

## Advancing Coronary Artery Disease Therapy: The Potential of Traditional Chinese Medicine Nanoparticles

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Received: 11 August 2024; Revised: 21 November 2024; Accepted: 24 November 2024

### ABSTRACT

Coronary artery disease (CAD) remains one of the leading causes of mortality worldwide, and conventional therapies, such as percutaneous coronary intervention (PCI), have inherent limitations. This review focuses on examining the potential role of nanoparticles loaded with Chinese medicine in CAD treatment. A comprehensive literature search was conducted to summarize the properties of nanovehicle systems, targeting mechanisms, and administration routes for various nanoparticles carrying Chinese medicine in the context of CAD therapy. Nanoparticle-based drug delivery platforms provide several advantages, including enhanced targeting efficiency, extended circulation time, and reduced systemic toxicity, highlighting their promise for CAD management. In summary, Chinese medicine-loaded nanoparticles represent a novel and promising strategy for treating CAD.

**Keywords:** Coronary artery disease, Nanoparticle, Targeting strategy, Drug delivery system

**How to Cite This Article:** Arakelyan S, Petrosyan N, Sargsyan H. Advancing Coronary Artery Disease Therapy: The Potential of Traditional Chinese Medicine Nanoparticles. *Interdiscip Res Med Sci Spec.* 2024;4(2):162-74. <https://doi.org/10.51847/hJ9QbdaPZZ>

### Introduction

Coronary heart disease develops when atherosclerotic plaques narrow or block the coronary arteries, restricting blood flow and causing damage to heart tissue. In China, both the prevalence and mortality of coronary artery disease (CAD) are rising. Estimates from 2020 indicate that around 330 million people suffer from cardiovascular diseases, with 11.39 million cases specifically attributed to coronary heart disease [1]. Current therapeutic approaches include percutaneous coronary intervention (PCI), coronary bypass surgery, and long-term use of anticoagulant, antiplatelet, and lipid-lowering drugs. Despite their effectiveness, these treatments can lead to adverse outcomes such as vascular restenosis, plaque progression, abnormal neovascularization, and drug-related systemic toxicity.

Advances in nanotechnology have opened new avenues for diagnosing and managing coronary heart disease. Applications range from targeted cardiovascular imaging and nanoeluting stents to sophisticated nanoparticle-based drug delivery systems. In particular, nanoparticle-mediated drug delivery has emerged as a promising strategy, offering improved targeting, reduced systemic side effects, and enhanced therapeutic potential for CAD patients [2]. This review examines the use of nanoparticle-based systems carrying Chinese medicine as an innovative approach for coronary heart disease therapy.

#### *Nanoparticle characteristics*

Nanoparticles have emerged as highly promising drug delivery vehicles due to their ability to target specific tissues, combined with favorable properties such as low toxicity, biodegradability, and biocompatibility [3]. In biomedical applications, nanotechnology plays a versatile role, including in medical imaging and diagnostics, drug and gene delivery, and as scaffolds in tissue engineering [4]. Among these, nanoparticle-based drug delivery

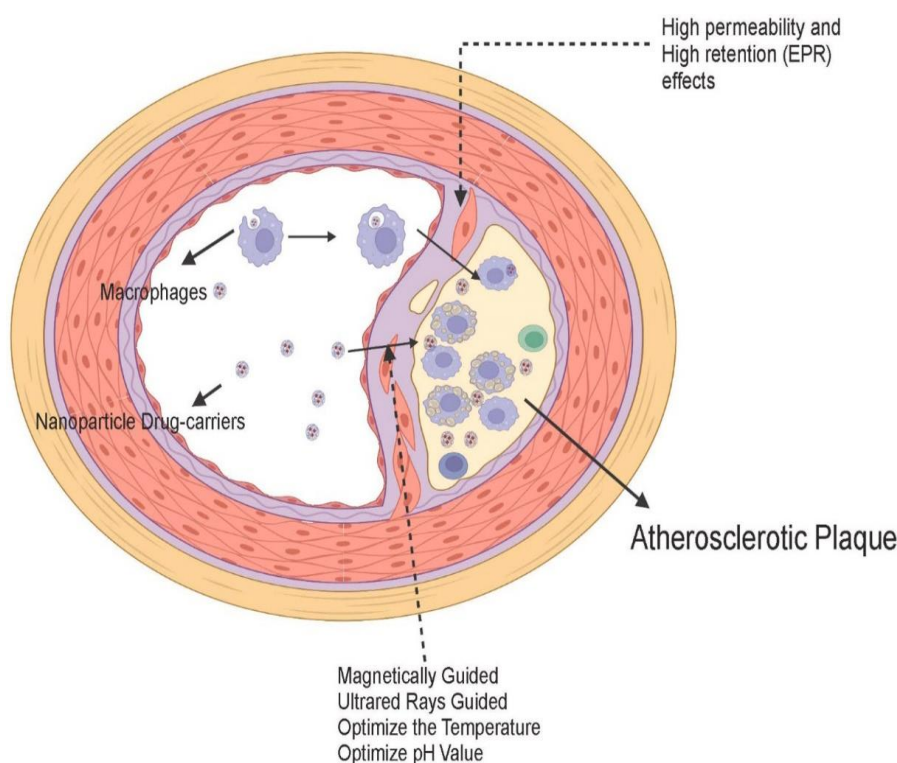
systems are particularly prevalent. These systems typically involve the integration of therapeutic agents with various nanoparticles, forming complexes that exploit the unique properties of nanomaterials to enhance targeted delivery.

Due to their nanoscale dimensions, nanoparticles can penetrate vascular endothelium and even cross the blood-brain barrier, facilitating efficient transport of therapeutic compounds. Additionally, parameters such as local temperature, protein activity, pH, and external stimuli—such as ultrasound, magnetic fields, or infrared radiation—can be optimized to achieve controlled and site-specific drug release. Nanoparticles provide a valuable solution for transporting CAD therapeutics that otherwise suffer from poor targeting, low bioavailability, and high tissue toxicity. Their large surface area-to-volume ratio allows the simultaneous encapsulation of multiple drugs or bioactive molecules [5]. Research has shown that nanoparticle-based delivery systems can protect drugs from rapid degradation, thereby extending their circulation time [6]. Moreover, targeted delivery via nanoparticles enhances therapeutic efficacy while minimizing systemic toxicity [7, 8].

### *Nanoparticle targeting strategies*

#### *Passive targeted transport*

The targeting strategies employed in nanoparticle-mediated drug delivery systems (NMDDs) can be broadly classified into passive and active approaches. Passive targeting exploits the properties of atherosclerotic plaques, which exhibit increased vascular permeability and compromised structural integrity, allowing nanoparticles carrying small-molecule drugs to preferentially accumulate in these regions [9]. Additionally, the infiltration of inflammatory cells within plaques further facilitates the localization of NMDDs, enhancing drug targeting [10]. Beyond tissue-specific permeability, targeted delivery can also be achieved by modulating internal or external factors, such as local temperature or applied magnetic fields [11] (**Figure 1**). For example, Li *et al.* developed a system combining urokinase with  $\text{Fe}_3\text{O}_4$  nanoparticles and demonstrated that the application of a magnetic field substantially increased the rate of thrombolysis [12].

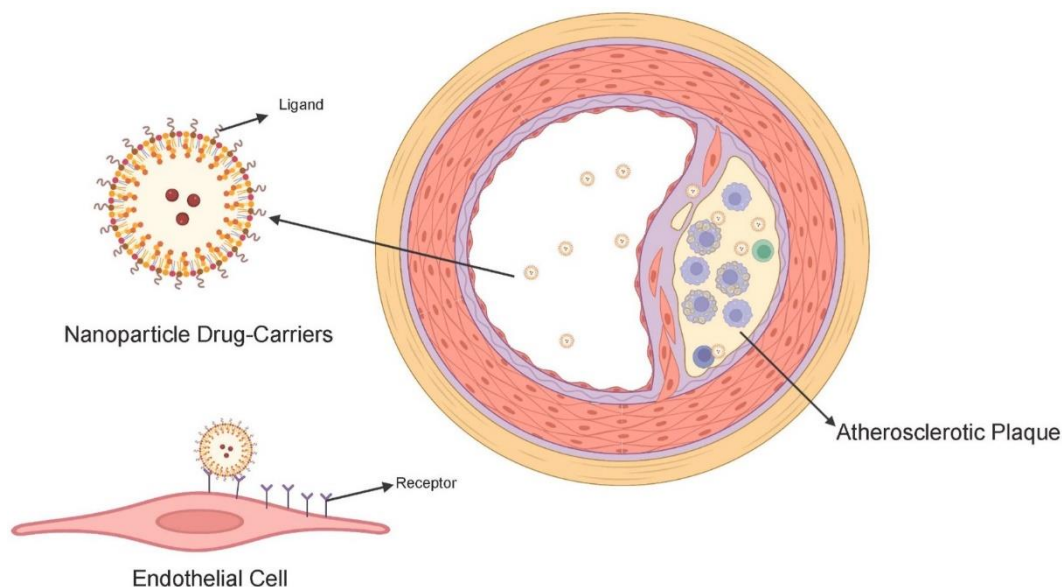


**Figure 1.** Passive Targeted Delivery of Nanoparticles.

#### *Active targeted transport*

While passive targeting can increase the accumulation of nanoparticles in specific tissues, it provides little control over their effects on surrounding healthy cells. To address this limitation, active targeting strategies are employed, in which nanoparticles are functionalized with specific molecules—such as antibodies, peptides, or ligands—that selectively bind to components of plaque tissue. This approach allows precise delivery to particular cell types

within the plaque, including vascular endothelial cells, macrophages, foam cells, and collagen in the vascular basement membrane [13] (**Figure 2**). For example, Benne *et al.* attached the cyclic peptide Lyp-1 to the surface of liposomes, enabling them to recognize and bind the p32 receptor on foam cells. This modification directs the liposomes preferentially to foam cells, achieving targeted delivery to arterial plaque [14].



**Figure 2.** Active Targeted Delivery of Nanoparticles.

For effective targeting, a strategy that combines both passive and active targeting is recommended. Nanocarriers take advantage of the enhanced permeability of plaque tissue for accumulation, while surface modifications enable precise interaction with specific components within the plaque. By integrating these approaches, drug loss or degradation can be minimized before the nanoparticles reach their intended target, improving delivery efficiency [15].

#### *Nanoparticle classification in CAD*

Nanoparticles can be divided based on their composition into organic types, including liposomes, micelles, dendrimers, and polymer-based particles, and inorganic types, such as those made from silicon, carbon, gold, or silver. Considering their biological behavior, nanoparticles may also be classified as biodegradable or responsive to specific stimuli. They exhibit a wide range of physical and chemical traits, including size, shape, density, and surface properties, which influence the efficiency of both passive and active targeting approaches [16]. Various nanoparticles have been widely explored for delivering drugs in the context of coronary artery disease (CAD), and their key features and advantages are summarized in **Table 1**.

**Table 1.** Types of Nanoparticles and advantages.

Nanoparticle Type	Drug	Model / Patient	CAD Model	Key Advantages	Reference
<b>Liposomes</b>	Prednisolone	Human atherosclerosis patients	Yes	Prolonged circulation time; improved delivery to atherosclerotic macrophages; no negative effects on cardiometabolic parameters	[17]
<b>Lipid Microsphere Nanoparticles</b>	Alprostadil	AMI patients post-PCI	Yes	Enhanced cardiac function and ventricular remodeling; reduced adverse event incidence	[18]
<b>PLGA Nanoparticles</b>	Pioglitazone	Mouse plaque rupture model	Yes	Targeted delivery to plaque macrophages; modulated plaque inflammation; decreased inflammatory cells; reduced fibrous cap	[19]

				thickness; stabilized plaque tissue	
	Pitavastatin	Patients with chronic limb-threatening ischemia	No	Demonstrated safety and good tolerability in patients	[20]
<b>Chitosan Nanoparticles</b>	Rosuvastatin	Hypercholesterolemic rabbits	Yes	Improved lipid-lowering effect; decreased heart valve calcification	[21]
<b>PEG-Coated Gold Nanoparticles</b>	—	Myocardial infarction rats	Yes	Reduced infarct size; improved systolic function; inhibited cardiac fibrosis; enhanced myocardial targeting and cardioprotection	[22]
<b>Ultrasmall Superparamagnetic Iron Oxide Nanoparticles</b>	—	Acute myocardial infarction patients	Yes	Enhanced macrophage targeting; excellent safety profile	[23]
	Fucoidan	Elastase-induced vascular injury rats	No	Improved sensitivity for thrombus-targeted imaging	[24]
	Tissue Plasminogen Activator	Embolic rat model	No	Enhanced thrombus targeting and thrombolytic efficiency	[25]

### *Liposomes*

**Liposome Nanoparticles:** Liposome nanoparticles are spherical structures composed of phospholipid bilayers [26]. They feature a hydrophilic interior and a hydrophobic exterior, allowing them to carry both water- and fat-soluble compounds. Liposomes are generally non-toxic and can avoid detection by immune cells. They provide sustained drug release, maintaining therapeutic levels in the body for longer periods, which enhances treatment effectiveness while reducing side effects. A randomized, placebo-controlled clinical study evaluating prednisolone-loaded liposomes in atherosclerotic macrophages showed that these nanoparticles significantly prolonged circulation time and improved macrophage targeting without negatively impacting cardiometabolic health [17].

**Lipid Microsphere Nanoparticles:** Lipid microsphere nanoparticles loaded with alprostadil have been extensively used for cardiovascular conditions, including myocardial infarction and angina. Alprostadil helps inhibit platelet aggregation, dilate blood vessels to improve microcirculation, expand coronary arteries, and increase myocardial perfusion [27]. In a randomized controlled trial with 300 AMI patients undergoing percutaneous coronary intervention (PCI), treatment with alprostadil combined with tanshinone IIa injections significantly enhanced cardiac function and ventricular remodeling after PCI and reduced the occurrence of adverse events [18].

### *Polymer nanoparticles*

**Polymeric Nanoparticles:** Polymeric nanoparticles, such as polylactic-co-glycolic acid (PLGA), polyethyleneimine, poly- $\epsilon$ -caprolactone (PCL), polyvinyl alcohol, and chitosan, are highly promising carriers for drug delivery [28]. These nanoparticles have a stable structure and consistent size, allowing precise regulation of drug release. They also exhibit excellent biocompatibility and minimal toxicity, generally without teratogenic effects. Upon degradation, polymeric nanoparticles break down into non-toxic oligomers that are compatible with most therapeutic agents. Their physical characteristics, including small size and high surface-to-volume ratio, enhance cellular uptake of drugs and improve bioavailability [29].

Despite these advantages, certain polymeric nanoparticles have limitations. For example, natural polymers like chitosan may degrade when exposed to biological fluids, reducing their effectiveness. Surface modifications can address these issues, improving both biocompatibility and targeting ability [30].

In experimental models, polymeric nanoparticles have demonstrated enhanced therapeutic outcomes. For instance, pioglitazone-loaded PLGA nanoparticles in a mouse atherosclerosis model outperformed free pioglitazone by significantly reducing the number and thickness of fibrous caps. This effect was attributed to targeted delivery to monocytes and macrophages, which regulated inflammation through receptor-mediated macrophage differentiation [19]. Similarly, Lin *et al.* developed a rosuvastatin-loaded chitosan nanoparticle system using ionic

gel preparation. In hypercholesterolemic rabbits, this nanoparticle formulation achieved greater lipid-lowering effects and reduced heart valve calcification compared to rosuvastatin alone [20].

Furthermore, in a phase I/IIa clinical trial, PLGA nanoparticles carrying pilavastatin demonstrated excellent safety and tolerability in patients with chronic limb-threatening ischemia, highlighting their potential as a therapeutic strategy for vascular diseases [21].

#### *Gold nanoparticles*

**Gold Nanoparticles:** Gold nanoparticles, as stable inorganic metal carriers, offer multiple advantages for cardioprotective drug delivery. Their low toxicity and non-immunogenic nature make them particularly suitable for clinical applications. Thanks to their unique structural properties, gold nanoparticles can effectively target ischemic tissues, enabling loaded drugs to accumulate efficiently and promote faster tissue recovery. They also support angiogenesis by delivering exogenous growth factors to damaged areas [31].

For example, metoprolol conjugated with gold nanoparticles selectively targets  $\beta_1$  receptors, showing twice the therapeutic effect in heart tissue affected by heart failure compared to the drug alone, while minimizing off-target side effects [32]. Additionally, polyethylene glycol-coated (PEGylated) gold nanoparticles have been shown to reduce infarct size by mitigating cardiomyocyte necrosis and apoptosis, and to regulate inflammation through modulation of collagen deposition. These findings suggest that gold nanoparticles or their polymeric derivatives could be promising candidates for cardiovascular therapies [22]. However, despite encouraging preclinical results, further studies are needed to confirm their safety and efficacy in clinical settings, particularly for acute myocardial infarction treatment.

#### *Magnetic nanoparticles*

**Magnetic Nanoparticles:** Magnetic nanoparticles are a type of stimulus-responsive nanomaterial that can be precisely guided using external magnetic fields, making them highly useful for targeted drug delivery and magnetic resonance imaging (MRI). These nanoparticles can carry cardiovascular drugs or MRI contrast agents directly to diseased tissues, providing novel therapeutic and diagnostic opportunities [33]. Among the various metals and metal oxides studied, iron oxide nanoparticles have gained regulatory approval from the FDA.

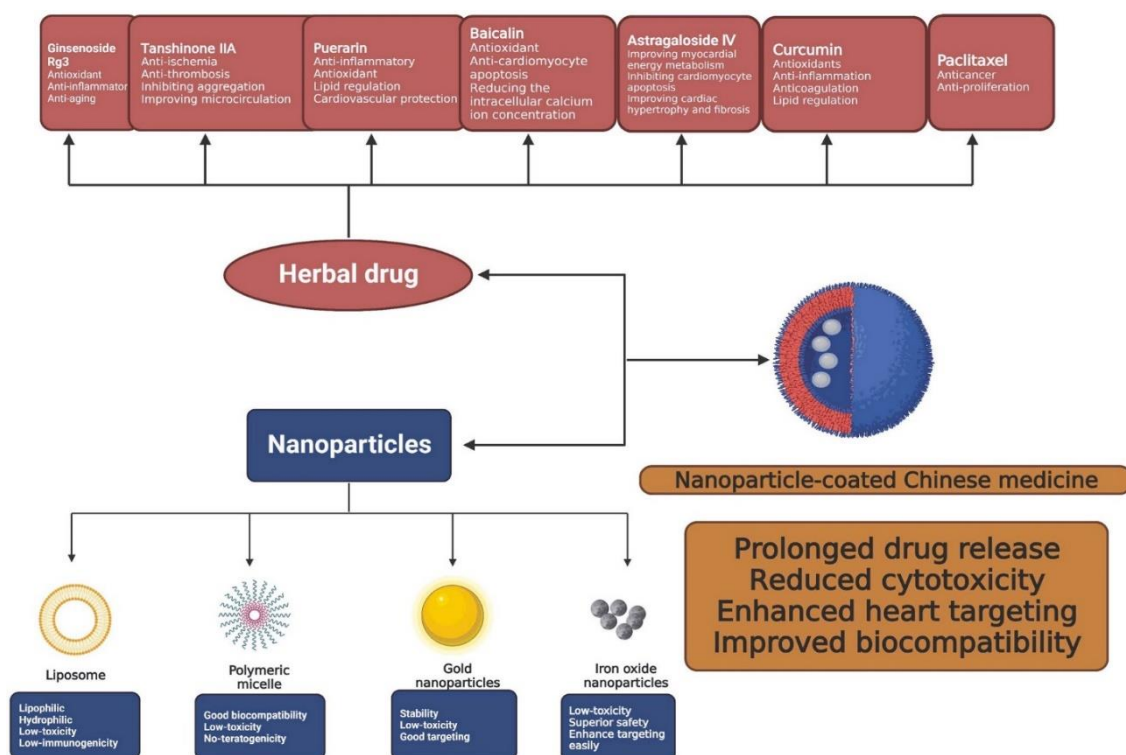
In cardiovascular applications, ultrasmall superparamagnetic iron oxide nanoparticles (USPIOs) have been shown to be safe and effective, offering superior detection of myocardial infarction-related macrophages compared to traditional gadolinium-based MRI agents [23]. Their small size allows them to penetrate the endothelium and accumulate within atherosclerotic plaques. For example, fucoidan-coated USPIOs (USPIO-FUCO) have been applied as MRI contrast agents to visualize thrombi in animal models by targeting activated platelets, demonstrating the potential of magnetic nanoparticles for enhanced coronary artery disease imaging [24].

Therapeutically, magnetic nanoparticles have been used to improve the efficacy of thrombolytic treatments. In embolized rat models, drugs such as tissue plasminogen activator bound to magnetic nanoparticles achieved effective clot dissolution at lower doses when guided by a magnetic field, compared to free drug administration [25]. Although some studies indicate that certain magnetic nanoparticles may cross the blood-brain barrier and cause neuronal damage, coating them with polymers has been shown to reduce toxicity [34]. Beyond iron oxide, other stimulus-responsive nanoparticles are available, each with unique properties that control drug release and targeting behavior depending on the therapeutic context.

#### *Nanoparticle-coated Chinese medicine in CAD*

In traditional Chinese medicine, research has highlighted the therapeutic potential of certain herbal extracts for managing coronary artery disease (CAD), due to their pronounced anti-inflammatory, antioxidant, lipid-regulating, and cardioprotective effects. As a result, Chinese medicine has gained attention as a promising treatment strategy. In this field, nanotechnology is currently being applied in two main ways. The first involves transforming active compounds into nanoscale suspensions or cocrystals, which increases their surface area, enhances solubility, and improves stability. For example, compounds such as curcumenol [35] and meletin [36] have been successfully formulated into nanosuspensions (**Figure 3**).

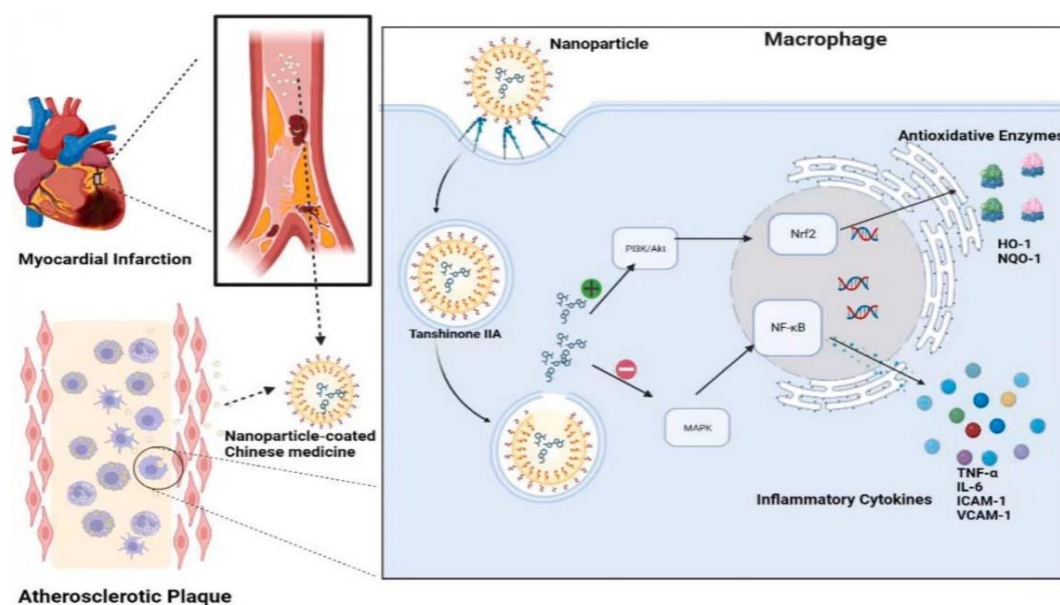




**Figure 3.** Mechanism of Nanoparticles in Coronary Artery Disease

The second application of nanotechnology in Chinese medicine involves using nanoparticles to deliver and transport active herbal compounds. Compared to conventional synthetic drugs, these natural compounds offer unique advantages, including broad biological activity and synergistic effects across multiple tissues and targets in the body [37]. Despite these benefits, clinical use of herbal active ingredients is often limited by poor absorption, low stability, restricted permeability, and potential toxicity to the liver and kidneys [38].

Nanotechnology provides a solution by enabling highly specific targeting of these compounds, overcoming many of their inherent limitations. Numerous nanoparticles have been successfully utilized as carriers for active ingredients from Chinese medicine, such as ginsenoside, puerarin, tanshinone IIA, baicalin, triptolide, and ligustrazine [39]. The next section presents several representative nanoparticle-based delivery systems for Chinese medicine compounds, summarized in **Table 2** and illustrated in **Figure 4**.



**Figure 4.** Nanoparticle-Enhanced Delivery of Chinese Herbal Medicines for the Treatment of Coronary Artery Disease

**Table 2.** Therapeutic Mechanisms and Benefits of Chinese Medicine Compounds Delivered via Nanoparticles in CAD

Herbal Drug / Compound	Nanocarrier System	Mechanism / Effect	Model / Patient	Observed Outcome	Reference
<b>Ginsenoside Rg3</b>	PEG-b-PPS nanoparticles	Antioxidant, anti-inflammatory, anti-aging	Ischemia-reperfusion rats	Improved cardiac function, reduced myocardial injury, decreased infarct size	[40]
<b>Puerarin</b>	RGD/PEG-SLNs	Anti-inflammatory, antioxidant, lipid regulation, cardioprotective	Myocardial infarction rats	Sustained release, enhanced ischemic myocardium targeting, reduced infarct size	[41]
	PEG-PE micelle nanoparticles	Sustained release, anti-apoptotic, reduces hemolysis	Acute myocardial ischemia rats	Reduced cardiomyocyte apoptosis, minimized hemolysis events	[42]
	PEG-PLGA micelle nanoparticles	Cardioprotective, targeted delivery	Acute myocardial ischemia rats	Enhanced ischemic myocardium targeting, lower myocardial enzyme levels, reduced infarct size	[43]
<b>Tanshinone IIA</b>	PEG-PE micelle nanoparticles	Anti-ischemic, anti-thrombotic, inhibits platelet aggregation, improves microcirculation	Acute myocardial ischemia rats	Prolonged release, targeted delivery to ischemic tissue	[44]
	Lipid-polymeric nanoparticles	Sustained release, enhanced targeting	Acute myocardial ischemia rats	Improved therapeutic efficacy and ischemic tissue targeting	[45]
<b>Baicalin</b>	PEG-PCL nanomicelles	Antioxidant, anti-apoptotic, reduces intracellular calcium in cardiomyocytes	Cardiac muscle cells	Prolonged release, enhanced mitochondrial targeting	[46]
	Lipid-polymer hybrid nanoparticles (LPNs)	Cardioprotective, anti-cytotoxic	Acute myocardial infarction rats	Prolonged release, enhanced myocardial targeting, reduced infarct size, lower cytotoxicity	[47]
<b>Astragaloside IV</b>	PEG-PE	Enhances myocardial energy metabolism, anti-apoptotic, improves hypertrophy and fibrosis	Cardiac muscle cells	Sustained release, improved mitochondrial targeting, increased anti-apoptotic effect	[48]
	PLGA-b-PEG-TPP polymer nanomicelles	Mitochondrial targeting, cardioprotective	Acute myocardial infarction rats	Enhanced mitochondrial delivery, improved cardiac function, reduced myocardial and mitochondrial injury, mitigated inflammation	[49]
<b>Curcumin</b>	Nanomicelles	Antioxidant, anti-inflammatory, anticoagulant, lipid-regulating	Patients post-coronary elective angioplasty	Improved lipid profile, reduced oxidative stress and inflammation	[50]
<b>Paclitaxel</b>	Albumin nanoparticles (Abraxane)	Anti-proliferative, anticancer	Advanced non-small cell lung cancer patients	Increased symptom remission, fewer adverse effects	[51]
	Liposomal nanoparticles	Anti-atherosclerotic	Aortic atherosclerosis patients	Reduced lesion size, lower incidence of toxic reactions	[52]

*Ginsenosides*

**Ginsenoside Rg3:** Ginsenoside, a bioactive component extracted from ginseng, exhibits notable anti-inflammatory and antioxidant effects, suggesting its potential for alleviating cancer-related symptoms and slowing aging. Among the various ginsenosides, Rg3 has been the focus of extensive clinical research. However, its therapeutic use in coronary artery disease (CAD) is limited by poor membrane permeability, low bioavailability, and a short half-life [53]. Despite these challenges, ginsenoside Rg3 has been shown to effectively suppress reactive oxygen species, contributing to the mitigation of myocardial ischemia. To overcome these limitations, Li *et al.* engineered PEG-b-PPS-Rg3 nanoparticles that are responsive to reactive oxygen species. These nanoparticles efficiently delivered ginsenoside Rg3, and in an ischemia-reperfusion rat model, they provided protection of cardiac diastolic function and reduced the size of myocardial infarctions [40].

#### *Puerarin*

**Puerarin:** Puerarin, a bioactive compound with antioxidant and anti-cancer activities, also exerts protective effects on the heart and liver, supporting its use in managing cardiovascular and cerebrovascular disorders. In clinical practice in China, puerose sodium chloride and puerose glucose injections have been approved to treat coronary artery disease (CAD), angina, myocardial ischemia or infarction, and retinal vein occlusion [54]. However, the compound's intrinsic properties—such as poor water solubility, limited permeability, and low bioavailability—hinder its effective absorption when taken orally [55]. Simply increasing the dosage is insufficient to improve its efficacy and may pose risks of systemic toxicity.

To overcome these pharmacokinetic limitations, researchers have turned to nanoparticle-based delivery systems. Strategies include lipid nanoparticles modified with cyclic RGD peptides and PEG, PEG-phosphatidylethanolamine (PEG-PE) micelles, and PEG-PLGA micelles [41–43]. Experimental studies have shown that these nanocarriers enhance puerarin's accumulation in cardiomyocytes, prolong its retention in the body, and improve cardioprotective outcomes, outperforming conventional administration of the drug [56].

#### *Tanshinone IIA*

**Tanshinone IIA:** Tanshinone IIA, derived from *Salvia miltiorrhiza*, offers several cardiovascular benefits, including reducing ischemic damage, preventing thrombosis, inhibiting platelet clumping, enhancing microcirculation, and protecting cardiomyocytes from hypoxia-induced injury—effects that parallel those observed with astragaloside IV [57]. However, its clinical utility is limited by poor water solubility and low bioavailability.

To improve delivery, Fang and colleagues encapsulated tanshinone IIA within PEG-PE nanoparticles using a membrane hydration approach. Experimental results showed that these nanoparticles could selectively accumulate in ischemic myocardial tissue while providing sustained drug release [44]. In a separate approach, Zhang *et al.* employed lipid-polymer hybrid nanoparticles with surface modifications to direct tanshinone IIA specifically to mitochondria in damaged cardiomyocytes. This targeted nanodelivery system outperformed free tanshinone IIA by enhancing cardiac accumulation, improving biocompatibility, prolonging release, and reducing infarct size in a rat coronary artery ligation model [45] (**Figure 4**).

#### *Baicalin*

**Baicalin:** Baicalin, the main bioactive constituent of *Scutellaria baicalensis*, possesses strong antioxidant activity and exerts cardioprotective effects by reducing cardiomyocyte apoptosis and lowering intracellular calcium levels [58]. Research has shown that baicalin can prevent mitochondrial damage—a key trigger for apoptosis—and activate protein kinase pathways, ultimately decreasing the extent of myocardial infarction [59]. However, its poor water solubility limits bioavailability and cellular uptake, restricting therapeutic efficacy.

To address these limitations, Li *et al.* developed PEG-b-polycaprolactone (PEG-PCL) nanomicelles to deliver baicalin with enhanced mitochondrial targeting. Studies demonstrated that these nanomicelles effectively localized baicalin to cardiomyocyte mitochondria, reducing caspase-3 activity and reactive oxygen species (ROS) levels associated with apoptosis, thereby improving anti-apoptotic effects in heart cells [46]. In another strategy, Wang *et al.* employed lipid-polymer hybrid nanoparticles that combined the advantages of liposomes and polymeric carriers to deliver baicalin. The nanoparticle surface was further modified with triphenylphosphonium (TPP) and atrial natriuretic peptide to specifically target infarcted cardiomyocytes. In vitro studies revealed that this modified system provided more sustained drug release and lower cytotoxicity compared to unmodified



nanoparticles, while in vivo biodistribution studies showed prolonged circulation time and greater accumulation in cardiac tissue [47].

#### *Astragaloside IV*

**Astragaloside IV:** Astragaloside IV, a key active component extracted from Astragalus, exerts cardioprotective effects by enhancing myocardial contractility, improving blood flow, and safeguarding ischemic heart tissue. It has also been shown to influence serum inflammatory markers in patients with stable coronary heart disease, demonstrating synergistic effects similar to combined astragalus and *Salvia miltiorrhiza* injections [60]. Like many other Chinese herbal compounds, its poor water solubility limits accumulation in cardiomyocytes, thereby reducing its therapeutic efficacy.

To address this challenge, Ye *et al.* coated astragaloside IV with PEG-PE, which enhanced delivery to cardiomyocytes and strengthened its anti-apoptotic effect. Experiments indicated that the nanoparticle formulation improved cellular uptake and localization in cardiomyocytes, resulting in more effective inhibition of apoptosis [48]. In another approach, Yang *et al.* designed PLGA-b-PEG-TPP polymeric nanomicelles loaded with astragaloside IV and coated with human platelet membranes to target cardiac tissue. Their study demonstrated that these nanomicelles significantly improved cardiac function, mitigated mitochondrial damage in the myocardium, and reduced inflammation following myocardial infarction, outperforming free astragaloside IV [49].

#### *Curcumin*

**Curcumin:** Curcumin, a bioactive polyphenolic compound extracted from turmeric, exhibits multiple pharmacological activities, including antioxidant, anti-inflammatory, anticoagulant, and lipid-regulating effects [61]. Nanoparticle formulations of curcumin have been increasingly explored for cardiovascular disease management. In a randomized, double-blind, placebo-controlled clinical trial with 90 patients undergoing coronary elective angioplasty, both curcumin and curcumin-loaded nanomicelles significantly improved lipid profiles, antioxidant capacity, and inflammatory markers compared to placebo. Notably, the nanomicelle formulation produced stronger effects than standard curcumin, indicating that nanoparticle delivery enhances bioavailability and cardioprotective efficacy [50].

In a separate clinical study, also randomized, double-blind, and placebo-controlled, curcumin nanoparticles were shown to reduce inflammation and lower lipoprotein levels in patients with type 2 diabetes and mild-to-moderate coronary artery disease, further supporting the therapeutic advantage of nanoformulations [62]

#### *Paclitaxel*

**Paclitaxel:** Paclitaxel, a bioactive compound extracted from medicinal plants, is widely used to treat various cancers, including breast, ovarian, and lung malignancies [63]. Its clinical application, however, is constrained by poor water solubility, which limits effective dosing. Early solubilization methods often caused severe adverse reactions, including hypersensitivity, kidney toxicity, neurotoxicity, and cardiac complications [64]. To overcome these issues, nanotechnology-based delivery strategies have been developed. Different nanoparticle platforms—such as polymeric micelles, liposomes, and albumin-based nanoparticles—have demonstrated promising results in enhancing paclitaxel delivery and safety [65].

Among these formulations, Abraxane, an albumin-bound paclitaxel nanoparticle, has become the preferred clinical approach. This system improves solubility, enhances tumor-targeting efficiency, reduces solvent-related toxicity, and allows higher drug loading. In a randomized clinical trial including 503 patients with advanced non-small cell lung cancer, treatment with Abraxane led to higher rates of symptom remission and fewer adverse effects, including neutropenia and peripheral neuropathy, compared to docetaxel [51].

Paclitaxel nanoparticles have also shown potential in cardiovascular disease therapy. In atherosclerotic rabbit models, liposomal paclitaxel nanoparticles effectively accumulated in plaque tissue and markedly reduced lesion size [66]. Similarly, a small clinical study with eight patients with aortic atherosclerosis reported that the nanoparticle formulation was well tolerated, with no nanoparticle-related toxicity [52]. These findings suggest that paclitaxel nanoparticles could be a promising approach for cardiovascular applications, though larger, well-controlled clinical trials are required to confirm their efficacy and safety in humans.

From their early use in cancer diagnosis and treatment to their emerging role in managing coronary heart disease (CAD), nanotechnology has shown tremendous promise in medicine. The unique properties of nanoparticles have expanded the scope of clinical diagnostics and therapeutic applications. In CAD, nanoparticle-based drug delivery systems have proven effective in targeting inflammation, modulating lipid levels, and preventing vascular plaque formation, thereby addressing some of the limitations inherent to traditional drug delivery methods. Combining nanotechnology with traditional Chinese medicine (TCM) presents a particularly promising avenue, given the rich diversity of bioactive compounds present in TCM. However, gaps remain in our understanding of both disease mechanisms and the optimal use of nanoparticles in TCM, which constrain further clinical and translational advances.

TCM encompasses a wide array of therapeutic approaches that utilize medicinal plants with distinct biological activities, acting on specific tissues and molecular targets. Active components derived from TCM have demonstrated antioxidant, anti-inflammatory, and anti-apoptotic effects on cardiomyocytes. Experimental studies, both *in vitro* and *in vivo*, indicate that nanoparticle-based delivery systems can enhance the therapeutic performance of these compounds in CAD. Nevertheless, several challenges remain. While individual TCM components have shown efficacy against atherosclerosis, effective CAD treatment often relies on combinations of multiple active ingredients. Interactions among these compounds are crucial for maximizing therapeutic outcomes and minimizing toxicity. Nanoparticle delivery of a single TCM component may limit efficacy, and combining nanoparticles with multiple TCM components could potentially disrupt these interactions or increase drug toxicity. Future research should aim to develop nanoparticle systems capable of delivering multiple active TCM ingredients simultaneously, providing a scientific basis for the optimization of multi-component TCM prescriptions.

Certain TCM-derived compounds, such as paclitaxel and curcumin, have already been successfully formulated into nanomedicines for CAD treatment, with encouraging results from clinical trials. However, broader randomized controlled trials with larger sample sizes are needed to validate and expand their clinical use.

Another limitation of current nanoparticle systems is the reliance on passive targeting, which can be less effective in infarcted myocardial tissue due to compromised blood flow. Advancing active targeting strategies by identifying new molecular targets and ligands may improve drug localization and therapeutic efficacy. Despite the growing body of research on nanoparticles, their translation into clinical practice faces several hurdles. Most studies have focused on therapeutic outcomes, often neglecting the *in vivo* metabolism and clearance of nanoparticles. Understanding these metabolic pathways is essential for ensuring safety. Additional challenges include minimizing systemic toxicity, achieving localized nanoparticle clearance, and stabilizing nanosized drug carriers. Moreover, the high cost of nanoparticle production presents a barrier to widespread clinical implementation.

With ongoing research and technological advances, it is anticipated that nanoparticle-mediated drug delivery will play an increasingly significant role in the diagnosis and treatment of CAD in the future.

**Acknowledgments:** We thank Jodi Smith, PhD ELS, from Liwen Bianji (Edanz) ([www.liwenbianji.cn](http://www.liwenbianji.cn)) for editing the English text of a draft of this manuscript. The figures were created using the online tool from BioRender website (<https://biorender.com/>).

**Conflict of Interest:** None

**Financial Support:** This study was supported by National Natural Science Foundation of China (No. 82274279, to Q.L.), Guangdong Provincial Bureau of Chinese medicine Fund Project (No. 20221360, to Q.L.), Municipal School (College) Joint Funding Project of Guangzhou Science and Technology Bureau (No. 202201020382, to R.Y.), Zhuhai Medical Science and Technology Research Fund Project (No. ZH24013310210002PWC, to Q.L.), Special Funding for Chinese medicine Science and Technology Research of Guangdong Provincial Hospital of Chinese Medicine (No. YN2020QN10, to Q.L.), and Municipal School (College) Joint Funding Project of Guangzhou Science and Technology Bureau (No. SL2023A03J00081, to Q.L.).

**Ethics Statement:** None

## References

1. The writing committee of the report on cardiovascular health and diseases in China, Key points of Report on Cardiovascular Health and Diseases in China 2020. *Chinese Journal of Cardiovascular Research* 40 (10) (2021) 1005–1009.
2. E. Kandaswamy, L. Zuo, Recent advances in treatment of coronary artery disease: role of science and Technology, *Int. J. Mol. Sci.* 19 (2) (2018).
3. Y. Fan, M. Marioli, K. Zhang, Analytical characterization of liposomes and other lipid nanoparticles for drug delivery, *J. Pharm. Biomed. Anal.* 192 (2021), 113642.
4. M. Chandarana, A. Curtis, C. Hoskins, The use of nanotechnology in cardiovascular disease, *Appl. Nanosci.* 8 (7) (2018) 1607–1619.
5. C. Kleinstreuer, Y. Feng, E. Childress, Drug-targeting methodologies with applications: a review, *World J Clin Cases* 2 (12) (2014) 742–756.
6. S. Zeng, et al., Cell membrane-coated nanomaterials for cancer therapy, *Mater Today Bio* 20 (2023), 100633.
7. S.P. Yoo, et al., Gadolinium-functionalized peptide amphiphile micelles for multimodal imaging of atherosclerotic lesions, *ACS Omega* 1 (5) (2016) 996–1003.
8. S. Li, et al., Application of chitosan/alginate nanoparticle in oral drug delivery systems: prospects and challenges, *Drug Deliv.* 29 (1) (2022) 1142–1149.
9. M. Alavi, M. Hamidi, Passive and active targeting in cancer therapy by liposomes and lipid nanoparticles, *Drug Metab Pers Ther* 34 (1) (2019).
10. N. Montelione, et al., Tissue engineering and targeted drug delivery in cardiovascular disease: the role of polymer nanocarrier for statin therapy, *Biomedicines* 11 (3) (2023).
11. M.F. Attia, et al., An overview of active and passive targeting strategies to improve the nanocarriers efficiency to tumour sites, *J. Pharm. Pharmacol.* 71 (8) (2019) 1185–1198.
12. Q. Li, et al., Thrombolysis enhancing by magnetic manipulation of Fe<sub>3</sub>O<sub>4</sub> nanoparticles, *Materials* 11 (11) (2018).
13. K.X. Tan, et al., Cardiovascular therapies utilizing targeted delivery of nanomedicines and aptamers, *Int. J. Pharm.* 558 (2019) 413–425.
14. N. Benne, et al., Complement receptor targeted liposomes encapsulating the liver X receptor agonist GW3965 accumulate in and stabilize atherosclerotic plaques, *Adv. Healthcare Mater.* 9 (10) (2020), e2000043.
15. Bhardwaj, et al., Stimuli-sensitive systems—an emerging delivery system for drugs, *Artif. Cells, Nanomed. Biotechnol.* 43 (5) (2015) 299–310.
16. J.M. Morachis, E.A. Mahmoud, A. Almutairi, Physical and chemical strategies for therapeutic delivery by using polymeric nanoparticles, *Pharmacol. Rev.* 64 (3) (2012) 505–519.
17. F.M. van der Valk, et al., Prednisolone-containing liposomes accumulate in human atherosclerotic macrophages upon intravenous administration, *Nanomedicine* 11 (5) (2015) 1039–1046.
18. Y. Lu, Y. Yan, X. Liu, Effects of alprostadil combined with tanshinone Ila injection on microcirculation disorder, outcomes, and cardiac function in AMI patients after PCI, *Ann. Palliat. Med.* 10 (1) (2021) 97–103.
19. T. Matoba, et al., Nanoparticle-mediated drug delivery system for atherosclerotic cardiovascular disease, *J. Cardiol.* 70 (3) (2017) 206–211.
20. L. Chen, C. Wang, Y. Wu, Cholesterol (Blood lipid) lowering potential of Rosuvastatin chitosan nanoparticles for atherosclerosis: preclinical study in rabbit model, *Acta Biochim. Pol.* 67 (4) (2020) 495–499.
21. T. Matsumoto, et al., Pitavastatin-incorporated nanoparticles for chronic limb threatening ischemia: a phase I/IIa clinical trial, *J. Atherosclerosis Thromb.* 29 (5) (2022) 731–746.
22. Tian, et al., Polyethylene-glycol-coated gold nanoparticles improve cardiac function after myocardial infarction in mice, *Can. J. Physiol. Pharmacol.* 96 (12) (2018) 1318–1327.
23. Yilmaz, et al., Imaging of myocardial infarction using ultrasmall superparamagnetic iron oxide nanoparticles: a human study using a multi-parametric cardiovascular magnetic resonance imaging approach, *Eur. Heart J.* 34 (6) (2013) 462–475.

24. M. Suzuki, et al., Ultrasmall superparamagnetic iron oxide nanoparticles coated with fucoidan for molecular MRI of intraluminal thrombus, *Nanomedicine* 10 (1) (2015) 73–87.
25. V.M. Martín Giménez, D.E. Kassuha, W. Manucha, *Nanomedicine applied to cardiovascular diseases: latest developments*, *Ther Adv Cardiovasc Dis* 11 (4) (2017) 133–142.
26. Y. Meng, X. Niu, G. Li, Liposome nanoparticles as a novel drug delivery system for therapeutic and diagnostic applications, *Curr. Drug Deliv.* 20 (1) (2022) 41–56.
27. W. Zhang, et al., Myocardial protective effect of intracoronary administration of nicorandil and alprostadil via targeted perfusion microcatheter in patients undergoing elective percutaneous coronary intervention: a randomized controlled trial, *Medicine* 100 (15) (2021).
28. F. Danhier, et al., PLGA-based nanoparticles: an overview of biomedical applications, *J. Contr. Release* 161 (2) (2012) 505–522.
29. Yang, et al., Impact of PEG chain length on the physical properties and bioactivity of PEGylated chitosan/siRNA nanoparticles in vitro and in vivo, *ACS Appl. Mater. Interfaces* 9 (14) (2017) 12203–12216.
30. J.T. Duskey, et al., Investigating novel syntheses of a series of unique hybrid PLGA-chitosan polymers for potential therapeutic delivery applications, *Polymers* 12 (4) (2020).
31. J. Zhang, A. Ma, L. Shang, Conjugating existing clinical drugs with gold nanoparticles for better treatment of heart diseases, *Front. Physiol.* 9 (2018) 642.
32. Y. Ni, et al., Bisoprolol reversed small conductance calcium-activated potassium channel (SK) remodeling in a volume-overload rat model, *Mol. Cell. Biochem.* 384 (1–2) (2013) 95–103.
33. Q. Zhou, L. Zhang, H. Wu, *Nanomaterials for cancer therapies*, *Nanotechnol. Rev.* 6 (5) (2017) 473–496.
34. Lombardo, M.A. Kiselev, M.T. Caccamo, Smart nanoparticles for drug delivery application: development of versatile nanocarrier platforms in biotechnology and nanomedicine, *J. Nanomater.* 2019 (2019) 1–26.
35. L.B.-t. Wang Wen-qian, C.U.I. Yan-li, Yi Wang, Yu Tian, C.H.E.N. Chang-qing, Research progress on structural modification of curcumin, *Drugs & Clinic* 33 (9) (2018) 2461–2465.
36. X. Liu, et al., [Preparation of nanosuspension of quercetin with a miniaturized milling method], *Zhongguo Zhongyao Zazhi* 42 (15) (2017) 2984–2988.
37. Z. Ma, et al., Traditional Chinese medicine-combination therapies utilizing nanotechnology-based targeted delivery systems: a new strategy for antitumor treatment, *Int. J. Nanomed.* 14 (2019) 2029–2053.
38. G. Cai-fang, et al., Application of nanotechnology in improving druggability of active ingredients of Chinese materia medica, *Chin. Tradit. Herb. Drugs* 49 (12) (2018) 2754–2762.
39. D.A. Hafez, et al., Nanomedicine-based approaches for improved delivery of phyto-therapeutics for cancer therapy, *Expet Opin. Drug Deliv.* 17 (3) (2020) 279–285.
40. L. Li, et al., Ginsenoside Rg3-loaded, reactive oxygen species-responsive polymeric nanoparticles for alleviating myocardial ischemia-reperfusion injury, *J. Contr. Release* 317 (2020) 259–272.
41. Z. Dong, et al., RGD modified and PEGylated lipid nanoparticles loaded with puerarin: formulation, characterization and protective effects on acute myocardial ischemia model, *Biomed. Pharmacother.* 89 (2017) 297–304.
42. W. Li, et al., Puerarin-loaded PEG-PE micelles with enhanced anti-apoptotic effect and better pharmacokinetic profile, *Drug Deliv.* 25 (1) (2018) 827–837.
43. X.Y. Liu, et al., [In vitro evaluation, cellular uptake and anti-acute myocardial ischemia effect of puerarin PEG-PLGA micelles], *Zhongguo Zhongyao Zazhi* 44 (11) (2019) 2244–2250.
44. F. Jun, et al., Preparation, in vitro release and cardiac targeting of Tanshinone IIA PEG PE nanomicelles in acute myocardial ischemia model rats, *Central South Pharmacy* 16 (7) (2018) 925–930.
45. S. Zhang, et al., Triphenylphosphonium and D- $\alpha$ -tocopheryl polyethylene glycol 1000 succinate-modified, tanshinone IIA-loaded lipid-polymeric nanocarriers for the targeted therapy of myocardial infarction, *Int. J. Nanomed.* 13 (2018) 4045–4057.
46. L.F. Li Jing, CHEN jianchao, Study on in Vitro Evaluation, Intracellular Distribution and Anti-apoptosis of Baicalin PEG-PCL Nanomicelle. *Chin J Mod Appl Pharm* 37 (12) (2020) 1427–1432.
47. J. Wang, S. Zhang, L. Di, Acute myocardial infarction therapy: in vitro and in vivo evaluation of atrial natriuretic peptide and triphenylphosphonium dual ligands modified, baicalin-loaded nanoparticulate system, *Drug Deliv.* 28 (1) (2021) 2198–2204.
48. Y.H. Yang, f.Z.J.L.H.Y., Preparation · Intracellular distribution and anti-cardiomyocyte apoptosis of

- astragaloside IV PEG-PE nanomicelles, *China Pharm.* 56 (10) (2021) 815–821.
49. L.L. Yang Ke, Guanwei Fan, Astragaloside IV- loaded heart-mitochondria dual-targeted nanomicelles improved heart injury after acute myocardial infarction 3 (3) (2022) 45–56.
50. B. Helli, et al., Curcumin nanomicelle improves lipid profile, stress oxidative factors and inflammatory markers in patients undergoing coronary elective angioplasty; A randomized clinical trial, *Endocr., Metab. Immune Disord.: Drug Targets* 21 (11) (2021) 2090–2098.
51. Y. Yoneshima, et al., Phase 3 trial comparing nanoparticle albumin-bound paclitaxel with docetaxel for previously treated advanced NSCLC, *J. Thorac. Oncol.* 16 (9) (2021) 1523–1532.
52. A.A. Shiozaki, et al., Treatment of patients with aortic atherosclerotic disease with paclitaxel-associated lipid nanoparticles, *Clinics* 71 (8) (2016) 435–439.
53. H. Kim, et al., Micro-/nano-sized delivery systems of ginsenosides for improved systemic bioavailability, *J Ginseng Res* 42 (3) (2018) 361–369.
54. Z. Zhang, T.N. Lam, Z. Zuo, Radix Puerariae: an overview of its chemistry, pharmacology, pharmacokinetics, and clinical use, *J. Clin. Pharmacol.* 53 (8) (2013) 787–811.
55. L. Zhang, Pharmacokinetics and drug delivery systems for puerarin, a bioactive flavone from traditional Chinese medicine, *Drug Deliv.* 26 (1) (2019) 860–869.
56. Y.X. Zhou, H. Zhang, C. Peng, Effects of puerarin on the prevention and treatment of cardiovascular diseases, *Front. Pharmacol.* 12 (2021), 771793.
57. D.C. Li, et al., [Research progress in the study of protective effect of tanshinone IIA on cerebral ischemic stroke], *Yao Xue Xue Bao* 50 (6) (2015) 635–639.
58. M.F. Li, et al., [Baicalin regulates STIM1-mediated calcium overload and reduces apoptosis of cardiomyocytes induced by lipopolysaccharide], *Zhonghua Yixue Zazhi* 99 (40) (2019) 3176–3182.
59. S. Hu, et al., Evidence construction of baicalin for treating myocardial ischemia diseases: a preclinical meta-analysis, *Phytomedicine* 107 (2022), 154476.
60. H. Yong-gui, et al., Mitochondrial mechanism of Astragaloside IV induced inhibition of GSK-3 $\beta$  in myocardial ischemia/reperfusion injury in rats, *Chin. Pharmacol. Bull.* 30 (3) (2014) 402–406.
61. B. Helli, et al., Curcumin nanomicelle improves lipid profile, stress oxidative factors and inflammatory markers in patients undergoing coronary elective angioplasty; A randomized clinical trial, *Endocr., Metab. Immune Disord.: Drug Targets* 21 (11) (2021) 2090–2098.
62. M. Dastani, et al., Three Months of Combination Therapy with Nano-Curcumin Reduces the Inflammation and Lipoprotein (A) in Type 2 Diabetic Patients with Mild to Moderate Coronary Artery Disease: Evidence of a Randomized, Double-Blinded, Placebo-Controlled Clinical Trial, *Biofactors*, 2022.
63. Y.-H. Yang, J.-W. Mao, X.-L. Tan, Research progress on the source, production, and anti-cancer mechanisms of paclitaxel, *Chin. J. Nat. Med.* 18 (12) (2020) 890–897.
64. Z.N. Al-Mahayri, M.M. AlAhmad, B.R. Ali, Current opinion on the pharmacogenomics of paclitaxel-induced toxicity, *Expet Opin. Drug Metabol. Toxicol.* 17 (7) (2021) 785–801.
65. L. Yinghui, et al., Research progress of paclitaxel nano-preparations, *Chinese Journal of Pharmaceutics (Online Edition)* 20 (5) (2022) 180–198.
66. F.L.T. Gomes, et al., Regression of atherosclerotic plaques of cholesterol-fed rabbits by combined chemotherapy with paclitaxel and methotrexate carried in lipid core nanoparticles, *J. Cardiovasc. Pharmacol. Therapeut.* 23 (6) (2018) 561–569.