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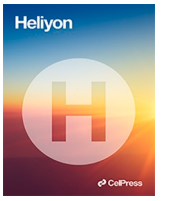

Review article

Potential role of Chinese medicine nanoparticles to treat coronary artery disease

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ABSTRACT

Coronary artery disease (CAD) is a leading cause of death worldwide, while conventional treatments such as percutaneous coronary intervention (PCI) have limitations. This review aims to explore the potential of nanoparticles loaded with Chinese medicine in the treatment of CAD. We conducted a comprehensive literature search to summarize the characteristics of nanovehicle systems, targeting strategies, and administration methods of various nanoparticles containing Chinese medicine for CAD treatment. Nanoparticle-based drug delivery systems, capable of delivering Chinese medicine, offer several advantages, including high targeting efficiency, prolonged half-life, and low systemic toxicity, making them promising for CAD treatment. Overall, nanoparticles containing Chinese medicine present a promising approach for the treatment of CAD.

1. Introduction

Coronary heart disease arises from the narrowing and blockage of coronary arteries due to coronary atherosclerosis, leading to inadequate blood supply and subsequent tissue damage in the heart. The incidence and mortality rates of coronary artery disease (CAD) have been on the rise in China. In 2020, it was estimated that approximately 330 million individuals were affected by cardiovascular diseases, with 11.39 million of them suffering from coronary heart disease [1]. The primary treatments for coronary heart disease include percutaneous coronary intervention (PCI), cardiac bypass surgery, and the long-term use of anti-coagulant, anti--platelet, and lipid-lowering medications. However, these interventions can give rise to complications such as neovascularization, plaque formation, vascular restenosis, and systemic toxicity induced by the medications.

The advent and progress of nanotechnology have significantly broadened the scope of diagnostic and therapeutic approaches in the field of coronary heart disease. Nanotechnology has found applications in various aspects of coronary heart disease management, including targeted cardiovascular imaging techniques, nanoeluting stents, and nanoparticle-based drug delivery systems. Among these, the nanoparticle-mediated targeted drug delivery system holds immense promise and offers distinct advantages for the treatment of patients with coronary artery disease (CAD) [2]. This review article focuses on the utilization of several nanoparticle-mediated drug delivery systems incorporating Chinese medicine for the treatment of coronary heart disease.

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1.1. Nanoparticle characteristics

Nanoparticles exhibit immense potential as drug carriers due to their drug-targeting capabilities, low toxicity, biodegradability, and biocompatibility [3]. In the field of medicine, nanotechnology finds diverse applications, including medical imaging and diagnosis, drug and gene delivery systems, and tissue engineering scaffolds [4]. Among these applications, the nanodrug loading system stands out as one of the most commonly utilized approaches, involving the combination of different nanoparticles with drugs to form complexes. This leverages the unique characteristics of nanomaterials for targeted drug delivery. With their small size, nanoparticles can traverse the endothelium of blood vessels and the blood-brain barrier, enabling efficient drug transport. Moreover, by optimizing parameters such as local temperature, protein activity, pH value, and external stimulation (e.g., ultrasonic field, magnetic field, and infrared rays), controlled and targeted drug administration can be achieved. Nanoparticles offer a promising means to transport CAD drugs with low targeting efficiency, limited bioavailability, and high tissue toxicity. Their high surface area-to-volume ratio allows for encapsulation and combination of multiple molecular drugs [5]. Previous studies have demonstrated that nanoparticle-based drug delivery systems effectively protect drugs from rapid inactivation, thereby prolonging their half-life [6]. Furthermore, nanoparticle targeting can be enhanced [7], leading to a reduction in drug toxicity [8].

2. Nanoparticle targeting strategies

2.1. Passive targeted transport

The targeting strategy of the nanoparticle-mediated drug delivery system (NMDD) can be categorized into passive and active methods. Passive targeting relies on the characteristics of atherosclerotic plaques in tissues with high permeability and weak structural integrity, allowing nanoparticles loaded with micromolecular drugs to penetrate and accumulate more easily in these tissues [9]. Furthermore, the presence of inflammatory cell congestion increases the likelihood of identifying NMDDs that enhance drug targeting [10]. Apart from tissue permeability, targeted drug delivery has been achieved by optimizing various internal or external parameters, such as temperature and magnetic field [11] (Fig. 1). For instance, Li et al. synthesized urokinase and dispersed Fe_3O_4 nanoparticles, and they discovered that the application of a magnetic field significantly enhances thrombolysis speed [12].

2.2. Active targeted transport

Passive targeted transport increases nanoparticle accumulation in local tissues, but it lacks control over the toxic effects on other cells. Building upon passive targeting, active targeted transport enhances drug targeting by modifying the nanoparticle surface with functional groups or active substances that specifically interact with plaque tissue, such as antibodies, peptides, and ligands [13].

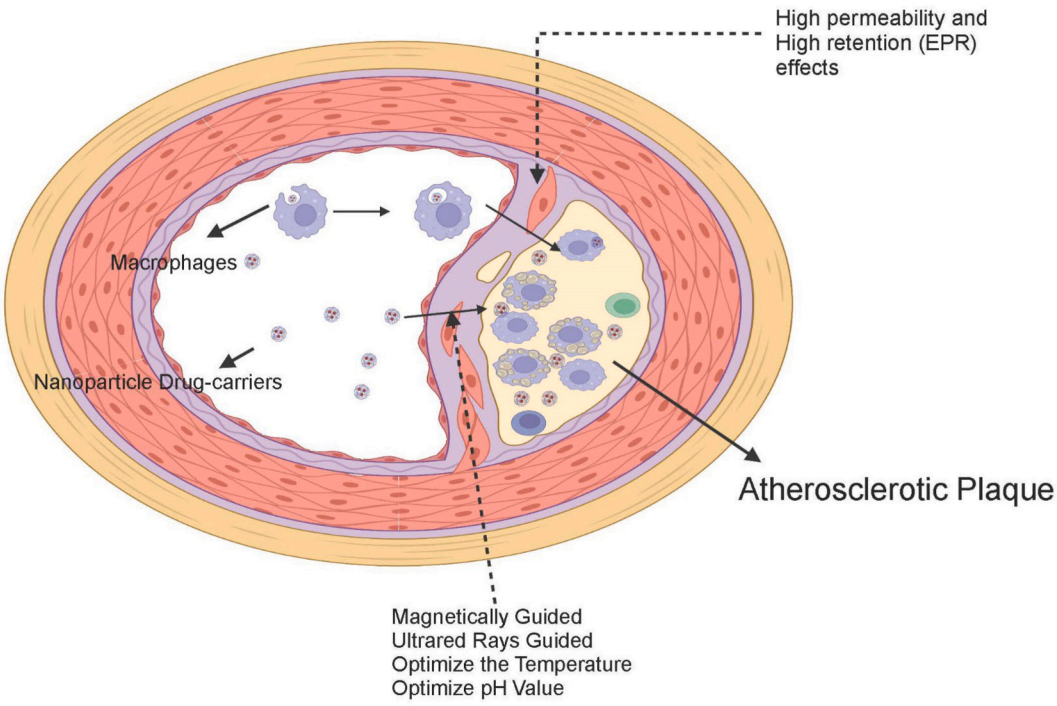

Fig. 1. Passive targeted transport of nanoparticles.

Different active substances are selected to target specific cells within the plaque tissue, including vascular endothelial cells, macrophages, foam cells, and vascular basement membrane collagen (Fig. 2). For instance, Benne et al. modified the liposome surface with the cyclic peptide Lyp-1, which actively binds to the p32 receptor expressed on foam cells. This modification enables preferential uptake of the liposome by foam cells, achieving active targeting of arterial plaque [14].

To achieve optimal targeting, a combination of passive and active targeting should be employed. Nanocarriers can effectively utilize the high permeability characteristics of plaque tissue, while functional modification allows for precise localization within the plaque tissue. The integration of these two strategies can more effectively prevent drug release or degradation before the nanoparticle reaches the plaque tissue [15].

3. Nanoparticle classification in CAD

Based on their physical properties, nanoparticles can be categorized into organic nanomaterials such as liposomes, micelles, dendrimers, and polymer nanoparticles, as well as inorganic nanomaterials including silicon, carbon-based, gold, and silver nanomaterials. Furthermore, based on their biological characteristics, nanoparticles can be classified into stimulus-responsive nanoparticles and biodegradable nanoparticles. These nanoparticles exhibit diverse biological and physical properties, including size, morphology, density, and surface chemistry. The effectiveness of both active and passive targeting strategies relies on the specific characteristics of the nanoparticles employed [16]. Numerous nanoparticles have been extensively investigated for drug delivery in coronary artery disease (CAD), and their descriptions are provided below (Table 1).

3.1. Liposomes

Liposome nanoparticles, resembling the spherical shape of cells, are composed of phospholipid bilayers [17]. These nanoparticles possess both lipophilic and hydrophilic properties, with a hydrophilic core and a hydrophobic surface. Liposomes exhibit low toxicity and evade immunocyte recognition. They demonstrate effective sustained drug release, prolonging the drug's presence in the body to enhance therapeutic efficacy while minimizing side effects. A randomized, placebo-controlled clinical trial investigating the accumulation of prednisolone-containing liposome nanoparticles in atherosclerotic macrophages revealed that these nanoparticles significantly extended circulation half-life and improved targeting of atherosclerotic macrophages without adversely affecting cardiometabolic parameters [18].

Lipid microsphere nanoparticles encapsulating alprostadil have been widely utilized in the treatment of myocardial infarction, angina, and other cardiovascular diseases. Alprostadil exerts inhibitory effects on platelet aggregation, promotes vasodilation to enhance microcirculation, dilates coronary arteries, and increases myocardial perfusion [19]. A randomized controlled trial involving 300 patients with acute myocardial infarction (AMI) who underwent percutaneous coronary intervention (PCI) demonstrated that the combination of alprostadil and tanshinone IIa injection notably improved cardiac function and ventricular remodeling post-PCI, while also reducing the incidence of adverse events [20].

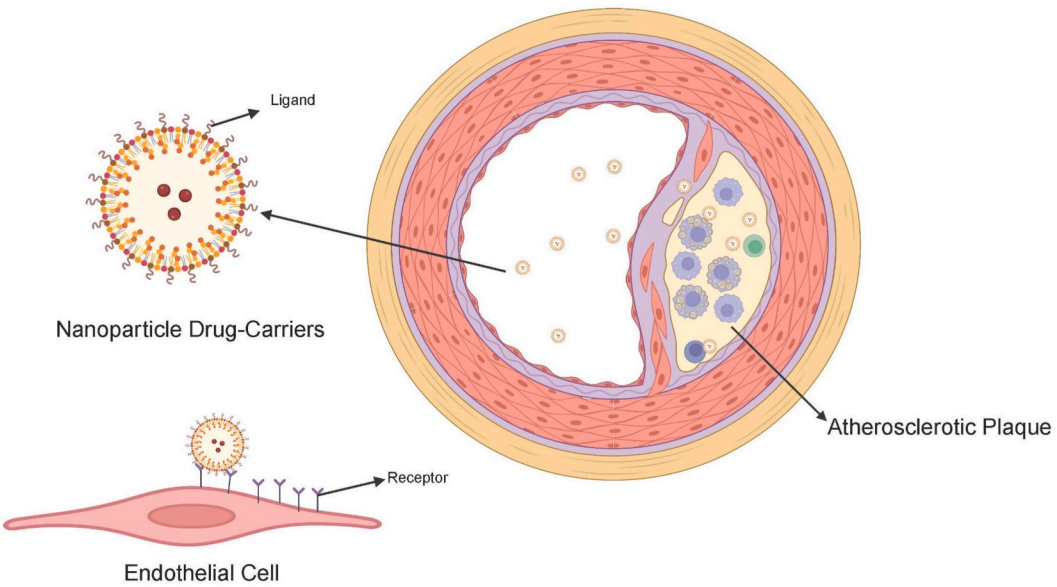

Fig. 2. Active targeted transport nanoparticles.

Table 1
Types of Nanoparticles and advantages.

Type	Drug	Model/Patient	CAD model included	Advantages	References
Liposomes	Prednisolone	Atherosclerosis humans	Yes	Prolong the circulation half-life Enhanced the targeting of atherosclerotic macrophages No adverse effect on cardiometabolic parameters	[18]
Lipid microsphere nanoparticles	Alprostadil	AMI patients who underwent PCI	Yes	Improved cardiac function and ventricular remodeling Reduced the incidence of adverse events	[20]
Poly (lactide-*co*-glycolide) nanoparticles	Pioglitazone	Plaque rupture mouse	Yes	Targeted macrophages in plaque tissue Regulate plaque inflammation Reduced inflammatory cells Effectively reduce the number of fibrous cap Stabilize plaque tissue	[24]
	Pilavastatin	Chronic limb threatening ischemia patients	No	Shown good safety and body tolerability in patients	[25]
Chitosan	Rosuvastatin	Hypercholesterolemia Rabbits	Yes	Better treatment effect of lowering blood lipid Reduce the calcification of heart valves	[26]
PEG-coated gold nanoparticles		Myocardial infarction rats	Yes	Reduced infarct size Improve cardiac systolic function Effectively inhibit cardiac fibrosis Enhanced infarct myocardial targeting and cardioprotective effects	[29]
Ultrasmall superparamagnetic iron oxide nanoparticles		Acute myocardial infarction patients	Yes	Enhanced macrophage targeting Superior safety	[31]
	Fucoidan	Elastase-induced vascular injury rats	No	More sensitive thrombus-targeted imaging	[32]
	Tissue plasminogen activator	Embolic rats	No	Enhanced thrombus targeting Enhanced thrombolytic activity	[33]

3.2. Polymer nanoparticles

Polymeric nanoparticles, including polylactic-*co*-glycolic acid (PLGA), polyethylene-imine, poly-Ɛ-caprolactone (PCL), polyvinyl alcohol, and chitosan, hold great promise as nanocarriers [21]. These nanoparticles possess a stable structure and uniform particle size, enabling precise control over drug release. Moreover, polymer nanoparticles exhibit excellent biocompatibility and low toxicity, typically devoid of teratogenic effects. Upon degradation, they yield non-toxic oligomerized end products that can coexist with most drugs. Leveraging their physical properties, such as size and large surface-to-volume ratio, polymer nanoparticles facilitate cellular drug absorption and enhance bioavailability [22]. However, polymer nanoparticles also exhibit limitations, such as the incompatibility of the natural polymer chitosan with biological fluids, leading to particle degradation and reduced efficacy. Nevertheless, surface modifications of nanoparticles can overcome this issue, enhancing their biocompatibility and targeting capabilities [23]. For instance, in a mouse model of atherosclerosis, pioglitazone-loaded PLGA nanoparticles demonstrated superior therapeutic outcomes compared to free pioglitazone. These results highlighted the significant reduction in the number and thickness of fibrous caps achieved by using nanoparticle-mediated drug delivery systems, as the modified PLGA nanoparticles targeted monocytes or macrophages and activated receptors that promoted macrophage differentiation to regulate inflammation [24]. Lin et al. developed a rosuvastatin-chitosan nanoloading vehicle system using an ionic gel preparation and conducted in vivo experiments in a hypercholesterolemia rabbit model. Their findings, published recently, demonstrated that the nanoloaded particle group exhibited a more pronounced effect on reducing blood lipid levels compared to the group receiving rosuvastatin alone. Additionally, the nanoloaded particle group showed a reduction in heart valve calcification compared to the rosuvastatin alone group [25]. In a phase I/IIa clinical trial, PLGA nanoparticles loaded with pilavastatin exhibited a favorable safety profile and tolerability in patients with chronic limb-threatening ischemia. This encouraging outcome suggests the potential of PLGA nanoparticles as a promising therapeutic strategy for vascular diseases [26].

3.3. Gold nanoparticles

Gold nanoparticles, as stable inorganic metal nanocarriers, possess several advantages that make them suitable for cardioprotective drug delivery. One key advantage is their reduced toxicity towards other cells and non-immunogenic nature, making them widely utilized in this field. Due to their unique structural characteristics, gold nanoparticles exhibit excellent targeting capabilities towards

ischemic tissues. Consequently, drugs loaded onto these nanoparticles can efficiently permeate and accumulate within the tissue, facilitating faster recovery of ischemic tissue and promoting angiogenesis by delivering exogenous growth factors [27]. To enhance drug transportation efficiency, metoprolol has been conjugated with gold nanoparticles, which selectively target β1 receptors. The conjugates have shown twice the efficacy in heart tissue affected by heart failure compared to the administration of drugs alone, while exhibiting minimal adverse effects in other tissues [28]. Polyethylene glycolylated (PEG) gold nanoparticles have been found to decrease the size of infarcted tissue by slowing down cardiomyocyte necrosis and apoptosis. Additionally, they exhibit control over inflammation through collagen deposition. Consequently, several studies have suggested the use of gold nanoparticles or gold nanoparticle multipolymers for the treatment of cardiovascular diseases [29]. While gold nanoparticles have shown promise in laboratory research for therapeutics targeting acute myocardial infarction, further investigation is required to determine their clinical utility and application.

3.4. Magnetic nanoparticles

Magnetic nanoparticles, as external stimulus-responsive nanomaterials, hold great potential for targeted drug delivery and utilization in magnetic resonance imaging (MRI) technology. By applying an external magnetic field, these nanoparticles can be directed towards specific targets. Magnetic nanoparticles can serve as safe carriers for magnetic resonance contrast agents or certain cardiovascular drugs, offering new possibilities in the field of cardiovascular medicine [30]. While various pure metals and metal oxides have been explored experimentally, the use of iron oxide nanoparticles has received authorization and clearance from the US Food and Drug Administration. In a clinical study focusing on cardiovascular imaging, ultrasmall superparamagnetic iron oxide nanoparticles demonstrated superior safety and the ability to better characterize myocardial infarction pathology by detecting macrophages, compared to gadolinium-based compounds [31]. Superparamagnetic iron oxide nanoparticles have shown effective permeation of blood vessel endothelium and accumulation in plaques. Suzuki et al. utilized fucoidan-coated ultrasmall superparamagnetic iron oxide nanoparticles (USPIO–FUCO) as an MRI contrast agent for arterial thrombi. By closely interacting with activated platelets, these nanoparticles enabled the detection of thrombi using MRI in animal models. This imaging study targeting thrombi suggests that magnetic nanoparticles have the potential to enhance imaging technologies for coronary artery disease [32]. In a rat model with embolization, magnetic nanoparticles have been utilized to enhance the local thrombolysis action of tissue-type plasminogen activators. By employing a magnetic field, the magnetic-assisted magnetic nanoparticle-bound drug demonstrated a significantly lower

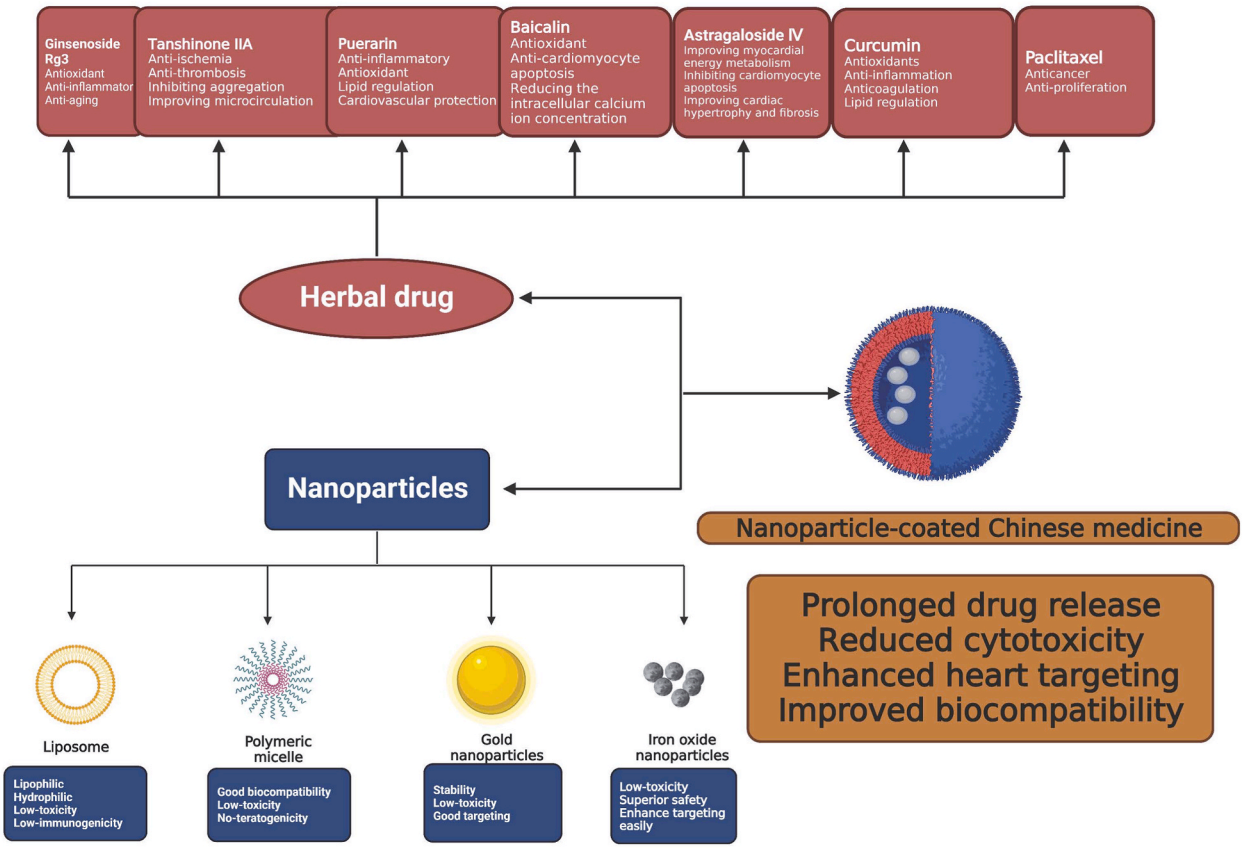

Fig. 3. Mechanism of action of nanoparticles on coronary artery disease.

dose requirement for clot dissolution compared to free drug administration [33]. Previous animal studies have indicated that certain magnetic nanoparticles can cross the blood-brain barrier and induce brain cell deformation, leading to toxicity. However, the application of a polymer coating has been found to mitigate magnetic nanoparticle toxicity [34]. Apart from magnetic nanoparticles, there are various other stimulus-responsive nanoparticles that can be employed in drug-loading systems, with different properties governing drug release and targeting conditions.

4. Nanoparticle-coated Chinese medicine in CAD

In the realm of Chinese medicine, previous studies have unveiled the potential of specific extracts in treating coronary artery disease (CAD) owing to their remarkable anti-inflammatory, anti-oxidative, lipid-regulating, and cardiovascular-protective properties.

Table 2
Mechanisms and advantages of nanoparticle-coated Chinese medicine in coronary artery disease.

Herbal drug	Nano-carriers	Effects	Model/Patient	Outcome	References
Ginsenoside Rg3	PEG-b-PPS nanoparticles	Antioxidant Anti-inflammatory Anti-aging	Ischemia-reperfusion rats	Effectively improve heart function Reduce myocardial injury Reduced infarct size	[41]
Puerarin	RGD/PEG-SLNs	Anti-inflammatory Antioxidant Lipid regulation Cardiovascular protection	Myocardial infarction rats	Prolonged release Enhanced Ischemic myocardium targeting Reduced infarct size	[44]
	PEG-PE micelles nanoparticles		Acute myocardial ischemia rats	Prolonged release Reduce the hemolysis events Reducing apoptosis	[45]
	PEG-PLGA micelles nanoparticles		Acute myocardial ischemia rats	Enhanced Ischemic myocardium targeting Reduced the myocardial enzymes Reduced infarct size	[46]
Tanshinone IIA	PEG-PE micelles nanoparticles	Anti-ischemia Anti-thrombosis Inhibiting platelet aggregation Improving microcirculation	Acute myocardial ischemia rats	Prolonged release Enhanced Ischemic myocardium targeting	[49]
	Lipid-polymeric nanoparticles		Acute myocardial ischemia rats	Prolonged release Enhanced Ischemic myocardium targeting Enhanced therapeutic efficacy	[50]
Baicalin	PEG-PCL nanomicelle	Antioxidant, Anti-cardiomyocyte apoptosis, Reducing the intracellular calcium ion concentration	Cardiac muscle cell	Prolonged release Enhanced mitochondrial targeting in cardiomyocytes	[53]
	Lipid polymer hybrid nanoparticles (LPNs)		Acute myocardial infarction rats	Prolonged release Enhanced myocardium targeting Reduced infarct size Reduced cytotoxicity	[54]
Astragaloside IV	Polyethylene glycol-derived phosphatidylethanolamine (PEG-PE)	Improving myocardial energy metabolism, Inhibiting cardiomyocyte apoptosis, Improving cardiac hypertrophy and fibrosis	Cardiac muscle cell	Prolonged release Enhanced mitochondrial targeting in cardiomyocytes Enhanced the anti-apoptotic effect	[56]
	PLGA-b-PEG-TPP polymer nanomicelles		Acute myocardial infarction rats	Enhanced mitochondrial targeting in cardiomyocytes Improved cardiac function, myocardial injury, mitochondrial injury, and cardiac inflammation	[57]
Curcumin	Nanomicelle	Antioxidants, Anti-inflammation Anticoagulation Lipid regulation	Patients who undergone coronary elective angioplasty	Improved lipoid profile, antioxidant indices, and inflammatory factors	[59]
Paclitaxel	Albumin nanoparticles (Abraxane)	Anticancer Anti-proliferation	Advanced non-small cell lung cancer patients	Increasing the objective symptom remission rates Reductced the incidence of adverse events	[64]
	Liposomal nanoparticles		Aortic atherosclerosis patients	Reduce lesion size Lower the incidence of toxic reactions	[66]

Consequently, Chinese medicine has emerged as a highly promising treatment avenue. In this context, nanotechnology is presently being harnessed in two distinct ways. The first approach involves processing the drug into a nanoscale suspension agent or cocrystals, thereby augmenting its specific surface area, solubility, and stability. Notably, certain medications like curcumenol [35] and meletin [36] have been successfully prepared as nanosuspensions (Fig. 3).

The second approach revolves around the loading and transportation of active substances from Chinese medicine by means of nanoparticles. These substances possess unique advantages over conventional synthetic drugs due to their natural compounds, which engender biological and synergistic activity across numerous tissues and targets within the human body [37]. However, the clinical application of active substances from Chinese medicine is impeded by challenges such as low absorption, stability, permeability, and potential hepatic and renal toxicity [38]. The advent of nanotechnology has opened up new avenues for exploring the active ingredients in Chinese medicine, as highly specific nanoparticle targeting can compensate for the limitations of these substances. Various nanoparticles have been successfully employed in drug-carrying systems for numerous active substances in Chinese medicine, including ginsenoside, puerarin, tanshinone IIA, baicalin, triptolide, and ligustrazine [39]. The following section describes several representative Chinese medicine nanovehicle systems in the present study (Table 2 and Fig. 4).

4.1. Ginsenosides

Ginsenoside, an active compound derived from ginseng, possesses anti-inflammatory and antioxidant properties, making it potentially valuable in alleviating cancer symptoms and delaying senescence. Among different types of ginsenosides, ginsenoside Rg3 has been widely studied in clinical research. However, its application in treating coronary artery disease (CAD) is hindered by challenges such as low membrane permeability, poor bioavailability, and a transient half-life [40]. Despite these limitations, ginsenoside Rg3 has demonstrated effective inhibition of reactive oxygen species, thereby aiding in the alleviation of myocardial ischemia symptoms. To address these issues, Li et al. developed PEG-b-PPS-Rg3 nanoparticles that respond well to reactive oxygen species. These nanoparticles effectively loaded and transported ginsenoside Rg3. In an ischemia-reperfusion rat model, the PEG-b-PPS-Rg3 nanoparticles exhibited cardiac diastolic function protection and reduced myocardial infarction size [41].

4.2. Puerarin

Puerarin, renowned for its antioxidant and anti-cancer properties, as well as its ability to safeguard heart and liver function, has

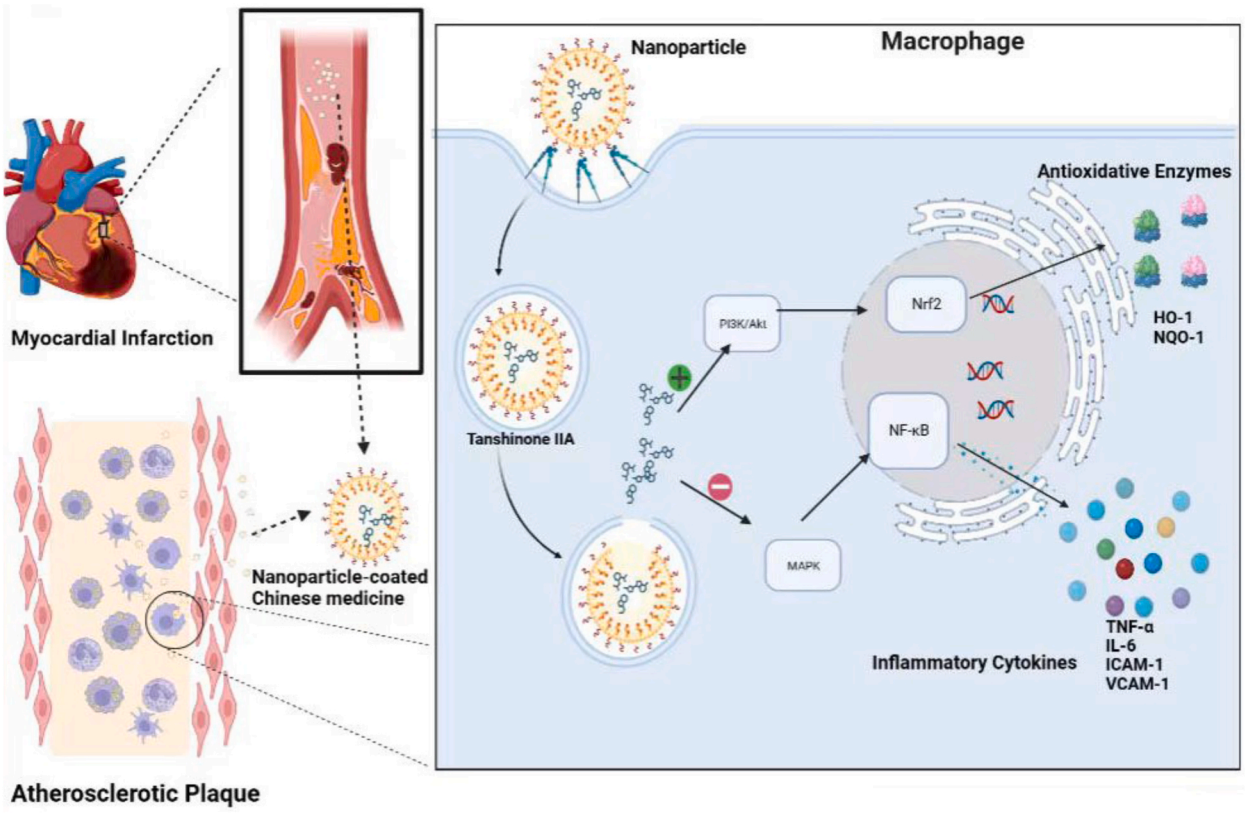

Fig. 4. Nanoparticle-coated Chinese medicine in regulating coronary artery disease.

found application in the treatment of various cardiovascular and cerebrovascular diseases. In China, both puerose sodium chloride and puerose glucose injections have received clinical approval as vasodilators for coronary artery disease (CAD), angina pectoris, myocardial ischemia or infarction, and retinal vein blockage [42]. However, puerarin's chemical composition imparts low solubility, permeability, and bioavailability, thereby resulting in poor absorption following oral administration [43]. Increasing the dosage of puerarin alone fails to enhance its efficacy and may even give rise to systemic toxicity. To overcome these challenges, the utilization of a nanodrug-carrying system has proven effective. Noteworthy nanocarrying systems for puerarin encompass cyclic arginyl-glycylaspartic acid (RGD)-modified and PEGylated lipid nanoparticles [44], PEG-derived phosphatidylethanolamine (PEG-PE) micelles [45], and PEG-PLGA micelles [46]. In vivo and in vitro experiments have demonstrated that these nanoparticles exhibit superior cardiomyocyte targeting and protective effects, extended in vivo retention time, and enhanced cardiomyocyte protection compared to puerarin alone [47].

4.3. Tanshinone IIA

Tanshinone IIA, an active ingredient derived from Salvia miltiorrhiza, has demonstrated a range of cardiovascular effects, including anti-ischemic and anti-thrombotic properties, inhibition of platelet aggregation, improvement of microcirculation, and attenuation of hypoxia-induced cardiomyocyte injury, which are similar to those of astragaloside IV [48]. However, the low solubility and poor bioavailability of tanshinone IIA present challenges. To overcome these limitations, Fang et al. employed the membrane hydration method to combine tanshinone IIA with PEG-PE nanoparticles. The results of in vitro and in vivo experiments demonstrated that tanshinone IIA-loaded PEG-PE nanoparticles exhibited excellent ischemic myocardial targeting and prolonged drug release time [49]. In another study, Zhang et al. utilized lipid-polymeric nanoparticles to deliver tanshinone IIA, achieving mitochondrial targeting in infarcted cardiac myocytes by modifying the nanoparticle surface. Compared to free tanshinone IIA, the modified nanoloaded vehicle system displayed higher biocompatibility, extended drug release time, significant accumulation in the heart, and reduced infarct size in a rat model of coronary artery ligation [50] (Fig. 4).

4.4. Baicalin

Baicalin, the primary active compound derived from Scutellaria baicalensis, exhibits antioxidant properties and pharmacological effects that can reduce cardiomyocyte apoptosis and intracellular calcium ion levels [51]. Previous studies have shown that baicalin inhibits mitochondrial damage, which can lead to apoptosis, and activates protein kinase pathways, resulting in a reduction in myocardial infarction area [52]. However, the low solubility of baicalin in water may hinder its bioabsorption and cellular uptake. To overcome these challenges, Li et al. utilized PEG-b polycaprolactone (PEG-PCL) to deliver baicalin, resulting in enhanced mitochondrial targeting. The findings demonstrated that baicalin-loaded PEG-PCL nanomicelles effectively targeted mitochondria in cardiomyocytes, leading to a reduction in caspase 3 activity and ROS levels associated with cardiomyocyte apoptosis, thereby exhibiting improved anti-myocardial apoptosis effects [53]. Alternatively, Wang et al. employed lipid-polymer hybrid nanoparticles with properties of both liposomal and polymeric nanoparticles to deliver baicalin. Additionally, they incorporated triphenylphosphonium (TPP) and atrial natriuretic peptide on the nanoparticle surface to enhance targeting towards infarcted cardiomyocytes. In vitro experiments revealed that the modified nanolipid vehicle system exhibited superior sustained drug release efficiency and lower cytotoxicity compared to nanoparticles without ligand modification. In vivo biodistribution evaluation demonstrated an extended circulation time within the body and increased accumulation in the heart for the nanolipid vehicle system [54].

4.5. Astragaloside IV

Astragaloside IV, derived from astragalus, possesses pharmacological effects such as improving myocardial contractility, blood supply, and protecting the ischemic myocardium. It also exhibits the combined effects of astragalus and salvia miltiorrhiza injections on serum inflammatory markers in patients with stable coronary heart disease [55]. However, similar to many active compounds in Chinese medicine, its poor water solubility hampers its aggregation in cardiomyocytes, thereby reducing its protective effect. To overcome this limitation, Ye et al. employed a coating of PEG-PE on astragaloside IV to enhance its cardiomyocyte targeting and strengthen its anti-myocardial apoptosis effect. The experiments demonstrated that the use of nanoparticles facilitated the entry and aggregation of astragaloside IV in cardiomyocytes, leading to a more potent anti-apoptotic effect [56]. Alternatively, Yang et al. developed PLGA-b-PEG-TPP polymer nanomicelles loaded with astragaloside IV and coated the polymer with a human platelet membrane to enable cardiac targeting. Their findings revealed that the drug-loaded nanomicelles significantly improved cardiac function, alleviated myocardial mitochondrial injury, and reduced cardiac inflammation after myocardial infarction compared to free astragaloside IV [57].

4.6. Curcumin

Curcumin, an active polyphenol compound derived from turmeric, possesses a wide range of pharmacological effects, including antioxidant, anti-inflammatory, anti-coagulation, and lipid regulation properties [58]. Various nanopreparations of curcumin have been utilized in the treatment of cardiovascular diseases. In a randomized double-blind, placebo-controlled clinical trial involving 90 patients who underwent coronary elective angioplasty, it was observed that curcumin nanomicelles and curcumin had significant effects on lipid profiles, antioxidant indices, and inflammatory factors compared to placebo. Notably, the effects were more

pronounced in the curcumin nanomicelle group than in the curcumin group [59]. This finding suggests that nanoparticles can effectively enhance the bioavailability of curcumin, leading to improved cardioprotective effects. Similarly, another randomized, double-blind, placebo-controlled clinical trial demonstrated that nanocurcumin reduces inflammation and lipoprotein levels in patients with type 2 diabetes and mild to moderate coronary artery disease [60].

4.7. Paclitaxel

Paclitaxel, an active compound derived from medicinal plants, has gained widespread use in clinical practice for the treatment of various tumors, including breast, ovarian, and lung cancers [61]. However, its limited solubility poses a challenge in delivering effective doses during tumor treatment. Early attempts to solubilize paclitaxel resulted in serious side effects, such as hypersensitivity, nephrotoxicity, neurotoxicity, and cardiotoxicity [62]. To overcome these issues, researchers have turned to nanotechnology as a promising approach for paclitaxel delivery. Several types of nanoparticles, including polymer micellar nanoparticles, liposomal nanoparticles, and albumin nanoparticles, have been utilized for paclitaxel delivery and have shown promising clinical outcomes [63]. Among these, Abraxane, which utilizes albumin nanoparticles as the carrier for paclitaxel, has emerged as the preferred clinical formulation. Albumin nanoparticles enhance paclitaxel solubility and tumor targeting, mitigate traditional solvent toxicity and side effects, and increase the drug load, resulting in a wide range of clinical benefits. In a randomized controlled clinical trial involving 503 patients with advanced non-small cell lung cancer, the Abraxane group exhibited a significant increase in objective symptom remission rates and a notable reduction in adverse events, such as neutropenia and peripheral neuropathy, compared to the docetaxel group [64]. Animal studies have demonstrated that liposome nanoparticles loaded with paclitaxel can effectively target plaque tissue and significantly reduce lesion size in an atherosclerotic rabbit model [65]. In another clinical trial involving eight patients with aortic atherosclerosis, the nanovehicle system exhibited a favorable safety profile, with no reported nanoparticle-related toxic reactions [66]. These results indicate the potential of paclitaxel nanoparticles in the treatment of cardiovascular diseases. However, further randomized controlled trials with larger sample sizes are still needed to demonstrate their safety and efficacy in humans.

5. Discussion

From the initial diagnosis and treatment of tumors to the current management of coronary heart disease, nanotechnology has emerged as a promising field in medicine. Nanotechnology offers unique advantages that enhance clinical diagnostic strategies and expand the therapeutic applications in clinical settings. Nanoparticle-mediated drug delivery systems play a crucial role in targeting inflammation, regulating lipid levels, and preventing vascular plaque formation in coronary artery disease (CAD), thus addressing the limitations of conventional drug delivery systems. The integration of nanotechnology with traditional Chinese medicine (TCM) holds great potential and has garnered interest from the pharmaceutical industry, given the rich repertoire of medicinal plants in TCM. However, there are still limitations in our understanding of diseases and the application of nanoparticles in TCM, which hinder further advancements in nanotechnology.

TCM encompasses a broad and versatile range of therapies that utilize medicinal plants, which possess unique advantages and exhibit various biological activities on tissues and molecular targets. Active components derived from Chinese medicine have demonstrated anti-cardiomyocyte apoptosis, antioxidant, and anti-inflammatory effects. In vivo and in vitro experiments have shown that nanovehicle systems enhance the therapeutic efficacy of active components from Chinese medicine in the treatment of coronary heart disease. However, further studies are needed to address several questions. Firstly, while individual active substances from TCM have shown beneficial effects on atherosclerosis, the treatment of CAD with TCM often requires a combination of multiple active substances. The interactions between different traditional Chinese medicines are critical for achieving desired therapeutic effects, as they can enhance efficacy or reduce toxicity of the treatment. The therapeutic efficacy of nanoparticles loaded with a single active substance from TCM is limited, and the combination of nanoparticles with TCM active substances may compromise their interactions and increase drug toxicity. Further studies should focus on transforming Chinese medicine from a single active substance to a system of multiple active substances combined with nanoparticles, providing experimental evidence for the development of TCM prescriptions. Additionally, certain active ingredients from traditional Chinese medicine, such as paclitaxel and curcumin, have been successfully formulated into nanomedicines for the treatment of coronary heart disease, with promising results from clinical trials. However, larger-scale randomized controlled trials are needed to expand the application of traditional Chinese medicine nanomedicines in clinical practice.

Furthermore, nanoparticles relying on passive targeting strategies may have limited efficacy in infarcted myocardial tissue due to poor blood flow supply. Future research should focus on active targeting strategies to identify new targets and ligands that can enhance drug targeting and therapeutic efficacy. Despite the numerous publications on various nanoparticles, their application in clinical practice requires further investigation to address several issues. Previous studies have primarily focused on the therapeutic effects of nanoparticles in coronary heart disease, overlooking the metabolic issues of nanoparticles in vivo. Understanding the metabolic pathways of nanoparticles is crucial for their safe use. Challenges such as reducing systemic toxicity, local removal of nanoparticles, and stabilizing nanosized drug carrier systems need to be addressed. Additionally, the high production costs of nanoparticles pose an obstacle to the future clinical application of nanotechnology. With increasing amounts of relevant research, it is believed that nanoparticle-mediated drug delivery systems will have a larger impact in the diagnosis and treatment of CAD in the future.

Founding

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Authors' contributions

Q.L. designed the study and finalized the manuscript. RY.Y., YM.G. and JY.Q. searched the literature and complete the first version of manuscript, Q.L. finished the manuscript corrections, the colleagues in acknowledgement and QQ.L. helped for language edition. All authors read, revised and approved the final manuscript.

Author contribution statement

All authors listed have significantly contributed to the development and the writing of this article.

Data availability statement

No data was used for the research described in the article.

Declaration of competing interest

The authors declared that there is no conflict of interest in the authorship and publication of this contribution.

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