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Review

A Review on the Role of Plant-Based Natural Antioxidant Metabolites in Oxidative Stress-Associated Myocardial Infarction: SAR Based Mechanistic Insights

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Abstract

Myocardial infarction (MI) has become one of the leading causes of mortality worldwide, and the prevalence is anticipated to rise considerably in the coming years. Among non-surgical procedures, chemical drugs, including diuretics, vasodilators, calcium channel blockers, β blockers, angiotensin converting enzyme inhibitors, are now in use to treat MI progression. These drugs often cause side effects and do not focus on mitigating oxidative stress, which has been recently proven to contribute to MI advancement. Naturally occurring antioxidant compounds, on the other hand, are safe, effective due to their multiple molecular targets, and have the potential to be used as lead compounds for finding novel drugs to therapeutically manage MI. Some of them, namely quercetin, puerarin, α-lipoic acid, and curcumin, have already made their way up to clinical trials. To develop and formulate natural antioxidant compounds as drugs against MI, it is crucial to comprehend their underlying mechanisms of cardio-protective activities and structure-activity relationships. This comprehensive review sheds light on the contribution of oxidative stress in the pathogenesis and progression of Myocardial Infarction, and highlights the cardio-protective roles of 51 natural antioxidant compounds along with their mechanistic insights and structure-activity relationships.

Keywords: myocardial infarction; reactive oxygen species; oxidative stress; antioxidant; phytochemicals; structure activity-relationship

1. Introduction

Myocardial infarction (MI) is a common clinical condition in cardiovascular diseases (CVDs) affecting cardiac tissues and ultimately leading to their necrosis due to blood perfusion arrest, failure in supplying oxygen and nutrients, and toxic substance accumulation (Frangogiannis, 2015; Fuentes et al., 2019). It is categorized into distinct classes based on pathological, clinical, and prognostic characteristics, as well as treatment options, such as type 1, type 2, type 3, type 4, and type 5 (Thygesen et al., 2018). Type 1 MI results from atherothrombotic coronary artery disease (CAD) (Thygesen et al., 2018), whereas Type 2 myocardial infarction (T2MI) occurs when the heart's demand for oxygen or supply of oxygen rises without a sudden disruption in atherothrombotic plaque (Sandoval & Jaffe, 2019). In type 2 myocardial infarction, the metabolic needs of myocardial cells are also greater than the amount of oxygen in blood (Musher et al., 2019). Although Type 3 MI is rare (as reflected by a study that found an annual incidence below 10 cases per 100,000 persons and a

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frequency of 3% to 4% among all MI types), it frequently causes sudden death even prior to the obtaining of biomarkers or ECG confirmation (Anderson & Morrow, 2017; Thygesen et al., 2018). Among other types, type 4 MI results from PCI (percutaneous coronary intervention) procedure and thrombosis of a coronary stent, while Type 5 MI is caused by coronary artery bypass grafting (CABG) (Anderson & Morrow, 2017) .

A key pathological hallmark of MI is oxidative stress, which describes a condition in which there is a mismatch between oxidants and antioxidants in the body (Navarro-Yepes et al., 2014). Oxidative stress is caused by an imbalance between the production of reactive oxygen and nitrogen species (ROS/RNS) and the amounts of enzymatic and non-enzymatic antioxidants. ROS and RNS are the two primary classes of free radicals involved in cellular redox signaling processes (Tern et al., 2021). Oxidative stress (OxS) and molecular damage are mainly caused by the overabundance of these free radicals, which are also the two most significant prooxidants. While the ROS encompass superoxide anion, hydroxyl radicals, and hydrogen peroxide, members of the RNS family include peroxynitrite and nitrosoperoxycarbonate. Peroxynitrite develops due to the reaction between superoxide and nitric oxide (NO), whereas nitrosoperoxycarbonate is created when peroxynitrite reacts with carbon dioxide (Chowdhury et al., 2015). Even though ROS play physiological roles possibly by controlling cardiomyocyte survival and death, their uncontrolled abundance deteriorates cardiac pathological conditions by inducing oxidative stress (Wu & Liu, 2022).

To defend against oxidative stress, which damages every component of the cell, cells depend mostly on antioxidant enzymes and non-enzymatic antioxidants, among others (Gulcin, 2025; Kozlov et al., 2024). Antioxidant enzymes, also termed as metalloproteins, fall under the class of proteins that catalyze the conversion of reactive oxygen species (ROS) and possibly their byproducts into more stable, generally less hazardous species. In pathological conditions like MI, where endogenous defenses are inadequate, there is a therapeutic need for exogenous antioxidants, and plant-produced natural antioxidants, including flavonoids, phenolics, and polyphenolics (hydrolysable and condensed tannins), have this therapeutic potential as they have been shown to prevent reactive oxygen species-induced oxidative stress (Thygesen et al., 2018). These natural bioactive compounds may lower oxidative stress in humans by getting rid of free radicals, slowing down lipid peroxidation, and stopping nitrosation reactions (Smit et al., 2020). In order to eliminate the free radicals that are produced as a byproduct of oxidative metabolism and to keep the redox balance in its proper place, natural antioxidants can work either independently or in conjunction with one another. Although current medications for treating MI include chemical drugs, their side effects on prolonged use and lack of ability to deal with the deeper root causes render the treatment less effective. Natural bioactive compounds, on the other hand, provide a safe, multi-targeted strategy. Therefore, scientific interest has grown in these compounds for developing safer and more effective drugs to fight the war against MI.

To enhance the understanding and optimization of these natural antioxidant compounds, it is imperative to study their SAR or structure-activity relationship. SAR unveils the impact of the structure of the molecule on its therapeutic activity. For example, the quantity and location of hydroxyl groups in flavonoids determine their ability to scavenge radicals, and the conjugated double bonds in carotenoids enable them to be better at quenching singlet oxygen. Moreover, during the journey of drug discovery, phytochemicals have to undergo critical scrutiny to be developed as valid therapeutic agents for MI. Such scrutiny looks at their structural attributes, SAR, and underlying mechanism of action to make sure that they are safe and effective. Thus, insights from SAR and mechanistic studies help promote potential compounds to clinical use from preliminary studies. Although there are mounting scientific data regarding the cardio-protective activity of these natural bioactive compounds, there is still a dearth of systematic investigations that link SAR to their cardio-protective action pathway in MI. To address this gap, this review aims to provide a concise summary of the role of oxidative stress in the development and progression of MI, highlight the identified natural antioxidant compounds that alleviate MI and its associated complications, and finally explore

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the SAR of some of the most promising compounds to understand how their structural features contribute to their cardio-protective activity.

2. Method

In order to garner relevant literature, well-known scientific databases, including Google Scholar, Springer Link, Science Direct, PubMed, Scopus, Web of Science, and the Wiley Online Library, were accessed. The search procedure was led by writing specific keywords such as “myocardial infarction”, “oxidative stress in myocardial infarction”, “natural antioxidant compounds”, “structure-activity relationship”, and “myocardial infarction mechanism”. Only publications published in the English language were considered, as articles in other languages could not be evaluated due to linguistic constraints. This review covered research studies on the following topics: association of oxidative stress with myocardial infarction, plant-derived anti-oxidant compounds with cardio-protective effects to alleviate MI, along with their underlying mechanisms of effects, and their SAR that contributes to these activities.

3. Oxidative Stress in MI Development

Free radicals are regarded as reactive chemical species that possess a single unpaired electron in the outermost orbital (Chandimali et al., 2025; Riley, 1994). They are capable of either donating or accepting electron species, therefore can act as both oxidant and reductant (Chaudhary et al., 2023; Cheeseman & Slater, 1993). The odd-numbered radical attacks molecules in its vicinity in order to attain stability. As a result, the attacked molecule loses its electron and converts into a radical family, initiating a reaction cascade that ultimately leads to cell death. The majority of free radicals that are engaged in impairing the biological system are known as oxygen free radicals; more particularly, “Reactive Oxygen Species” (ROS). These ROS induces myocardial damage during ischemia or reperfusion (G. Gong et al., 2025). Free radicals have been proven both deleterious and beneficial for the biological system. On the one side, at low concentrations, they are required for the maturation of cellular structures and the regulation of the host defense mechanism. Free radicals are released by the body’s phagocytes (neutrophils, macrophages, monocytes) and aid in destroying and invading pathogenic agents. The production of ROS and RNS by non-phagocytic NADPH oxidase isoforms plays a vital role in modulating intracellular signaling cascades in various types of cells, including fibroblasts, vascular smooth muscle cells, endothelial cells, cardiac myocytes, and thyroid cells. Free radical nitric oxides and superoxide play a significant role in the biological regulatory system. Nitric oxide radical is a crucial intracellular messenger for regulating blood flow, thrombosis, and neural activities (Pacher et al., 2007). On the other side, free radicals have an influence on a number of pathological conditions like diabetes, cancer, rheumatoid arthritis, inflammation, asthma, cardiovascular disease, muscular dystrophy, intestinal tract disease, progerias, atherosclerosis, parkinson’s disease, cataract, ischemia, and so forth (Phaniendra et al., 2015; Reddy, 2023). Overproduction or excessive accumulation of free radicals alters homeostasis, which subsequently gives rise to pathological conditions. For example, hydroxyl radical and peroxynitrite in excess can damage cell membranes and lipoproteins by lipid peroxidation that leads to the formation of malondialdehyde (MDA) and conjugated diene compounds, which are mutagenic and cytotoxic.

Oxidative stress occurs due to the imbalance between free radical generation and antioxidant defensive mechanisms. In other words, the term “oxidative stress” refers to the disruption between reduced to oxidized glutathione or (GSH/GSSG) or NADPH/NADP+ ratios (Kurian et al., 2016). It can be a consequence of either- due to the impairment of the antioxidant system caused by malnutrition (inadequate consumption of vitamin C, vitamin E, sulphur-containing amino acids) or by the excessive production of free radicals, including ROS and RNS (due to external or internal stimulus). Cells can bear up mild oxidative stress because there is an upregulation of the antioxidant system in response to that mild rise, so that cells can cope with the raised situation. For example, if experimental rats are continuously exposed to higher level of oxygen, they develop better oxygen

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tolerance in comparison to control rats due to antioxidant system elevation in lungs (Halliwell, 2012). But when this adaptive capacity of the cell exceeds, it starts to experience oxidative stress. Oxidative stress asserts to play role in plethora of diseases including atherosclerosis, inflammatory diseases (arthritis, glumerulonephritis, vasculitis, lupus erythematous, respiratory distress syndrome), ageing process, fibromyalgia, AIDS, emphysema, hemochromatosis, hypertension, preeclampsia, gastric ulcers, neurological disorders (Alzheimer's disorder, parkinson's disease, muscular dystrophy), and so on (Islam et al., 2025; Lobo et al., 2010). Oxidative stress manifests cellular derangement like DNA strand breakage, elevation in cytosolic free calcium, cell membranes and transport proteins damage, and release of transition metal ions that finally results in cell death (Halliwell, 2012).

3.1. Pathophysiology of Oxidative Stress Associated MI:

There is growing evidence which indicates that oxidative stress has an important role in the pathophysiology of myocardial infarction (MI) (Neri et al., 2015; van der Pol et al., 2019). A contemporary hot subject is the oxidative stress theory, which holds that excessive production and accumulation of ROS cause cardiac damage (Wen et al., 2021). The multifaceted roles of oxidative stress in MI pathogenesis are summarized and presented in Figure 1. MI occurs in a series of events after the supply of oxygen in cardiovascular tissue is acutely hampered, mostly due to coronary thrombosis resulting from atherosclerotic plaque rapture, a condition known as ischemia. This shifts cellular respiration to anaerobic, and also increases intracellular calcium level that results in cell swelling, rupture, and mostly cell death by both necrosis and apoptosis (Fuentes et al., 2019; Hausenloy & Yellon, 2013). When the supply of oxygen to tissue is reestablished, reactive oxygen species are produced in cardiac muscle cells that contribute to the prognosis of this disease. Mitochondria, as well as some other cardiovascular enzymes such as NADPH oxidase (NOX), nitric oxide synthase (when uncoupled), and xanthine oxidase are responsible for the generation of ROS. Though several antioxidant systems are present to counter the deleterious effect of ROS, sometimes a disproportion between pro-oxidant and antioxidant systems occurs, which leads to a situation known as "oxidative stress" (Fuentes et al., 2019; González-Montero et al., 2018; Hori & Nishida, 2009). This disproportion impairs mitochondrial functions. Consequently, even more ROS are produced, increasing the level of inflammatory cytokines, which in turn induces further production of ROS and damages vital cellular structures, including mitochondria. This disastrous loop of mitochondrial failure, increased oxidative stress, and cellular destruction keeps ramping up and eventually expedites MI progression (Cai et al., 2023; Ide et al., 2001). Moreover, ROS and inflammatory cytokines trigger the increased activation of matrix metalloproteins (MMPs) and excessive deposition of collagen. MMPs are enzymes responsible for the degradation of the extracellular matrix components (ECM), including collagen that offers cardiac muscle its structural stability and tensile strength. Even though in normal circumstances MMPs have a crucial role in tissue remodeling, ROS and inflammatory cytokines mediated overactivation of them during the initial stage of MI speeds up ECM and collagen breakdown, leading to diminishing strength of cardiac muscle. This is succeeded by an excess accumulation of collagen, a condition referred to as fibrosis, which leads to an increase in the stiffness of the cardiac muscle. Both processes aid in the alterations of the ventricular remodeling of injured myocardium following MI. Also, high levels of ROS in impaired cardiac muscle cells can lead to substantial oxidative damage to DNA. Consequently, an enzyme called ribonuclease polymerase gets activated, and its hyperactivity hampers regular cell metabolism and triggers the secretion of inflammatory mediators, which are intricately associated with cardiac remodeling and heart (Q. Guo et al., 2024; R. Yang et al., 2018). In addition to DNA-damaging mechanisms, ROS can directly initiate cascades of intracellular signals that exacerbate cardiac damage. For example, Hydrogen peroxide directly stimulates the production of tumor necrosis factor α (TNF-α) via the p38 mitogen-activated protein kinase (MAPK) pathway that mediates myocardial dysfunction and apoptosis (Fuentes et al., 2019; Meldrum et al., 1998). Likewise, in experimental rat models of heart failure, the superoxide anion in the aorta was observed

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to be markedly increased in the same p38 MAPK pathway in addition to the elevated level of the NOX subunit p47phox (Widder et al., 2004).

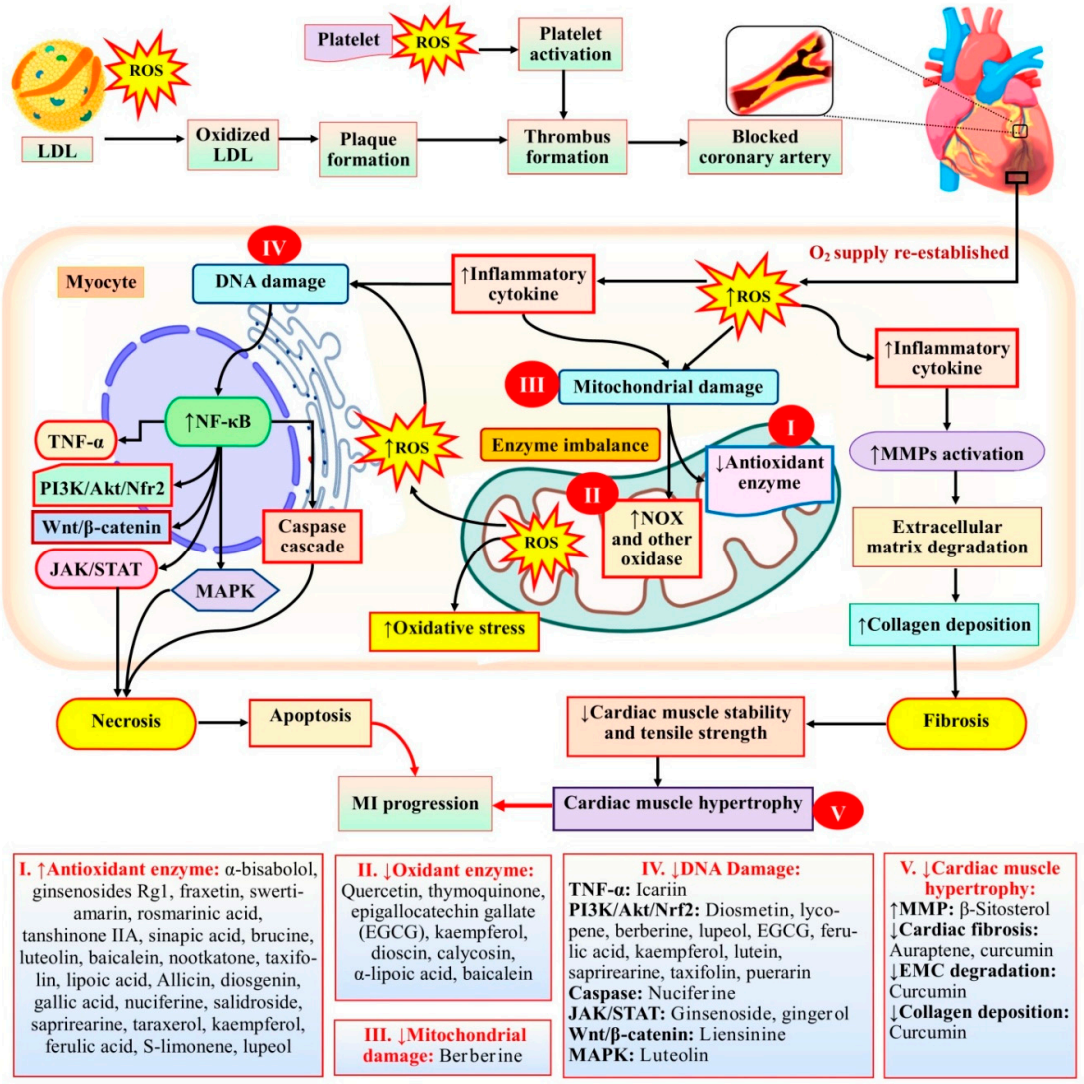

Figure 1. Impact of natural compounds on alleviating oxidative stress associated MI progression.

Furthermore, in post-myocardial infarction patients, a consistently high level of hydroxyl radical production was reported to be associated with the likelihood of progressing towards heart failure according to a clinical study (Valgimigli et al., 2004). These aforementioned oxidizing species can further oxidize LDL, leading to a rise of oxidized LDL or oxLDL in the circulation. Elevated concentration of Circulating oxLDL is linked with various cardiovascular diseases, including atherosclerosis (S. Gao & Liu, 2017; Poznyak et al., 2021; Zingg et al., 2021). Apart from inflicting direct damage, ROS also function as secondary messengers in cardiac signaling pathways. For instance, Src family of tyrosine kinases, MAPKs, small GTP-binding proteins, and cytokines are all activated by ROS. These subsequently induce the activation of nuclear transcription factors connected to the cellular stress responses, which eventually result in cell hypertrophy and apoptosis (Sia et al., 2002). Activated platelets also produce ROS, which is crucial in controlling platelet response to thrombus development. In addition to established activities that promote the growth of atherothrombotic plaques, changes in platelet hemostatic characteristics may promote the progression of injury at the infarct zone (Hori & Nishida, 2009).

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3.2. Impact of Oxidative Stress on MI Complications

Mechanical complications, which are the most common within the first week after myocardial infarction, include left ventricular free wall rupture, ventricular septal rupture with acute ventricular septal defect, papillary muscle rupture with severe mitral regurgitation, pseudo-aneurysm, true aneurysm, and hemodynamically significant right ventricular infarction (F. F. Gong et al., 2020; Reeder, 1995). Pseudoaneurysm, a rare complication of MI, particularly may occur when the visceral, parietal, or both pericardia retain the blood leaked due to the hemorrhagic process resulting from the rupture of the cardiac wall (Ashraf et al., 2021). Some of the other common complications associated with an acute MI are cardiogenic shock, acute pulmonary edema, pericarditis, and heart failure (F. F. Gong et al., 2020; Hubbard, 2003). Cardiac myocyte apoptosis, chronic neurohumoral activation, and ventricular remodeling also occur following MI and ischemia reperfusion (Jenča et al., 2021; Mihalko et al., 2019).

Oxidative stress has a strong impact on MI complications. In myocardial reperfusion injury, the restoration of blood flow to the already existent ischemic zone causes a significant increase in ROS, which quickly and severely damages crucial bio-molecular constituents of the myocardium. Thus, the myocardium loses its structural integrity and functionality to a great extent. This phenomenon is accompanied by several post-MI complications, including lethal reperfusion, no-reflow phenomenon, myocardial stunning, and reperfusion arrhythmias. Post-MI patients who also have diabetes mellitus experience worsened oxidative stress conditions (González-Montero et al., 2018). It is because the constant presence of hyperglycemia is reported to promote oxidative stress succeeding MI, causing endothelial dysfunction and the advancement of atherosclerosis (Kitano et al., 2016). This obstructs the coronary supply of oxygenated blood to the myocardium, thereby further deteriorating the condition of heart cells. So, together, diabetes and myocardial ischemia induce oxidative stress, which causes cardiac tissue to overexpress iNOS and increase NO production. Inhibited NADPH activity may interact with the latter, causing the generation of peroxynitrites and a decrease in NO bioavailability. These responses are closely tied to the rise in cytokine production and apoptosis inside the myocardium, which increases necrosis and disrupts the post-MI recovery of cardiac cells (Filippo et al., 2006).

4. Biomarkers of Oxidative Stress in MI

There are numerous biomarkers of oxidative stress which are present in patients with MI, indicating an association between oxidative stress and MI (Table 1). For example, according to a study by Feng et al., MI patients have higher levels of advanced oxidation protein products (AOPP) in their blood (Feng et al., 2010). Normally, the H_2O_2-myeloperoxidase (MPO) system uses plasma proteins to react with chlorinated oxidants, such as hypochlorous acid, and produce AOPP. AOPPs are unique indicators of oxidant-mediated protein degradation because they possess di-tyrosine. Albumin is the primary carrier of AOPP in the bloodstream (Melough et al., 2017). Protein carbonyl, a significant biomarker for protein oxidation, is made when proteins react with lipid peroxidation products or when certain amino acid residues oxidize. According to another study, protein carbonyl was found significantly higher in patients with MI than in controls, indicating the ROS-driven oxidative protein damage as a result of MI (Shahzad et al., 2018).

It is worthwhile to mention that ROS causes the oxidation of LDL, which raises the levels of circulating oxidized LDL (oxLDL), a marker that has been linked to the emergence of CVDs. oxLDL stimulates the growth and accumulation of foam cells in atherosclerotic plaques, which may then favor platelet activation and cause a cycle of oxidative damage. This establishes the link between atherosclerosis and platelet oxidative stress (Fuentes et al., 2019). Also, lipid peroxidation products such as MDA, HNE, and F2-isoprostanes which are derived from polyunsaturated arachidonic acid are important biomarkers for oxidative stress linked to cardiovascular complications (Tsikas, 2017). Several studies found that an increased level of MDA and F2-isoprostanes are associated with

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exacerbation of MI (Babu et al., 2010; Davies & Roberts II, 2011; Kharb & Singh, 2000; Mythiili & Malathi, 2015; Yin et al., 2019).

Several vitamins such as vitamin A, C, and E act as antioxidants and protect the body from harm by neutralizing free radicals. A study revealed that patients with acute MI who were hospitalized to intensive care had significantly lower levels of vitamins E and C, except for vitamin A which did not differ significantly (Ismail et al., 2018). Another study reported that individuals with AMI had relatively low levels of vitamins E and C than controls (Singh et al., 2004). This is in line with the findings of Singh et al. who reported that lipid peroxide levels were much greater in AMI patients compared to controls, whereas vitamins C, E, A, and β-carotene decreased dramatically (Singh et al., 1994).

The term "superoxide dismutase" refers to a protein family that includes Mn-SOD and Cu-Zn-SOD. The spontaneous conversion of superoxide radicals to H_2O_2 is accelerated by SOD activity. The catalase enzyme may eliminate the final byproduct H_2O_2 of the dismutation cycle. Glutathione peroxidase (GPx) uses GSH as its substrate to catalyze peroxide reduction, turning it to GSSG or glutathione disulfide (Rodrigo et al., 2013). According to an investigation, patients with MI and ischemic heart disease had considerably lower SOD, CAT, and GPx activity than healthy controls (Hazini et al., 2015; Rodrigo et al., 2013). Additionally, smokers with AMI had significantly lower SOD, CAT, and GPx activity than nonsmokers, making these people more susceptible to oxidative stress (Metta et al., 2015). It has been noted that SOD and CAT activity in the erythrocytes of AMI patients has been decreased due to elevated peroxidation (Anbarasi et al., 2006; Scott et al., 1991). In the erythrocytes of AMI patients, there has been evidence of reduced GPx activity. Because GSH is one of the substrates for GPx, a drop in GSH levels may also result in a decrease in GPx activity. Accordingly, it has been demonstrated that individuals with AMI have considerably lower GSH concentrations in plasma and erythrocytes (Ścibior et al., 2008; Serdar et al., 2006; Tavares et al., 2012). So, levels of SOD, CAT, GPx, and GSH are decreased in MI due to oxidative stress which was confirmed by several studies (Aladag et al., 2021; Freitas et al., 2014; Khan et al., 2013; Shahzad et al., 2018). The amount of zinc, magnesium, and calcium in the body is related to oxidative stress. For instance, zinc levels and oxidative stress have an opposing connection. Zinc deficiency causes many cell lines to produce more ROS. It has been reiterated that zinc supplementation can lower elevated levels of ROS. Superoxide dismutase 1 (SOD 1), an antioxidant enzyme that scavenges superoxide anion, uses zinc as a cofactor. The decrease in serum zinc levels during acute tissue injury, such as MI, has long been known. According to a previous study, MI patients had significantly lower serum zinc levels within the first three days than the control group. In MI patients, Zn may therefore be a helpful oxidative marker (S. Choi et al., 2018). A lack of magnesium also increases the formation of free radicals linked to MI (Kharb & Singh, 2000). It is noteworthy to mention that Mg exhibits antiarrhythmic properties in MI. Acute MI is more likely to be fatal and is related to low serum Mg levels. Mg shortage worsens MI through increasing oxidative stress-induced ischemia damage and mitochondrial dysfunction (M. Liu & Dudley, 2020).

Oxidative stress can lead to cellular abnormalities, including a decrease in the activity of the (Na+K)-ATPase, which in turn increases calcium influx, and suppresses the sarcolemma calcium pump ATPase, hence lowering calcium efflux. Moreover, it has been observed that oxidative stress decreases the sarcoplasmic reticulum calcium pump ATPase, which prevents calcium from being secreted from the cardiomyocytes. Eventually, ROS causes intracellular calcium accumulation and cell death by depressing the calcium-regulating system. Additionally, a rise during ischemia causes xanthine dehydrogenase to change into xanthine oxidase, which then causes an increase in superoxide generation (González-Montero et al., 2018).

Table 1. Biomarkers of oxidative stress in Myocardial infarction.

Biomarker	Role in MI pathophysiology	Reference
Advanced oxidation protein	Advanced oxidation protein products (AOPP), indicative of extensively oxidized proteins, were significantly elevated in acute	(Feng et al., 2010)

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products (AOPPs)	MI patients experiencing acute hyperglycemia. These pro-inflammatory mediators directly disrupt HDL metabolism and may play a crucial role in the progression of cardiovascular disease.	
Protein carbonyl (PC) content	The protein carbonyl (PC) content, a widely recognized marker of protein oxidation, was found to be elevated in acute MI patients, suggesting protein damage as a result of acute MI.	(Maneewong et al., 2011)
Oxidized LDL (oxLDL)	Oxidized LDL (oxLDL) promotes the proliferation and buildup of foam cells within atherosclerotic plaques, potentially triggering platelet activation and perpetuating a cycle of oxidative damage. This further confirms connection between atherosclerosis and platelet oxidative stress.	(Jiang et al., 2022)
Lipid peroxidation products	Lipid peroxidation products (MDA, HNE, and F2-isoprostanes) derived from arachidonic acid as serve as biomarkers of oxidative stress related to CVD. Increased levels of MDA and F2-isoprostanes are linked to the worsening of MI, reported by multiple investigations.	(Minuz et al., 2006)
SOD, CAT, and GPx	In MI or IHD patient, SOD, CAT, and GPx levels are significantly low compared to healthy subjects. Here, elevated peroxidation plays important role.	(Aladag et al., 2021)
Antioxidant Vitamins	AMI had notably lower levels of vitamins C, E, A, and β-carotene compared to the control group.	(Riccioni et al., 2012; Singh et al., 1994)
Zinc and magnesium	Low serum zinc levels during acute tissue injury such as MI are observed. Similarly, magnesium deficiency Increases ROS generation associated with MI. Magnesium usually plays a preventive role in MI. Hence, lower serum Mg levels are linked to a higher fatality risk in AMI.	(M. Liu et al., 2020; Tanita et al., 2024)

5. Natural Antioxidant Products Based Therapeutic Approaches for MI

In recent years, scientists have realized how crucial oxidative stress is to the emergence of MI (W. Guo et al., 2023). Excessive oxidative stress may be a factor in the ischemia/reperfusion injury which accounts for MI-related mortality. This revelation prompts researchers to explore innovative therapeutic approaches that specifically target this particular path in the context of anti-MI drugs (Rhana et al., 2022). Considering this, in this section, we have provided an overview of bioactive natural compounds reported for potential MI management focusing on mitigating oxidative stress. A summary of reported natural bioactive compounds and their mechanistic insights into cardioprotection in MI is also presented in Table 2.

Scopoletin

Scopoletin, a prominent phytoalexin present in many plant species, particularly those belonging to the Convolvulaceae, Ulmaceae, Solanaceae, Compositae, Oleaceae, Rutaceae, and Aceraceae families, has been revealed to have a strong capacity to scavenge free radicals. A pre-treatment with scopoletin, according to Rong et al. (Rong et al., 2022), significantly decreased heart-to-body weight ratio, cardiac diagnostic markers, MDA, inflammatory indicators, and apoptotic markers, as well as elevated levels of antioxidant enzymes. As a result, histological features similar to inflammation and necrosis were reversed in the MI model.

Shikimic acid

Shikimic acid (SA), a plant derived phenolic compound, is one of the major intermediate products formed in the shikimate pathway in a number of plants (Bochkov et al., 2012). It exhibits notable pharmacological effects, including antioxidant (M. Estevez & J. Estevez, 2012), anti-inflammatory (Rabelo et al., 2016), anti-platelet, and antithrombotic activities (Veach et al., 2016). SA

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has been shown to reduce MDA levels and enhance SOD activity, thereby minimizing oxidative stress and cellular damage (Khattak et al., 2025). Moreover, it reduces pro-inflammatory cytokines, such as TNF-α and IL-1β, which contribute to ventricular remodeling, inflammation, and cardiomyocyte apoptosis after myocardial infarction (Rabelo et al., 2016).

Nerolidol

Nerolidol is a plant derived sesquiterpene alcohol commonly found in lavender, lemongrass, and ginger (Chan et al., 2016). It is reported for a wide number of pharmacological activities like antioxidant, anticancer, antinociceptive, anti-inflammatory activities (Ayhan et al., 2025; Fonsêca et al., 2016; Tousif et al., 2025). A recent research has demonstrated its effectiveness in prevention of myocardial damage when administered for long time in animal models (Asaikumar et al., 2019). Another research reported the cardioprotective role of nerolidol in MI where different oxidative stress markers were found to be altered. It significantly increased SOD activity and reduced lipid peroxidation and carbonyl levels leading to minimizing isoproterenol-induced heart damage (Asaikumar et al., 2019; Gonçalves et al., 2022).

Biochanin-A

Biochanin-A (BCA) is an O-methylated isoflavonoid found in plants like red clover, soy, alfalfa sprouts, peanuts, and chickpea. Govindasami et al. have studied the impact of BCA on MI which revealed that this compound showed cardioprotection in MI by reducing lipid peroxidation and increasing antioxidant enzyme function (Govindasami et al., 2020).

Diosmetin

Diosmetin is a citrus fruits derived mono-methoxy flavonoid commonly found in lemons and olives. It is also extracted from medicinal herbs like *Rosmarinus officinalis*. Diosmetin is reported for inhibiting MDA formation as well as restoring antioxidant enzyme functions in myocardium (Ahmad et al., 2023). In a H9c2 cell line based study on hypoxia-afflicted damaged myocardium, Si et al. reported that Diosmetin reduces the apoptosis of myocardium via the autophagy induction by activating AMPK (Si et al., 2020). This study suggested Diosmetin as a potential drug candidate in the treatment of myocardial infarction.

10-gingerol

10-gingerol is a phenolic compound found in ginger, a popular spice of cooking. It has been reported for potential role in diminishing ROS levels in cells. Previous research showed that this phytocompound exhibits protective activity against MI in both in vitro and in vivo experiments. The underlying mechanism is activation of JAK2/STAT3 signaling pathway and prevention of oxidative stress leading to reduction of apoptosis (Han et al., 2022).

Quercetin

Quercetin is a potent flavonoid commonly found in wide varieties of plants. It is also very commonly found in vegetables, fruits, berries, and teas. This compound is reported to increase the level of nitric oxide in the ischemic myocytes of myocardium (P. G. Li et al., 2012). It also exhibits the potential to inhibit several oxidative enzymes like oxidases and lipoxygenases. More recently, it is known as potent antioxidant medication (Sadik et al., 2003; W. Zhang et al., 2023). A recent study conducted by Kozhukhov et al. has revealed that quercetin aids in protecting the heart by reducing the infarct size and stopping intramyocardial haemorrhage, when administered as intravenous infusion alongside the conventional treatment in patients following the first incidence of ST elevation MI (Kozhukhov et al., 2024).

Lycopene

An integrated experiment by Guo, Huang and Li provided a theoretical basis for the antioxidant effect of lycopene in both preventing and curing MI (W. Guo et al., 2023). The research demonstrated that lycopene can effectively neutralize free radicals and stimulate the transcription of downstream antioxidant enzymes via activating the Nrf2/HO-1 pathway.

Berberine (Ber)

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Doxorubicin (DOX)-induced MI damage has been acknowledged as a significant side effect of cancer chemotherapy. The goal of an experimental investigation by Y. Wang *et al.* (Y. Wang et al., 2023) was to determine whether Ber, an isoquinoline alkaloid initially isolated from Chinese goldthread (*Coptis chinensis*), could offer defense against this problem. Berberine has a wide spectrum of biological roles, including antioxidant function. The study reveals that myocardial damage was prevented by pretreatment with Ber as it reduced the formation of ROS and MDA and raised SOD activity via triggering the Nrf2-mediated pathway.

Ellagic acid

Ellagic acid (EA) is an antioxidant and anti-inflammatory polyphenol that is mostly present in pomegranates, blackberries, raspberries, strawberries, cranberries, walnuts, pecans, and wolfberries (Costa et al., 2022). Plenty of studies reported that EA treatment prevented lipid peroxidation (Osawa et al., 1987) , oxidant-induced endothelial dysfunction, and atherosclerosis (Y. Ding et al., 2014), in addition to inhibiting the isoproterenol-induced cardiac necrosis in rats (Kannan & Quine, 2011) . Additionally, EA improved the structural and functional recovery of myocardial energy metabolism when paired with indapamide, a thiazide diuretic prescribed for hypertension. Moreover, oral administration of EA reduces ROS production and blocks the CaMKII signaling pathway, which improves left ventricular diastolic dysfunction in rats with ovariectomies. Therefore, EA seems like a viable option for the treatment of clinical conditions like hypertension, heart failure, and MI (Costa et al., 2022) .

Thymoquinone

Thymoquinone (TQ) is the primary active component of *Nigella sativa*, giving *Nigella sativa* its anti-inflammatory and antioxidant potentials. To further understand how TQ affects oxidative stress, inflammation, apoptosis as well as how it protects cardiac mtDNA in an experimentally induced MI model, an experimental study was conducted by Khalifa, Rashad and El-Hadidy (Khalifa et al., 2021). The finding demonstrates that pre- and co-administration of TQ reduced the oxidative stress linked to the occurrence of MI, reversed the changes in histoarchitecture, and retained the amount of cardiac mtDNA. These characteristics enhance the cardiac advantages resulting from using TQ as a natural cardio-protective agent.

Lupeol

A pentacyclic triterpenoid molecule known as lupeol is abundantly present in edible plants like olive oil, strawberries, etc. According to Moris et al. (Moris et al., 2017), unusual ROS production and NF-κB activation are key determinants of the severity of myocardial damage. Also, Nrf2 has been linked to the control of oxidative stress responses as a key transcription factor. In order to find out whether lupeol has protective benefits against myocardial ischemia/reperfusion injury (I/R) via modulating NF-κB & Nrf2 signaling pathways, Li et al.(J. Li et al., 2022) used myocardial I/R rat models. The results revealed that lupeol dramatically altered NF-κB and Nrf2 signaling, suggesting that it may be an effective treatment for preventing I/R-induced myocardial infarction.

S-Limonene

S-Limonene (SL) is one of the most prevalent monoterpenes discovered in lemon and orange peels. To assess the potential therapeutic use of SL in an isoproterenol-induced MI animal model, an investigation was conducted by Rhana et al. (Rhana et al., 2022). The findings demonstrated that s-limonene supports cardio-protection against MI injury, most likely via decreasing elevated Ca2+ and reducing oxidative stress via CaMKII. This makes it a potentially effective choice for the treatment of MI.

Ferulic acid

Ferulic acid (FA), a polyphenol generated from plants, is widely present in cereals, vegetables, and fruits. FA is well known for its anti-inflammatory properties. According to *Pandi* et al.(Pandi et al., 2022), FA's cardio protective effects mainly involve modulating cellular antioxidants, ROS-

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mediated oxidative stress, apoptosis, inflammation, and autophagy. FA primarily modulates PI3K/Akt dependant Nrf2 signaling pathway.

Kaempferol

Kaempferol is an active phytoconstituent of *Amaranthus viridis*. An ISO-induced rat model was used by *Krishna* et al. to study the cardioprotective effects of kaempferol (Krishna et al., 2023). The study reported that kaempferol can improve antioxidant response by reducing myocardial oxidative stress via the Nrf-2/Ho-1 signaling pathway, which is principally responsible for its cardioprotective effects against ISO-Induced MI in rats.

Icariin

Icariin is the primary bioactive medicinal ingredient identified from *Epimedii herba*. Inhibition of oxidative stress, attenuation of DNA damage, prevention of mitochondrial oxidative damage, and reduction of cardiomyocyte apoptosis are just a few of the many potential pathways that could underlie icariin's cardioprotective benefits. An in silico study by Ke et al. (Ke et al., 2023) hypothesized that, suppressed oxidative stress may be related to icariin's protective effects against MI. This protective characteristic makes icariin a candidate for treating MI.

Liensinine

The *Nelumbo nucifera* Gaertn. seed embryo contains a naturally occurring bisbenzylisoquinoline alkaloid liensinine (LSN), which has been shown to have several antioxidant and cardiovascular potentials. A research conducted by Shen et al. assessed the cardioprotective activities of LSN following MI which demonstrated its novel cardioprotective function. This compound has significant potential to protect myocytes from oxidative stress induced damage in MI by downregulating Wnt/β-catenin signaling pathway (F. Shen et al., 2023). This finding supports the novel therapeutic role of LSN in ischemic heart diseases as well.

Taraxerol

Taraxerol is a plant derived naturally occurring pentacyclic triterpenoid with diverse medicinal properties. Recent studies investigated it's possible cardioprotective activity to prevent MI which revealed that it increases antioxidant enzymes like SOD and reduces pro-inflammatory cytokines leading to protect heart from ISO-induced damage (Aodah et al., 2023).

Dioscin

Dioscin is a natural phytocompound present in numerous medicinal plants belonging to *Dioscorea* and *Liliaceae* families. Several studies have shown that dioscin can lower oxidative stress and inflammation in rats with cardiac ischemia-reperfusion. Dioscin showed significant potential to prevent MI by controlling inflammation and oxidative stress that are mediated by BMP4/NOX1 (Z. Zhang et al., 2022).

Salvianolic acid B

Salvianolic acid B (Sal B), derived from the herb *Salvia miltiorrhiza* has numerous health benefits. It works against oxidative stress, inflammation, liver fibrosis, and cancer. Numerous in vitro and in vivo studies suggest that in myocardial damage models, Sal B inhibits ferroptosis by activating the Nrf2 signaling pathway, thereby offering protection against MI (Y. Shen et al., 2022).

Hinokitiol (β-thujaplicin)

Hinokitiol (β-thujaplicin), a plant derived biocompound resembling to tropolone, obtained from cupressaceous plant's wood, exhibits bioactivities like antibacterial, anticancer, anti-inflammatory, and antioxidant activities (Hachlafi et al., 2021). A research done by Xiao et al. stated that this compound reduces apoptosis by downregulating autophagy flux (H. Xiao et al., 2022).

Saprirearine

Saprirearine, is a diterpenoid derived from *Salvia prionitis*. Recent research on this compound explored that it possesses cardioprotective activity on hypoxic/re-oxygenated H9c2 cardiomyocytes model of MI. The underlying mechanism involves enhancing mitochondrial dysfunction and

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preventing oxidative stress, thereby preventing mitochondria-mediated cell death. Apart from that, it also activates Nrf2 which synergistically fosters cardioprotection(G. Zhang et al., 2022).

Auraptene

Auraptene is a citrus peel-derived component, and has a variety of pharmacological properties that makes it useful in treating MI. Sunagawa et al. found that auraptene drastically reduced MI-induced systolic dysfunction in MI-affected rats and improved posterior wall thickness (Sunagawa et al., 2022). Auraptene therapy was used to counteract MI-induced reductions in the expression of PPARα-dependent genes.

Notoginsenoside R1

In China, cardiovascular problems are frequently prevented and treated using *Panax notoginseng*, a well-known traditional Chinese medication. One of *P. notoginseng's* main active ingredients, notoginsenoside R1 (NGR1), possesses anti-inflammatory, antioxidant, and anti-apoptotic activities (J. Xiao et al., 2018). According to Zhu and Wan, NGR1 produces superior therapeutic effects on MI (Zhu & Wan, 2023). The reporting of Xu et al. suggests that NGR1 controls the JAK2/STAT3 signaling pathway in hypoxia/reoxygenation (H/R)-treated H9C2 cells to enhance proliferation and prevent apoptosis (H. Xu et al., 2022). NGR1 also slowed the in vivo course of MI.

Salidroside (SAL)

SAL has several pharmacological properties that boost immunity, improve tolerance to hypoxia, and reduce free radical induced damage. A thorough investigation by Fan et al. into SAL's ability to prevent harm has revealed that it can act in a variety of ways to fight oxidation, inflammation, and apoptosis (Fan et al., 2022). In that study, SAL greatly improved the remodeling process of MI and decreased cardiac damage by reducing oxidative and inflammatory effects via the PI3K/AKT/Nrf2/HO-1 pathway. This suggests that SAL could be used to treat MI effectively.

Psoralidin (PSO)

Adriamycin (ADR) is an effective and widely used broad-spectrum anticancer medication. However, ADR's cumulative and dose-dependent cardiotoxicity severely restricts its clinical use. A natural phenolic coumarin called psoralidin (PSO), which was reported to have reduced ADR-induced cardiotoxicity, is extracted from the seeds of the medicinal plant *Psoralea corylifolia* L. PSO demonstrates a variety of biological actions, including anti-inflammatory, anti-allergic, antibacterial, antidepressant, and antioxidant properties. According to Liang et al., PSO significantly decreased ADR-induced excessive ROS buildup in cardiomyocytes (Liang et al., 2022). It also increased the levels of Nrf2, NQO1, and HO-1, suggesting that it may prevent oxidative stress and ultimately lessen the cardiotoxicity caused by ADR.

Calycosin

Calycosin is one of the *Radix astragali's* main active ingredients, having cardioprotective qualities. In order to figure out if calycosin can reduce oxidative stress and oxidative stress-induced cardiac apoptosis in newborn cardiomyocytes (NCMs) via activation of aldehyde dehydrogenase 2 (ALDH2), calycosin has been studied in vivo and in vitro by Ding et al.(W. jun Ding et al., 2023). The results strongly support the potential therapeutic application of calycosin in MI by strongly indicating that it lowers oxidative stress and oxidative stress-induced apoptosis through the control of ALDH2 signaling.

Emodin

It has been demonstrated that the principal active ingredient in traditional Chinese medicine rhubarb, an anthraquinone derivative, emodin possesses anticancer, antibacterial, immunomodulatory, and antioxidant properties. To generate fresh concepts for the clinical management of post-MI heart failure (MI HF), the effect of emodin on myocardial cells was investigated in an experimental rat model by Liu and Ning (J. Liu & Ning, 2021). According to the research, emodin has the potential to be a therapeutic option because it can considerably enhance

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energy metabolism, lower the pace at which myocardial tissues undergo apoptosis, and improve cardiac function in post-MI HF rats.

Nuciferine

Nuciferine, an aporphine alkaloid that is mostly found in *Nelumbo nucifera* leaves, has been linked to anti-cancer, anti-oxidant, anti-tumor, and insulin secretor actions. An investigation was carried out by HarishKumar and Selvaraj to assess the cardioprotective effects of nuciferine (HarishKumar & Selvaraj, 2022). There, isoproterenol (ISO) was first used to cause MI in Wistar rats, and then nuciferine was administered orally as a pretreatment. In rats with MI, the pretreatment with nuciferine greatly raised the amount of endogenous antioxidants and reduced lipid peroxidation. In a different study on acute myocardial infarction mice model, Xie et al. found that regulation of PI3K/AKT pathway is responsible for the cardioprotective function of nuciferine (Xie et al., 2024). In light of this, nuciferine may be employed as plant-based cardioprotective drugs.

Gallic acid

Gallic acid, a phenolic substance present in many plants, such as gallnuts, sumac, witch hazel, tea leaves, oak bark, and grape seeds, has shown impressive outcomes in the treatment of ailments caused by oxidative stress. Several studies explored that the isoprenaline (ISO)-induced myocardial infarction (MI) in rat model can possibly be improved by gallic acid (Abdelhalim et al., 2021; Shackebaei et al., 2022). The findings provide evidence that gallic acid reduces the oxidative damage induced by ISO, activates endogenous natural antioxidant enzymes, and guards the heart against MI.

Diosgenin

Diosgenin is a bioactive steroidal sapogenin molecule. It is found largely in *Rhizoma polgonati*, *Smilax china*, and *Trigonella foenum-graecum* along with other plants (Semwal et al., 2022). Liu and his team evaluated the cardioprotective effects of diosgenin molecule on MI mice models (X. Liu et al., 2024). The study revealed that diosgenin minimizes oxidative stress in myocardial infarction-damaged cardiac tissue of rat. Diosgenin also has cholesterol-lowering traits, which may assist to prevent and control cardiovascular disease (Sun et al., 2021). Another study on MI model of wister rat exhibited that diosgenin along with exercise show cardio-protective activity because it has antioxidant and free radical scavenging potential (Salimeh et al., 2013).

Puerarin

Puerarin is the principal isoflavone obtained from *Radix puerariae*. It has anti-inflammatory, anti-oxidative, and anti-apoptotic properties. An experimental model is developed and examined to find out if puerarin pretreatment enhances heart function in AMI (F. Chen et al., 2021). The outcomes demonstrated that pretreatment with puerarin in AMI can significantly enhance cardiac function by preventing myocardial apoptosis. The PI3K/Akt pathway in cardiomyocytes may be activated in order to mediate the molecular mechanism of this protective action.

Bakuchiol

Bakuchiol (BAK) is a bioactive compound extracted from the seeds of the *Psoralea corylifolia* plant. It is known to have preventive effects against cardiac complications due to its anti-oxidant and anti-inflammatory capabilities. BAK has shown cardio-protective activity by alleviating hyperglycemia-induced diabetic cardiomyopathy, improving aortic banding-induced pathological cardiac hypertrophy, and attenuating MIRI-induced mitochondrial oxidative damage in isolated heart cells. BAK maintains cardiac function following MI and also protects the heart from harmful remodeling. It most likely acts by inhibiting the gene expression of ERK2 and TGF-β1 (Duan et al., 2021).

β-Sitosterol

β-Sitosterol is a phytosterol, isolated from *Nepeta deflersiana*. There are mounting evidences establishing β-sitosterol's protective effects on cardiovascular illnesses. In a recent mechanistic investigation by Wong et al., it was discovered that β-sitosterol effectively increased cellular glutathione redox cycling, thereby reducing oxidative damage in rat cardiomyocytes (Wong et al.,

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2014). Additionally, rat cardiac damage induced by isoproterenol, was prevented by β-sitosterol. Moreover, β-sitosterol demonstrated protective effects against carbon tetrachloride generated hepatotoxicity in rats via enhancing mitochondrial glutathione redox cycling. Another study by Lin et al. found that β-sitosterol provided protection against the damage that hypoxia/reoxygenation-induced cardiomyocyte injury and cardiac I/R injury caused to cells in culture. Also, the regulation of PPARc/NF-κB signaling after myocardial I/R injury may contribute to the β-sitosterol-mediated cardioprotective effects (Lin et al., 2020).

Allicin

Allicin, a very effective natural antimicrobial compound found in garlic, prevents the growth of numerous pathogens (Choo et al., 2020). Gao et al. demonstrated that allicin could alleviate myocardial infarction in I/R by exerting a cardioprotective effect via promoting SHP2 axis to inhibit p-PERK-mediated oxidative stress (T. Gao et al., 2024). Allicin was utilized to treat rats using a myocardial infarction rat model in order to study the effects of allicin on myocardial infarction (W. Xu et al., 2020). It demonstrated how allicin works with oxidative stress markers, apoptosis-related proteins, and the JNK signaling cascade to minimize oxidative stress damage and cardiomyocyte death in a rat model of myocardial infarction. Hence, the therapeutic impact of allicin on myocardial infarction should be further investigated using a large sample size of clinical patients.

α-lipoic acid

α-lipoic acid (ALA) is a powerful antioxidant that occurs in nature and has a wide range of antioxidant potential that may increase its effectiveness in disease states where oxidative stress plays a vital role in cardiovascular pathophysiology. In a mouse model of AMI, the cardioprotective potential of ALA was investigated by Yang et al. (Z. Yang et al., 2020). The study showed that daily administration of ALA not only decreased oxidative stress during both the acute phase immediately following an AMI and the chronic remodeling phase that followed, but also protected the heart from future attacks and helped maintain cardiac structure and function throughout the progression of LVR post-AMI.

Taxifolin

Taxifolin (TAX) is a naturally occurring flavonoid that is mostly found in olive oil, grapes, and onions. It has a number of pharmacological effects, including anti-inflammatory and radical-scavenging capabilities. TAX protects against ISO-induced acute myocardial injury through the activation of the Nrf2/HO-1 signaling pathway, attenuation of oxidative tissue injury, attenuation of key regulators of the inflammatory response and apoptosis. Thus, TAX may be of use to find a novel cardioprotective treatment for acute MI. However, it requires additional investigation in prospective human trials (Obeidat et al., 2022).

Nootkatone

Nootkatone (NKT), a naturally occurring bioactive sesquiterpene which is widely present in grapefruit, is one of many well-known plant-derived substances. It has gained attention for its potential health advantages and pharmacological activities. Meeran et al. looked into NKT's ability to protect against MI in the heart of rats (Meeran et al., 2021). The results showed that, in ISO-induced MI, NKT's protective actions occur by activating the PI3K/Nrf2/Akt signaling cascades and moderating aberrant TLR4/NF-κB/MAPK signaling, which in turn reduced oxidative stress, inflammation, and apoptosis.

Formononetin

It has been widely reported that the isoflavone formononetin (FN), which is found in many plants but is particularly abundant in *Trifolium pratense* (red clover) and the Chinese herbal supplement *Astragalus membranaceus*, has a variety of pharmacological properties, including antioxidant, cardioprotective and neuroprotective activity, vasorelaxant, anticancer, anti-inflammatory, and antiviral activity. Wang et al. designed an experimental investigation to better understand how FN affects myocardial ischemia/reperfusion injury (MIRI) (D. S. Wang et al., 2020).

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The results demonstrated that FN alleviated MIRI in rats and reduced the activation of the NLRP3 inflammasome through the regulation of ROS-TXNIP-NLRP3 pathway.

Curcumin

Curcumin is a polyphenolic compound commonly found in turmeric. It is reported to prevent myocardial injury by reducing oxidative stress, inflammation, apoptosis, and fibrosis. Pretreatment with curcumin alleviates MIRI induced mitochondrial oxidative damage (Mokhtari-Zaer et al., 2019). Xiao et al. reported that curcumin prevents myocardial fibrosis most possibly via the activation of SIRT1(J. Xiao et al., 2016). Therefore, it can be used alongside the conventional therapy for the better management of myocardial fibrosis following MI.

Baicalein

Baicalein, the primary bioactive component found in the roots of *Scutellaria baicalensis* and *Scutellaria lateriflora*, has a wide range of pharmacological activities, including anti-inflammatory, anti-cancer, anxiolytic, antidepressant, and antioxidant action. Kumar et al. assessed the effects of baicalein pretreatment on ISO-induced MI and looked into potential causes (Kumar et al., 2016). The results of their investigation suggest that pretreatment with baicalein protects the rat myocardium from ISO-induced myocardial infarction. Additionally, Baicalein preserves the cardiac enzyme functioning, sustains the integrity of the myocardium, inhibits oxidative-nitrosative stress, boosts the antioxidant defense system, and suppresses NF-κB protein production, which minimizes necrosis or/and cell death in rats with myocardial infarction.

Luteolin

Luteolin is a falconoid substance with anti-inflammatory, antioxidant, and anti-tumor properties. It can be obtained from traditional Chinese remedies. Recently, it has been used in clinical treatment for the prevention of IHD and MIRI. Luteolin markedly reduces the elevated ROS generation due to its ability to balance out oxidant/antioxidant system. According to Yu et al. in vivo and in vitro myocardial ischemia/reperfusion has been successfully treated with luteolin (Yu et al., 2015). The ROS system and MAPK pathways may be involved in mediating the effect, which improves mitochondrial function by inhibiting the phosphorylation of JNK and p38 MAPK, facilitating the activation of ERK1/2, increasing the transcription of Mn-SOD's mRNA. This advantage, together with luteoline's safety, made it a viable treatment option for MIRI.

Brucine

MI-related harms can be mitigated and significant advantages can be achieved by combining antioxidant and anti-inflammatory functions. In this context, the major bioactive alkaloid from *Strychnos nux-vomica* seeds, brucine, which has anti-inflammatory and antioxidant characteristics, could be quite effective in treating MI. An extensive study by Liu et al. showed that oral brucine preparation protected rat myocardium from ISO-induced myocardial damage (B. Liu et al., 2021). Brucine successfully reduced the extent of the infarct by boosting endogenous antioxidants, lowering the status of the marker enzymes TBARS and LOOH, and ameliorating histopathological damage.

Sinapic acid

Sinapic acid (SA) is a widely distributed, orally accessible phytochemical with anti-inflammatory and peroxynitrite-scavenging properties. It is present in various foods, including cereals, citrus, berry fruits, vegetables, cereal grains, and oilseed crops. SA was observed to show an altered lipid profile, reduced myocardial infarct size, and improved lysosomal membrane damage in ISO exposed rats. A research was conducted to divulge the protective function of SA on cardiac mitochondrial damage in rats with ISO-induced myocardial infarction (Stanely Mainzen Prince et al., 2020). It was found that pretreatment and cotreatment with SA elevated the levels of antioxidants and protected heart mitochondria in ISO-treated rats by reducing oxidative stress.

Tanshinone IIA

Tanshinone IIA (TIIA) is a natural compound obtained from the roots of *Salvia miltiorrhiza* Bunge. Several researches have shown that TIIA has antioxidant, anti-cancer, and anti-inflammatory

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properties (R. Guo et al., 2020). TIIA is utilized to treat cardiovascular disorders, because it can improve myocardial metabolic dysfunction caused by hypoxia. It can also improve coronary blood flow. It is reported that TIIA therapy can lessen infarction and boost myocardial regeneration and contractility (X. Zhang et al., 2019). Moreover, CHEN et al. found that, TIIA might alleviate cardiac dysfunction and fibrosis in heart failure (HF) of MI-rats by preventing oxidative stress (CHEN et al., 2021). The imbalance between antioxidant and oxidant levels was also rectified by TIIA.

Rosmarinic acid

Rosmarinic acid (RA) is a bioactive phytochemical isolated from the *Rosmarinus officinalis* plant. It has particularly drawn scientific interest due to its antioxidant, anti-inflammatory, anti-depressive, and anti-proliferative properties. RA is able to treat MI associated depression because it has multidimensional pharmacological effects. Verma et al. investigated the possible benefits of RA on comorbidly depressed MI rat models (Verma et al., 2022). The study was designed in a way that the depression (maternal stress) affected the severity of MI. The study divulged that the anti-inflammatory, anti-oxidative, anti-depressive, and brain-derived neurotrophic factor modulatory capabilities of RA provide cardio-protection to test animals against MI.

Swertiamarin

Swertiamarin is a naturally occurring plant glycoside. It is found abundantly in *Enicostemma littorale Blume (E. littorale)* along with variety of other plant species. Swertiamarin is reported for its anti-diabetic, antinociceptive, antilipidemic, hepatoprotective, anti-obesity, anti-malarial, anti-leprosy, antioxidant, and anti-inflammatory activities (Leong et al., 2016). The cardioprotective effect of swertiamarin was investigated by Wang et al. which demonstrated that pre-treatment with swertiamarin reduced oxidative stress while increasing levels of cellular antioxidants in MI rat models (T. Wang et al., 2022). The underlying mechanism could be attributed to its ability to lower ROS by scavenging ROS radicals and by simultaneously activating the genes which encode antioxidant/antioxidant enzymes. The study also found decreased levels of the pro-inflammatory cytokines TNF-α and IL-6 and a significant protection against histological changes in rats with ISO-induced MI.

Fraxetin

Fraxetin is a coumarin derived from the *Fraxinus rhynchophylla* plant. Dual antioxidative action of fraxetin against metals and free radicals has been proven by Thuong et al.(Thuong et al., 2009). According to that study, fraxetin is a more effective free radical scavenger than other antioxidants such as esculetin and caffeic acid. Among numerous studies, Yin et al. looked into the cardioprotective abilities of fraxetin (Fx) in experimental rats with myocardial infarction (Yin et al., 2022). The study showed that, besides improving antioxidant activity and decreasing free radicals, fraxetin also reduces cardiac tissue inflammation and damage, supporting its cardioprotective effects in rats following MI.

Ginsenoside Rg1

Ginsenoside Rg1 (Rg1) is a saponin of the protopanaxtriol type. It has the ability to provide protection to the mitochondria and ischemic myocardium. Rg1 has several functions, including the prevention of apoptosis and oxidative damage, as well as the stimulation of blood vessel and cardiomyocytes regeneration. An analysis by Yang, Jiang and Xing on the protective effect of Rg1 on myocardial ischemic injury in rats after AMI revealed that, Rg1 may increase the rate of recovery of cardiomyocytes, lower the rate of cardiomyocyte apoptosis, lessen myocardial infarction area, elevate microvessel density in infract area, and preserve myocardial cells after AMI by means of antioxidant damage mechanisms (C. Yang et al., 2022). It is therefore a potential therapeutic candidate for MI due to these attributes.

Lutein

Lutein (LU) is a naturally occurring plant-derived oxygenated carotenoid. It is found in a variety of fruits and vegetables, particularly in spinach and egg yolks. LU has been reported to show

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numerous pharmacological properties, such as anti-inflammatory, antioxidant, and anti-apoptotic actions (Fuad et al., 2020). A study designed by Abdelmonem et al. investigated the possible preventative role of LU against ISO-induced MI (Abdelmonem et al., 2021). The study concluded that, LU may lessen the severity of the condition in rats by improving endogenous antioxidant defense and regulating the MIAT/miR200a/Nrf2 pathway.

α-Bisabolol

α-Bisabolol is a sesquiterpene alcohol which is present in the essential oils of several different plants, such as chamomile (*Chamomilla recutita* L.), salvia (*Salvia runcinata*), *Plinia cerrocampanensis*, and wood of candeia (*Eremanthus erythropappus*) (Kamatou & Viljoen, 2009). It has been demonstrated that bisabolol has anti-inflammatory, antimutagenic, gastroprotective, antispasmodic, and antioxidant activities (Eddin et al., 2022). As free radical-mediated oxidative stress is crucial for MI development, Meeran et al. carried out an investigation to see how α-Bisabolol affects lipid peroxidation, nonenzymatic antioxidants, and hemodynamics in ISO-induced MI (Meeran et al., 2018). The in vivo and in vitro hemodynamic and biochemical data were obtained from that study. The study revealed that, bisabolol protects the myocardium of ISO-induced MI rat models due to its powerful anti-lipid and antioxidant effects. The reversal of altered lipid peroxidation and nonenzymatic antioxidant status was observed following the treatment with α-Bisabolol.

Table 2. Reported natural bioactive compounds and their mechanistic insights into cardioprotection in MI.

Compound	Source	Assay	Model	Effect & mechanism	Application	Reference
Scopoletin	Convovulaceae (*convolvulus tricolor*), Ulmaceae, Solanaceae	In vivo	Albino Sprague-Dawley male rats	Prevents oxidative stress by reducing MDA level & by increasing the levels of antioxidant enzymes (SOD and CAT)	MI	(Rong et al., 2022)
Shikimic acid	*Illicium verum, Liquidambar styraciflua, Pinus sylvestris, Malus pumila*	In vitro, in vivo	Sprague-Dawley rats	Decreases MDA level and increases SOD activity, and thereby decreasing the cellular damage caused by free radicals	MI	(Khattak et al., 2025)
Nerolidol	lavender, lemon grass, and ginger	In vivo	male Wistar normotensive rats	Increases SOD activity and reduces lipid peroxidation and carbonyl levels	MI	(Gonçalves et al., 2022)
Biochanin A	Red Clover, Soy, Alfalfa Sprouts, Peanuts, And Chickpea	In vivo	Male Wistar rats	i) Protects from oxidative stress by enhancing the levels of GPx, GST, GSH, and GRD ii) Increases activities of enzymatic antioxidants, such as (SOD) and (CAT) & reduces MDA levels		(Govindasami et al., 2020)
Diosmetin	Lemon peel and Citrus Fruit (*Olea europaea L*)	In vivo, In vitro	Rat model, H9c2 cell line	i) Protects against oxidative stress by inhibiting the generation of MDA and restoring the antioxidant enzymes (SOD, GPX, CAT). ii) Activates β 1-adrenergic receptors iii) Reduces apoptosis of myocardium via the	MI	(Ahmad et al., 2023; Si et al., 2020)

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				autophagy induction by activating AMPK		
10-gingerol	Ginger	In vivo	Sprague-Dawley (SD) rats	Minimizes oxidative stress by reducing ROS & MDA & increasing SOD, CAT, and GSH levels; Activates JAK2/STAT3 pathway	MI	(Han et al., 2022)
Quercetin	Apple, Onion, Tea	Clinical trial	Human	May Increase in the content of nitric oxide & metabolism of leukotriene and thereby decreasing oxidative stress & inflammation	ST elevated MI	(Kozhukhov et al., 2024)
Lycopene	Tomato	In vitro	HMEC-1 cell,ECV-304 cell	Minimizes oxidative stress by declining ROS & MDA levels, restores GSH,GCLC,GCLM expression & activates the SIRT1/Nrf2/HO-1 pathway	MI	(W. Guo et al., 2023)
Berberine	Chinese goldthread (*Coptis chinensis*)	In vivo	Wild-type male SD rats	Inhibits oxidative stress and mitochondrial injury by up-regulating the expression of Nrf2, HO1, TFAM, as well as decreasing MDA & increasing SOD levels	Myocardial injury	(Y. Wang et al., 2023)
Ellagic acid	Pomegranates, Blackberries, Raspberries, Strawberries, Cranberries, Walnuts, Pecans, Wolfberry	In vivo	Female Wistar rats	Increases SOD activity and reduces ROS & CaMKII phosphorylation	MI induced LVDD	(Costa et al., 2022)
Thymoquinone	*Nigella Sativa*	In vivo	Male albino rats	Decreases MDA & ROS, & significantly elevates GSH, GPx,SOD, CAT, as well as preserves the cardiac mtDNA content	MI	(Khalifa et al., 2021)
Epigallocatechin Gallate	Green tea (*Camellia sinensis*)	In vitro, in vivo	H9C2 cardiomyocytes, male C57BL/6 mice	i) MDA levels & the expression of Bax & p-PI3K/PI3K, p-Akt/Akt are significantly decreased, and the activity of SOD & expression of Bcl-2 are significantly increased ii) Antihypertensive effect by reducing oxidative stress through down-regulation of vascular NADPH oxidase activity	Myocardial Ischemia-reperfusion Injury(MIRI)	(FU et al., 2019; Mohd Sabri et al., 2022)
Lupeol	Olive Oil, Strawberry	In vivo	SD rats	Suppresses the ROS & MDA expression & increases the level of SOD, GSH, GPx, as	MIRI	(J. Li et al., 2022)

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				well as enhances the expression of Nrf2/HO-1		
S-limonene	Lemons and Oranges peel	In vivo	Wistar rats	Inhibits increased Ca^{2+} and attenuates oxidative stress via CaMKII, as well as causes the restoration of SOD, GPx activity	MI	(Rhana et al., 2022).
Ferulic acid	Grain bran, Whole grain foods, Citrus fruits, Banana, Coffee, Cabbage, Celery and Carrots	In vitro, in vivo	H9c2 cell, C5/BL/6 J mice	Reduces oxidative stress by alleviating MDA, Restores SOD, CAT, GPx, GST & GSH levels, as well as minimizes apoptosis and activates Nrf2 signaling pathway	Arrhythmia, MI, Myocardial Hypertrophy	(Pandi et al., 2022)
Kaempferol	*Amaranthus viridis*	In vivo	Male wistar rats	Attenuates oxidative stress by elevating GSH, and decreasing lipid peroxidation, along with suppressing ROS & NOx, in addition to restoring the activity of SOD, CAT, GPx, GR, GST, and up-regulating the Nrf2/HO1 pathway	MI & post MI damage	(Krishna et al., 2023)
Icariin	*Epimedii Herba*	In silico	—	Potential targets are EGFR, AKT1, TP53, JUN, ESR1, PTGS2, TNF, RELA, HSP90AA1, BCL2L1 & protective effect is associated with inhibited oxidative stress	MI	(Ke et al., 2023)
Liensinine	*Nelumbo nucifera Gaertn*	In vitro, in vivo	Human AC16, rat H9c2 cells, male C57BL/6 mice	Protects against ischemic and oxidative stress-induced DNA damage via inhibiting Wnt/β-catenin signaling pathway activation	MI induced ischemic injury	(F. Shen et al., 2023)
Taraxerol	Asteraceae family (*Taraxacum officinale*)	In vivo	Male SD rats	Decreases MDA levels & increases the activity of SOD and GPx	MI	(Aodah et al., 2023)
Dioscin	*Dioscorea nipponica Makino*	In vitro, in vivo	HL-1 cells, C57BL/6 mice	Increases the viability of HL-1 cells and inhibits ROS level along with decreasing LDH,CK-MB, cTnI, MDA & increasing SOD by down-regulating BMP4/NOX1-mediated oxidative stress	MI injury	(Z. Zhang et al., 2022)
Salvianolic acid B	*Salvia miltiorrhiza*	In vivo	SPF-grade male rats	Inhibits MI-induced ferroptosis by alleviating iron overload and oxidative stress through activating the Nrf2 signaling pathway	MI	(Y. Shen et al., 2022)

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Hinokitiol (β-thujaplicin)	Cupressaceae (*Chamaecyparis obtusa*)	In vitro	Human AC16 cells	Protects cardio-myocytes by increasing p21 expression through GSK3β/p21 signaling	MIRI	(H. Xiao et al., 2022)
Saprirearine	*Salvia prionitis*	In vitro	Rat H9c2	Oxidative state is reversed by decreasing ROS & MDA & increasing the activity of SOD and CAT. It also activates Nrf2 Pathway	MI	(G. Zhang et al., 2022)
Auraptene	*Citrus hassaku*	In vitro, in vivo	Rat Neonatal cardiomyocytes, SD rats	Represses MI-induced cardiac hypertrophy & left ventricular systolic dysfunction by activating PPARα	MI	(Sunagawa et al., 2022)
Notoginsenoside R1	*Panax notoginseng*	In vitro, in vivo	Rat H9C2 cell, male SD rats	Regulates the proliferation and apoptosis of H9C2 cells & attenuates MI by activating the JAK/STAT3 signaling pathway.	MI	(H. Xu et al., 2022)
Salidroside	*Rhodiola rosea L.*	In vivo	Male wild-type SD rats	Increases SOD and CAT activities and decreases MDA and LDH content, along with significantly promoting p-PI3k,p-AKT,Nrf2 and HO-1 expression	MI	(Fan et al., 2022)
Psoralidin	*Psoralea corylifolia L*	In vitro, in vivo	HL-1 cells, male BALB/c mice	Upregulates expression of Bcl2/Bax,Nrf2,NQO1,HO-1,NRF1,TFAM,UCP2, and inhibits oxidative stress by upregulating the expression of Nrf2,HO-1,NQO1	Cardiotoxicity (MI, HF)	(Liang et al., 2022)
Calycosin	*Radix Astragali*	In vitro In vivo	Neonatal cardiomyocytes. C57BL/6 male mice	Inhibits cell apoptosis and oxidative stress by reducing ROS,4-HNE & MDA levels via activating ALDH2	MI	(W. jun Ding et al., 2023)
Emodin	Rhubarb	In vivo	Male SD rats	Declines levels of cTnI and PGC-1 & the expressions of complex I and p-ERK in myocardial tissues	Post MI HF	(J. Liu & Ning, 2021)
Nuciferine	*Nelumbo nucifera*	In vivo, in silico	Male Wistar rats	Mitigates oxidative stress by decreasing ROS & MDA levels along with increasing SOD,CAT,GSH, and enhances the up-regulation of Bcl-2, in addition to the down-regulation of Bax,Cas-9 & Cas-3	MI	(HarishKumar & Selvaraj, 2022)
Gallic acid	Gallnuts, Sumac, Witch hazel, Tea leaves, Oak bark, and Grape seeds	In vivo	Male albino rats	Attenuates the oxidative stress by restoring the activity of SOD, GSH & decreases MDA level.	MI	(Abdelhalim et al., 2021; Shackebaei et al., 2022)

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Diosgenin	*Rhizoma polgonati*, *Smilax china*, *Trigonella foenum-graecum*	In vivo	Mice, male albino wistar rats	Minimizes oxidative stress by increasing activity of SOD, CAT, GSH, GPx, GST & reducing ROS formation	MI	(X. Liu et al., 2024) (Semwal et al., 2022) (Sun et al., 2021) (Salimeh et al., 2013)
Puerarin	*Radix puerariae*	In vivo	Male SD rats	Activates the PI3K/Akt signaling pathway	AMI	(F. Chen et al., 2021)
Bakuchiol	*Psoralea Corylifolia*	In vivo	Wild-Type C57/BL 6N Mice	Produces cardioprotective effects by inhibiting the gene expression of ERK2 and TGF-β1.	MI	(Duan et al., 2021)
β-Sitosterol	*Nepeta deflersiana*	In vitro	H9c2 cells	Reduces oxidative stress and promotes mitochondrial function by inhibiting cell apoptosis and ROS production, and increasing MMP	MIRI	(Lin et al., 2020)
Allicin	Garlic	In vivo	Male SD rats	Increases SOD, CAT, GSH-Px activities and decreases MDA levels, along with significantly regulating the JNK signaling pathway.	MI	(W. Xu et al., 2020)
Alpha-Lipoic Acid	Broccoli	In vivo	C57Bl/6 mice	Reduces oxidative stress by decreasing ROS & MDA & plasma nitrate/nitrite & Myeloperoxidase	AMI	(Z. Yang et al., 2020)
Taxifolin	Olive Oil, Grapes, Onions	In vivo	Swiss albino mice	Attenuates cardiac injury by CK-MB, cTnI, LDH, and protects against oxidative stress via reduction in MDA, protein carbonyl, and NO contents, and increase in SOD,CAT,GSH, as well as activates cardiac Nrf2/HO-1 signaling pathway	MI Other CVDs	(Obeidat et al., 2022)
Nootkatone	Grapefruit	In vivo	Male wistar albino rats	Protects myocardium by inhibiting the release of CK, LDH, & troponin-T into the serum, Minimizes oxidative stress by increasing in the activities of SOD, CAT, GSH, vitamin-C,vitamin-E via modulation of PI3K/Akt/Nrf2 signaling pathway.	MI	(Meeran et al., 2021)
Formononetin	*Trifolium pratense* (red clover)	In vitro, in vivo	NCMs, male SD rats	Mitigates the elevation of ROS & inhibits the activation of NLRP3 inflammasome via the suppression of ROS-TXNIP-NLRP3 pathway	MIRI	(D. S. Wang et al., 2020)

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Curcumin	Turmeric (*Curcuma longa*)	In vitro, in vivo	Wistar rat's cardiac fibroblasts, wild-type male mice	Alleviates cardiac fibrosis by regulating collagen deposition, ECM degradation, and CFs' proliferation and migration, as well as produces antioxidative stress effects by attenuating the down-regulation of SIRT1	MI-induced cardiac fibrosis	(J. Xiao et al., 2016)
Baicalein	*Scutellaria baicalensis, Scutellaria lateriflora*	In vivo	Male Wistar albino rats	i) Exerts significant antioxidant activity by declining nitric oxide and lipid peroxidation (MDA) and enhancing SOD, catalase and GSH activity ii) Suppresses ferroptosis in cardiomyocytes via reducing ROS and MDA	MIRI MI	(Kumar et al., 2016) (I. C. Wang et al., 2023)
Luteolin	Carrots, Olive Oil, Peppers, Rosemary	In vitro, in vivo	H9c2 cell, male SD rats	i) Increases T-SOD activity, and decreases LDH, CK, MDA level, along with decreasing the ROS generation and modulation of MAPK pathway ii) Suppresses ferroptosis in cardiomyocytes via reducing ROS and MDA	MIRI MI	(Yu et al., 2015) (I. C. Wang et al., 2023)
Brucine	*Strychnos nux-vomica* seeds	In vivo	Male wistar rats	Increases enzymatic antioxidants activities such as SOD, CAT, GPx, GSH, GSSG, GSH/GSSG ratio, and elevates the Na+/K+-ATPase activity	MI	(B. Liu et al., 2021)
Sinapic acid	Citrus and Berry fruits, Vegetables, Cereals and Oilseed	In vivo	Male Albino wistar rats	Prevents oxidative stress by reducing the level of TBARS, & improving SOD, GPx, and GSH levels, as well as protects the heart mitochondria for its anti-lipid peroxidation effect	MI	(Stanely Mainzen Prince et al., 2020)
Tanshinone IIA	*Salvia miltiorrhiza* Bunge	In vivo	Male SD rats	Attenuates oxidative stress by decreasing MDA, superoxide anions and Nox activity levels & by increasing SOD activity	MI	(CHEN et al., 2021)
Rosmarinic acid	*Rosmarinus officinalis*	In vivo	Rats	Exerts potent cardio-protective effects by increasing BDNF, IL-10, GSH, and SOD activity	Depression induced MI	(Verma et al., 2022)
Swertiamarin	*Enicostemma littorale* Blume	In vivo	Albino male wistar rats	Alleviates oxidative stress by reducing MDA, PC levels, and raising GSH, SOD, CAT, GPx, GST, GR, and TAC levels	MI	(T. Wang et al., 2022)
Fraxetin	*Fraxinus rhynchophylla*	In vivo	Male wistar rats	Reduces oxidative stress by preventing the rise of MDA levels & elevating the levels of SOD, GSH, CAT, and GPx,	MI	(Yin et al., 2022)

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				along with blocking lipid peroxidation & increasing Na+/K+ATPase levels		
Ginsenosides Rg1	*Panax ginseng*	In vivo	Wistar rats	Scavenges oxygen free radicals by SOD and GSH-Px contents	MI	(C. Yang et al., 2022)
Lutein	Spinach and Egg Yolks	In vivo	Male wistar rats	Reduces ROS by Nrf2 activation, leading to the down-regulation in TXINP expression that increases thioredoxin, and GSH content	MI	(Abdelmonem et al., 2021)
α-bisabolol	*Chamomilla recutita L, Salvia runcinata, Plinia cerrocampanens, Eremanthus erythropappus*	In vivo	Male albino wistar rats	Exerts free radical scavenging effect by reducing the concentrations of lipid peroxidation products & restoring the concentrations of GSH and vitamin-C	MI	(Meeran et al., 2018)

6. Reported SAR of Natural Antioxidant Compounds Used as Therapeutics for MI

6.1. Quercetin

Quercetin is a phenolic compound, specifically a flavonol. It contains a specialized polyphenolic structure composed of two benzene rings linked by a pyrone ring. It contains five hydroxyl groups (-OH) responsible for donating hydrogen atoms, which help in the neutralization of reactive oxygen species (ROS), resulting in antioxidant defense in MI (Figure 2). In myocytes, -OH groups in ring A and B function as free radical scavengers and facilitate the relaxation of vascular tissues. The C pyrone ring containing C2=C3 and 4-carbonyl group is responsible for binding to matrix metalloproteinase 9 (MMP-9), leading to enhancing recovery of myocardial tissue and lessening post-MI remodeling. Bioavailability is directly impacted by O-glycosylation substitutions. Derivatives, such as quercetin-3-O-glucoside, exhibit tissue-specific targeting and altered bioavailability (Alizadeh & Ebrahimzadeh, 2022; Magar & Sohng, 2020).

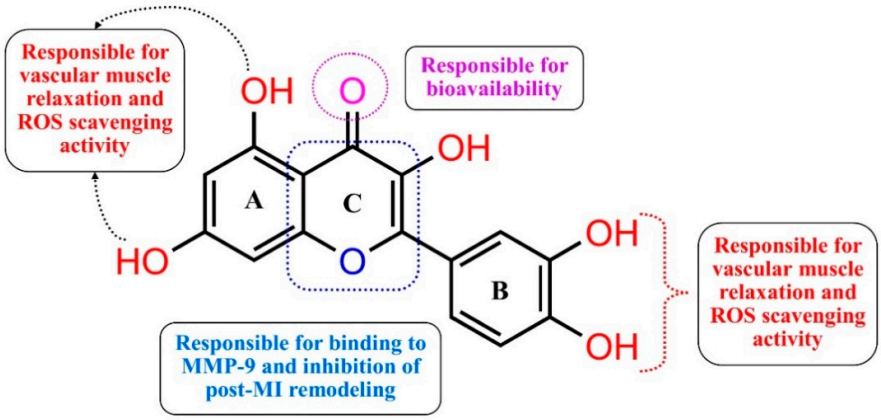

Figure 2. Structure activity relationship of Quercetin.

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6.2. Resveratrol

A stilbenoid polyphenol, resveratrol, is made up of two benzene rings joined by an ethylene (1,2-diphenylethylene) backbone. Three hydroxyl groups (-OH) are joined to the benzene rings at particular locations to form the core structure, which is trans-3,5,4′-trihydroxystilbene. Stilbene backbone, along with its arrangement, is mandatory to exert cardioprotective activity in MI (Figure 3). Modification of this core leads to a lack of inhibition of endothelin-1, which enhances myocardial necrosis and arrhythmogenesis, thereby worsening the MI. Apart from that, the number and position of –OH groups are directly related to endothelin-1 inhibition activity. Modification is possible only in the case of –OH groups. For example, 2 –OH groups in the 4 and 4′ position form 4,4′-dihydroxy-trans-stilbene, which is reported to show more potent cardioprotective activity than resveratrol. The antioxidant activity of this compound is also due to the presence of multiple –OH groups (Szekeres et al., 2010).

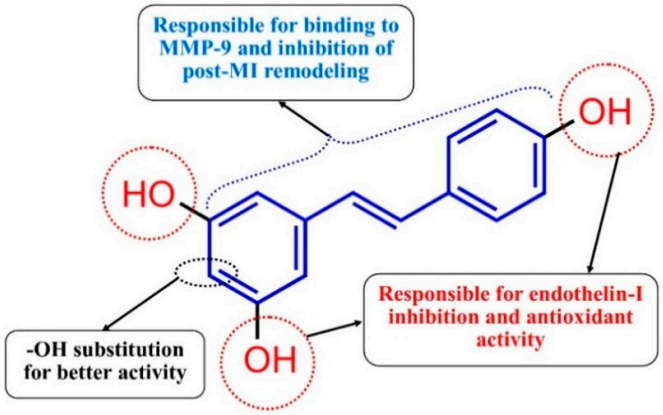

Figure 3. Structure activity relationship of Resveratrol.

6.3. Ellagic Acid

Ellagic acid, a natural polyphenolic compound, is reported to show effectiveness in MI treatment due to its process antioxidant and anti-inflammatory activities. The presence of multiple hydroxyl groups (-OH) at positions 3, 3′, 4, and 4′ enhances its radical scavenging capacity, reducing oxidative stress and lipid peroxidation in myocytes. Oral bioavailability of this compound is affected due to the polar –OH moieties. Besides, the polar moieties are also responsible for extensive phase-II metabolism and rapid clearance. Cellular signaling for inflammation, as well as optimal interaction with molecular target, is dependent on conjugated (C=O) structure (Figure 4). Apart from that, the presence of two lactone rings is essential for structural stability as well as bonding to target sites (Y. Chen et al., 2020; Mari Kannan & Darlin Quine, 2011; Yamasan et al., 2021).

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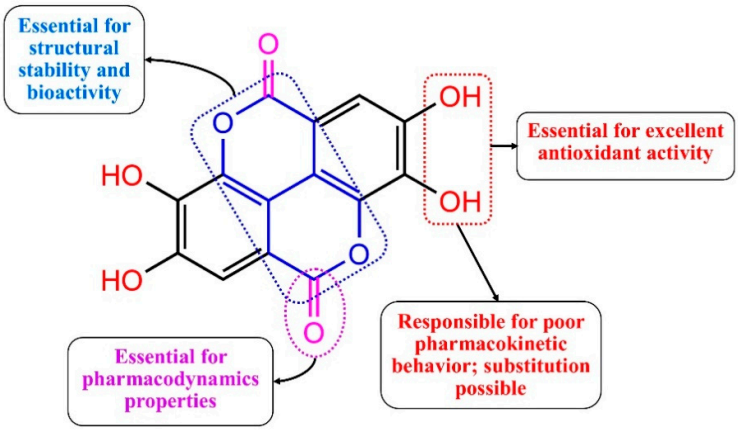

Figure 4. Structure activity relationship of Ellagic Acid.

6.4. Biochanin A

Biochanin A is an O-methylated isoflavone containing a core isoflavone scaffold attached with a number of substituents. Isoflavone scaffold, also known as 3-phenylchromen-4-one, is essential for maintaining structural rigidity and pertaining affinity to the target site for vasodilation during MI. In ring A, the 5,7-dihydroxy groups (-OH) are essential for antioxidant activity, leading to the prevention of oxidative damage of myocytes during MI. In B ring, the 4′-methoxy group (C-O-C) facilitates oral absorption due to its lipophilic nature, thus increasing oral bioavailability (Figure 5). Apart from that, it is essential for blocking cytokine expression and preventing inflammation(Sarfraz et al., 2020; J. Zhang et al., 2010).

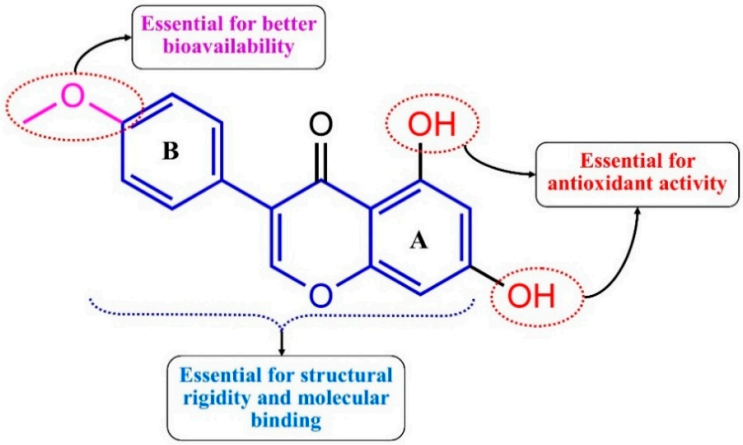

Figure 5. Structure activity relationship of Biochanin A.

6.5. 10-Gingerol

10-Gingerol, a phenolic compound, is a beta-hydroxy ketone, specifically a 5-hydroxydecan-3-one substituted by a 4-hydroxy-3-methoxyphenyl moiety at position 1. The presence of aromatic ring in the compound is essential for stabilization of the structure and molecular binding. It exhibits cardioprotective activity in MI by potent antioxidant and anti-inflammatory properties. The presence of phenolic hydroxyl group (-OH) is responsible for the strong antioxidant activity (Figure 6). The C-3 ketone group (C=O) and the extended aliphatic 10 chained hydrocarbon side chain add the

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lipophilic behavior, thus facilitating bioavailability and intracellular signaling process (H. Choi et al., 2017).

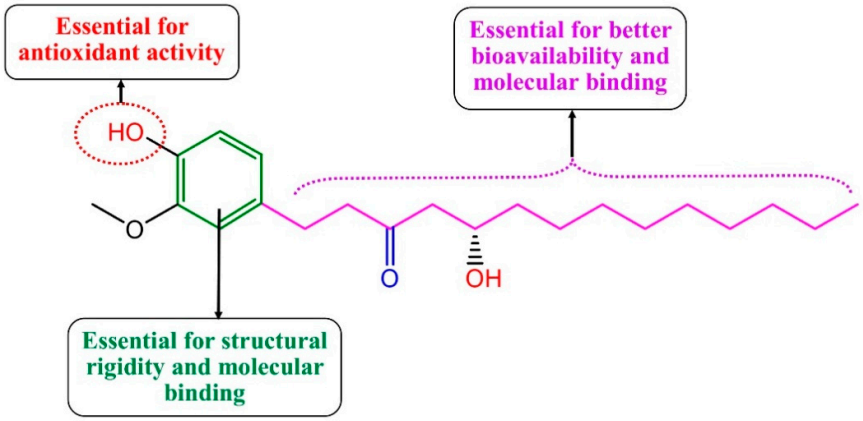

Figure 6. Structure activity relationship of 10-Gingerol.

6.6. Epigallocatechin Gallate

Epigallocatechin gallate, a 3-flavanol, is basically a catechin esterified with gallic acid. It contains a pyran ring, C, which is esterified at position 3 with gallate and is linked to three aromatic rings, A, B, and D. It shows strong cardioprotective activity in MI due to its unique polyphenolic structure with multiple –OH groups. The –OH groups and the gallate molecule are crucial for high antioxidant activity. The B-ring is essential for chelation of metal and excellent antioxidant activity (Figure 7). The A-ring and the attached pyran ring, C, are essential for molecular interaction with inflammatory signaling targets (Renzetti et al., 2020; Zuhra et al., 2022).

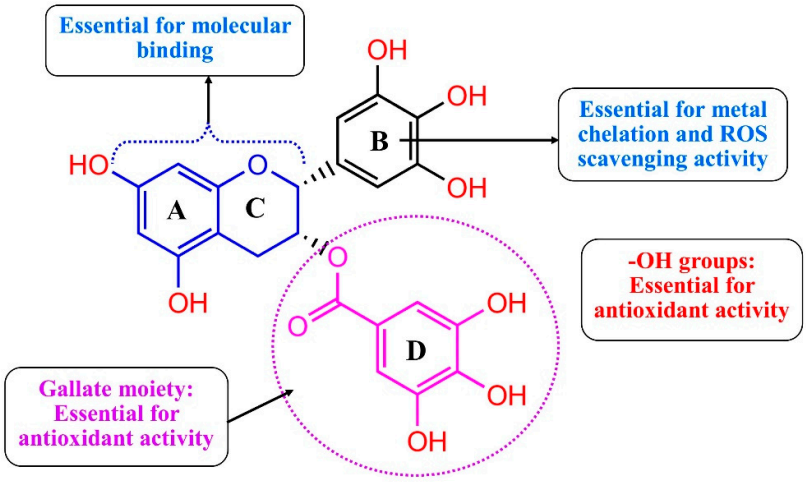

Figure 7. Structure activity relationship of Epigallocatechin Gallate.

6.7. Scopoletin

Scopoletin, also known as 7-hydroxy-6-methoxycoumarin, is a natural coumarin derivative reported for cardioprotective properties in MI due to its anti-inflammatory, antioxidant, and vasorelaxant activities. It contains core coumarin scaffold, which is key to showing antioxidant and anti-inflammatory activities. The 7-hydroxyl group (7-OH) is responsible for free radical scavenging

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and antioxidant activity. The 6-methoxy group (6-OCH_3) is responsible for oral absorption and bioavailability as well as vasorelaxation. Substitution on the aromatic ring produces different types of analogs (Figure 8). Any analog containing nucleophilic moiety shows better antioxidant activity but easily gets metabolized. Analog with electrophiles shows opposite effects (Luo et al., 2018).

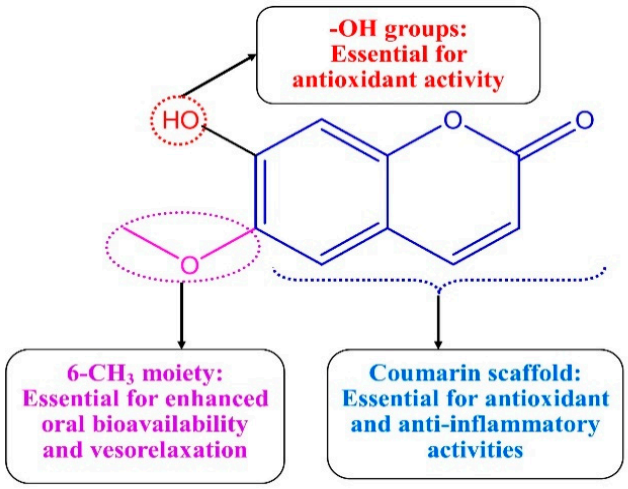

Figure 8. Structure activity relationship of Scopoletin.

7. Clinical Trial

Numerous plant-derived compounds which were reported to undergo clinical trials for the treatment of MI and oxidative stress include quercetin, puerarine, curcumin, α-lipoic acid, and lycopene (Figure 9). Among them, Quercetin underwent a multicenter randomized controlled trial where its cardioprotective potential was assessed in ST-elevated MI patients (Kozhukhov et al., 2024). This study reported that quarcetine is able to decrease the infarct size and prevent the intramyocardial hemorrhage when administered intravenously along with standard therapy. In another clinical trial, puerarin was investigated to examine whether it is effective in treating acute MI (L. Xiao et al., 2005). The study concluded that puerarin is capable of reducing infarct size. Moreover, to check if curcumin supplementation combined with piperine is able to mitigate myocardial injury succeeding acute MI, a randomized double blind clinical trial was conducted, which stated that supplementation with curcumin markedly diminishes HbA1C, LDL, ALT, and ALP, while increasing HDL level in acute MI patients (Tabaee et al., 2021). However, no influence was noticed on ejection fraction and cardiac troponin 1 level. Also, post non-Q MI patients who have type 2 diabetes mellitus went through a separate clinical trial where they were administered α-lipoic acid for a duration of 4 months in addition to oral antidiabetic medication and basic cardiovascular drugs (Altunina et al., 2020). The trial observed a reduction in CRP, IL-6, and TNF-α. Therefore, the investigation suggested the use of α-lipoic acid for the above-mentioned patients due to its antioxidant potential, along with vasorelaxation and anti-inflammatory properties. Furthermore, a clinical trial involving lycopene-enriched tomatoes was carried out (Burton-Freeman et al., 2012). The trial came to the conclusion that consumption of lycopene enrich tomatoes could reduce postprandial oxidative stress and inflammatory response.

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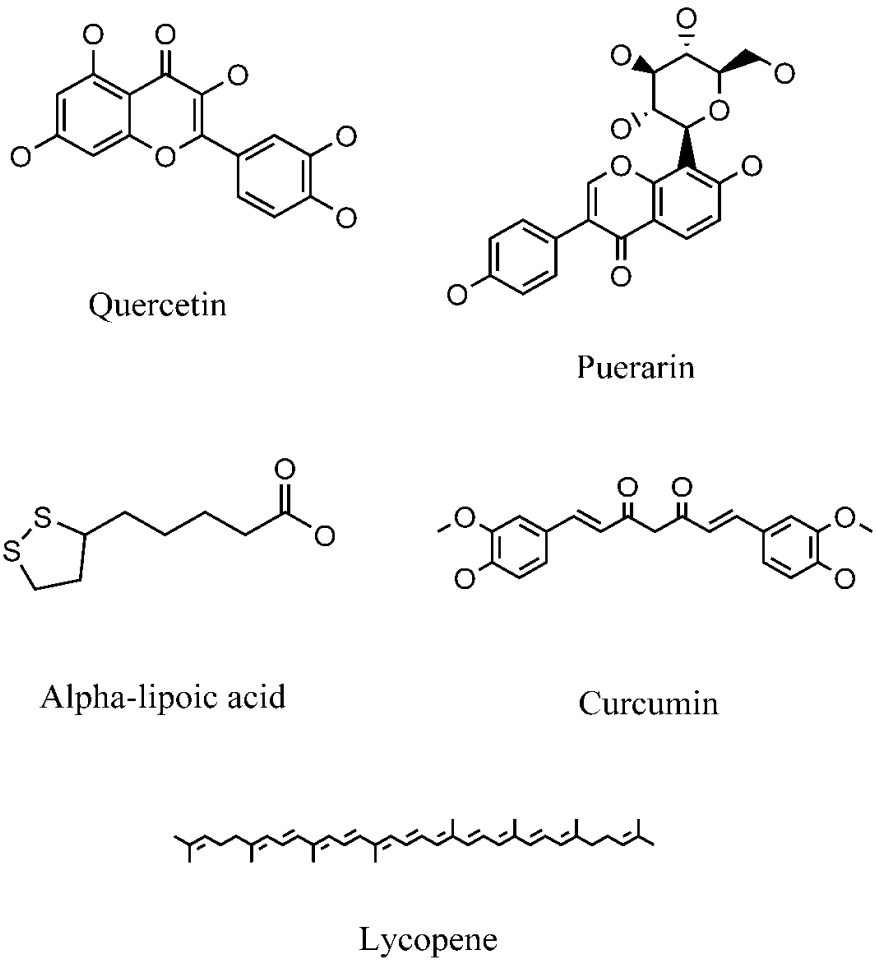

Figure 9. Plant-derived compounds under clinical trial for MI and oxidative stress management.

8. Conclusions

This review summarizes the evidence that confirms the contribution of oxidative stress in the pathogenesis and progression of myocardial infarction. It also sheds light on the underlying cardio-protective mechanisms of bioactive 51 natural antioxidant compounds, along with the reported structure-activity relationships of 7 of them. Considering the vast number of naturally occurring bioactive antioxidant compounds, the number of antioxidant compounds that have been investigated to treat myocardial infarction is comparable to the tip of the iceberg. The structure-activity relationship regarding the cardio-protective activity of these compounds reported is even too little. Although plenty of researchers have focused on finding the potential cardio-protective activity of natural antioxidant compounds against MI, the overwhelming majority of them have used animal models. Moreover, a single, naturally occurring, unmodified antioxidant compound hasn't fulfilled all the requirements to be a novel drug to date. Therefore, this review recommends the continuation of more work regarding the structural modification of the already explored compounds to find a more potent and safer drug for the purpose of bringing them from laboratory to bedside. To facilitate the structural modification, this review also suggests the conduction of newer works exploring the structure-activity relationship of natural antioxidant compounds with a focus on their development and formulation as drugs.

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References

1. Abdelhalim, A., Mahmoud, S., Nur, N., Shaban, M., Mansour, S., & Ibrahim, S. (2021). Cardioprotective Effects of Gallic Acid on an Isoprenaline-Induced Myocardial Infarction Rat Model. *International Journal of Nutrition, Pharmacology, Neurological Diseases*, *11*(2), 174–179. https://doi.org/10.4103/IJNPND.IJNPND_100_20
2. Abdelmonem, M., Ibrahim, S. M., Essam, R. M., Amin, H. A. A., & Abd-Elmawla, M. A. (2021). Lutein exerts its cardioprotective effect against the experimental model of isoprenaline-induced myocardial infarction via MIAT/miR-200a/Nrf2/TXINP pathway. *Journal of Biochemical and Molecular Toxicology*, *35*(11). https://doi.org/10.1002/JBT.22899;REQUESTEDJOURNAL:JOURNAL:10990461;SUBPAGE:STRING:ACCESS
3. Ahmad, T., Khan, T., Kirabo, A., & Shah, A. J. (2023). Antioxidant Flavonoid Diosmetin Is Cardioprotective in a Rat Model of Myocardial Infarction Induced by Beta 1-Adrenergic Receptors Activation. *Current Issues in Molecular Biology*, *45*(6), 4675–4686. https://doi.org/10.3390/cimb45060297
4. Aladag, N., Asoglu, R., Ozdemir, M., Asoglu, E., Atabey, R. D., Demir, C., & Demir, H. (2021). Oxidants and antioxidants in myocardial infarction (mi); investigation of ischemia modified albumin, malondialdehyde, superoxide dismutase and catalase in individuals diagnosed with st elevated myocardial infarction (stemi) and non-stemi (nstemi). *Journal of Medical Biochemistry*, *40*(3), 286–294. https://doi.org/10.5937/jomb0-28879
5. Alizadeh, S. R., & Ebrahimzadeh, M. A. (2022). Quercetin derivatives: Drug design, development, and biological activities, a review. *European Journal of Medicinal Chemistry*, *229*, 114068. https://doi.org/10.1016/J.EJMECH.2021.114068
6. Altunina, N. V., Lizogub, V. G., & Bondarchuk, O. M. (2020). Alpha-Lipoic Acid as a Means of Influence on Systemic Inflammation in Type 2 Diabetes Mellitus Patients with Prior Myocardial Infarction. *Journal of Medicine and Life*, *13*(1), 32–36. https://doi.org/10.25122/jml-2020-0018
7. Anbarasi, K., Vani, G., Balakrishna, K., & Devi, C. S. S. (2006). Effect of bacoside A on brain antioxidant status in cigarette smoke exposed rats. *Life Sciences*, *78*(12), 1378–1384. https://doi.org/10.1016/j.lfs.2005.07.030
8. Anderson, J. L., & Morrow, D. A. (2017). Acute Myocardial Infarction. *The New England Journal of Medicine*, *376*(21), 2053–2064. https://doi.org/10.1056/NEJMra1606915
9. Aodah, A. H., Devi, S., Alkholifi, F. K., Yusufoglu, H. S., Foudah, A. I., & Alam, A. (2023). Effects of Taraxerol on Oxidative and Inflammatory Mediators in Isoproterenol-Induced Cardiotoxicity in an Animal Model. *Molecules*, *28*(10), 1–14. https://doi.org/10.3390/molecules28104089
10. Asaikumar, L., Vennila, L., Akila, P., Sivasangari, S., Kanimozhi, K., Premalatha, V., & Sindhu, G. (2019). Preventive effect of nerolidol on isoproterenol induced myocardial damage in Wistar rats: Evidences from biochemical and histopathological studies. *Drug Development Research*, *80*(6), 814–823. https://doi.org/10.1002/DDR.21564
11. Ashraf, H., Sadatnaseri, A., Aminorroaya, A., Kuhi, Z., Zandi, N., & Saleh, S. K. (2021). Left ventricular pseudoaneurysm as a complication of myocardial infarction; a case series and review of the literature. *Frontiers in Emergency Medicine*, *5*(3). https://doi.org/10.18502/FEM.V5I3.5892
12. Ayhan, İ., Turkmen, N. B., Taslidere, A., Aydin, M., & Ciftci, O. (2025). Protective Effect of Nerolidol on Paclitaxel-Induced Reproductive Toxicity in Rats: Oxidative Stress and Inflammation. *Basic and Clinical Pharmacology and Toxicology*, *136*(2), e14126. https://doi.org/10.1111/BCPT.14126;PAGE:STRING:ARTICLE/CHAPTER

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13. Babu, S., Shetty, J. K., & Prakash, M. (2010). Total thiols and MDA levels in patients with acute myocardial infarction before and after reperfusion therapy. *Online Journal of Health and Allied Sciences*, *9*(3), 1–4.
14. Bochkov, D. V., Sysolyatin, S. V., Kalashnikov, A. I., & Surmacheva, I. A. (2012). Shikimic acid: Review of its analytical, isolation, and purification techniques from plant and microbial sources. *Journal of Chemical Biology*, *5*(1), 5–17. https://doi.org/10.1007/s12154-011-0064-8
15. Burton-Freeman, B., Talbot, J., Park, E., Krishnankutty, S., & Edirisinghe, I. (2012). Protective activity of processed tomato products on postprandial oxidation and inflammation: A clinical trial in healthy weight men and women. *Molecular Nutrition and Food Research*, *56*(4), 622–631. https://doi.org/10.1002/mnfr.201100649
16. Cai, S., Zhao, M., Zhou, B., Yoshii, A., Bugg, D., Villet, O., Sahu, A., Olson, G. S., Davis, J., & Tian, R. (2023). Mitochondrial dysfunction in macrophages promotes inflammation and suppresses repair after myocardial infarction. *Journal of Clinical Investigation*, *133*(4). https://doi.org/10.1172/JCI159498
17. Chan, W. K., Tan, L. T. H., Chan, K. G., Lee, L. H., & Goh, B. H. (2016). Nerolidol: A sesquiterpene alcohol with multi-faceted pharmacological and biological activities. *Molecules*, *21*(5), 529. https://doi.org/10.3390/molecules21050529
18. Chandimali, N., Bak, S. G., Park, E. H., Lim, H. J., Won, Y. S., Kim, E. K., Park, S. I., & Lee, S. J. (2025). Free radicals and their impact on health and antioxidant defenses: a review. *Cell Death Discovery*, *11*(1). https://doi.org/10.1038/s41420-024-02278-8
19. Chaudhary, P., Janmeda, P., Docea, A. O., Yeskaliyeva, B., Abdull Razis, A. F., Modu, B., Calina, D., & Sharifi-Rad, J. (2023). Oxidative stress, free radicals and antioxidants: Potential crosstalk in the pathophysiology of human diseases. *Frontiers in Chemistry*, *11*, 1158198. https://doi.org/10.3389/fchem.2023.1158198
20. Cheeseman, K. H., & Slater, T. F. (1993). An introduction to free radical biochemistry. *British Medical Bulletin*, *49*(3), 481–493.
21. Chen, F., Chen, Z. Q., Wang, H., & Zhu, J. J. (2021). Puerarin pretreatment inhibits myocardial apoptosis and improves cardiac function in rats after acute myocardial infarction through the PI3K/Akt signaling pathway. *Advances in Clinical and Experimental Medicine*, *30*(3), 255–261. https://doi.org/10.17219/ACEM/131754
22. CHEN, R., CHEN, W., HUANG, X., & RUI, Q. (2021). Tanshinone IIA attenuates heart failure via inhibiting oxidative stress in myocardial infarction rats. *Molecular Medicine Reports*, *23*(6), 1–10. https://doi.org/10.3892/mmr.2021.12043
23. Chen, Y., Xu, L., Wang, Y., Chen, Z., Zhang, M., Panichayupakaranant, P., & Chen, H. (2020). Study on the active polyphenol constituents in differently colored Rubus Chingii Hu and the structure-activity relationship of the main ellagitannins and ellagic acid. *Lwt- Food Science and Technology*, *121*, 108967. https://doi.org/10.1016/j.lwt.2019.108967
24. Choi, H., Ham, S. Y., Cha, E., Shin, Y., Kim, H. S., Bang, J. K., Son, S. H., Park, H. D., & Byun, Y. (2017). Structure-Activity Relationships of 6- and 8-Gingerol Analogs as Anti-Biofilm Agents. *Journal of Medicinal Chemistry*, *60*(23), 9821–9837. https://doi.org/10.1021/acs.jmedchem.7b01426
25. Choi, S., Liu, X., & Pan, Z. (2018). Zinc deficiency and cellular oxidative stress: Prognostic implications in cardiovascular diseases review-article. *Acta Pharmacologica Sinica*, *39*(7), 1120–1132. https://doi.org/10.1038/aps.2018.25
26. Choo, S., Chin, V. K., Wong, E. H., Madhavan, P., Tay, S. T., Yong, P. V. C., & Chong, P. P. (2020). Review: antimicrobial properties of allicin used alone or in combination with other medications. *Folia Microbiologica*, *65*(3), 451–465. https://doi.org/10.1007/S12223-020-00786-5
27. Chowdhury, R., Alam, D. S., Fakir, I. I., Adnan, S. D., Naheed, A., Tasmin, I., Monower, M. M., Hossain, F., Hossain, F. M., Rahman, M. M., Afrin, S., Roy, A. K., Akter, M., Sume, S. A., Biswas, A. K., Pennells, L., Surendran, P., Young, R. D., Spackman, S. A., … Di Angelantonio, E. (2015). The Bangladesh Risk of Acute Vascular Events (BRAVE) study: Objectives and design. *European Journal of Epidemiology*, *30*(7), 577–587. https://doi.org/10.1007/s10654-015-0037-2
28. Costa, B. M., Mengal, V., Brasil, G. A., Peluso, A. A., Treebak, J. T., Endlich, P. W., de Almeida, S. A., & de Abreu, G. R. (2022). Ellagic acid prevents myocardial infarction-induced left ventricular diastolic

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dysfunction in ovariectomized rats. *The Journal of Nutritional Biochemistry*, *105*, 108990. https://doi.org/10.1016/J.JNUTBIO.2022.108990

29. Davies, S. S., & Roberts II, L. J. (2011). F2-isoprostanes as an indicator and risk factor for coronary heart disease Sean. *Free Radical Biology and Medicine*, *50*(5), 559–566. https://doi.org/https://doi.org/10.1016/j.freeradbiomed.2010.11.023
30. Ding, W. jun, Chen, G. hong, Deng, S. hui, Zeng, K. feng, Lin, K. li, Deng, B., Zhang, S. wei, Tan, Z. Bin, Xu, Y. cai, Chen, S., Chen, J. bang, Chen, T. fang, Tan, Y. zhen, Zhou, Y. chun, Zhang, J. zhi, & Liu, B. (2023). Calycosin protects against oxidative stress-induced cardiomyocyte apoptosis by activating aldehyde dehydrogenase 2. *Phytotherapy Research*, *37*(1), 35–49. https://doi.org/10.1002/PTR.7591
31. Ding, Y., Zhang, B., Zhou, K., Chen, M., Wang, M., Jia, Y., Song, Y., Li, Y., & Wen, A. (2014). Dietary ellagic acid improves oxidant-induced endothelial dysfunction and atherosclerosis: Role of Nrf2 activation. *International Journal of Cardiology*, *175*(3), 508–514. https://doi.org/10.1016/J.IJCARD.2014.06.045
32. Duan, Y.-J., Shen, Z.-X., Huang, T., Gu, H.-H., Wu, Y.-T., Sun, Y.-M., & Wang, J. (2021). Bakuchiol protects against adverse cardiac remodeling after myocardial infarction. *Ethiopian Journal of Health Development*, *35*(3), 208–219.
33. Eddin, L. B., Jha, N. K., Goyal, S. N., Agrawal, Y. O., Subramanya, S. B., Bastaki, S. M. A., & Ojha, S. (2022). Health Benefits, Pharmacological Effects, Molecular Mechanisms, and Therapeutic Potential of α-Bisabolol. *Nutrients*, *14*(7), 1370. https://doi.org/10.3390/nu14071370
34. Fan, Y., Wang, W., Tian, L., & Yin, J. (2022). Salidroside induced repair of myocardial infarction through Nrf2/HO-1. *Brazilian Journal of Pharmaceutical Sciences*, *58*, 1–9. https://doi.org/10.1590/s2175-97902022e20218
35. Feng, Y., Shen, C., Ma, G., Wang, J., Chen, Z., Dai, Q., Zhi, H., Yang, C., Fu, Q., Shang, G., & Guan, Y. (2010). Prolonged pain to hospital time is associated with increased plasma advanced oxidation protein products and poor prognosis in patients with percutaneous coronary intervention for ST-elevation myocardial infarction. *Heart and Vessels*, *25*(5), 374–378. https://doi.org/10.1007/s00380-009-1220-8
36. Filippo, C. Di, Cuzzocrea, S., Rossi, F., Marfella, R., & D'Amico, M. (2006). Oxidative stress as the leading cause of acute myocardial infarction in diabetics. *Cardiovascular Drug Reviews*, *24*(2), 77–87. https://doi.org/10.1111/j.1527-3466.2006.00077.x
37. Fonsêca, D. V., Salgado, P. R. R., de Carvalho, F. L., Salvadori, M. G. S. S., Penha, A. R. S., Leite, F. C., Borges, C. J. S., Piuvezam, M. R., Pordeus, L. C. de M., Sousa, D. P., & Almeida, R. N. (2016). Nerolidol exhibits antinociceptive and anti-inflammatory activity: involvement of the GABAergic system and proinflammatory cytokines. *Fundamental & Clinical Pharmacology*, *30*(1), 14–22. https://doi.org/10.1111/FCP.12166
38. Frangogiannis, N. G. (2015). Pathophysiology of Myocardial Infarction. *Comprehensive Physiology*, *5*(4), 1841–1875. https://onlinelibrary.wiley.com/doi/abs/10.1002/j.2040-4603.2015.tb00664.x
39. Freitas, F., Brucker, N., Durgante, J., Bubols, G., Bulcão, R., Moro, A., Charão, M., Baierle, M., Nascimento, S., Gauer, B., Sauer, E., Zimmer, M., Thiesen, F., Castro, I., Saldiva, P., & Garcia, S. C. (2014). Urinary 1-hydroxypyrene is associated with oxidative stress and inflammatory biomarkers in acute myocardial infarction. *International Journal of Environmental Research and Public Health*, *11*(9), 9024–9037. https://doi.org/10.3390/ijerph110909024
40. FU, W., ZENG, M., CHEN, J., FENG, G., GUAN, P., & ZHONG, C. (2019). Study on Mechanism of Epigallocatechin Gallate Alleviating Myocardial Ischemia-reperfusion Injury by Inhibiting Cardiomyocyte Apoptosis. *China Pharmacy*, *12*, 2187–2192. http://dx.doi.org/
41. Fuad, N. I. N., Sekar, M., Gan, S. H., Lum, P. T., Vaijanathappa, J., & Ravi, S. (2020). Lutein: A comprehensive review on its chemical, biological activities and therapeutic potentials. *Pharmacognosy Journal*, *12*(6), 1769–1778. https://doi.org/10.5530/pj.2020.12.239
42. Fuentes, E., Moore-Carrasco, R., de Andrade Paes, A. M., & Trostchansky, A. (2019). Role of Platelet Activation and Oxidative Stress in the Evolution of Myocardial Infarction. *Journal of Cardiovascular Pharmacology and Therapeutics*, *24*(6), 509–520. https://doi.org/10.1177/1074248419861437
43. Gao, S., & Liu, J. (2017). Association between circulating oxidized low-density lipoprotein and atherosclerotic cardiovascular disease. *Chronic Diseases and Translational Medicine*, *3*, 89–94.

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Preprints.org (www.preprints.org) | NOT PEER-REVIEWED | Posted: 22 May 2026 doi:10.20944/preprints202605.1521.v1

44. Gao, T., Liu, M., Fu, D., Xue, Y., Liao, J., Yang, P., & Li, X. (2024). Allicin treats myocardial infarction in I/R through the promotion of the SHP2 axis to inhibit p-PERK-mediated oxidative stress. *Aging (Albany NY)*, *16*(6), 5207. https://doi.org/10.18632/AGING.205640
45. Gonçalves, M. S. S., Silva, E. A. P., Santos, D. M., Santana, I. R., Souza, D. S., Araujo, A. M., Heimfarth, L., Vasconcelos, C. M. L., Santos, V. C. O., Santos, M. R. V., de S. S. Barreto, R., Quintans Júnior, L. J., & Barreto, A. S. (2022). Nerolidol attenuates isoproterenol-induced acute myocardial infarction in rats. *Naunyn-Schmiedeberg's Archives of Pharmacology*, *395*(3), 353–363. https://doi.org/10.1007/s00210-022-02202-w
46. Gong, F. F., Vaitenas, I., Malaisrie, S. C., & Maganti, K. (2020). Mechanical Complications of Acute Myocardial Infarction: A Review. *JAMA Cardiology*, *6*(3), 341–349. https://doi.org/10.1001/jamacardio.2020.3690
47. Gong, G., Wan, W., Zhang, X., Chen, X., & Yin, J. (2025). Management of ROS and Regulatory Cell Death in Myocardial Ischemia – Reperfusion Injury. *Molecular Biotechnology*, *67*(5), 1765–1783. https://doi.org/10.1007/s12033-024-01173-y
48. González-Montero, J., Brito, R., Gajardo, A. I., & Rodrigo, R. (2018). Myocardial reperfusion injury and oxidative stress: Therapeutic opportunities. *World Journal of Cardiology*, *10*(9), 74–86. https://doi.org/10.4330/wjc.v10.i9.74
49. Govindasami, S., Uddandrao, V. V. S., Raveendran, N., & Sasikumar, V. (2020). Therapeutic Potential of Biochanin-A Against Isoproterenol-Induced Myocardial Infarction in Rats. *Cardiovascular & Hematological Agents in Medicinal Chemistry*, *18*(1), 31–36. https://doi.org/10.2174/1871525718666200206114304
50. Gulcin, İ. (2025). Antioxidants: a comprehensive review. In *Archives of Toxicology* (Vol. 99, Issue 5). https://doi.org/10.1007/s00204-025-03997-2
51. Guo, Q., Wang, J., Ni, C., Pan, J., Zou, J., Shi, Y., Sun, J., Zhang, X., Wang, D., & Luan, F. (2024). Research progress on the natural products in the intervention of myocardial infarction. *Frontiers in Pharmacology*, *15*(August), 1–32. https://doi.org/10.3389/fphar.2024.1445349
52. Guo, R., Li, L., Su, J., Li, S., Duncan, S. E., Liu, Z., & Fan, G. (2020). Pharmacological activity and mechanism of tanshinone iia in related diseases. *Drug Design, Development and Therapy*, *14*, 4735–4748. https://doi.org/10.2147/DDDT.S266911
53. Guo, W., Huang, D., & Li, S. (2023). Lycopene alleviates oxidative stress-induced cell injury in human vascular endothelial cells by encouraging the SIRT1/Nrf2/HO-1 pathway. *Clinical and Experimental Hypertension*, *45*(1). https://doi.org/10.1080/10641963.2023.2205051
54. Hachlafi, N. El, Lakhdar, F., Khouchlaa, A., Bakrim, S., El Omari, N., Balahbib, A., Shariati, M. A., Zengin, G., Fikri-Benbrahim, K., Orlando, G., Ferrante, C., Meninghi, L., & Bouyahya, A. (2021). Health Benefits and Pharmacological Properties of Hinokitiol. *Processes* , *9*(9), 1680. https://doi.org/10.3390/PR9091680
55. Halliwell, B. (2012). Free radicals and antioxidants: Updating a personal view. *Nutrition Reviews*, *70*(5), 257–265. https://doi.org/10.1111/j.1753-4887.2012.00476.x
56. Han, X., Qi, J., Yang, Y., Zheng, B., Liu, M., Liu, Y., Li, L., Guan, S., Jia, Q., & Chu, L. (2022). Protective mechanisms of 10-gingerol against myocardial ischemia may involve activation of JAK2/STAT3 pathway and regulation of Ca2+ homeostasis. *Biomedicine and Pharmacotherapy*, *151*(April), 113082. https://doi.org/10.1016/j.biopha.2022.113082
57. HarishKumar, R., & Selvaraj, C. I. (2022). Nuciferine from Nelumbo nucifera Gaertn. attenuates isoproterenol-induced myocardial infarction in Wistar rats. *Biotechnology and Applied Biochemistry*, *69*(3), 1176–1189. https://doi.org/10.1002/bab.2194
58. Hausenloy, D. J., & Yellon, D. M. (2013). Myocardial ischemia-reperfusion injury: A neglected therapeutic target. *Journal of Clinical Investigation*, *123*(1), 92–100. https://doi.org/10.1172/JCI62874
59. Hazini, A., Cemek, M., Işildak, I., Alpdaıtaş, S., Önül, A., Şenel, Ü., Kocaman, T., Dur, A., Iraz, M., & Uyarel, H. (2015). Investigation of ischemia modified albumin, oxidant and antioxidant markers in acute myocardial infarction. *Advances in Interventional Cardiology/Postepy w Kardiologii Interwencyjnej*, *11*(4), 298–303. https://doi.org/10.5114/pwki.2015.55600
60. Hori, M., & Nishida, K. (2009). Oxidative stress and left ventricular remodelling after myocardial infarction. *Cardiovascular Research*, *81*(3), 457–464. https://doi.org/10.1093/cvr/cvn335

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61. Hubbard, J. (2003). Complications associated with myocardial infarction. *Nursing Times*, *99*(15), 28–29. https://europepmc.org/article/med/12733287
62. Ide, T., Tsutsui, H., Hayashidani, S., Kang, D., Suematsu, N., Nakamura, K. I., Utsumi, H., Hamasaki, N., & Takeshita, A. (2001). Mitochondrial DNA damage and dysfunction associated with oxidative stress in failing hearts after myocardial infarction. *Circulation Research*, *88*(5), 529–535. https://doi.org/10.1161/01.RES.88.5.529
63. Islam, M. A., Alam, M. A., Ahmed, S., Rakib, A., Uddin, M. G., Islam, M. N., Etu, F. S., Masud, M. I. U., & Uddin, S. M. N. (2025). The Relationship Between Lipid Peroxidation, Serum Antioxidant Vitamin, Inflammatory Biomarker, Trace Elements, and Macro-Minerals With Bangladeshi Fibromyalgia Patients: A Case-Control Study. *Health Science Reports*, *8*(9), e71222. https://doi.org/10.1002/HSR2.71222;PAGE:STRING:ARTICLE/CHAPTER
64. Ismail, M. K., Samera, M. Y., & Abid, S. K. (2018). Oxidative stress markers and antioxidant activity in patients admitted to Intensive Care Unit with acute myocardial infarction. *International Journal of Health Sciences*, *12*(5), 14–19.
65. Jenča, D., Melenovský, V., Stehlik, J., Staněk, V., Kettner, J., Kautzner, J., Adámková, V., & Wohlfahrt, P. (2021). Heart failure after myocardial infarction: incidence and predictors. *ESC Heart Failure*, *8*, 222–237.
66. Jiang, H., Zhou, Y., Nabavi, S. M., Sahebkar, A., Little, P. J., Xu, S., Weng, J., & Ge, J. (2022). Mechanisms of Oxidized LDL-Mediated Endothelial Dysfunction and Its Consequences for the Development of Atherosclerosis. *Frontiers in Cardiovascular Medicine*, *9*(June), 1–11. https://doi.org/10.3389/fcvm.2022.925923
67. Kamatou, G. P. P., & Viljoen, A. M. (2009). A Review of the Application and Pharmacological Properties of α-Bisabolol and α-Bisabolol-Rich Oils. *Journal of the American Oil Chemists' Society* , *87*(1), 1–7. https://doi.org/10.1007/S11746-009-1483-3
68. Kannan, M. M., & Quine, S. D. (2011). Ellagic acid ameliorates isoproterenol induced oxidative stress: Evidence from electrocardiological, biochemical and histological study. *European Journal of Pharmacology*, *659*(1), 45–52. https://doi.org/10.1016/j.ejphar.2011.02.037
69. Ke, Z., Wang, Y., Silimu, G., Wang, Z., & Gao, A. (2023). Pharmacology-Based Prediction of the Targets and Mechanisms for Icariin against Myocardial Infarction. *Medicina*, *59*(3). https://doi.org/10.3390/medicina59030420
70. Khalifa, A. A., Rashad, R. M., & El-Hadidy, W. F. (2021). Thymoquinone protects against cardiac mitochondrial DNA loss, oxidative stress, inflammation and apoptosis in isoproterenol-induced myocardial infarction in rats. *Heliyon*, *7*(7), e07561. https://doi.org/10.1016/j.heliyon.2021.e07561
71. Khan, H. A., Alhomida, A. S., Sobki, S. H., Habib, S. S., Aseri, Z. Al, Khan, A. A., & Moghairi, A. Al. (2013). Serum markers of tissue damage and oxidative stress in patients with acute myocardial infarction. *Biomedical Research*, *24*(1), 15–20.
72. Kharb, S., & Singh, V. (2000). Magnesium deficiency potentiates free radical production associated with myocardial infarction. *The Journal of the Association of Physicians of India*, *48*(5), 484–485. https://europepmc.org/article/med/11273138
73. Khattak, M., Khan, I. A., Shah, N., Abdulsamad, S. A., Naeem, A. A., & Shah, A. J. (2025). Shikimic acid, a phenolic acid reverses isoproterenol-induced myocardial infarction in rat model. *Phytomedicine Plus*, *5*(2), 100788. https://doi.org/10.1016/j.phyplu.2025.100788
74. Kitano, D., Takayama, T., Nagashima, K., Akabane, M., Okubo, K., Hiro, T., & Hirayama, A. (2016). A comparative study of time-specific oxidative stress after acute myocardial infarction in patients with and without diabetes mellitus. *BMC Cardiovascular Disorders*, *16*(1), 1–6. https://doi.org/10.1186/s12872-016-0259-6
75. Kozhukhov, S., Parkhomenko, A., Lutay, Y., & Dovganych, N. (2024). Impact of quercetin in patients with myocardial infarction. A multicenter, randomized, and open-label pilot study. *Hellenic Journal of Cardiology*, *76*, 68–74. https://doi.org/10.1016/j.hjc.2023.08.004
76. Kozlov, A. V., Javadov, S., & Sommer, N. (2024). Cellular ROS and Antioxidants: Physiological and Pathological Role. *Antioxidants*, *13*(5), 1–11. https://doi.org/10.3390/antiox13050602
77. Krishna, P. S., Ramesh Kumar, N., Swathi, Rani, S., & Roja Rani, A. (2023). Amaranthus viridis methanolic extract and its active compound kaempferol ameliorate myocardial infarction induced by isoproterenol

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through decreasing oxidative stress and cell death via Nrf-2/HO-1 and MMP/Bax/Bcl-2/TLR-4 pathways in rats. *Comparative Clinical Pathology* , *32*(4), 661–670. https://doi.org/10.1007/S00580-023-03474-1

78. Kumar, M., Kasala, E. R., Bodduluru, L. N., Dahiya, V., & Lahkar, M. (2016). Baicalein protects isoproterenol induced myocardial ischemic injury in male Wistar rats by mitigating oxidative stress and inflammation. *Inflammation Research*, *65*(8), 613–622. https://doi.org/10.1007/s00011-016-0944-z
79. Kurian, G. A., Rajagopal, R., Vedantham, S., & Rajesh, M. (2016). The Role of Oxidative Stress in Myocardial Ischemia and Reperfusion Injury and Remodeling: Revisited. *Oxidative Medicine and Cellular Longevity*, *2016*. https://doi.org/10.1155/2016/1656450
80. Leong, X. Y., Thanikachalam, P. V., Pandey, M., & Ramamurthy, S. (2016). A systematic review of the protective role of swertiamarin in cardiac and metabolic diseases. *Biomedicine & Pharmacotherapy*, *84*, 1051–1060. https://doi.org/10.1016/J.BIOPHA.2016.10.044
81. Li, J., Ma, X., Yang, J., Wang, L., Huang, Y., & Zhu, Y. (2022). Lupeol Alleviates Myocardial Ischemia-Reperfusion Injury in Rats by Regulating NF-κB and Nrf2 Pathways. *The American Journal of Chinese Medicine*, *50*(5), 1269–1280. https://doi.org/10.1142/S0192415X22500525
82. Li, P. G., Sun, L., Han, X., Ling, S., Gan, W. T., & Xu, J. W. (2012). Quercetin induces rapid eNOS phosphorylation and vasodilation by an Akt-independent and PKA-dependent mechanism. *Pharmacology*, *89*(3–4), 220–228. https://doi.org/10.1159/000337182
83. Liang, Z., Chen, Y., Wang, Z., Wu, X., Deng, C., Wang, C., Yang, W., Tian, Y., Zhang, S., Lu, C., & Yang, Y. (2022). Protective effects and mechanisms of psoralidin against adriamycin-induced cardiotoxicity. *Journal of Advanced Research*, *40*, 249–261. https://doi.org/10.1016/j.jare.2021.12.007
84. Lin, F., Xu, L., Huang, M., Deng, B., Zhang, W., Zeng, Z., & Yinzhi, S. (2020). β-Sitosterol Protects against Myocardial Ischemia/Reperfusion Injury via Targeting PPARγ/NF-κB Signalling. *Evidence-Based Complementary and Alternative Medicine*, *2020*(1), 2679409. https://doi.org/https://doi.org/10.1155/2020/2679409
85. Liu, B., Zhang, Y., Wu, Q., Wang, L., & Hu, B. (2021). Alleviation of isoprenaline hydrochloride induced myocardial ischemia injury by brucine through the inhibition of Na+/K+-ATPase. *Experimental Gerontology*, *149*(324). https://doi.org/10.1016/j.exger.2021.111332
86. Liu, J., & Ning, L. (2021). Protective role of emodin in rats with post-myocardial infarction heart failure and influence on extracellular signal-regulated kinase pathway. *Bioengineered*, *12*(2), 10246–10253. https://doi.org/10.1080/21655979.2021.1983977
87. Liu, M., & Dudley, S. C. (2020). Magnesium, Oxidative Stress, Inflammation, and Cardiovascular Disease. *Antioxidants* , *9*(10), 907. https://doi.org/10.3390/ANTIOX9100907
88. Liu, M., Samuel C. Dudley, J., Liu, M., & Samuel C. Dudley, J. (2020). Magnesium, Oxidative Stress, Inflammation, and Cardiovascular Disease. *Antioxidants* , *9*(10), 1–31. https://doi.org/10.3390/ANTIOX9100907
89. Liu, X., Shen, D., Liu, L., Peng, Y., & Lu, Q. (2024). Diosgenin improves post-myocardial infarction cardiac function via HAND2-induced angiogenesis. *Biochemical and Biophysical Research Communications*, *712–713*, 149941. https://doi.org/10.1016/J.BBRC.2024.149941
90. Lobo, V., Patil, A., Phatak, A., & Chandra, N. (2010). Free radicals, antioxidants and functional foods: Impact on human health. *Pharmacognosy Reviews*, *4*(8), 118.
91. Luo, J., Lai, T., Guo, T., Chen, F., Zhang, L., Ding, W., & Zhang, Y. (2018). Synthesis and Acaricidal Activities of Scopoletin Phenolic Ether Derivatives: QSAR, Molecular Docking Study and in Silico ADME Predictions. *Molecules* , *23*(5), 995. https://doi.org/10.3390/MOLECULES23050995
92. M. Estevez, A., & J. Estevez, R. (2012). A Short Overview on the Medicinal Chemistry of (−)-Shikimic Acid. *Mini-Reviews in Medicinal Chemistry*, *12*(14), 1443–1454. https://doi.org/10.2174/13895712803832735/CITE/REFWORKS
93. Magar, R. T., & Sohng, J. K. (2020). A Review on Structure, Modifications and Structure-Activity Relation of Quercetin and Its Derivatives. *Journal of Microbiology and Biotechnology*, *30*(1), 11–20. https://doi.org/10.4014/jmb.1907.07003
94. Maneewong, K., Mekrungruangwong, T., Luangaram, S., Thongsri, T., & Kumphune, S. (2011). Combinatorial determination of ischemia modified albumin and protein carbonyl in the diagnosis of

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NonST-elevation myocardial infarction. *Indian Journal of Clinical Biochemistry*, *26*(4), 389–395. https://doi.org/10.1007/s12291-011-0118-2

95. Mari Kannan, M., & Darlin Quine, S. (2011). Pharmacodynamics of ellagic acid on cardiac troponin-T, lyosomal enzymes and membrane bound ATPases: Mechanistic clues from biochemical, cytokine and in vitro studies. *Chemico-Biological Interactions*, *193*(2), 154–161. https://doi.org/10.1016/j.cbi.2011.06.005
96. Meeran, M. F. N., Azimullah, S., Adeghate, E., & Ojha, S. (2021). Nootkatone attenuates myocardial oxidative damage, inflammation, and apoptosis in isoproterenol-induced myocardial infarction in rats. *Phytomedicine*, *84*, 153405. https://doi.org/10.1016/j.phymed.2020.153405
97. Meeran, M. F. N., Laham, F., Al-Taee, H., Azimullah, S., & Ojha, S. (2018). Protective effects of α-bisabolol on altered hemodynamics, lipid peroxidation, and nonenzymatic antioxidants in isoproterenol-induced myocardial infarction: In vivo and in vitro evidences. *Journal of Biochemical and Molecular Toxicology*, *32*(10), 1–6. https://doi.org/10.1002/jbt.22200
98. Meldrum, D. R., Dinarello, C. A., Cleveland, J., Cain, B. S., Shames, B. D., Meng, X., Harken, A. H., Zwischenberger, J. B., & Billiar, T. R. (1998). Hydrogen peroxide induces tumor necrosis factor α-mediated cardiac injury by a P38 mitogen-activated protein kinase-dependent mechanism. *Surgery*, *124*(2), 291–297. https://doi.org/10.1016/S0039-6060(98)70133-3
99. Melough, M. M., Sun, X., & Chun, O. K. (2017). The role of AOPP in age-related bone loss and the potential benefits of berry anthocyanins. *Nutrients*, *9*(7). https://doi.org/10.3390/nu9070789
100. Metta, S., Basalingappa, D. R., Uppala, S., & Mitta, G. (2015). Erythrocyte antioxidant defenses against cigarette smoking in ischemic heart disease. *Journal of Clinical and Diagnostic Research*, *9*(6), BC08-BC11. https://doi.org/10.7860/JCDR/2015/12237.6128
101. Mihalko, E. P., Huang, K., Sproul, E. P., Cheng, K., & Brown, A. C. (2019). Targeted treatment of ischemic and fibrotic complications of myocardial infarction using a dual-delivery microgel therapeutic. *Transactions of the Annual Meeting of the Society for Biomaterials and the Annual International Biomaterials Symposium*, *40*, 440. https://doi.org/10.1021/acsnano.8b01977
102. Minuz, P., Fava, C., & Lechi, A. (2006). Lipid peroxidation, isoprostanes and vascular damage. *Pharmacological Reports*, *58*(SUPPL.), 57–68.
103. Mohd Sabri, N. A., Lee, S. K., Murugan, D. D., & Ling, W. C. (2022). Epigallocatechin gallate (EGCG) alleviates vascular dysfunction in angiotensin II-infused hypertensive mice by modulating oxidative stress and eNOS. *Scientific Reports*, *12*(1), 1–11. https://doi.org/10.1038/s41598-022-21107-5
104. Mokhtari-Zaer, A., Marefati, N., Atkin, S. L., Butler, A. E., & Sahebkar, A. (2019). The protective role of curcumin in myocardial ischemia–reperfusion injury. *Journal of Cellular Physiology*, *234*(1), 214–222. https://doi.org/10.1002/JCP.26848
105. Moris, D., Spartalis, M., Spartalis, E., Karachaliou, G. S., Karaolanis, G. I., Tsourouflis, G., Tsilimigras, D. I., Tzatzaki, E., & Theocharis, S. (2017). The role of reactive oxygen species in the pathophysiology of cardiovascular diseases and the clinical significance of myocardial redox. *Annals of Translational Medicine*, *5*(16), 1–11. https://doi.org/10.21037/atm.2017.06.27
106. Musher, D. M., Abers, M. S., & Corrales-Medina, V. F. (2019). Acute Infection and Myocardial Infarction. *New England Journal of Medicine*, *380*(2), 171–176. https://doi.org/10.1056/nejmra1808137
107. Mythiili, S., & Malathi, N. (2015). Diagnostic markers of acute myocardial infarction. *Biomedical Reports*, *3*(6), 743–748. https://doi.org/10.3892/br.2015.500
108. Navarro-Yepes, J., Burns, M., Anandhan, A., Khalimonchuk, O., Del Razo, L. M., Quintanilla-Vega, B., Pappa, A., Panayiotidis, M. I., & Franco, R. (2014). Oxidative stress, redox signaling, and autophagy: Cell death versus survival. *Antioxidants and Redox Signaling*, *21*(1), 66–85. https://doi.org/10.1089/ars.2014.5837
109. Neri, M., Fineschi, V., Paolo, M., Pomara, C., Riezzo, I., Turillazzi, E., & Cerretani, D. (2015). Cardiac Oxidative Stress and Inflammatory Cytokines Response after Myocardial Infarction. *Current Vascular Pharmacology*, *13*(1), 26–36. https://doi.org/10.2174/15701611113119990003
110. Obeidat, H. M., Althunibat, O. Y., Alfwuaires, M. A., Aladaileh, S. H., Algefare, A. I., Almuqati, A. F., Alasmari, F., Aldal'in, H. K., Alanezi, A. A., Alsuwayt, B., & Abukhalil, M. H. (2022). Cardioprotective Effect of Taxifolin against Isoproterenol-Induced Cardiac Injury through Decreasing Oxidative Stress,

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Inflammation, and Cell Death, and Activating Nrf2/HO-1 in Mice. *Biomolecules*, *12*(11), 1–16. https://doi.org/10.3390/biom12111546

111. Osawa, T., Ide, A., Su, J. de, & Namiki, M. (1987). Inhibition of in vitro lipid peroxidation by ellagic acid. *Journal of Agricultural and Food Chemistry*, *35*(5), 808–812. https://doi.org/10.1021/JF00077A042
112. Pacher, P., Beckman, J. S., & Liaudet, L. (2007). Nitric oxide and peroxynitrite in health and disease. *Physiological Reviews*, *87*(1), 315–424. https://doi.org/10.1152/physrev.00029.2006
113. Pandi, A., Raghu, M. H., Chandrashekar, N., & Kalappan, V. M. (2022). Cardioprotective effects of Ferulic acid against various drugs and toxic agents. *Beni-Suef University Journal of Basic and Applied Sciences*, *11*(1). https://doi.org/10.1186/s43088-022-00273-5
114. Phaniendra, A., Jestadi, D. B., & Periyasamy, L. (2015). Free Radicals: Properties, Sources, Targets, and Their Implication in Various Diseases. *Indian Journal of Clinical Biochemistry*, *30*(1), 11–26. https://doi.org/10.1007/s12291-014-0446-0
115. Poznyak, A. V., Nikiforov, N. G., Markin, A. M., Kashirskikh, D. A., Myasoedova, V. A., Gerasimova, E. V., & Orekhov, A. N. (2021). Overview of OxLDL and Its Impact on Cardiovascular Health: Focus on Atherosclerosis. *Frontiers in Pharmacology*, *11*(January), 1–11. https://doi.org/10.3389/fphar.2020.613780
116. Rabelo, T. K., Guimarães, A. G., Oliveira, M. A., Gasparotto, J., Serafini, M. R., de Souza Araújo, A. A., Quintans-Júnior, L. J., Moreira, J. C. F., & Gelain, D. P. (2016). Shikimic acid inhibits LPS-induced cellular pro-inflammatory cytokines and attenuates mechanical hyperalgesia in mice. *International Immunopharmacology*, *39*, 97–105. https://doi.org/10.1016/j.intimp.2016.07.016
117. Reddy, V. P. (2023). Oxidative Stress in Health and Disease. *Biomedicines*, *11*(11). https://doi.org/10.3390/biomedicines11112925
118. Reeder, G. S. (1995). Identification and Treatment of Complications of Myocardial Infarction. *Mayo Clinic Proceedings*, *70*(9), 880–884. https://doi.org/10.4065/70.9.880
119. Renzetti, A., Betts, J. W., Fukumoto, K., & Rutherford, R. N. (2020). Antibacterial green tea catechins from a molecular perspective: Mechanisms of action and structure-activity relationships. *Food and Function*, *11*(11), 9370–9396. https://doi.org/10.1039/d0fo02054k
120. Rhana, P., Barros, G. M., Santos, V. C. de O., Costa, A. D., Santos, D. M. dos, Fernandes-Braga, W., Durço, A. O., Santos, M. R. V., Roman-Campos, D., Vasconcelos, C. M. L. de, Cruz, J. S., & Souza, D. S. (2022). S-limonene protects the heart in an experimental model of myocardial infarction induced by isoproterenol: Possible involvement of mitochondrial reactive oxygen species. *European Journal of Pharmacology*, *930*(April). https://doi.org/10.1016/j.ejphar.2022.175134
121. Riccioni, G., D'Orazio, N., Salvatore, C., Franceschelli, S., Pesce, M., & Speranza, L. (2012). Carotenoids and vitamins C and E in the prevention of cardiovascular disease. *International Journal for Vitamin and Nutrition Research*, *82*(1), 15–26. https://doi.org/10.1024/0300-9831/a000090
122. Riley, P. A. (1994). Free radicals in biology: Oxidative stress and the effects of ionizing radiation. *International Journal of Radiation Biology*, *65*(1), 27–33. https://doi.org/10.1080/09553009414550041;WEBSITE:WEBSITE:TFOPB;REQUESTEDJOURNAL:JOURNAL:IRAB20;PAGEGROUP:STRING:PUBLICATION
123. Rodrigo, R., Libuy, M., Feliú, F., & Hasson, D. (2013). Oxidative Stress-Related Biomarkers in Essential Hypertension and Ischemia-Reperfusion Myocardial Damage. *Disease Markers*, *35*(6), 773–790.
124. Rong, N., Yang, R., Ibrahim, I. A. A., & Zhang, W. (2022). Cardioprotective Role of Scopoletin on Isoproterenol-Induced Myocardial Infarction in Rats. *Applied Biochemistry and Biotechnology* , *195*(2), 919–932. https://doi.org/10.1007/S12010-022-04123-Z
125. Sadik, C. D., Sies, H., & Schewe, T. (2003). Inhibition of 15-lipoxygenases by flavonoids: structure–activity relations and mode of action. *Biochemical Pharmacology*, *65*(5), 773–781. https://doi.org/10.1016/S0006-2952(02)01621-0
126. Salimeh, A., Mohammadi, M., & Rashidi, B. (2013). Preconditioning with diosgenin and treadmill exercise preserves the cardiac toxicity of isoproterenol in rats. *Journal of Physiology and Biochemistry*, *69*(2), 255–265. https://doi.org/10.1007/s13105-012-0208-5
127. Sandoval, Y., & Jaffe, A. S. (2019). Type 2 Myocardial Infarction: JACC Review Topic of the Week. *Journal of the American College of Cardiology*, *73*(14), 1846–1860. https://doi.org/10.1016/j.jacc.2019.02.018

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128. Sarfraz, A., Javeed, M., Shah, M. A., Hussain, G., Shafiq, N., Sarfraz, I., Riaz, A., Sadiqa, A., Zara, R., Zafar, S., Kanwal, L., Sarker, S. D., & Rasul, A. (2020). Biochanin A: A novel bioactive multifunctional compound from nature. *Science of the Total Environment*, *722*, 137907. https://doi.org/10.1016/J.SCITOTENV.2020.137907
129. Ścibior, D., Skrzycki, M., Podsiad, M., & Czeczot, H. (2008). Glutathione level and glutathione-dependent enzyme activities in blood serum of patients with gastrointestinal tract tumors. *Clinical Biochemistry*, *41*(10–11), 852–858. https://doi.org/10.1016/J.CLINBIOCHEM.2008.03.005
130. Scott, M. D., Lubin, B. H., Zuo, L., & Kuypers, F. A. (1991). Erythrocyte defense against hydrogen peroxide: Preeminent importance of catalase. *The Journal of Laboratory and Clinical Medicine*, *118*(1), 7–16. https://doi.org/10.5555/URI:PII:002221439190110S
131. Semwal, P., Painuli, S., Abu-Izneid, T., Rauf, A., Sharma, A., Daştan, S. D., Kumar, M., Alshehri, M. M., Taheri, Y., Das, R., Mitra, S., Emran, T. Bin, Sharifi-Rad, J., Calina, D., & Cho, W. C. (2022). Diosgenin: An Updated Pharmacological Review and Therapeutic Perspectives. *Oxidative Medicine and Cellular Longevity*, *2022*. https://doi.org/10.1155/2022/1035441
132. Serdar, Z., Aslan, K., Dirican, M., Sarandöl, E., Yeşilbursa, D., & Serdar, A. (2006). Lipid and protein oxidation and antioxidant status in patients with angiographically proven coronary artery disease. *Clinical Biochemistry*, *39*(8), 794–803. https://doi.org/10.1016/j.clinbiochem.2006.02.004
133. Shackebaei, D., Hesari, M., Ramezani-Aliakbari, S., Hoseinkhani, Z., & Ramezani-Aliakbari, F. (2022). Gallic acid protects against isoproterenol-induced cardiotoxicity in rats. *Human and Experimental Toxicology*, *41*, 1–10. https://doi.org/10.1177/09603271211064532
134. Shahzad, S., Hasan, A., Faizy, A. F., Mateen, S., Fatima, N., & Moin, S. (2018). Elevated DNA Damage, Oxidative Stress, and Impaired Response Defense System Inflicted in Patients With Myocardial Infarction. *Clinical and Applied Thrombosis/Hemostasis*, *24*(5), 780–789. https://doi.org/10.1177/1076029617725602
135. Shen, F., Wu, C., Zhong, X., Ma, E., Peng, J., Zhu, W., Wo, D., & Ren, D. ni. (2023). Liensinine prevents ischemic injury following myocardial infarction via inhibition of Wnt/β-catenin signaling activation. *Biomedicine and Pharmacotherapy*, *162*(March). https://doi.org/10.1016/j.biopha.2023.114675
136. Shen, Y., Shen, X., Wang, S., Zhang, Y., Wang, Y., Ding, Y., Shen, J., Zhao, J., Qin, H., Xu, Y., Zhou, Q., Wang, X., & Shen, J. (2022). Protective effects of Salvianolic acid B on rat ferroptosis in myocardial infarction through upregulating the Nrf2 signaling pathway. *International Immunopharmacology*, *112*, 109257. https://doi.org/10.1016/J.INTIMP.2022.109257
137. Si, Q., Shi, Y., Huang, D., & Zhang, N. (2020). Diosmetin alleviates hypoxia-induced myocardial apoptosis by inducing autophagy through AMPK activation. *Molecular Medicine Reports*, *22*(2), 1335–1341. https://doi.org/10.3892/mmr.2020.11241
138. Sia, Y. T., Parker, T. G., Liu, P., Tsoporis, J. N., Adam, A., & Rouleau, J. L. (2002). Improved post-myocardial infarction survival with probucol in rats: Effects on left ventricular function, morphology, cardiac oxidative stress and cytokine expression. *Journal of the American College of Cardiology*, *39*(1), 148–156. https://doi.org/10.1016/S0735-1097(01)01709-0
139. Singh, R. B., Niaz, M. A., Sharma, J. P., Kumar, R., Bishnoi, I., & Begom, R. (1994). Plasma levels of antioxidant vitamins and oxidative stress in patients with acute myocardial infarction. *Acta Cardiologica*, *49*(5), 441–452. https://europepmc.org/article/med/7839763
140. Singh, R. B., Pella, D., Neki, N. S., Chandel, J. P., Rastogi, S., Mori, H., Otsuka, K., & Gupta, P. (2004). Mechanisms of acute myocardial infarction study (MAMIS). *Biomedicine & Pharmacotherapy*, *58*(SUPPL. 1), S111–S115. https://doi.org/10.1016/S0753-3322(04)80018-0
141. Smit, M., Coetzee, A. R., & Lochner, A. (2020). The Pathophysiology of Myocardial Ischemia and Perioperative Myocardial Infarction. *Journal of Cardiothoracic and Vascular Anesthesia*, *34*(9), 2501–2512. https://doi.org/10.1053/j.jvca.2019.10.005
142. Stanely Mainzen Prince, P., Dey, P., & Roy, S. J. (2020). Sinapic acid safeguards cardiac mitochondria from damage in isoproterenol-induced myocardial infarcted rats. *Journal of Biochemical and Molecular Toxicology*, *34*(10), 2–7. https://doi.org/10.1002/jbt.22556
143. Sun, F., Yang, X., Ma, C., Zhang, S., Yu, L., Lu, H., Yin, G., Liang, P., Feng, Y., & Zhang, F. (2021). The effects of diosgenin on hypolipidemia and its underlying mechanism: A review. *Diabetes, Metabolic Syndrome and Obesity*, *14*, 4015–4030. https://doi.org/10.2147/DMSO.S326054

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144. Sunagawa, Y., Kawaguchi, S., Miyazaki, Y., Katanasaka, Y., Shimizu, K., Shimizu, S., Hamabe-horiike, T., Kawase, Y., Mori, K., Murakami, A., Hasegawa, K., Morimoto, T., Hospital, N., Hospital, S. G., Pharmacology, C., & Hospital, S. G. (2022). Auraptene, a Citrus Peel-derived Natural Product, Prevents Myocardial Infarction- Induced Heart Failure by Activating PPARα in Rats. *Phytomedicine*, *107*, 154457.
145. Szekeres, T., Fritzer-Szekeres, M., Saiko, P., & Jäger, W. (2010). Resveratrol and resveratrol analogues-structure-activity relationship. *Pharmaceutical Research*, *27*(6), 1042–1048. https://doi.org/10.1007/s11095-010-0090-1
146. Tabaee, S., Sahebkar, A., Aghamohammadi, T., Pakdel, M., Dehabeh, M., Sobhani, R., Alidadi, M., Majeed, M., & Mirhafez, S. R. (2021). The Effects of Curcumin Plus Piperine Supplementation in Patients with Acute Myocardial Infarction: A Randomized, Double-Blind, and Placebo-Controlled Trial. *Advances in Experimental Medicine and Biology*, *1328*, 199–211. https://doi.org/10.1007/978-3-030-73234-9_13
147. Tanita, A., Namiuchi, S., Onodera, K., Sunamura, S., Ogata, T., Noda, K., & Takii, T. (2024). Serum zinc concentration in patients with myocardial infarction: a retrospective study. *BMC Cardiovascular Disorders*, *24*(1), 107. https://doi.org/10.1186/S12872-024-03776-4
148. Tavares, A. M. V., Da Rosa Araujo, A. S., Llesuy, S., Khaper, N., Rohde, L. E., Clausell, N., & Belló-Klein, A. (2012). Early loss of cardiac function in acute myocardial infarction is associated with redox imbalance. *Experimental and Clinical Cardiology*, *17*(4), 263–267.
149. Tern, P. J. W., Ho, A. K. H., Sultana, R., Ahn, Y., Almahmeed, W., Brieger, D., Chew, D. P., Fong, A. Y. Y., Hwang, J., Kim, Y., Komuro, I., Maemura, K., Mohd-Ali, R., Quek, D. K. L., Reid, C., Tan, J. W. C., Wan-Ahmad, W. A., Yasuda, S., & Yeo, K. K. (2021). Comparative overview of ST-elevation myocardial infarction epidemiology, demographics, management, and outcomes in five Asia-Pacific countries: A meta-analysis. *European Heart Journal - Quality of Care and Clinical Outcomes*, *7*(1), 6–17. https://doi.org/10.1093/ehjqcco/qcaa057
150. Thuong, P. T., Pokharel, Y. R., Lee, M. Y., Kim, S. K., Bae, K. H., Su, N. D., Oh, W. K., & Kang, K. W. (2009). Dual anti-oxidative effects of fraxetin isolated from Fraxinus rhinchophylla. *Biological and Pharmaceutical Bulletin*, *32*(9), 1527–1532. https://doi.org/10.1248/bpb.32.1527
151. Thygesen, K., Alpert, J. S., Jaffe, A. S., Chaitman, B. R., Bax, J. J., Morrow, D. A., White, H. D., Corbett, S., Chettibi, M., Hayrapetyan, H., Roithinger, F. X., Aliyev, F., Sujayeva, V., Claeys, M. J., Smajić, E., Kala, P., Iversen, K. K., Hefny, E. El, Marandi, T., … Parkhomenko, A. (2018). Fourth Universal Definition of Myocardial Infarction (2018). *Journal of the American College of Cardiology*, *72*(18), 2231–2264. https://doi.org/10.1161/CIR.0000000000000617
152. Tousif, M., Nadeem, M., Tabassum, M., Rizvi, M. M. A., & Haque, S. E. (2025). Anticancer efficacy of nerolidol, cyclophosphamide, and their combination against breast cancer cell line MCF-7. *Medical Oncology*, *42*(10), 1–10. https://doi.org/10.1007/s12032-025-02997-7
153. Tsikas, D. (2017). Assessment of lipid peroxidation by measuring malondialdehyde (MDA) and relatives in biological samples: Analytical and biological challenges. *Analytical Biochemistry*, *524*, 13–30. https://doi.org/10.1016/j.ab.2016.10.021
154. Valgimigli, M., Merli, E., Malagutti, P., Soukhomovskaia, O., Cicchitelli, G., Antelli, A., Canistro, D., Francolini, G., Macrì, G., Mastrorilli, F., Paolini, M., & Ferrari, R. (2004). Hydroxyl radical generation, levels of tumor necrosis factor-alpha, and progression to heart failure after acute myocardial infarction. *Journal of the American College of Cardiology*, *43*(11), 2000–2008. https://doi.org/10.1016/j.jacc.2004.01.036
155. van der Pol, A., van Gilst, W. H., Voors, A. A., & van der Meer, P. (2019). Treating oxidative stress in heart failure: past, present and future. *European Journal of Heart Failure*, *21*(4), 425–435. https://doi.org/10.1002/ejhf.1320
156. Veach, D., Hosking, H., Thompson, K., & Santhakumar, A. B. (2016). Anti-platelet and anti-thrombogenic effects of shikimic acid in sedentary population. *Food and Function*, *7*(8), 3609–3616. https://doi.org/10.1039/c6fo00927a
157. Verma, H., Bhattacharjee, A., Shivavedi, N., & Nayak, P. K. (2022). Evaluation of rosmarinic acid against myocardial infarction in maternally separated rats. *Naunyn-Schmiedeberg's Archives of Pharmacology*, *395*(10), 1189–1207. https://doi.org/10.1007/s00210-022-02273-9

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158. Wang, D. S., Yan, L. Y., Yang, D. Z., Lyu, Y., Fang, L. H., Wang, S. B., & Du, G. H. (2020). Formononetin ameliorates myocardial ischemia/reperfusion injury in rats by suppressing the ROS-TXNIP-NLRP3 pathway. *Biochemical and Biophysical Research Communications*, *525*(3), 759–766. https://doi.org/10.1016/j.bbrc.2020.02.147
159. Wang, I. C., Lin, J. H., Lee, W. Sen, Liu, C. H., Lin, T. Y., & Yang, K. T. (2023). Baicalein and luteolin inhibit ischemia/reperfusion-induced ferroptosis in rat cardiomyocytes. *International Journal of Cardiology*, *375*, 74–86. https://doi.org/10.1016/J.IJCARD.2022.12.018
160. Wang, T., Wu, S., Ibrahim, I. A. A., & Fan, L. (2022). Cardioprotective Role of Swertiamarin, a Plant Glycoside Against Experimentally Induced Myocardial Infarction via Antioxidant and Anti-inflammatory Functions. *Applied Biochemistry and Biotechnology* , *195*(9), 5394–5408. https://doi.org/10.1007/S12010-022-04094-1
161. Wang, Y., Liao, J., Luo, Y., Li, M., Su, X., Yu, B., Teng, J., Wang, H., & Lv, X. (2023). Berberine Alleviates Doxorubicin-Induced Myocardial Injury and Fibrosis by Eliminating Oxidative Stress and Mitochondrial Damage via Promoting Nrf-2 Pathway Activation. *International Journal of Molecular Sciences*, *24*(4). https://doi.org/10.3390/ijms24043257
162. Wen, Z. J., Xin, H., Wang, Y. C., Liu, H. W., Gao, Y. Y., & Zhang, Y. F. (2021). Emerging roles of circRNAs in the pathological process of myocardial infarction. *Molecular Therapy Nucleic Acids*, *26*(December), 828–848. https://doi.org/10.1016/j.omtn.2021.10.002
163. Widder, J., Behr, T., Fraccarollo, D., Hu, K., Galuppo, P., Tas, P., Angermann, C. E., Ertl, G., & Bauersachs, J. (2004). Vascular endothelial dysfunction and superoxide anion production in heart failure are p38 MAP kinase-dependent. *Cardiovascular Research*, *63*(1), 161–167. https://doi.org/10.1016/j.cardiores.2004.03.008
164. Wong, H. S., Chen, N., Leong, P. K., & Ko, K. M. (2014). β-Sitosterol enhances cellular glutathione redox cycling by reactive oxygen species generated from mitochondrial respiration: Protection against oxidant injury in H9c2 cells and rat hearts. *Phytotherapy Research*, *28*(7), 999–1006. https://doi.org/10.1002/ptr.5087
165. Wu, T., & Liu, W. (2022). Functional hydrogels for the treatment of myocardial infarction. *NPG Asia Materials*, *14*(9). https://doi.org/10.1038/s41427-021-00330-y
166. Xiao, H., Liang, S., Cai, Q., Liu, J., Jin, L., Yang, Z., & Chen, X. (2022). Hinokitiol Protects Cardiomyocyte from Oxidative Damage by Inhibiting GSK3 β-Mediated Autophagy. *Oxidative Medicine and Cellular Longevity*, *2022*. https://doi.org/10.1155/2022/2700000
167. Xiao, J., Sheng, X., Zhang, X., Guo, M., & Ji, X. (2016). Curcumin protects against myocardial infarction-induced cardiac fibrosis via SIRT1 activation in vivo and in vitro. *Drug Design, Development and Therapy*, *10*, 1267–1277. https://doi.org/10.2147/DDDT.S104925
168. Xiao, J., Zhu, T., Yin, Y. zhang, & Sun, B. (2018). Notoginsenoside R1, a unique constituent of Panax notoginseng, blinds proinflammatory monocytes to protect against cardiac hypertrophy in ApoE-/- mice. *European Journal of Pharmacology*, *833*, 441–450. https://doi.org/10.1016/J.EJPHAR.2018.07.004
169. Xiao, L., Gao, L., & Ma, S. (2005). Comparative study on effects of puerarin and granulocyte colony-stimulating factor in treating acute myocardial infarction. *Chinese Journal of Integrated Traditional and Western Medicine*, *25*(3), 210–213.
170. Xie, W., Chen, S., Wang, W., Qin, X., Kong, C., & Wang, D. (2024). Nuciferine reduces vascular leakage and improves cardiac function in acute myocardial infarction by regulating the PI3K/AKT pathway. *Scientific Reports 2024 14:1*, *14*(1), 1–11. https://doi.org/10.1038/s41598-024-57595-w
171. Xu, H., Zhang, X., Shi, Y., Yu, K., & Jiang, Y. (2022). Notoginsenoside R1 relieves the myocardial infarction via activating the JAK2/STAT3 signaling pathway in vivo and in vitro. *Bioengineered*, *13*(3), 5653–5662. https://doi.org/10.1080/21655979.2022.2037366
172. Xu, W., Li, X. P., Li, E. Z., Liu, Y. F., Zhao, J., Wei, L. N., & Ma, L. (2020). Protective Effects of Allicin on ISO-Induced Rat Model of Myocardial Infarction via JNK Signaling Pathway. *Pharmacology*, *105*(9–10), 505–513. https://doi.org/10.1159/000503755
173. Yamasan, B. E., Mercan, T., Erkan, O., & Ozdemir, S. (2021). Ellagic Acid Prevents Ca2+ Dysregulation and Improves Functional Abnormalities of Ventricular Myocytes via Attenuation of Oxidative Stress in Pathological Cardiac Hypertrophy. *Cardiovascular Toxicology*, *21*(8), 630–641. https://doi.org/10.1007/s12012-021-09654-1

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174. Yang, C., Jiang, G., & Xing, Y. (2022). Protective Effect of Ginsenosides Rg1 on Ischemic Injury of Cardiomyocytes After Acute Myocardial Infarction. *Cardiovascular Toxicology*, *22*(10–11), 910–915. https://doi.org/10.1007/s12012-022-09767-1
175. Yang, R., Chang, Q., Meng, X., Gao, N., & Wang, W. (2018). Prognostic value of Systemic immune-inflammation index in cancer: A meta-analysis. *Journal of Cancer*, *9*(18), 3295–3302. https://doi.org/10.7150/jca.25691
176. Yang, Z., Tian, Y., Berr, S. S., & French, B. A. (2020). Therapeutic Efficacy of Alpha-Lipoic Acid against Acute Myocardial Infarction and Chronic Left Ventricular Remodeling in Mice. *Cardiology Research and Practice*, *2020*, 1–8.
177. Yin, Y., Han, W., & Cao, Y. (2019). Association between activities of SOD, MDA and Na+-K+-ATPase in peripheral blood of patients with acute myocardial infarction and the complication of varying degrees of arrhythmia. *Hellenic Journal of Cardiology*, *60*(6), 366–371. https://doi.org/10.1016/j.hjc.2018.04.003
178. Yin, Y., Wang, L., Chen, G., & You, H. (2022). Effect of Fraxetin on Oxidative Damage Caused by Isoproterenol-Induced Myocardial Infarction in Rats. *Applied Biochemistry and Biotechnology*, *194*(12), 5666–5679. https://doi.org/10.1007/s12010-022-04019-y
179. Yu, D., Li, M., Tian, Y., Liu, J., & Shang, J. (2015). Luteolin inhibits ROS-activated MAPK pathway in myocardial ischemia/reperfusion injury. *Life Sciences*, *122*, 15–25. https://doi.org/10.1016/j.lfs.2014.11.014
180. Zhang, G., Zhang, D., Zhang, X., Yu, K., & Jiang, A. (2022). Saprirearine protects H9c2 cardiomyocytes against hypoxia/ reoxygenation-induced apoptosis by activating Nrf2. *Acta Biochimica Polonica*, *69*(2), 429–436. https://doi.org/10.18388/abp.2020_5892
181. Zhang, J., Du, F., Peng, B., Lu, R., Gao, H., & Zhou, Z. (2010). Structure, electronic properties, and radical scavenging mechanisms of daidzein, genistein, formononetin, and biochanin A: A density functional study. *Journal of Molecular Structure: THEOCHEM*, *955*(1–3), 1–6. https://doi.org/10.1016/j.theochem.2010.04.036
182. Zhang, W., Zheng, Y., Yan, F., Dong, M., & Ren, Y. (2023). Research progress of quercetin in cardiovascular disease. *Frontiers in Cardiovascular Medicine*, *10*(November), 1–17. https://doi.org/10.3389/fcvm.2023.1203713
183. Zhang, X., Wang, Q., Wang, X., Chen, X., Shao, M., Zhang, Q., Guo, D., Wu, Y., Li, C., Wang, W., & Wang, Y. (2019). Tanshinone IIA protects against heart failure post-myocardial infarction via AMPKs/mTOR-dependent autophagy pathway. *Biomedicine & Pharmacotherapy*, *112*, 108599. https://doi.org/10.1016/J.BIOPHA.2019.108599
184. Zhang, Z., Zhao, X., Gao, M., Xu, L., Qi, Y., Wang, J., & Yin, L. (2022). Dioscin alleviates myocardial infarction injury via regulating BMP4/NOX1-mediated oxidative stress and inflammation. *Phytomedicine*, *103*, 154222. https://doi.org/10.1016/J.PHYMED.2022.154222
185. Zhu, T., & Wan, Q. (2023). Pharmacological properties and mechanisms of Notoginsenoside R1 in ischemia-reperfusion injury. *Chinese Journal of Traumatology*, *26*(1), 20–26. https://doi.org/10.1016/J.CJTEE.2022.06.008
186. Zingg, J. M., Vlad, A., & Ricciarelli, R. (2021). Oxidized ldls as signaling molecules. *Antioxidants*, *10*(8), 1184. https://doi.org/10.3390/antiox10081184
187. Zuhra, K., Petrosino, M., Gupta, B., Panagaki, T., Cecconi, M., Myrianthopoulos, V., Schneiter, R., Mikros, E., Majtan, T., & Szabo, C. (2022). Epigallocatechin gallate is a potent inhibitor of cystathionine beta-synthase: Structure-activity relationship and mechanism of action. *Nitric Oxide*, *128*(July), 12–24. https://doi.org/10.1016/j.niox.2022.07.007

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