initiation and activation process of NLRP3 inflammatory bodies, reduce Caspase-1 activation, mitigate myocardial inflammatory damage, and improve cardiac function in CHD rats [56]. Additionally, Tongxinluo Capsules, a widely used Chinese patent medicine for coronary heart disease treatment, can reduce myocardial ischemia-reperfusion injury by inhibiting endothelial cell pyroptosis, with mechanisms involving the NLRP3/Caspase-1/GSDMD signaling pathway. This study identified 40 key targets through network pharmacology, confirming that Tongxinluo can improve cardiac function, reduce myocardial enzymes and inflammatory markers, downregulate pyroptosis-related factors, and protect microcirculatory barrier integrity [32]. Relevant clinical reviews also indicate that Tongxinluo Capsules demonstrated efficacy and good tolerability in clinical trials for coronary heart disease [57]. Linggui Zhugan Decoction inhibits cardiomyocyte pyroptosis by suppressing the NLRP3/Caspase-1 signaling pathway. Studies show [58] that this formula significantly reduces apoptosis rates, inhibits pyroptosis, and decreases mRNA and protein expression levels of NLRP3, ASC, Caspase-1, and GSDMD, suggesting that Linggui Zhugan Decoction exerts cardioprotective effects by regulating the NLRP3/Caspase-1 pathway. Research has confirmed [31] that Lingbao Huxin Dan alleviates myocardial injury in rats with myocardial infarction (MI), reducing infarct size, inflammatory responses, myocardial ischemia, serum IL-1β and IL-18 levels, as well as NLRP3 and Caspase-1 levels in myocardial tissue. This indicates that Lingbao Huxin Dan mitigates myocardial injury by inhibiting the NLRP3/Caspase-1 cell pyroptosis signaling pathway.

5. Brief summary

As a common cardiovascular disease, CHD has a complex pathogenesis involving the regulation of multiple signaling pathways. Recent studies have demonstrated that the NLRP3/Caspase-1

signaling axis plays a significant role in the pathophysiology of CHD. This pathway influences processes such as cardiomyocyte pyroptosis and inflammatory responses by modulating the levels of NLRP3, Caspase-1, IL-1β, and IL-18, representing one of the key molecular mechanisms in the development and progression of CHD. This article systematically reviews how various monomers and compound formulations of traditional Chinese medicine can inhibit the NLRP3/Caspase-1 signaling pathway, thereby reducing cardiomyocyte pyroptosis and inflammatory responses, and improving cardiac function. Based on these findings, targeted modulation of this signaling pathway has become an important therapeutic approach in traditional Chinese medicine for CHD intervention.

Traditional Chinese Medicine (TCM) intervenes in coronary heart disease (CHD) by regulating the NLRP3/Caspase-1 signaling pathway, which not only provides new theoretical support for TCM treatment of CHD but also offers scientific basis and direction for novel drug development. By deeply elucidating the interaction mechanisms between active components of Chinese herbal medicines and NLRP3 inflammasomes as well as their downstream molecules, it is expected to enhance drug targeting affinity and bioavailability, thereby developing more efficient and low-toxicity anti-CHD drugs and promoting the application of TCM in CHD treatment. Current research is primarily limited to cellular models and animal experiments, and future studies urgently need to extend to clinical applications, evaluating the clinical efficacy and safety of TCM in modulating the NLRP3/Caspase-1 pathway in CHD patients, exploring the value of relevant biomarkers in clinical diagnosis and prognosis assessment, and integrating genomic and metabolomic data to investigate activation characteristics of the NLRP3/Caspase-1 pathway in patients with different TCM syndromes. These efforts aim to guide precision individualized TCM therapy and advance the modernization and sustainable development of TCM in CHD prevention and treatment.

References

[1] Libby P, Theroux P. Pathophysiology of coronary artery disease. Circulation. 2005. 111(25): 3481-3488.

[2] Collaborators GBoCDaR2. Global, Regional, and National Burden of Cardiovascular Diseases and Risk Factors in 204 Countries and Territories, 1990-2023. J Am Coll Cardiol. 2025. 86(22): 2167-2243.

[3] Liu M, He X, Yang X, Wang Z. 2024 annual report on cardiovascular health and diseases in China: Data and trend. Chin Med J (Engl). 2025. 138(23): 3037-3049.

[4] Tao S, Tang X, Yu L, et al. Prognosis of coronary heart disease after percutaneous coronary intervention: a bibliometric analysis over the period 2004-2022. Eur J Med Res. 2023. 28(1): 311.

[5] RASHEDI S, KEYKHAEI M, SATO A, et al. Anticoagulation and Antiplatelet Therapy for Atrial Fibrillation and Stable Coronary Disease: Meta-Analysis of Randomized Trials[J]. J Am Coll Cardiol, 2025,85(11):1189-1203.

[6] Zhang Yu, Li Yuqi, Ding Qi, et al. Research progress on the treatment of unstable angina pectoris with coronary heart disease using traditional Chinese medicine [J]. Journal of Modern Integrated Traditional Chinese and Western Medicine, 2025,34(07):1013-1017.

[7] ATTIQ A, AFZAL S, AHMAD W, et al. Hegemony of inflammation in atherosclerosis and coronary artery disease[J]. Eur J Pharmacol, 2024,966:176338.

[8] LIBBY P, SOEHNLEIN O. Inflammation in atherosclerosis: Lessons and therapeutic implications[J]. Immunity, 2025,58(10):2383-2401.

[9] XING Y, LIN X. Challenges and advances in the management of inflammation in atherosclerosis[J]. J Adv Res, 2025, 71:317-335.

[10] AJOOLABADY A, PRATICO D, LIN L,et al. Inflammation in atherosclerosis: pathophysiology and mechanisms[J]. Cell Death Dis, 2024,15(11):817.

[11] GUO X, FENG X, YANG Y, et al. Spermidine attenuates chondrocyte inflammation and cellular pyroptosis through the AhR/NF-κB axis and the NLRP3/caspase-1/GSDMD pathway[J]. Front Immunol, 2024,15:1462777.

[12] Pan Xubiao, Li Xiangyu, Wang Zhixin, et al. Research progress on the NLRP3-(Caspase-1)/IL-1β signaling pathway [J]. China Medical Guide, 2019,16(01):41-44.

[13] STARK K, MASSBERG S. Interplay between inflammation and thrombosis in cardiovascular pathology[J]. Nat

Rev Cardiol, 2021,18(9):666-682.
[14] CHEN Y, YE X, ESCAMES G, et al. The NLRP3 inflammasome: contributions to inflammation-related diseases[J]. Cell Mol Biol Lett, 2023,28(1):51.
[15] WU Q, YANG H, ZHANG H, et al. IP3R2-mediated Ca2+ release promotes LPS-induced cardiomyocyte pyroptosis via the activation of NLRP3/Caspase-1/GSDMD pathway[J]. Cell Death Discov, 2024,10(1):91.
[16] JIA Z, ZHANG X, LI Z, et al. Hydrogen sulfide mitigates ox-LDL-induced NLRP3/caspase-1/GSDMD dependent macrophage pyroptosis by S-sulfhydrating caspase-1[J]. Mol Med Rep, 2024,30(2)
[17] KODI T, SANKHE R, GOPINATHAN A, et al. New Insights on NLRP3 Inflammasome: Mechanisms of Activation, Inhibition, and Epigenetic Regulation[J]. J Neuroimmune Pharmacol, 2024,19(1):7.
[18] LV J, MUHAMMAD F, WANG Z, et al. Defective RuO(2) Nanospheres Attenuate Osteoarthritis Progression via Suppressing the ROS/NLRP3/Caspase-1 Signaling Pathway[J]. ACS Nano, 2025,19(25):23080-23095.
[19] Cui Xinyu, Li Haolin, Li Weiqing, et al. Effects of Yiqi Juanbi Formula on pyroptosis of chondrocytes in collagen-induced arthritis rats via NF-κB/NLRP3/Caspase-1 signaling pathway[J]. Chinese Patent Medicine, 2025,47(09):2880-2887.
[20] Cai M, Zhang YN. Effects of Panax notoginseng total saponins on pyroptosis of chondrocytes in osteoarthritis rats through regulation of TLR4/NLRP3/Caspase-1 signaling pathway [J]. Chinese Journal of Traditional Medicine Information, 2023,40(02):11-17.
[21] LIU S, SONG X, SUN Y, et al. Kai-Xin-San ameliorates mild cognitive impairment in SAMP8 mice by inhibiting neuroinflammation and pyroptosis via NLRP3/Caspase-1 pathway modulation[J]. Front Pharmacol, 2025,16:1528011.
[22] SHUAIHUI Q, QIQI Y, JUN Y, et al. Effects of Huayu Tongluo moxibustion on learning and memory ability and neuronal injury in the hippocampal CA1 region in vascular dementia rats via the NLRP3/Caspase-1/GSDMD signaling pathway[J]. Chinese Acupuncture and Moxibustion, 2025,45(11):1591-1599.
[23] Xie Xiaofang, Zhao Zhanqing, Fu Meichui. Effect of ligustrazine on pyroptosis in sepsis-induced lung injury rats by regulating NLRP3/Caspase-1 signaling pathway [J]. China Journal of Pharmacy, 2023,58(19):1744-1751.
[24] Zhao Guanyu, Xin Ruihua, Qiu Zhengying, et al. Mechanism of Wumei Pill-induced pyroptosis in colonic epithelial cells of ulcerative colitis mice based on NLRP3/Caspase-1/GSDMD signaling pathway[J]. Chinese Herbal Medicine, 2023,54(24):8086-8093.
[25] Zhao Zhuo. Effects of Banxia Xiexin Decoction on inflammatory responses in ulcerative colitis rats via the NLRP3/Caspase-1 pyroptosis signaling pathway [D]. Shenyang: Liaoning University of Traditional Chinese Medicine, 2024.
[26] MA X, YANG Y, LI H, et al. Periplogenin inhibits pyroptosis of fibroblastic synoviocytes in rheumatoid arthritis through the NLRP3/Caspase-1/GSDMD signaling pathway[J]. Int Immunopharmacol, 2024,133:112041.
[27] LI H, LI X, XU G, et al. Minocycline alleviates lipopolysaccharide-induced cardiotoxicity by suppressing the NLRP3/Caspase-1 signaling pathway[J]. Sci Rep, 2024,14(1):21180.
[28] MA X, ZHAO X, YANG Y, et al. Paeonol inhibits NETs-mediated foam cell inflammation through the CitH3/NLRP3/caspase-1 signaling pathway in atherosclerosis[J]. Int Immunopharmacol, 2025,151:114340.
[29] HOU C, JIANG X, SHENG W, et al. Xinmaikang (XMK) tablets alleviate atherosclerosis by regulating the SREBP2-mediated NLRP3/ASC/Caspase-1 signaling pathway[J]. J Ethnopharmacol, 2024,319(Pt 2):117240.
[30] WANG L H, GU Z W, LI J, et al. Isorhynchophylline inhibits inflammatory responses in endothelial cells and macrophages through the NF-κB/NLRP3 signaling pathway[J]. BMC Complement Med Ther, 2023,23(1):80.
[31] Tan Yu, Chai Hua, Ma Xiaojuan. Effect of Lingbao Huxindan on the pyroptosis signaling pathway of NLRP3/Caspase-1 in myocardial tissue of myocardial infarction rats [J]. China Journal of Integrated Traditional and Western Medicine, 2023,43(01):90-96.
[32] XUAN W, YUN-LONG H, TONG-XING W, et al. Tongxinluo alleviates myocardial ischemia-reperfusion injury by inhibiting the pyroptosis of endothelial cells via the NLRP3/Caspase-1/GSDMD signaling pathway[J]. J Mol Histol, 2025,56(5):302.
[33] CHAI R, YE Z, XUE W, et al. Tanshinone IIA inhibits cardiomyocyte pyroptosis through TLR4/NF-κB p65 pathway after acute myocardial infarction[J]. Front Cell Dev Biol, 2023,11:1252942.
[34] Ji Chengfeng, Wang Chen, Zhang Hexiang, et al. Protective effect of dihydrodanshenone on myocardial ischemia-reperfusion injury in cardiomyocytes [J]. Northwest Journal of Pharmacy, 2023,38(06):77-82.
[35] XU S, ILYAS I, LITTLE P J, et al. Endothelial Dysfunction in Atherosclerotic Cardiovascular Diseases and Beyond: From Mechanism to Pharmacotherapies[J]. Pharmacol Rev, 2021,73(3):924-967.
[36] He Tingting, Zhang Xulin, Jia Zhenli, et al. Hydrogen sulfide inhibits pyroptosis of vascular endothelial cells induced by oxidized low-density lipoprotein by downregulating the NLRP3/caspase-1 signaling pathway [J]. China Journal of Pathophysiology, 2021,37(10):1738-1746.
[37] Yang Jiale, Shen Xiangchun. Luteolin improves LPS+ATP-induced inflammatory response and pyroptosis in endothelial cells by inhibiting the NLRP3/caspase-1 signaling pathway [J]. China Pharmacological Bulletin, 2022, 38(08):1196-1201.

[38] GAO J, GAO Z. The regulatory role and mechanism of USP14 in endothelial cell pyroptosis induced by coronary heart disease[J]. Clin Hemorheol Microcirc, 2024,86(4):495-508.
[39] WU J, HE S, SONG Z, et al. Macrophage polarization states in atherosclerosis[J]. Front Immunol, 2023,14: 1185587.
[40] Song Luxia. Mechanistic study on Qingxin Jieyu Formula regulating macrophage polarization to stabilize atherosclerotic vulnerable plaques [D]. Beijing: Beijing University of Chinese Medicine, 2024.
[41] LIU Z, LV L, WEI J, et al. Cordycepin attenuates NLRP3/Caspase-1/GSDMD-mediated LPS-induced macrophage pyroptosis[J]. Front Pharmacol, 2025,16:1526616.
[42] Xiao Min, Xiang Jingjing, Wang Wei, et al. Jinxiangdan inhibits the NLRP3/IL-1β/Caspase-1 signaling pathway to alleviate myocardial ischemia-reperfusion injury in rats [J]. China Journal of Experimental Formulary Science, 2021,27(20):87-94.
[43] Li SH, Li QJ, Zhou C, et al. Resveratrol regulates pyroptosis of vascular smooth muscle cells mediated by NLRP3 inflammasome to combat atherosclerosis [J]. Drug Evaluation Research, 2022,45(10):1972-1979.
[44] QIN J, YANG Q, WANG Y, et al. The role of pyroptosis in heart failure and related traditional chinese medicine treatments[J]. Front Pharmacol, 2024,15:1377359.
[45] Fan Xingyu, Liao Xiaoqian, Huang Shumin, et al. Exploring the regulation of cellular pyroptosis by Shenfu Injection on chronic heart failure based on the NLRP3/caspase-1 pathway [J]. China Journal of Traditional Chinese Medicine, 2023,48(23):6475-6482.
[46] Liang Guoqing, Xia Ran, Wang Yinyan, et al. Effects of Shenqi Jianxin Formula on pyroptosis in cardiomyocytes of chronic heart failure model rats based on the NLRP3/Caspase-1 signaling pathway[J]. Chinese Journal of Traditional Chinese Medicine, 2024,65(01):94-102.
[47] ZHANG L, LI Y, FAN C D, et al. Chinese medicinal formula Fu Xin decoction against chronic heart failure by inhibiting the NLRP3/caspase-1/GSDMD pyroptotic pathway[J]. Biomed Pharmacother, 2024,174:116548.
[48] ZHANG J, XUE S, CHEN H, et al. Exploring the Mechanism of Si-miao-yong-an Decoction in the Treatment of Coronary Heart Disease based on Network Pharmacology and Experimental Verification[J]. Comb Chem High Throughput Screen, 2024,27(1):57-68.
[49] ZHAO J, WANG Z, YUAN Z, et al. Baicalin ameliorates atherosclerosis by inhibiting NLRP3 inflammasome in apolipoprotein E-deficient mice[J]. Diab Vasc Dis Res, 2020,17(6):1479164120977441.
[50] YUAN Y, LIU H, MENG Q. The Cardioprotective Effects and Mechanisms of Astragalus-Safflower Herb Pairs on Coronary Heart Disease Identified by Network Pharmacology and Experimental Verification[J]. Front Biosci (Landmark Ed), 2023,28(5):94.
[51] WEN J, CHANG Y, HUO S, et al. Tanshinone IIA attenuates atherosclerosis via inhibiting NLRP3 inflammasome activation[J]. Aging (Albany NY), 2020,13(1):910-932.
[52] SILVIS M J M, FIOLET A T L, OPSTAL T S J, et al. Colchicine reduces extracellular vesicle NLRP3 inflammasome protein levels in chronic coronary disease: A LoDoCo2 biomarker substudy[J]. Atherosclerosis, 2021, 334: 93-100.
[53] Chen Yulin, He Yingying, Hu Kai, et al. Effects and mechanisms of Trichosanthes seed exosome vesicles in preventing and treating atherosclerosis [J]. China Tissue Engineering Research, 2026,30(07):1768-1781.
[54] Zhao D, Huang Y, Chen Wenxuan, et al. Exploring the mechanism of Danzhuanshuan Tea on coronary heart disease complicated with depression in mice based on network pharmacology and NLRP3 inflammatory pathway[J]. Chinese Journal of New Drugs and Clinical Pharmacology, 2024,35(10):1552-1561.
[55] Chang Yanbin, Li Yan, Zhang Lili, et al. Study on the mechanism of modified Wenden Decoction inhibiting NLRP3-mediated pyroptosis of endothelial cells in preventing coronary heart disease with phlegm-stasis syndrome [J]. Journal of Modern Integrated Traditional Chinese and Western Medicine, 2022,31(20):2808-2812+2905.
[56] 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[J]. Phytomedicine, 2024,131:155773.
[57] WANG J, LI T L, CHANG P F, et al. Clinical effects and mechanisms of a Chinese patent medicine, Tongxinluo capsule, as an adjuvant treatment in coronary heart disease[J]. Heliyon, 2024,10(6):e27460.
[58] ZHAO X, DING H, MA Y, et al. Ling-Gui-Zhu-Gan decoction inhibits cardiomyocyte pyroptosis via the NLRP3/Caspase-1 signaling pathway[J]. Tissue Cell, 2024,91:102588.