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Biogenic Nanoparticles in Cardiovascular Disease: Current Insights and Future Prospects

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Abstract

Cardiovascular diseases, particularly myocardial infarction (MI), remain the leading cause of mortality worldwide. The search for novel therapeutic strategies has led to growing interest in green-synthesized nanoparticles as supportive agents in cardiovascular therapy. These biofunctionalized nanoparticles, derived from natural sources such as plants and microbes, offer several advantages, including eco-friendly synthesis, low-cost production, enhanced biocompatibility, improved bioavailability, and reduced toxicity. Nanoparticles target mitochondrial membranes in ischemic cardiomyocytes, where they deliver reactive oxygen species scavengers to alleviate oxidative stress. They have been shown to lower blood pressure, suppress nuclear factor kappa B (NF-κB) signaling, and reduce the expression of pro-inflammatory cytokines such as interleukin-1β (IL-1β) and tumor necrosis factor-alpha (TNF-α). Moreover, we highlight advances in nanoparticle-mediated gene regulation, including the delivery of small interfering RNA (siRNA) to silence key atherogenic targets such as proprotein convertase subtilisin/kexin type 9 (PCSK9) and apolipoprotein B (ApoB). They have demonstrated anti-atherosclerotic activity by reducing foam cell formation in THP-1 monocyte-derived macrophages and inhibiting apoptosis, lipid peroxidation, and production of NADPH-derived superoxides, and stabilizing levels of serum creatine and cardiotropins in myocardial infarcted animals. This review synthesizes current scientific evidence on the clinical relevance and mechanistic pathways of green nanoparticles in cardiovascular medicine, aiming to guide future research and inspire the development of next-generation therapeutics.

Keywords

Green Synthesis, Nanoparticles, Cardiovascular, Diseases

1. Introduction

Nowadays, cardiovascular diseases (CVD), particularly myocardial infarction (MI), are the major cause of mortality worldwide. In 2003, the World Health Organization (WHO) estimated the number of deaths by MI at 7.3 million [1]. Most of the deaths are in people more than 65 years old. The risk of MI increases with age from 45 years old for a man and from 55 years old for a woman. The latter produce oestrogens, which play a protective role. However, after menopause, the risk increases as for a man. The WHO estimates that 23.6 million people will die from cardiovascular disease (CVD) by 2030, despite improvements in the prevention and treatment of the condition [2]. These diseases would remain the leading cause of mortality worldwide. Nanomedicine is a promising route to improving the diagnosis and treatment of cardiovascular diseases (CVD), which are a leading cause of mortality worldwide [3]. Different classes of nanoparticles (NPs) have been evaluated. This has occurred in a multitude of in vitro and in vivo studies. The types of NPs include organic NPs, such as dendrimers and lipid-based NPs; inorganic NPs, such as carbon and metal-based NPs; and organic-inorganic mixed NPs, such as magnetoliposomes [4]. The main classes of nanomaterials that have been used in CVD are micelles, liposomes, polymeric nanoparticles, dendrimers, carbon nanotubes, inorganic nanoparticles, and crystalline nanoparticles such as gold, silver, or silica [5] [6]. Nanoparticles (NPs) are promising tools to improve the diagnosis and treatment of cardiovascular diseases. Parameters such as small size (from about 1 to 100 nm) allow easy uptake by the cells and the high surface-area-to-volume ratio, which controls the absorptions and sustained release of drugs, attest to the choice of nanoparticles. Metallic NPs have been applied in both drug delivery and diagnosis. The common metallic NPs are iron, copper, gold, silver, gadolinium, zinc oxide, titanium oxide, cerium oxide, and selenium [7]. Due to their unique physicochemical properties, including biocompatibility, high stability, and special surface chemistry, some of these nanoparticles are important metal oxides that are used in optical, medical, and catalytic applications [8]. Chemical methods are used to synthesise them, and these methods mostly employ toxic reducing agents. This poses numerous hazards to the environment. For instance, the pyrometallurgical method, which involves operating at high temperatures, requires a significant amount of energy [9]. This has made people more aware of environmental contamination and more interested in studying green synthesis methods. AgNPs released to the aquatic environment were estimated at about 0.01 $\mu g \cdot L^{-1}$ [10]. Researchers used a safe approach for nanoparticle production. This approach is also non-toxic, eco-friendly, and low-cost, known as biological synthesis and has been used in recent decades. Green synthesis of nano-

particles involves the use of various natural, renewable sources as alternatives to toxic chemicals such as plant extracts from leaves [11], flowers [12], roots, peelings [13], fruits [14], and seeds [15], as well as bacteria and yeast. These sources are believed to reduce and stabilise the process [16]. These biological substances are relatively safer and biodegradable. Green synthesis uses renewable feedstocks that are applied in green synthesis by using plant extract as reductants and stabilisers. In addition, green solvents such as water, CO_2 supercritical and ethanol replaced toxic organic solvents in the green synthesis process [17]. Plant extracts contain compounds such as polyphenols, flavonoids, terpenoids, carbohydrates, enzymes, etc., which are natural oxidants [18]. The antioxidant capacity of plant extracts or microorganisms results in their high reduction capacity, which increases the efficiency of nanoparticle synthesis [18]. Another application concerns the coating of nanoparticles. Nanoparticles produced by bacteria are often coated with proteins, improving stability and adding biological activities. Extracts of *Darjeeling tea* have been investigated as coatings for silver nanoparticles (AgNPs) to provide stability against agglomeration and to reduce toxicity [19]. Au NPs are used as carriers of bioactive molecules such as anticancer agents, which is of great help to the treatment of diseases, particularly cancer [20]. A phenolic-rich avocado peel extract encapsulated in Bovine Serum Albumin NPs may offer a novel and effective approach to lowering cholesterol levels and reducing the risk of CVDs [21]. Optimizing the therapeutic impact of metal nanoparticles requires a complex understanding and careful control of how the NPs interact with biological systems.

The consumption of herbal medicinal products is increasing around the world. Almost one-third of the marketed pharmaceuticals are natural products and derivatives [22], and about 80% of the world's population uses old-method medicines for their remediation [23]. Populations use medicinal products in classic formulations such as powders, solutions, capsules, tablets, ointments, creams, etc. Otherwise, natural products are recently formulated in nanoparticulate forms [24]. The bioavailability of natural products is a significant concern. However, many alternate strategies are available; among them is nanotechnology [25].

In this paper, we reviewed applications of nanoparticles-based natural products in cardiovascular diseases.

2. Advantages of Green Synthesis

Green synthesis, which uses biological methods to produce nanoparticles, has a number of advantages over traditional chemical methods [26]. Reduction in toxic chemicals: Green synthesis uses biological agents, such as plant extracts, bacteria, or fungi, which reduces or eliminates the need for harmful chemicals and organic solvents. Biodegradability: The materials and agents used in green synthesis are often biodegradable, which minimizes environmental impact and reduces waste [27]. Safety and non-toxicity: Green synthesis methods are generally safer for workers and consumers, as they avoid the use of hazardous chemicals. Nanopar-

ticles produced by biological methods are often less toxic and safer for use in medical and environmental applications. Economic efficiency: Green synthesis can reduce production costs by using renewable resources and avoiding the complex purification steps often required in chemical methods. Plant extracts and microorganisms are often available in abundance and can be grown sustainably [28]. Ease of implementation: Green synthesis methods are often simpler and require fewer steps than chemical methods, making them easier to implement on a large scale. Synthesis conditions can be easily adjusted to suit specific needs, allowing flexibility in production [29].

3. Mechanisms of Green Synthesis

The precise process of biosynthesis of metal oxide nanoparticles using plant extracts has not yet been validated. However, it has been suggested that polar groups take charge of NP synthesis [30] [31]. It appears that, initially, the lone pair electrons present in the ascorbic acid polar groups have the opportunity to occupy the Zn^{2+} orbital. Subsequently, Zn^{2+} is covered by the polar groups to form a complex compound within the nanometric models of metabolites. Finally, the reaction could lead to the formation of ZnONPs via calcination (**Figure 1**) [32]. **Figure 1** shows how zinc oxide nanocrystals can be made from rambutan bark extract. The p-track conjugation effect occurs when the ester oxygen atom and the phenolic hydroxyl groups of the polyphenols interact. This effect occurs when

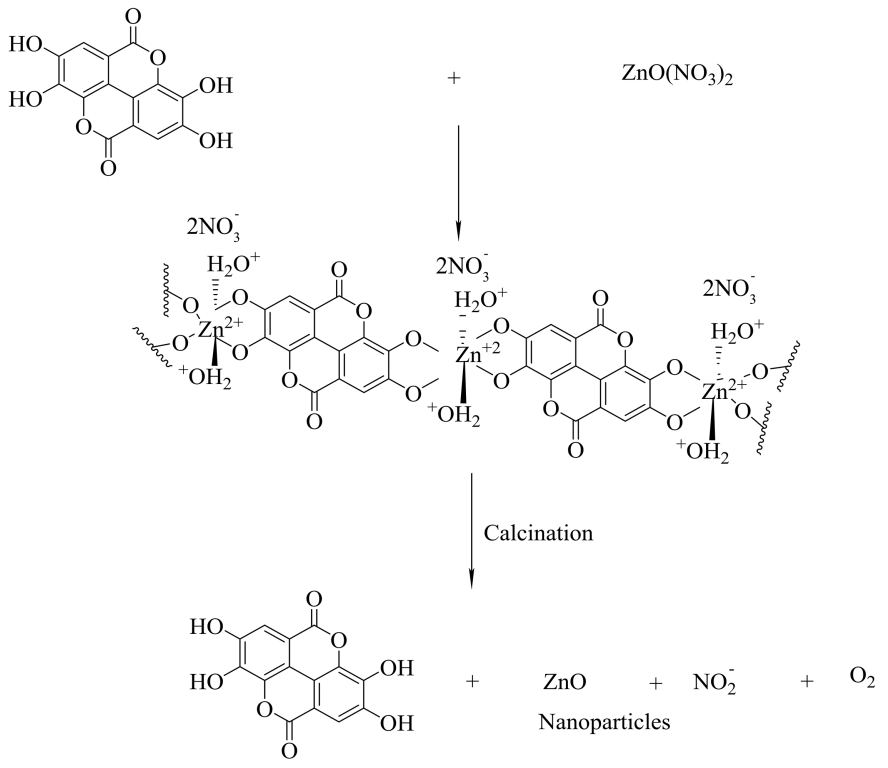

Figure 1. Potential process for creating ZnO nanocrystals using rambutan skin extracts [32].

the hydroxyl groups join with the metal to form a phenolic complex (a zinc-ellagate complex) through a process called chelation. These complexes decompose directly at 450˚C, resulting in the formation of zinc oxide nanostructures [33]. As shown in **Figure 2**, the process for creating ZnONPs using a lemon zest extract is illustrated. Carotenoid, limonoid, and flavonoid molecules can interact with zinc (Zn^{2+}), forming complex zinc-carotenoid, limonoid, and flavonoid molecules (**Figure 2**). After the complexation reactions had taken place, the solution was applied to the substrate, which was then dried and annealed. During this process, the complex molecules were converted into ZnONPs [34]. The flavonoid-rich extract of *Hagenia abyssinica* (Bruce) J. F. Gmel interacts with metal ions due to its carbonyl functional groups. This releases reactive hydrogen, which transforms the flavonoid enol into its ketone form and leads to the formation of Ag^0 (**Figure 3**) [35].

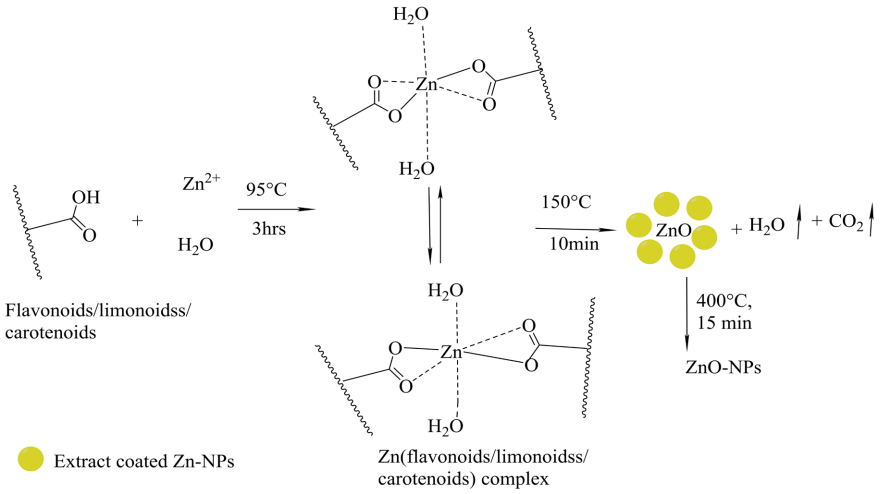

Figure 2. Possible mechanism for the formation of ZnO nanoparticles [34].

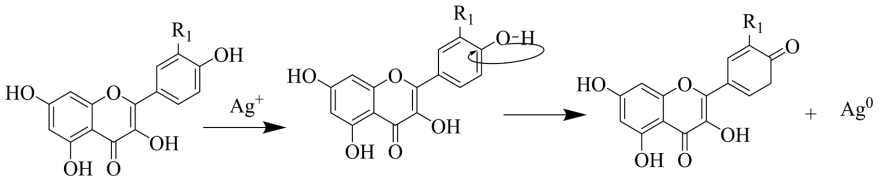

Figure 3. Flavonoids induce phyto-reduction of Ag+ to AgNPs [35].

4. Green Synthesis Methods of Nanoparticles

4.1. Plant-Based Synthesis

Nanoparticles produced by natural products known as biodegradable nanoparticles have advantages of increased stability (**Figure 4**) [36]. In 2022, N. Jayarambabu *et al.* used an extract of *Curcuma longa* to produce copper nanoparticles simply and economically, without using harmful compounds. The nanoparticles produced have an average size ranging from 5 to 25 nm, are crystalline in nature, and are free from impurities (CuO, Cu_2O). Antibacterial activity tests were carried

out on nanoparticles against Gram-positive (*Bacillus subtilis*) and Gram-negative (*Escherichia coli*) bacteria. The Gram-positive bacteria showed increased sensitivity, with more extensive zones of inhibition [37]. In 2012, Sontara Konwar Boruah *et al.* used the synthesis of gold nanoparticles from the young leaves and buds of tea (*Camellia Sinensis*). The gold ions are transformed into gold nanoparticles by the reducing action of the polyphenols present in the tea extract. Formation of the nanoparticles was confirmed by observing peaks at 534 and 752 nm in the UV-visible absorption spectrum, which indicates the presence of surface plasmon resonance. The AuNPs range in size from 2.94 to 45.58 nm, with an average size of 13.14 nm. They exhibit spherical, hexagonal, and triangular morphologies and fluorescence with emissions measured at 450 nm and 705 nm [38]. In 2019, C.A. Soto-Robles *et al.* used Hibiscus sabdariffa extract at concentrations of 1%, 4%, and 8% as a reducing and stabilizing agent for the manufacture of ZnO nanoparticles. ZnO NPs are characterized by a hexagonal crystalline structure (Wurtzite), a particle size ranging from 8 to 30 nm, and a band gap that decreases from 2.96 eV to 2.77 eV as a function of extract concentration. Similarly, ZnO NPs showed high efficiency in the degradation of methylene blue, reaching 97% in 150 minutes of UV exposure [39]. In 2023, Amin Sadeghi Dousari *et al.* synthesized silver, zinc, copper, iron, bismuth, and gold nanoparticles using *Mentha pulegium* [40]. These nanoparticles range in size from 4 to 320 nm and in shape, being spherical, cubic, and hexagonal. Silver and zinc nanoparticles are effective against *Escherichia coli* and *Staphylococcus aureus*. They inhibit the development of certain species of fungi. These fungi are resistant to traditional antifungals. They are also cytotoxic against cancer cells [40]. In 2015, A. Jafarizada *et al.* used *Mentha* and *Pelargonium* extracts to synthesize gold nanoparticles [41]. The elements present in the extracts have characteristics that favor the conversion of gold into nanoparticles and their stabilization, thus preventing their tendency to agglomerate. The nanoparticles demonstrated significant stability over time and under various temperatures, with a uniform size, attesting to their potential for use in the biomedical field [41]. In 2019, Samira Shahriyari Rad *et al.*, *synthesized* zinc oxide nanoparticles (ZnO NPs), using an aqueous extract of *Mentha pulegium* leaves [27]. The ZnO nanoparticles demonstrated significant antibacterial action against *Escherichia coli* (Gram-negative) and *Staphylococcus aureus* (Gram-positive). Tests indicate that the impact is more marked on Gram-positive bacteria. Several mechanisms are attributed to the antibacterial effect of ZnO NPs, including disruption of the bacterial cell membrane and production of reactive oxygen species (ROS), which damage cellular elements [27]. Iron oxide nanoparticles were made from *Mentha Pulegium* L leaf extract in 2020 by Abderrahmane Bouafia *et al.* The formation of iron oxide nanoparticles is confirmed by absorption maxima located between 275 and 301 nm, and the size of the nanoparticles, ranging from 22 to 34 nm, is affected by different concentrations of $FeCl_3$ [29]. ZnO nanoparticles were synthesized by combining a 10% extract of *Ocimum basilicum* (used as a reducing and stabilizing agent) with a zinc acetate dihydrate solution [42]. They were then

dried and calcined to obtain a hexagonal crystal structure with an average size of 30 to 40 nm. ZnONPs have been tested against *Staphylococcus aureus* and *Escherichia coli*, as well as a fungus called *Aspergillus niger*. The nanoparticles demonstrated significant suppression of microbial growth, with inhibition diameters of 31.05 mm, 36.15 mm, and 24.10 mm respectively. The minimum inhibition threshold (MIC) was 312.5 µg/mL for the bacteria and 5000 µg/mL for the fungus [42]. In 2022, Aayasha Negi *et al.* used an extract from the roots of *Taraxacum officinale radix* (dandelion) to produce zinc nanoparticles (ZnONPs) [43]. Their formation was validated by UV absorption at 365 nm. The ZnO-NPs produced were hexagonal in shape and had an average size of approximately 23.35 nm. Evaluation of the zeta potential indicates significant stability of the nanoparticles. ZnO-NPs proved effective against various pathogenic bacteria (*Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, and *Streptococcus pneumoniae*), with zones of inhibition varying according to the concentrations used. An ability to capture DPPH radicals was noted, with an estimated IC_{50} of 127.75 mg/ml, indicating a promising antioxidant potential. ZnO-NPs also acted as catalysts for the degradation of industrial dyes such as methylene blue, rhodamine B, and acridine orange, proving their effectiveness in the treatment of wastewater under sunlight [43]. In 2024, K. Kasthuri *et al.* used dandelion extract and zinc sulphate heptahydrate to synthesize ZnO nanoparticles [28]. ZnONPs were 85% effective against *Escherichia coli* and *Staphylococcus aureus*, reduced the growth of certain fungal species by 70%, and reduced the viability of human cancer cells (MCF-7) by 60% [28]. In 2022, Nguyen Duy Hai *et al.* used mango leaf extract as a reducing and stabilizing agent to produce AgNPs in an environmentally friendly way [44]. They studied the impact of the reaction, the volume of the $AgNO_3$ solution, and the pH on the creation of AgNPs. The nanoparticles demonstrate high efficiency in reducing organic dyes, particularly crystal violet, with a 98.83% reduction accompanied by ultrasound support. The latter show appreciable sensitivity for the detection of hydrogen peroxide (H_2O_2) and mercury ions (Hg^{2+}), with detection thresholds of 20.21 µg/L and 25.87 µg/L respectively. These nanoparticles effectively curb the proliferation of various Gram-positive, Gram-negative bacteria, and fungi with an efficacy rate exceeding 85% [44].

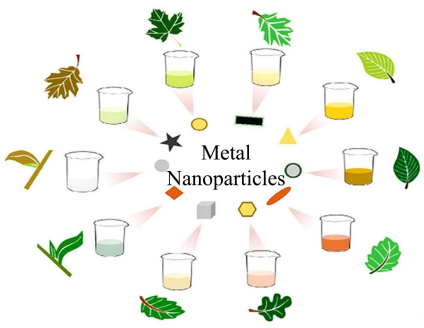

Figure 4. Plant-based metal nanoparticles [36].

4.2. Microorganism-Mediated Synthesis

In 2014 Zhe Li, Lei Wang *et al.*, used bacterial cellulose (BC) as a reducing and protective agent in the formation of AgNPs, the process being carried out at a pressure of 0.103 MPa and a temperature of 121˚C for a period of 10 minutes [45]. BC membranes incorporating AgNPs were tested against bacteria such as *Escherichia coli*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*, demonstrating an antimicrobial capacity in excess of 99.9%. Because of their antibacterial and biocompatible characteristics, BC-AgNPs nanocomposites could be used to manufacture antimicrobial dressings and materials intended for implantation [45]. In the same year C. Ganesh Kumar *et al.*, used the supernatant from the culture of the *Delftia sp. strain* KCM-006 to generate gold nanoparticles (AuNPs), without the use of chemical reducing agents. The nanoparticles produced are monodisperse, spherical, exhibit photoluminescence and a crystalline structure, with an average diameter of 11.3 nm and notable stability (zeta potential of −25 mV). These nanoparticles (RSV-AuNPs) have been grafted with resveratrol, an anticancer agent, which increases their efficacy compared with resveratrol alone. Experiments carried out in vitro on lung cancer cells (A549) show that RSV-AuNPs are 65% more effective than resveratrol alone. The research indicates that these nanoparticles could serve as effective carriers for targeted delivery of cancer drugs [46]. In 2020 Sohier M. Syame *et al.* confirmed the green production of AgNPs by lactic acid bacteria, in particular *Lactobacillus plantarum* and *Lactobacillus brevis*, using UV-visible spectroscopy at 410 nm [47]. The nanoparticles were spherical in shape and varied in size between 5 and 40 nm. The nanoparticles produced were evaluated for their potential antimicrobial activity, showing greater efficacy against Gram-negative bacteria (*Escherichia coli*, *Pseudomonas aeruginosa*) than Gram-positive bacteria (*Staphylococcus aureus*, *Enterococcus faecalis*), as well as against *Candida albicans* [47]. Nanoparticles derived from algae, particularly those based on gold and silver, have antimicrobial, antifouling, and photocatalytic properties. They can be used for bioremediation, in biosensors, and for medical diagnostics. Nanoparticles derived from algae have shown great promise in removing contaminants from wastewater [48]. In 2023, a study by Ahmed E. Alprol and colleagues revealed a new method for synthesizing ZnO-NPs [49]. This innovative approach avoids the use of toxic substances commonly employed in conventional methods, using algae extracts as an alternative. Algae, in particular marine macroalgae and microalgae, contain a plethora of bioactive elements and facilitate the manufacture of ZnO-NPs that are biocompatible, economical, and non-toxic. Several sectors use these nanoparticles, including photocatalysis, biological wastewater treatment, medical equipment, the cosmetics industry, and sensors [49]. In 2014 Ganesan Arun *et al.*, examined the production of AgNPs using the fungus *Schizophyllum commune*. Several techniques, including UV-Visible spectrum, FTIR, and scanning electron microscopy (SEM), were used to analyze the synthesized nanoparticles, confirming their formation and structure

[50]. The nanoparticles demonstrated significant action against bacteria such as *E. coli*, *Bacillus subtilis*, *Klebsiella pneumoniae*, and *Pseudomonas fluorescens*. They curb the proliferation of harmful dermatophytes such as *Trichophyton simii*, *Trichophyton mentagrophytes*, and *Trichophyton rubrum*. A cytotoxicity test (MTT test) carried out on HEP-2 cells from a human laryngeal carcinoma revealed a cell death rate that depended on the nanoparticle concentration. The ecological production route for AgNPs by Schizophyllum commune represents a promising alternative to chemical techniques and shows significant potential for applications in the biomedical field [50]. In 2018 Zsófia Molnár *et al.*, synthesized gold nanoparticles (AuNPs) using extracts of thermophilic filamentous fungi, providing an efficient and scalable method for their synthesis [51]. The AuNPs produced vary in size (from 6 to 40 nm) and distribution depending on the fungus used and the experimental conditions. The use of fungi encourages production that is more respectful of the environment, but it is essential to understand the functions of the biomolecules involved [51]. Prince Clarance *et al.* used *Fusarium solani* to produce gold nanoparticles using an environmentally-friendly method [52]. These nanoparticles have a ruby red hue and a fixed absorption maximum at 551 nm, with an average size ranging from 40 to 45 nm. The nanoparticles were examined on cervical (HeLa) and breast (MCF-7) cancer cells. They demonstrated dose-dependent cytotoxicity, with IC_{50} values of 0.8 ± 0.5 µg/mL (MCF-7) and 1.3 ± 0.5 µg/mL (HeLa). They induce apoptosis and modify the cell cycle of cancer cells, suggesting their use in chemotherapy with reduced systemic toxicity [52]. In 2014, Aniket Gade *et al.*, used the fungus *Phoma glomerata* for the ecological and cost-effective production of AgNPs [53]. FTIR spectroscopy indicates that a protein shell surrounds the nanoparticles, enhancing their stability. Methods such as transmission electron microscopy (TEM), X-ray diffraction (XRD), and nanoparticle analysis (NPA) validate their polydisperse and spherical nature [53]. In 2012 Guangquan Li *et al.*, used the fungus *Aspergillus terreus* to decrease Ag^+ ions to AgNPs via compounds released in its culture environment [54]. The reaction took place at room temperature and was monitored by UV-Vis spectroscopy. The nanoparticles produced ranged in size from 1 to 20 nm and were well dispersed. It appears that the presence of NADH and NADH-dependent enzymes promotes the reduction of silver ions. It is likely that this reaction is an enzymatic process occurring outside the cell. AgNPs have demonstrated considerable activity against various pathogenic bacteria (such as *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa*). They also inhibited the proliferation of harmful fungi, including certain species of *Candida* and *Aspergillus* [54]. The production of AgNPs outside cells by *Aspergillus sydowii* was verified using colour change, UV spectroscopy, and electron microscopy [55]. They succeeded in obtaining spherical particles ranging in size from 1 to 24 nm, with a cubic-type crystalline structure. The AgNPs demonstrated effective action against several harmful fungal species, including Candida, *Aspergillus*, and *Fusarium*, as well as inhibiting the multiplication of HeLa and MCF-7 cancer cells at precise concentrations [56].

5. Green Nanoparticles on Cardiovascular Complications

5.1. Organic Nanoparticles (ONPs)

Their highly biodegradable and biocompatible vehicles for drug and cell delivery make ONPs well suited to a variety of applications. Their ease of synthesis and increasing biological stability are characteristics of organic NPs. The chemistry of lipid-based NPs is characterized by their cell membrane. In contrast, inorganic NPs are recognized by their electrical properties. The treatment or prevention of cardiovascular diseases (CVDs) has involved the use of medicinal plant-based nanoformulations. The treatment or diagnosis of cardiovascular pathologies is done indirectly through the genes expressed during a dysfunction, with these genes being the key to identifying the problem. The uptake of minimally modified low-density lipoprotein (LDL) and oxidized LDL (oxLDL) is increased by scavenger receptors expressed by macrophages [57]. Native low-density lipoproteins (LDLs) naturally accumulate during the progression of atherosclerosis. They accumulate cholesterol and transform it into foam cells. These cells secrete many inflammatory factors, including MCP-1, which produces more monocytes and induces an increase in macrophages and foam cells in the artery wall. Macrophages play an important role in the progression of atherosclerosis. The death of foam cells induces lipid accumulation in the artery wall and provokes the formation of atherosclerotic plaques [58].

5.1.1. Natural Polymeric Nanoparticles

Drug delivery nanosystems can be made from a variety of polymers. Plant-based polymers are natural and have several advantages over inorganic polymers. Thanks to these advantages, plant-based natural polymers are particularly notable in the study of cardiovascular diseases and are being investigated for use in the treatment of CVDs for imaging, diagnosis, and drug delivery. Cur-Bio PLGA NPs, a polynutrient-based nanomedicine, demonstrated anti-atherosclerotic activity by reducing foam cell formation in THP-1 monocyte-derived macrophages [59]. Curcumin (Cur) is a natural polyphenol that belongs to the curcuminoid family and is derived from the rhizomes of Curcuma longa. Bioperine (Bio) is a natural bioenhancer derived from Piper nigrum. One anti-atherosclerotic therapeutic strategy involves developing curcumin-loaded linear dendrimer-type methoxy poly(ethylene glycol)-b-poly(ε-caprolactone) copolymer nanoparticles, which reduce atherosclerotic lesions and have plaque-stabilising properties compared to curcumin alone [60]. Natural bio-enhancers are agents that increase the effectiveness and bioavailability of drugs when co-administered [61]. Two different ratios of curcumin were tested. Bioperine was tested for its inhibitory effect on oxidised low-density lipoprotein (Ox-LDL)-induced foam cell formation. The results showed that Cur-Bio PLGA NPs at ratios of 1:0 and 2:10 maintained cell viability in THP-1 monocyte-derived macrophages at over 80% throughout the experiment. Curcumin and resveratrol co-loaded into polymeric micelles exhibited cardioprotective effects in a cell model of doxorubicin-induced cardiotoxicity [62]. Curcumin-

loaded copolymer PEG-pol (ethylene glycol) methyl ether-block-poly (D, L-lactide)-block-decane inhibited apoptosis, lipid peroxidation, and production of NADPH-derived superoxides induced by exposure of cardiomyocytes to palmitate [63] and activated the AMP-activated protein kinase, and regulated the expression of downstream proteins [64]. Nabofa *et al.* demonstrated that the curcumin-nisin-based PLA nanoparticles formulation provided a significant level of cardioprotection in a guinea pig myocardial infarction model [65]. In a rat model, the delivery of curcumin encapsulated in carboxymethyl chitosan nanoparticles conjugated to a myocyte-specific homing peptide to pathological myocardium was found to reduce cardiac hypertrophy and apoptosis [66]. Resveratrol (3, 5, 4'-trihydroxystilbene) is one of the non-flavonoid polyphenolic compounds. It increases eNOS production, inhibits lipid peroxidation [67] [68] mitogen-activated protein (MAP) kinases and iNOS activities [69], and has anti-inflammatory effects through the down-regulation of pro-inflammatory mediators like COX-1 and COX-2; eNOS activity/expression protects the effect of resveratrol against vascular damage in cardiovascular diseases. The limitations of resveratrol are poor water solubility, a short biological half-life, chemical instability, and rapid metabolism [67] [70]. Thus, nanoparticle delivery systems represent an ideal way to carry resveratrol to target tissues and ensure bioavailability [67]. Resveratrol-loaded polymeric nanoparticles are no bigger than 100 nm, enabling them to easily pass through the membrane. Cheng *et al.* reported that dual-shell polymeric nanoparticles (MCTD-NPs), which utilise a multistage continuous targeted strategy to deliver ROS scavengers specifically to the mitochondria of ischaemic cardiomyocytes, distribute resveratrol in the ischaemic myocardium and reduce infarct size in myocardial ischaemia/reperfusion injury in rats [71]. Hardy *et al.* reported that exposure of hearts to resveratrol-loaded nanoparticles allowed the late release of creatine kinase and lactate dehydrogenase, which are injured myocardium markers [72]. Quercetin has important cardioprotective effects, and preventive effects in dyslipidaemia, endothelial dysfunction, and platelet aggregation [73]. It lowered blood pressure [74], reduced transcription of NF-kB [75], and decreased IL-1β, and TNF-α [76]. In spite of all these, quercetin's therapeutic target is limited due to its poor solubility, instability in the physiological medium, and low bioavailability [77] [78]. Therefore, polymeric nanoparticles solve these limitations. Quercetin-loaded PLA nanoencapsulation demonstrated higher water solubility and sustained release of the drug, leading to better bioavailability and stability of quercetin. Comparison of quercetin- and catechin-loaded PLGA nanoparticles showed that quercetin was more slowly released from PLGA, probably due to the carbonyl and carboxyl interactions of the polymer and flavonoid molecules. A novel system of polymeric PLGA nanoparticles loaded with quercetin and fabricated via the electrohydrodynamic atomization process may have great potential in the prevention of atherosclerosis and other related cardiovascular diseases [78]. Curcumin exhibits many physiological activities, such as antioxidant, anti-inflammatory, and anti-proliferative effects. These properties protect the heart against

the development of cardiac hypertrophy, cardiotoxicity, and heart failure. It also showed beneficial effects in the atherosclerotic process and in diabetic cardiovascular complications [79]. Like other natural polyphenolic compounds, curcumin has limitations that restrict its clinical use, such as poor bioavailability and absorption, and rapid metabolism. Curcumin-loaded polymeric nanoparticle systems solve all these problems. Carlson *et al.* demonstrated the cardioprotective effects of combining curcumin and resveratrol in polymeric micelles in a cell model of doxorubicin-induced cardiotoxicity, reducing apoptosis and ROS formation [62].

5.1.2. Lipid Nanoparticles

Lipid nanoparticles are an option for administering drugs to the myocardium. They can include hydrophilic and lipophilic materials, and their morphology is comparable to cell membranes [80]. They have the capacity to introduce a variety of biomaterials such as peptides, proteins, nucleic acids, imaging agents, and low-weight drugs into the intended tissue [81].

Liposome therapy and diagnostic applications are the commonly injured areas in which pharmaceuticals are used. Liposomes are spherical, self-closing structures composed of one or more concentric lipid bilayers with aqueous phase between and within the lipid bilayers [82]. Liposomes are small vesicles with a diameter of 20 nm to 2.5 μm. They can be fabricated from one or more non-concentric or concentric membranes. Acute parameters may influence drug encapsulation efficiency and half-life in circulation, including vesicle size and number of bilayers. Liposomes can be categorized as unilamellar vesicles, multilamellar vesicles (MLV, >500 nm), or multivesicular vesicles (MVV, >1000 nm) based on the size and quantity of bilayers [83]. The first medication delivery method utilizing nanoparticles is liposome-encapsulated doxorubicin (Doxil), used to treat AIDS-related Kaposi's sarcoma, multiple myeloma, and ovarian cancer [84]. Then, liposomes began to be explored for other biomedical applications, including alternative therapeutics for CVDs. Despite the lack of liposomal drug formulations available for CVD treatment, liposomes have made significant steps in improving the effectiveness of cardiovascular drug delivery. For example, liposomes altered lipid metabolism in small and large models by delivering small interfering ribonucleic acid (siRNA) to suppress the expression of proprotein convertase subtilisin-kexin type 9 (PCSK9) and apolipoprotein B. This resulted in a decrease in low-density lipoprotein levels [85]. It has also been envisaged to use lipid nanoparticles for messenger RNA delivery (mRNA) with applications in various CVDs. Recent studies have explored the synergy of mRNA and lipidic nanocarriers for improving cardiac function and regeneration [86], decreasing low-density lipoprotein cholesterol levels [87], and treating endotheliopathy associated with vascular senescence.

(-)-Epigallocatechin-3-gallate (EGCG) possesses the potential to decrease the release of inflammatory factors and reduce cholesterol accumulation in macrophages [88]. Besides, EGCG is unstable in water and physiological fluid *in vitro*. Nanoencapsulation of EGCG in nanostructured lipid carriers (NLCE) and chi-

tosan-coated NLCE (CSNLCE) showed potential as tools to inhibit atherosclerosis through decreasing macrophage cholesterol content and MCP-1 expression [58].

The NLRP3 inflammasome protein complex is a vital player in the innate immune system. Its activation is regulated through a two-step process. First, it must be primed and then assembled [89]. Inappropriate activation of the NLRP3 inflammasome has been implicated in atherosclerosis [90]. Thus, the NLRP3 inflammasome has been considered a desirable drug target. Dietary vesicle-like nanoparticles (VLNs) have high therapeutic potential. They are bioavailable, stable, and bioactive. Their membranes enclose the biomolecules inside the nanoparticles, are resistant to solutions in the stomach and intestines, and protect the biomolecules from degradation [91]. They can be extracted from vegetables, including the genus *Allium*, such as garlic, leek, onion, and scallion [92]. Liu *et al.* showed that oral administration or intravenous administration of garlic chive-derived vesicle-like nanoparticles (GC-VLNs) suppresses NLRP3 inflammasome activation, and the phospholipid 1,2-dilinoleoyl-sn-glycerol-3-phosphocholine (DLPC) in GC-VLNs is responsible for this phenomenon [93]. *Drococephalum moldavica* L., belonging to the Labiatae family, possesses total flavonoids including Italiani, luteolin, and rosmarinic acid, which play important roles in *D. moldavica* pharmacological action. Studies showed the effectiveness of the total flavonoids of *D. Moldavica* solid lipid NPs (TFDM-SLNPs) against coronary artery occlusion-induced myocardial ischemia-reperfusion injury in rats. Treatment of the rat group with the TFDM-SLNPs formulation induced smaller infarct size, lower LDH activity, and lower CK level, indicating an improved cardioprotective effect of TFDM-SLNPs compared with TFDM alone. TFDM-SLNPs also improved the integrity of the myocardial membrane and fibres while significantly reducing the IL-1β and TNF-α levels.

Type of Treatment	Medical Applications	Ref
Vesicles formulated with phospholipids, PEG-HS, and istaroxime	Acute and chronic heart failure	[94]
Biomimetic liposomes	Anti-inflammatory treatment of MI	[95]
Liposome/DNA complexes immobilized on the stainless-steel surface	Coronary restenosis	[96]
Liposome plasmid DNA complexes with TATp	Transfection of cardiomyocytes in the ischemic zone	[97]
Targeted liposomes loaded with ATP	Cardioprotective effect	[98]
Liposomes coated with polyethylene glycol containing gadodiamide	Enhance MR angiography	[99]

5.1.3. Dendrimers Nanoparticles

Dendritic polymers have been explored for various applications in the diagnosis and treatment of cardiovascular diseases. Dendrimers can be tailored to deliver

anti-inflammatory, anti-thrombotic, or vasodilator drugs directly to the affected sites, minimizing systemic side effects. They have been used for delivering the thrombus-dissolving enzyme natto kinase (NT) and as nanocarriers of pegylated peptide based on different generations (G2-G4) of dendritic polyglutamic acid [100].

5.1.4. Carbon-Based Nanoparticles (CNTs)

CNTs or nanocarbons were discovered in 1991, and they attracted a significant amount of interest from the scientific community due to their chemical, mechanical, and electronic properties. Their usage has gradually expanded in the biomedical field and may offer advanced treatment options that transcend the shortcomings of currently available therapies against cardiovascular diseases [101]. CNTs interact with cardiomyocytes and promote electrical conductivity. The CNT and cardiomyocyte interface allows changes in scaffold morphology and results in the proliferation of cells, and their differentiation and maturation into a cardiac lineage. Vertically aligned nanotubes (VA-CNTs), considered green carbon nanotubes, can be synthesized using natural palm oil as the carbon source.

5.2. Metallic Nanoparticles (MNPs)

Inorganic nanoparticles are recognized for their electrical properties that allow magnetic-guided delivery of therapeutic and diagnostic imaging. They enable adequate tissue penetration and are timely degraded but are sometimes very toxic. The toxicity of MNPs depends on many parameters such as size, shape, coating, method of synthesis, dispersion, and charge [102]. MNP coatings considerably affect toxicity through the modification of uptake and localization. Research on the impact of nanomaterials on living organisms and ecosystems requires nanotoxicological studies; the accumulation and distribution of nanomaterials within individual organisms and the food chain should first be revealed [103]. Mechanistically, it is agreed that MNP toxicity arises from the production of reactive oxygen species (ROS), which cause oxidative stress. The toxicity of Ag^{+}, the EC_{50} was 0.39 ± 0.32 $mg{\cdot}L^{-1}$ for Chlorella sp., and the LC_{50} of *Moina macrocopa*, *Barbonymus gonionotus*, and *Chironomus spp* were 0.026 ± 0.43 $mg{\cdot}L^{-1}$, 0.057 ± 1.15 $mg{\cdot}L^{-1}$, and 0.042 ± 0.19 $mg{\cdot}L^{-1}$, respectively. Besides, the EC_{50} of AgNPs was 0.89 ± 0.68 $mg{\cdot}L^{-1}$ for Chlorella sp., and the LC50 of *M. macrocopa*, *B. gonionotus*, and *Chironomus spp* were 1.11 ± 0.86 $mg{\cdot}L^{-1}$, 1.76 ± 0.19 $mg{\cdot}L^{-1}$, and 1.08 ± 1.21 $mg{\cdot}L^{-1}$, respectively. The results of the bioaccumulation study indicated that the highest bioaccumulation factor (BAF) of Ag^{+} was 101.84 $L{\cdot}g^{-1}$ in Chlorella sp., and the lowest BAF of AgNPs was 1.89 $L{\cdot}g^{-1}$ in *B. gonionotus* [104]. Hence, there is a need to produce MNPs using plant extracts of phytochemicals that have strong antioxidant properties.

5.2.1. Silver Nanoparticles

AgNPs have a role in reducing oxidative stress by scavenging ROS. As glucose-induced ROS-mediated oxidative stress in cardiomyocytes has been associated

with diabetic cardiomyopathy [105]. With high costs and many toxicity issues associated with the chemical synthesis of AgNPs, many efforts were made toward the formulation of efficient and safe green methods for AgNPs synthesis [106]. Plant extracts provide efficient and safe AgNPs due to the presence of a biologically active component. Neha *et al.* used *Sygyzium cumini* (Sm) extract to reduce silver ion and form an active surface with bioactive compounds as ligands, which were absent in the chemically synthesized AgNPs [107]. They evaluated lipid peroxide formation as an indicator of oxidative stress in cardiac cells. With treatment using AgNPs and *S. cumini* separately in glucose-stressed cells, the inhibition was reduced to about 1.5-fold compared to stressed cells. AgNPs prevent oxidative and cellular damage due to their antioxidant characteristics. This means that AgNPs have significant cardioprotection on glucose-stressed cells. Diabetics are more prone to develop cardiovascular complications than non-diabetics. This means that further investigations in this regard are a prime necessity. A multitude of natural products is used for drug preparations targeting diabetic cardiomyopathy [108]. Previous studies showed that methanol extract of *Syzygium cumini* suppresses high glucose-induced stress by reducing the overproduction of ROS and collagen content in H9c2 cardiomyocytes [109]. *S. cumini* has a dual role as an antidiabetic and cardioprotective agent in combating cardiac stress associated with high glucose levels [107]. *S. cumini* nanoparticles (AgNPs) were synthesized and characterized for their cardioprotective potential under high glucose, as diabetes is associated with an increased incidence of heart failure. Atale *et al.* evaluated the antioxidant activity of AgNPs on DPPH and ABTS. Results showed for the DPPH assay 66 (±1.23), 60.29 (±0.02), and 68.35 (±1.15) % inhibition by AgNPs, *S. cumini* and gallic acid, respectively, at the concentration of 1 mg/mL. For ABTS radicals, they observed 86 (±1.19), 85.67 (±1.27), and 89.91 (±1.25) percentage inhibition by AgNPs, *S. cumini*, and BHT, respectively, at the concentration of 1 mg/mL. These results showed that AgNPs possess better antioxidant activity for DPPH and ABTS compared to *S. cumini* extract.

5.2.2. Iron Nanoparticles

Previous studies demonstrated that the Fenton reaction and protein aggregation caused iron NP's toxic effects. Top-down and bottom-up approaches are two major synthetic routes for iron nanoparticles. The surface structure of iron nanoparticles synthesized from these methods affects environmental remediation [110]. Green synthesis of iron nanoparticles through plant extracts is an eco-friendly, stable, and economical method. Phytochemicals have been used in medicine, nutraceuticals, and food additives [111]. Secondary metabolites present in the extracts of seeds, pericarp, leaves, tea, and flowers are natural reducing agents that can reduce iron precursors and prevent the aggregation of iron nanoparticles [112]. Polyphenols are reducing chelators that can form complexes with iron ions and reduce these ions to iron nanoparticles. The reducing potential of polyphenols induces the iron ion conversion from Fe^{3+} to Fe^{2+} ($E^0_{Fe3+/Fe2+}$ = 0.77 V). Plant extracts contain different reducing and stabilizing components that can participate

in iron nanoparticle synthesis. The composition of the plant extracts establishes the characteristics of the synthesized iron nanoparticles [113]. Xiu *et al.* reported green synthesis of FeNPs using *Centaurea alba* extract and investigated their atherosclerotic properties [114]. *Centaurea*, being one of the largest plant species with over 700 diverse species, is generally found in different parts of Asian countries [115]. Studies reported in the *Centaurea aura* leaf extract the presence of organic compounds including sesquiterpene lactones [116], flavone [117], flavonoid [118], lignans, and alkaloids [119]. This species has been reported to have antimicrobial, anti-cancer, and antioxidant properties [120]. Previous works show strong evidence of the enhancement of therapeutic properties of metallic nanoparticles synthesized by antioxidant-rich ethnomedicinal plants. TEM and SEM determined the morphological features of the FeNPs. More analyses such as UV-Vis and FT-IR have been evaluated. The anti-atherosclerosis effect of FeNPs was evaluated by LDL and cholesterol levels. After feeding rats with a high-cholesterol supplement diet followed by administration of FeNPs, the level of LDL and cholesterol was reduced. Various studies showed the underlying effects of FeNPs in ECTs, such as vasculogenesis, angiogenesis, and magnetic-responsive stimulation, inducing cardiomyocyte actuation and crosstalk improvement between the cells, among other properties [121]-[124]. An iron nanoparticle-mediated tissue engineering platform was used to evaluate the repairing potential of Mesenchymal Stem Cells (MSCs) [125]. Moreover, it was demonstrated that FeNPs have induced the formation of electrophysiological cardiac biomarkers and a cardiac repair-favorable paracrine profile, which indicates the potential of conventional MSCs in repairing cardiac tissues [125].

5.2.3. Zinc Oxide Nanoparticles

The augmentation of hyperglycaemia and its complications by environmentally synthesised zinc oxide nanocrystals (ZnO-NPs) was evaluated. The ZnO-NPs were synthesised using environmentally benign, biodegradable hydroxyethyl cellulose (HEC) [126]. The particle size, morphological structure, purity, and crystallinity of ZnO NPs were analysed using transmission electron microscopy (TEM), X-ray diffraction (XRD), and scanning electron microscopy with energy-dispersive X-ray spectroscopy (SEM-EDS). HES is a natural, biodegradable, and biocompatible polymer which acts as a stabilising agent to prevent agglomeration of the ZnO NPs, as well as a structure-directing agent. Endothelial dysfunction is a well-known predictor of cardiovascular disease and atherosclerosis. The vascular complications of diabetes are the most serious manifestations of the disease. Hyperglycaemia can increase C-reactive protein (CRP) and cytokines such as interleukins (IL-1 and IL-6), contributing to cardiovascular disease development. Levels of interleukin-1 (IL-1α), C-reactive protein (CRP), and asymmetric dimethylarginine (ADMA) increase with endothelial dysfunction. An elevated CRP level induces the downregulation of nitric oxide (NO) production by inhibiting endothelial nitric oxide synthase (eNOS), thereby increasing the risk of cardiovascular complications [127]. Male albino rats that were diabetic and treated with ZnO-

NPs showed a significant increase in CRP, IL-1, and ADMA levels, alongside a reduction in NO levels. These results confirmed that the reported approach of environmentally synthesising and applying a new generation of nanoparticles to treat diabetic complications considerably enhances atherosclerosis selectively. The effects of Artemisia herba alba leaf extract (AHALE) and AHALE zinc oxide nanoparticles (AHALE-ZnONPs) were evaluated in male rats against isoproterenol (ISO)-induced myocardial infarction (MI) [128]. *Artemisia herba alba* is known as traditional medicine against many diseases [129]. The substance is characterized by a significant quantity of antioxidants, cineole, Artemisia ketone, phenolic compounds, flavonoids, and camphene [130]. These secondary metabolites are highly effective at preventing the generation of ROS [131]. Cosmetic creams that protect the skin from carcinogens are manufactured using formulations of Artemisia herba alba nanoparticles coated on ZnO nanoparticles [132]. AHALE-ZnO-NPs have been prepared by mixing 1 mM of aqueous extract solution with fresh AHALE and ZnO-NPs at a ratio of 9:1 (v:v). The mixture was placed in a shaker at 28˚C ± 3˚C with constant rotation for several hours. UV-visible spectrophotometry was used to demonstrate the biosynthesis of AHALE-ZnO-NPs. X-ray diffraction was measured using an X-ray diffraction meter. Hitachi electron microscopy (S-4160) was used to analyse the size and shape. Finally, the particle sizes were measured using a Malvern Zetasizer Nano ZS [128]. Following the treatment of adult Wistar rats with ISO, the results revealed an increase in the concentrations of the CK, CK-MB, AST, ALT, and LDH enzymes, which are indicative of the extent of myocardial infarction. Pretreating the rats with AHALE-ZnO-NPs for four weeks reduced the enzyme activity in the serum of the animals exposed to ISO later [128]. This shows the protective effect of AHALE-ZnO-NPs on the heart muscle that was exposed to the ISO.

5.2.4. Gold Nanoparticles

Metal nanoparticles have received a lot of attention. AuNPs have received particular attention. This is due to their unique and tuneable surface plasmon resonance (SPR) [133]. The green synthesis of AuNPs has recently attracted scientific attention. The reduction potential of plant extracts or phytochemicals enables the reduction of gold salts to AuNPs. Plants that are rich in polyphenols, flavonoids, amino acids, thiols, and hydroxyl compounds offer efficient reduction potentials. Gold is generally used in the form of gold (III) chloride trihydrate ($HAuCl_4 \cdot 3H_2O$). The synthesis of Au^0 involves the bio-reduction of AuCl4 ions using phytochemicals. The synthesis of AuNPs was shown by Ibrar *et al.* to be stabilized and reduced by partial purification of ethyl acetate/n-hexane (40:60 v/v) from the crude methanolic extract of Paeonia emodi by HPLC [134]. The lower concentration of Pe.EA 40 is not enough for proper reduction and stabilization of NPs. Therefore, 3 mg/mL of Pe.EA 40 and 0.5 mM of gold mixed in a 1:1 v/v ratio was the best condition for the synthesis of Pe.EA 40-AuNPs with a maximum intensity of the characteristic SPR peak. The cardioprotective effect of Pe.EA 40-AuNPs was also shown at a 40 mg/kg dose. Pe.EA 40-AuNPs reduced the levels of ALT, AST, CPK,

and LDH to 60.74 ± 2.79, 75.47 ± 1.67, 80.48 ± 2.64, and 247.57 ± 5.57 IU/L respectively [134]. This can be explained by Pe.EA 40-AuNPs increased solubility and permeability through its loading in NPs [135].

Gold nanoparticles synthesized from the root of *Euphorbia fischeriana* were confirmed using a UV-visible spectrophotometer, Fourier-transform infrared spectroscopy (FTIR), a high-resolution transmission electron microscope (HRTEM), and X-ray diffraction. The combination of *Euphorbia fischeriana* root extract and gold nanoparticles (EF-AuNPs) was evaluated in relation to heart weight in cases of myocardial infarction [136]. Isoprenaline-induced myocardial damage established the increase in TBARS and LOOH of heart tissues and a decline in antioxidant enzymes such as SOD, CAT, GPx, and GSH [137]. After isoprenaline administration, pre-treatment with EF-AuNPs (50 mg/kg b·w) illustrated stabilized levels of serum creatine and cardiotropins in myocardial infarcted animals [136]. This means that EF-AuNPs prevented cardiac injury by equalizing the free radicals formed by isoprenaline. The cardioprotective nature of proanthocyanidin (PAC)-synthesized gold nanoparticles was evaluated. Reduction of gold ions to AuNPs during exposure to proanthocyanidin extracted from grape seeds was detected by the color change from brownish yellow to ruby red and was examined by UV-vis spectroscopy [138]. This phenomenon is due to the excitation of the surface plasmon vibrations in the AuNPs. Myocardial injury was induced in Wistar strain male albino rats by injection of 85 mg/kg of isoproterenol daily for two consecutive days and then sacrificed [139]. PAC-synthesized AuNPs showed cardioprotective action in isoproterenol-induced myocardial injury at the lowest dosage (9 mg/kg) [138]. Yang Liu *et al.* showed that gold nanoparticles exert cardioprotective properties by suppressing isoproterenol-induced inflammation [140]. This was associated with PPAR-gamma expression upregulation and NF-kB phosphorylation inhibition in the myocardial infarction mice and suppressed the increased enzyme levels induced by isoproterenol treatment.

Aortic flow, cardiac output, and work, reflecting systolic heart function, were remarked in diabetic patients, indicating that diabetes affects heart function [141]. Treatment with gold nanoparticles-based *Calendula officinalis* extract (COAuNPs) significantly improves cardiac output and cardiac work, suggesting that CO-AuNPs may have beneficial effects on the heart in a diabetic state [142]. The phosphorylation of STAT3 was significantly elevated in the diabetes group, which was attenuated by COAuNPs treatment. It means that COAuNPs also had no effects on the proapoptotic Bax and antiapoptotic Bcl-XL proteins [142].

The integration of NPs with cardiac patches has a profound influence on the mechanical and adhesive properties, impacting tissue morphogenesis and guiding cell self-assembly [143]. AuNPs have been identified as potential contenders in tissue engineering and biosensing areas due to their biocompatibility, inertness towards cells, and ability to exhibit localized surface plasmon resonance (LSPR) within the visible spectrum [144]. The integration of AuNPs synthesized using *Avena sativa* L. extract showed a potential increase in the conductivity of the ma-

trix and improved the transmission of electrical signals among heart cells [145]. The chemical structure of ellagic acid, characterized by the presence of four hydroxyl groups and two lactone moieties, shows an exceptional propensity to trap free radicals through electron donation. This structure incorporates both lipophilic and hydrophilic domains and imposes constraints on its clinical applicability [146]. The synthesized ellagic acid-AuNPs (EA-AuNPs), with good biocompatibility and bioactivity, showed that they might alleviate myocardial injury by inhibiting ROS-induced oxylipin level alterations [147]. EA-AuNPs also inhibited the ISO-induced increase in cardiac enzyme activity. The treatment with EA-AuNPs enhanced the activities of CAT, GSH-PX, and SOD to normal levels [147]. These results indicated that EA-AuNP treatment could improve the antioxidant activity of cardiomyocytes to counteract oxidative damage. Tissue damage in MI generates high levels of ROS, leading to oxidative stress and cell apoptosis, with H_2O_2 as a major constituent [148]. The results of Annexin V/7-AAD flow assays indicated that EA-AuNPs treatment reduced the proportion of apoptotic cells (1.47% ± 0.69% early and 0.31% ± 0.20% late apoptotic cells), similar to the levels observed in the control group. ISO-induced hypertrophic cardiomyoblasts were shown to be correlated with ROS production. AuNPs synthesized using *Imperata cylindrica* extract showed that they attenuated cardiomyoblast hypertrophy by decreasing ROS [149]. This means that they may also influence possible therapeutic resources in the treatment of various cardiovascular disorders linked to oxidative stress. They can break down various types of ROS, in contrast to enzymes which can break specific radicals [149].

5.2.5. Copper Nanoparticles

The biological properties of copper nanoparticles (CuNPs) are well understood due to their high surface area compared to the bulk state. The most common routes for synthesizing CuNPs are wet chemical reduction, solvothermal reduction, electrochemical reduction, sonochemical reduction, microwave irradiation, thermal reduction, photochemical reduction, microemulsion reduction, electrode discharge reduction, gamma radiolysis, and biosynthesis [150]. Some of these methods involve the use of toxic reagents and solvents. Therefore, in recent years, researchers have focused on synthesizing CuNPs using green chemistry methods. To illustrate, in 2019, Maruthupantdy *et al.* synthesized CuO nanoparticles using Camellia japonica leaf extract. The synthesis of Cu_2O nanoparticles using *Prunus serotine* Ehrh. was carried out by Kumar *et al.* in 2020. var. capuli cherry extract. In 2020, the synthesis of Cu nanoparticles by Wang *et al.* used green coffee bean extract. Jayakodi *et al.* reported the production of copper oxide nanoparticles (CuO NPs) via green synthesis using Azadirachta indica (Ai) flower extract [151]. The synthesized Au-CuONPs were characterised using zeta potential, TGA, SEM, and TEM analyses. The most common method of synthesising copper oxide nanoparticles is to chemically reduce copper using organic and inorganic reducing agents [152]. Scientists synthesised nanoparticles using plant extracts. These

plant-based nanoparticles are prepared without toxic reagents and are much safer [153]. *Azadirachta indica* (neem) is a traditional plant that grows in tropical and subtropical climates and has many applications in medical science. The leaves, flowers, and fruits of the neem tree have chemotherapeutic properties [154]. After administration of DOX, which induced H9c2 cell damage by apoptosis and ROS, treatment with *Ai*-CuO nanoparticles, cured with different concentrations (5, 10, and 20 μg/mL) [151]. Hyperlipidemia is one of the major agents in the occurrence of atherosclerosis and cardiovascular diseases and is one of the most common causes of death from cardiovascular diseases [155]. It is characterized by a rise in the amount of apolipoprotein B, cholesterol, low-density particles (LDL), triglycerides, and free fatty acids and a reduction in the concentration of high-density particles (HDL) in plasma. Most of the medicines used to treat hyperlipidaemia are in different groups and each of them has its own mechanism, such as hydroxymethylglutaryl coenzyme A reductase inhibitors, nicotinic acid group, cholesterol absorption inhibitors, and fibrates, which are one of the winners of bile acids [155] [156]. The copper NPs green-mediated by *Ginkgo biloba* increased the level of +dP/dt, −dP/dt, SV, ESP, cardiac mitochondrial swelling, and cardiac mitochondrial membrane potential changes, and decreased the level of HR, cardiac mitochondrial ROS production, EDP, visceral fat, plasma glucose, plasma total cholesterol, body weight, cardiac MDA, plasma MDA, HOMA index, plasma insulin, and LF/HF ratio [157].

5.2.6. Mesoporous Silica Nanoparticles

Doxorubicin (DOX) is known as an efficacious drug against cancers such as solid tumours, leukaemia, soft tissue sarcoma, breast cancer, small cell carcinoma of the lung, and oesophageal carcinomas. However, its clinical usefulness is restricted due to its toxicities to cardiac tissues [158]. Studies have confirmed the effect of curcumin-loaded mesoporous silica nanoparticles (MSNs) against doxorubicin-induced myocardial toxicity in rats [159]. This latter is a traditional medicinal plant used in India. It possesses pharmacological properties such as antioxidant, hepatoprotective, anti-inflammatory, anti-thrombosis, and anti-apoptotic activities [79] [160]. Pre-treatment with MSNs (200 mg/kg) followed by DOX administration significantly protected the myocardium from the toxic effects of DOX by decreasing the level of malondialdehyde (MDA) and increasing the GSH, SOD, and CAT levels in cardiac tissue. MSNs are among the most efficient carriers used for the delivery of cardioprotective drugs and stem cell therapy due to their high drug-loading capacity and biocompatibility [161]. For instance, 5-azacytidine (5-aza) was successfully loaded into the pores of MSNs, and these nanocontainers were then coated with poly(allylamine hydrochloride) (PAH). These released drug molecules selectively induced the differentiation of ESCs (P19 cells) to cardiomyocytes. This result was confirmed by the resultant changes in the histone modifications on the regulatory regions of differentiation genes and cardiac marker genes [161]. Ascorbic acid loading by tetramethyl rhodamine (TRITC)-conju-

gated MSNs repaired the myocardium damage [162].

5.2.7. Magnesium Oxide Nanoparticles

Magnesium oxide nanoparticles (MgO NPs) have gained high attention in many industrial and commercial applications due to their unique physicochemical characteristics, including minimal toxicity, cationic capability, resistance to corrosion, dielectric behavior, optical clarity, superior stability, and redox potential [163]. Green MgO NPs synthesized using plant extracts showed the least biological toxicity with immense antioxidant, anti-inflammatory, antimicrobial, and anticancer properties. The MgO-NPs *Tamarindus indica* seeds showed cardioprotective effects by reducing the expression of the apoptotic genes p53 and Caspase-3 while restoring the levels of SOD gene expression [164]. These compounds, as powerful antioxidants, can protect the heart from DOX-induced cardiotoxicity. MgO-NPs based on aqueous *Tarenna asiatica* fruit extract inhibited adenosine di-phosphate (ADP)-induced platelet aggregation, but they did not show haemolytic, haemorrhagic, or edema-inducing properties [165]. These NPs possess potential in mitigating cardiac damage induced by DOX, both as pretreatment and cotreatment. Oral administration of Pulp MgO NPs decreased serum cTnL, CK-MB, and AST levels. The cardioprotective potential of Pulp MgO NPs was attributed to the normalization of cardiac biomarkers [165].

6. Future Prospects of Green Nanoparticles

Green-synthesized nanoparticles (GSNPs) are set to transform the treatment of cardiovascular disease (CVD) through a variety of innovative applications. A significant development is the creation of stimuli-responsive GSNPs that release drugs in response to specific conditions, such as pH changes, oxidative stress, or enzyme activity, at diseased cardiovascular sites. This targeted delivery approach significantly enhances therapeutic precision while minimizing systemic toxicity. Another promising innovation is the design of bioactive GSNPs that act as drug carriers and exert intrinsic therapeutic effects due to the medicinal properties of natural extracts, such as those derived from African medicinal plants, used in their synthesis. These nanoparticles may help to combat inflammation, oxidative stress, and endothelial dysfunction, all of which play a central role in the progression of CVD. In the field of cardiac regeneration, GSNPs are being investigated for use in injectable nano scaffolds or engineered cardiac patches to support tissue repair and neovascularization following myocardial infarction. Combining GSNPs with biomaterials such as hydrogels or biopolymers can enhance their retention, stability, and biological activity within damaged tissues. Looking to the future, integrating GSNPs with wearable devices for real-time cardiovascular monitoring and controlled, on-demand drug release could be transformative. The convergence of nanotechnology and smart health systems could transform chronic disease management. Furthermore, eco-friendly innovations, such as biowaste-derived synthesis methods and scalable, low-cost production techniques, will be essential in

enhancing the accessibility and sustainability of GSNPs, thereby facilitating their transition from laboratory to clinical application.

The development of multifunctional nanoparticles, where imaging and therapy are combined into a single nano-vehicle, allows simultaneous diagnosis, real-time tracking during therapy, and targeted treatment. Challenges and opportunities at the intersection of nanomedicine innovation and regulatory evolution are a significant concern. It is important to support researchers and stakeholders in navigating the regulatory landscape, facilitating the successful commercialization and clinical translation of nanoparticle-based therapeutics.

7. Conclusion

The synergistic combination of bioactive phytochemicals and microorganisms with nanotechnology, enclosed in nanoparticles, has demonstrated significant progress in the improvement of anti-cardiovascular disease treatments. These findings suggest that green nanoparticles derived from natural sources could be employed for cardioprotection, warranting further investigation for potential clinical applications. Green synthesis uses biological agents such as plant extracts, bacteria, or fungi, reducing or eliminating the need for harmful chemicals and organic solvents. The materials and agents used in green synthesis are often biodegradable, minimizing environmental impact and reducing waste. Green nanoparticles exhibit anti-atherosclerotic activity by reducing foam cell formation in THP-1 monocyte-derived macrophages, protecting against coronary artery occlusion-induced myocardial ischemia-reperfusion injury in rats, and exhibiting anti-inflammatory effects through the downregulation of pro-inflammatory mediators such as COX-1 and COX-2. Furthermore, eNOS activity/expression protects the effect of resveratrol against vascular damage in cardiovascular diseases. This review demonstrates the need for interdisciplinary research to ensure the safe and effective clinical translation of these findings. The ease of synthesis and increasing biological stability of green nanoparticles make them useful for the prevention or treatment of cardiovascular diseases (CVDs). Treatment or diagnosis of cardiovascular pathologies is indirect, involving genes expressed during dysfunction. Therefore, green nanoparticles play an important role in reshaping the future of cardiovascular therapy. To extend to, the development of industrial methods for the production of nanocarriers with controlled and repeatable physicochemical properties while maintaining economic profitability remains a key challenge. Fulfilling these conditions is necessary for introducing nanotechnology as a standard method in modern cardiovascular medicine.

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Conflicts of Interest

The authors report that there are no competing interests to declare.

References

[1] Baudin, B., Cohen, A., Berthelot-Garcias, E., Meuleman, C., Dufaitre, G., Ederhy, S., *et al.* (2009) Données épidémiologiques des maladies cardiovasculaires et prise en charge des accidents cardiovasculaires. *Revue Francophone des Laboratoires*, **2009**, 27-39. https://doi.org/10.1016/s1773-035x(09)70198-4

[2] World Health Organization (2014) World Health Organization in Global Status Report on Noncommunicable Diseases 2014. World Health Organization. https://www.who.int/publications/i/item/9789241564854

[3] Gundogdu, E., Senyigit, Z. and Ilem-Ozdemir, D. (2014) Nanomedicine for the Diagnosis and Treatment of Cardiovascular Disease: Current Status and Future Perspective. *Cardiovascular Disease*, Concept Press Ltd., 187-201.

[4] Fan, C., Zhang, E., Joshi, J., Yang, J., Zhang, J. and Zhu, W. (2020) Utilization of Human Induced Pluripotent Stem Cells for Cardiac Repair. *Frontiers in Cell and Developmental Biology*, **8**, Article 36. https://doi.org/10.3389/fcell.2020.00036

[5] Smith, B.R. and Gambhir, S.S. (2017) Nanomaterials for *in Vivo* Imaging. *Chemical Reviews*, **117**, 901-986. https://doi.org/10.1021/acs.chemrev.6b00073

[6] Felici, A., Di Mascolo, D., Ferreira, M., Lauciello, S., Bono, L., Armirotti, A., *et al.* (2021) Vascular-Confined Multi-Passage Discoidal Nanoconstructs for the Low-Dose Docetaxel Inhibition of Triple-Negative Breast Cancer Growth. *Nano Research*, **15**, 482-491. https://doi.org/10.1007/s12274-021-3507-8

[7] Patra, J.K., Das, G., Fraceto, L.F., Campos, E.V.R., Rodriguez-Torres, M.D.P., Acosta-Torres, L.S., *et al.* (2018) Nano Based Drug Delivery Systems: Recent Developments and Future Prospects. *Journal of Nanobiotechnology*, **16**, Article No. 71. https://doi.org/10.1186/s12951-018-0392-8

[8] Chavali, M.S. and Nikolova, M.P. (2019) Metal Oxide Nanoparticles and Their Applications in Nanotechnology. *SN Applied Sciences*, **1**, Article No. 607. https://doi.org/10.1007/s42452-019-0592-3

[9] Nagar, A., Kumar, A., Parveen, S., Kumar, A., Dhasmana, H., Husain, S., *et al.* (2020) Zinc Oxide Nanoflowers Synthesized by Sol-Gel Technique for Field Emission Displays (FEDs). *Materials Today*: *Proceedings*, **32**, 402-406. https://doi.org/10.1016/j.matpr.2020.02.087

[10] Tiede, K., Boxall, A.B.A., Tiede, D., Tear, S.P., David, H. and Lewis, J. (2009) A Robust Size-Characterisation Methodology for Studying Nanoparticle Behaviour in 'Real' Environmental Samples, Using Hydrodynamic Chromatography Coupled to ICP-MS. *Journal of Analytical Atomic Spectrometry*, **24**, 964-972. https://doi.org/10.1039/b822409a

[11] Devi, H.S., Boda, M.A., Shah, M.A., Parveen, S. and Wani, A.H. (2018) Green Synthesis of Iron Oxide Nanoparticles Using *Platanus orientalis* Leaf Extract for Antifungal Activity. *Green Processing and Synthesis*, **8**, 38-45. https://doi.org/10.1515/gps-2017-0145

[12] Sone, B.T., Diallo, A., Fuku, X.G., Gurib-Fakim, A. and Maaza, M. (2020) Biosynthesized CuO Nano-Platelets: Physical Properties & Enhanced Thermal Conductivity Nanofluidics. *Arabian Journal of Chemistry*, **13**, 160-170. https://doi.org/10.1016/j.arabjc.2017.03.004

[13] Ehrampoush, M.H., Miria, M., Salmani, M.H. and Mahvi, A.H. (2015) Cadmium Re-

moval from Aqueous Solution by Green Synthesis Iron Oxide Nanoparticles with Tangerine Peel Extract. *Journal of Environmental Health Science and Engineering*, **13**, Article No. 84. https://doi.org/10.1186/s40201-015-0237-4

[14] Kumar, B., Smita, K., Cumbal, L., Debut, A. and Angulo, Y. (2017) Biofabrication of Copper Oxide Nanoparticles Using Andean Blackberry (*Rubus glaucus* Benth.) Fruit and Leaf. *Journal of Saudi Chemical Society*, **21**, S475-S480. https://doi.org/10.1016/j.jscs.2015.01.009

[15] Dhand, V., Soumya, L., Bharadwaj, S., Chakra, S., Bhatt, D. and Sreedhar, B. (2016) Green Synthesis of Silver Nanoparticles Using Coffea Arabica Seed Extract and Its Antibacterial Activity. *Materials Science and Engineering*: *C*, **58**, 36-43. https://doi.org/10.1016/j.msec.2015.08.018

[16] Pillai, A.M., Sivasankarapillai, V.S., Rahdar, A., Joseph, J., Sadeghfar, F., Anuf A, R., *et al.* (2020) Green Synthesis and Characterization of Zinc Oxide Nanoparticles with Antibacterial and Antifungal Activity. *Journal of Molecular Structure*, **1211**, Article ID: 128107. https://doi.org/10.1016/j.molstruc.2020.128107

[17] Abdullah, F.H., Abu Bakar, N.H.H. and Abu Bakar, M. (2020) Low Temperature Biosynthesis of Crystalline Zinc Oxide Nanoparticles from Musa Acuminata Peel Extract for Visible-Light Degradation of Methylene Blue. *Optik*, **206**, Article ID: 164279. https://doi.org/10.1016/j.ijleo.2020.164279

[18] Nadeem, M., Khan, R., Afridi, K., Nadhman, A., Ullah, S., Faisal, S., *et al.* (2020) Green Synthesis of Cerium Oxide Nanoparticles (CeO_2 NPs) and Their Antimicrobial Applications: A Review. *International Journal of Nanomedicine*, **15**, 5951-5961. https://doi.org/10.2147/ijn.s255784

[19] Nune, S.K., Chanda, N., Shukla, R., Katti, K., Kulkarni, R.R., Thilakavathy, S., *et al.* (2009) Green Nanotechnology from Tea: Phytochemicals in Tea as Building Blocks for Production of Biocompatible Gold Nanoparticles. *Journal of Materials Chemistry*, **19**, 2912-2920. https://doi.org/10.1039/b822015h

[20] Kumari, P. and Meena, A. (2020) Green Synthesis of Gold Nanoparticles from *Lawsoniainermis* and Its Catalytic Activities Following the Langmuir-Hinshelwood Mechanism. *Colloids and Surfaces A*: *Physicochemical and Engineering Aspects*, **606**, Article ID: 125447. https://doi.org/10.1016/j.colsurfa.2020.125447

[21] Teixeira, L.M., Reis, C.P. and Pacheco, R. (2024) Potential of Application of Natural Product Nanoparticles in Hypercholesterolemia. *Chemistry Proceedings*, 16, Article 84. https://doi.org/10.3390/ecsoc-28-20168

[22] Xu, B., Watkins, R., Wu, L., Zhang, C. and Davis, R. (2015) Natural Product-Based Nanomedicine: Recent Advances and Issues. *International Journal of Nanomedicine*, **10**, 6055-6074. https://doi.org/10.2147/ijn.s92162

[23] Bodeker, G., Bhat, K.K.S., Burley, J. and Vantomme, P. (1997) Medicinal Plants for Forest Conservation and Health Care. FAO, 100-108.

[24] Chen, S., Li, Q., McClements, D.J., Han, Y., Dai, L., Mao, L., *et al.* (2020) Co-Delivery of Curcumin and Piperine in Zein-Carrageenan Core-Shell Nanoparticles: Formation, Structure, Stability and *in Vitro* Gastrointestinal Digestion. *Food Hydrocolloids*, **99**, Article ID: 105334. https://doi.org/10.1016/j.foodhyd.2019.105334

[25] Fazal, H., Abbasi, B.H., Ahmad, N. and Ali, M. (2016) Elicitation of Medicinally Important Antioxidant Secondary Metabolites with Silver and Gold Nanoparticles in Callus Cultures of *Prunella vulgaris* L. *Applied Biochemistry and Biotechnology*, **180**, 1076-1092. https://doi.org/10.1007/s12010-016-2153-1

[26] Parveen, K., Banse, V. and Ledwani, L. (2016) Green Synthesis of Nanoparticles: Their Advantages and Disadvantages. *AIP Conference Proceedings*, **1724**, Article ID:

020048. https://doi.org/10.1063/1.4945168

[27] Rad, S.S., Sani, A.M. and Mohseni, S. (2019) Biosynthesis, Characterization and Antimicrobial Activities of Zinc Oxide Nanoparticles from Leaf Extract of *Mentha pulegium* (L.). *Microbial Pathogenesis*, **131**, 239-245. https://doi.org/10.1016/j.micpath.2019.04.022

[28] Kasthuri, K., Kishor Kumar, J., Rajkumar, P., Amala Jeya Ranchani, A. and Jayaprakash, K. (2024) Bio-Inspired Synthesis of ZnO Nanoparticles Using Taraxacum Officinale for Antibacterial, Antifungal, and Anticancer Applications. *Inorganic Chemistry Communications*, **170**, Article ID: 113409. https://doi.org/10.1016/j.inoche.2024.113409

[29] Bouafia, A. and Laouini, S.E. (2020) Green Synthesis of Iron Oxide Nanoparticles by Aqueous Leaves Extract of *Mentha pulegium* L.: Effect of Ferric Chloride Concentration on the Type of Product. *Materials Letters*, **265**, Article ID: 127364. https://doi.org/10.1016/j.matlet.2020.127364

[30] Jha, A.K. and Prasad, K. (2010) Green Synthesis of Silver Nanoparticles Using *Cycas* Leaf. *International Journal of Green Nanotechnology: Physics and Chemistry*, **1**, P110-P117. https://doi.org/10.1080/19430871003684572

[31] Medina-Ramirez, I., Bashir, S., Luo, Z. and Liu, J.L. (2009) Green Synthesis and Characterization of Polymer-Stabilized Silver Nanoparticles. *Colloids and Surfaces B: Biointerfaces*, **73**, 185-191. https://doi.org/10.1016/j.colsurfb.2009.05.015

[32] Jafarirad, S., Mehrabi, M., Divband, B. and Kosari-Nasab, M. (2016) Biofabrication of Zinc Oxide Nanoparticles Using Fruit Extract of *Rosa canina* and Their Toxic Potential against Bacteria: A Mechanistic Approach. *Materials Science and Engineering: C*, **59**, 296-302. https://doi.org/10.1016/j.msec.2015.09.089

[33] Yuvakkumar, R., Suresh, J., Nathanael, A.J., Sundrarajan, M. and Hong, S.I. (2014) Novel Green Synthetic Strategy to Prepare ZnO Nanocrystals Using Rambutan (*Nephelium lappaceum* L.) Peel Extract and Its Antibacterial Applications. *Materials Science and Engineering: C*, **41**, 17-27. https://doi.org/10.1016/j.msec.2014.04.025

[34] Çolak, H. and Karaköse, E. (2017) Green Synthesis and Characterization of Nanostructured ZnO Thin Films Using Citrus Aurantifolia (Lemon) Peel Extract by Spin-Coating Method. *Journal of Alloys and Compounds*, **690**, 658-662. https://doi.org/10.1016/j.jallcom.2016.08.090

[35] Melkamu, W.W. and Bitew, L.T. (2021) Green Synthesis of Silver Nanoparticles Using *Hagenia abyssinica* (*Bruce*) J.F. Gmel Plant Leaf Extract and Their Antibacterial and Anti-Oxidant Activities. *Heliyon*, **7**, e08459. https://doi.org/10.1016/j.heliyon.2021.e08459

[36] Shafey, A.M.E. (2020) Green Synthesis of Metal and Metal Oxide Nanoparticles from Plant Leaf Extracts and Their Applications: A Review. *Green Processing and Synthesis*, **9**, 304-339. https://doi.org/10.1515/gps-2020-0031

[37] Jayarambabu, N., Akshaykranth, A., Venkatappa Rao, T., Venkateswara Rao, K. and Rakesh Kumar, R. (2020) Green Synthesis of Cu Nanoparticles Using Curcuma Longa Extract and Their Application in Antimicrobial Activity. *Materials Letters*, **259**, Article ID: 126813. https://doi.org/10.1016/j.matlet.2019.126813

[38] Schreiber, M., Vivekanandhan, S., Kumar Mohanty, A. and Misra, M. (2012) A Study on the Electrospinning Behaviour and Nanofibre Morphology of Anionically Charged Lignin. *Advanced Materials Letters*, **3**, 476-480. https://doi.org/10.5185/amlett.2012.icnano.336

[39] Soto-Robles, C.A., Luque, P.A., Gómez-Gutiérrez, C.M., Nava, O., Vilchis-Nestor, A.R., Lugo-Medina, E., *et al.* (2019) Study on the Effect of the Concentration of *Hi-*

biscus sabdariffa Extract on the Green Synthesis of ZnO Nanoparticles. *Results in Physics*, **15**, Article ID: 102807. https://doi.org/10.1016/j.rinp.2019.102807

[40] Dousari, A.S., Hosseininasab, S.S., Akbarizadeh, M.R., Naderifar, M. and Satarzadeh, N. (2023) *Mentha pulegium* as a Source of Green Synthesis of Nanoparticles with Antibacterial, Antifungal, Anticancer, and Antioxidant Applications. *Scientia Horticulturae*, **320**, Article ID: 112215. https://doi.org/10.1016/j.scienta.2023.112215

[41] Jafarizad, A., Safaee, K., Gharibian, S., Omidi, Y. and Ekinci, D. (2015) Biosynthesis and *In-Vitro* Study of Gold Nanoparticles Using Mentha and Pelargonium Extracts. *Procedia Materials Science*, **11**, 224-230. https://doi.org/10.1016/j.mspro.2015.11.113

[42] Saka, A., Jule, L.T., Soressa, S., Gudata, L., Nagaprasad, N., Seenivasan, V., *et al.* (2022) Biological Approach Synthesis and Characterization of Iron Sulfide (FeS) Thin Films from Banana Peel Extract for Contamination of Environmental Remediation. *Scientific Reports*, **12**, Article No. 10486. https://doi.org/10.1038/s41598-022-14828-0

[43] Negi, A., Gangwar, R., Kumar Vishwakarma, R. and Singh Negi, D. (2022) Antibacterial, Antioxidant and Photodegradation Potential of ZnO Nanoparticles Mediated via Roots of Taraxacum Officinale Radix. *Materials Today*: *Proceedings*, **57**, 2435-2443. https://doi.org/10.1016/j.matpr.2022.02.019

[44] Hai, N.D., Dat, N.M., Huong, L.M., Tai, L.T., Thinh, D.B., Nam, N.T.H., *et al.* (2022) Phytosynthesis of Silver Nanoparticles Using Mangifera Indica Leaves Extract at Room Temperature: Formation Mechanism, Catalytic Reduction, Colorimetric Sensing, and Antimicrobial Activity. *Colloids and Surfaces B*: *Biointerfaces*, **220**, Article ID: 112974. https://doi.org/10.1016/j.colsurfb.2022.112974

[45] Li, Z., Wang, L., Chen, S., Feng, C., Chen, S., Yin, N., *et al.* (2014) Facilely Green Synthesis of Silver Nanoparticles into Bacterial Cellulose. *Cellulose*, **22**, 373-383. https://doi.org/10.1007/s10570-014-0487-9

[46] Ganesh Kumar, C., Poornachandra, Y. and Mamidyala, S.K. (2014) Green Synthesis of Bacterial Gold Nanoparticles Conjugated to Resveratrol as Delivery Vehicles. *Colloids and Surfaces B*: *Biointerfaces*, **123**, 311-317. https://doi.org/10.1016/j.colsurfb.2014.09.032

[47] Syame, S.M., Mansour, A.S., Khalaf, D.D., Ibrahim, E.S. and Gaber, E.S. (2020) Green Synthesis of Silver Nanoparticles Using Lactic Acid Bacteria: Assessment of Antimicrobial Activity. *World's Veterinary Journal*, **10**, 625-633. https://doi.org/10.54203/scil.2020.wvj75

[48] Khan, F., Shahid, A., Zhu, H., Wang, N., Javed, M.R., Ahmad, N., *et al.* (2022) Prospects of Algae-Based Green Synthesis of Nanoparticles for Environmental Applications. *Chemosphere*, **293**, Article ID: 133571. https://doi.org/10.1016/j.chemosphere.2022.133571

[49] Alprol, A.E., Mansour, A.T., El-Beltagi, H.S. and Ashour, M. (2023) Algal Extracts for Green Synthesis of Zinc Oxide Nanoparticles: Promising Approach for Algae Bioremediation. *Materials*, **16**, Article 2819. https://doi.org/10.3390/ma16072819

[50] Arun, G., Eyini, M. and Gunasekaran, P. (2014) Green Synthesis of Silver Nanoparticles Using the Mushroom Fungus *Schizophyllum commune* and Its Biomedical Applications. *Biotechnology and Bioprocess Engineering*, **19**, 1083-1090. https://doi.org/10.1007/s12257-014-0071-z

[51] Molnár, Z., Bódai, V., Szakacs, G., Erdélyi, B., Fogarassy, Z., Sáfrán, G., *et al.* (2018) Green Synthesis of Gold Nanoparticles by Thermophilic Filamentous Fungi. *Scientific Reports*, **8**, Article No. 3943. https://doi.org/10.1038/s41598-018-22112-3

[52] Clarance, P., Luvankar, B., Sales, J., Khusro, A., Agastian, P., Tack, J., *et al.* (2020)

Green Synthesis and Characterization of Gold Nanoparticles Using Endophytic Fungi *Fusarium solani* and Its *In-Vitro* Anticancer and Biomedical Applications. *Saudi Journal of Biological Sciences*, **27**, 706-712. https://doi.org/10.1016/j.sjbs.2019.12.026

[53] Gade, A., Gaikwad, S., Duran, N. and Rai, M. (2014) Green Synthesis of Silver Nanoparticles by *Phoma glomerata*. *Micron*, **59**, 52-59. https://doi.org/10.1016/j.micron.2013.12.005

[54] Li, G., He, D., Qian, Y., Guan, B., Gao, S., Cui, Y., *et al.* (2011) Fungus-mediated Green Synthesis of Silver Nanoparticles Using *Aspergillus terreus*. *International Journal of Molecular Sciences*, **13**, 466-476. https://doi.org/10.3390/ijms13010466

[55] Alhazzazi, T.Y., Alzebiani, N.A., Alotaibi, S.K., Bogari, D.F., Bakalka, G.T., Hazzazi, L.W., *et al.* (2016) Awareness and Attitude toward Using Dental Magnification among Dental Students and Residents at King Abdulaziz University, Faculty of Dentistry. *BMC Oral Health*, **17**, Article No. 21. https://doi.org/10.1186/s12903-016-0254-4

[56] Wang, D., Xue, B., Wang, L., Zhang, Y., Liu, L. and Zhou, Y. (2021) Fungus-Mediated Green Synthesis of Nano-Silver Using *Aspergillus sydowii* and Its Antifungal/Antiproliferative Activities. *Scientific Reports*, **11**, Article No. 10356. https://doi.org/10.1038/s41598-021-89854-5

[57] Guyton, J.R. and Klemp, K.F. (1996) Development of the Lipid-Rich Core in Human Atherosclerosis. *Arteriosclerosis, Thrombosis, and Vascular Biology*, **16**, 4-11. https://doi.org/10.1161/01.atv.16.1.4

[58] Zhang, J., Nie, S. and Wang, S. (2013) Nanoencapsulation Enhances Epigallocatechin-3-Gallate Stability and Its Antiatherogenic Bioactivities in Macrophages. *Journal of Agricultural and Food Chemistry*, **61**, 9200-9209. https://doi.org/10.1021/jf4023004

[59] Pillai, S.C., Borah, A., Le, M.N.T., Kawano, H., Hasegawa, K. and Kumar, D.S. (2021) Co-delivery of Curcumin and Bioperine via PLGA Nanoparticles to Prevent Atherosclerotic Foam Cell Formation. *Pharmaceutics*, **13**, Article 1420. https://doi.org/10.3390/pharmaceutics13091420

[60] Meng, N., Gong, Y., Zhang, J., Mu, X., Song, Z., Feng, R., *et al.* (2018) A Novel Curcumin-Loaded Nanoparticle Restricts Atherosclerosis Development and Promotes Plaques Stability in Apolipoprotein E Deficient Mice. *Journal of Biomaterials Applications*, **33**, 946-954. https://doi.org/10.1177/0885328218815328

[61] Randhawa, G., Kullar, J. and Rajkumar, (2011) Bioenhancers from Mother Nature and Their Applicability in Modern Medicine. *International Journal of Applied and Basic Medical Research*, **1**, 5-10. https://doi.org/10.4103/2229-516x.81972

[62] Carlson, L.J., Cote, B., Alani, A.W.G. and Rao, D.A. (2014) Polymeric Micellar Co-Delivery of Resveratrol and Curcumin to Mitigate *in Vitro* Doxorubicin-Induced Cardiotoxicity. *Journal of Pharmaceutical Sciences*, **103**, 2315-2322. https://doi.org/10.1002/jps.24042

[63] Li, J., Zhou, Y., Zhang, W., Bao, C. and Xie, Z. (2017) Relief of Oxidative Stress and Cardiomyocyte Apoptosis by Using Curcumin Nanoparticles. *Colloids and Surfaces B: Biointerfaces*, **153**, 174-182. https://doi.org/10.1016/j.colsurfb.2017.02.023

[64] Zhang, J., Wang, Y., Bao, C., Liu, T., Li, S., Huang, J., *et al.* (2019) Curcumin-Loaded PEG-PDLLA Nanoparticles for Attenuating Palmitate-Induced Oxidative Stress and Cardiomyocyte Apoptosis through AMPK Pathway. *International Journal of Molecular Medicine*, **44**, 672-682. https://doi.org/10.3892/ijmm.2019.4228

[65] Nabofa, W.E.E., Alashe, O.O., Oyeyemi, O.T., Attah, A.F., Oyagbemi, A.A.,

Omobowale, T.O., *et al.* (2018) Cardioprotective Effects of Curcumin-Nisin Based Poly Lactic Acid Nanoparticle on Myocardial Infarction in Guinea Pigs. *Scientific Reports*, **8**, Article No. 16649. https://doi.org/10.1038/s41598-018-35145-5

[66] Ray, A., Rana, S., Banerjee, D., Mitra, A., Datta, R., Naskar, S., *et al.* (2016) Improved Bioavailability of Targeted Curcumin Delivery Efficiently Regressed Cardiac Hypertrophy by Modulating Apoptotic Load within Cardiac Microenvironment. *Toxicology and Applied Pharmacology*, **290**, 54-65. https://doi.org/10.1016/j.taap.2015.11.011

[67] R. Neves, A., Lucio, M., L.C. Lima, J. and Reis, S. (2012) Resveratrol in Medicinal Chemistry: A Critical Review of Its Pharmacokinetics, Drug-Delivery, and Membrane Interactions. *Current Medicinal Chemistry*, **19**, 1663-1681. https://doi.org/10.2174/092986712799945085

[68] de la Lastra, C.A. and Villegas, I. (2007) Resveratrol as an Antioxidant and Pro-Oxidant Agent: Mechanisms and Clinical Implications. *Biochemical Society Transactions*, **35**, 1156-1160. https://doi.org/10.1042/bst0351156

[69] Liao, P., Ng, L., Lin, L., Richardson, C.D., Wang, G. and Lin, C. (2010) Resveratrol Arrests Cell Cycle and Induces Apoptosis in Human Hepatocellular Carcinoma Huh-7 Cells. *Journal of Medicinal Food*, **13**, 1415-1423. https://doi.org/10.1089/jmf.2010.1126

[70] Frémont, L. (2000) Biological Effects of Resveratrol. *Life Sciences*, **66**, 663-673. https://doi.org/10.1016/s0024-3205(99)00410-5

[71] Cheng, Y., Liu, D., Zhang, C., Cui, H., Liu, M., Zhang, B., *et al.* (2019) Mitochondria-targeted Antioxidant Delivery for Precise Treatment of Myocardial Ischemia-Reperfusion Injury through a Multistage Continuous Targeted Strategy. *Nanomedicine: Nanotechnology, Biology and Medicine*, **16**, 236-249. https://doi.org/10.1016/j.nano.2018.12.014

[72] Hardy, N., Viola, H.M., Johnstone, V.P.A., Clemons, T.D., Cserne Szappanos, H., Singh, R., *et al.* (2014) Nanoparticle-Mediated Dual Delivery of an Antioxidant and a Peptide against the L-Type Ca^{2+} Channel Enables Simultaneous Reduction of Cardiac Ischemia-Reperfusion Injury. *ACS Nano*, **9**, 279-289. https://doi.org/10.1021/nn5061404

[73] Patel, R.V., Mistry, B.M., Shinde, S.K., Syed, R., Singh, V. and Shin, H. (2018) Therapeutic Potential of Quercetin as a Cardiovascular Agent. *European Journal of Medicinal Chemistry*, **155**, 889-904. https://doi.org/10.1016/j.ejmech.2018.06.053

[74] Porcu, E.P., Cossu, M., Rassu, G., Giunchedi, P., Cerri, G., Pourová, J., *et al.* (2018) Aqueous Injection of Quercetin: An Approach for Confirmation of Its Direct *in Vivo* Cardiovascular Effects. *International Journal of Pharmaceutics*, **541**, 224-233. https://doi.org/10.1016/j.ijpharm.2018.02.036

[75] Kleemann, R., Verschuren, L., Morrison, M., Zadelaar, S., van Erk, M.J., Wielinga, P.Y., *et al.* (2011) Anti-Inflammatory, Anti-Proliferative and Anti-Atherosclerotic Effects of Quercetin in Human *in Vitro* and *in Vivo* Models. *Atherosclerosis*, **218**, 44-52. https://doi.org/10.1016/j.atherosclerosis.2011.04.023

[76] Zahedi, M., Ghiasvand, R., Feizi, A., Asgari, G. and Darvish, L. (2013) Does Quercetin Improve Cardiovascular Risk Factors and Inflammatory Biomarkers in Women with Type 2 Diabetes: A Double-Blind Randomized Controlled Clinical Trial. *International Journal of Preventive Medicine*, **4**, 777-785.

[77] Salehi, B., Machin, L., Monzote, L., Sharifi-Rad, J., Ezzat, S.M., Salem, M.A., *et al.* (2020) Therapeutic Potential of Quercetin: New Insights and Perspectives for Human Health. *ACS Omega*, **5**, 11849-11872. https://doi.org/10.1021/acsomega.0c01818

[78] Giannouli, M., Karagkiozaki, V., Pappa, F., Moutsios, I., Gravalidis, C. and Logothetidis, S. (2018) Fabrication of Quercetin-Loaded PLGA Nanoparticles via Electrohydrodynamic Atomization for Cardiovascular Disease. *Materials Today*: *Proceedings*, **5**, 15998-16005. https://doi.org/10.1016/j.matpr.2018.05.044

[79] Li, H., Sureda, A., Devkota, H.P., Pittalà, V., Barreca, D., Silva, A.S., *et al.* (2020) Curcumin, the Golden Spice in Treating Cardiovascular Diseases. *Biotechnology Advances*, **38**, Article ID: 107343. https://doi.org/10.1016/j.biotechadv.2019.01.010

[80] Duan, Y., Gong, K., Xu, S., Zhang, F., Meng, X. and Han, J. (2022) Regulation of Cholesterol Homeostasis in Health and Diseases: From Mechanisms to Targeted Therapeutics. *Signal Transduction and Targeted Therapy*, **7**, Article No. 265. https://doi.org/10.1038/s41392-022-01125-5

[81] Mulder, W.J.M., Strijkers, G.J., van Tilborg, G.A.F., Griffioen, A.W. and Nicolay, K. (2006) MR in Biomedicine: An International Journal Devoted to the Development and Application of Magnetic Resonance *In Vivo* 2006, **19**, 142-164.

[82] Shade, C.W. (2016) Liposomes as Advanced Delivery Systems for Nutraceuticals. *Integrative Medicine* (*Encinitas*, *Calif.*), **15**, 33-36.

[83] Wang, S., Chen, Y., Guo, J. and Huang, Q. (2023) Liposomes for Tumor Targeted Therapy: A Review. *International Journal of Molecular Sciences*, **24**, Article 2643. https://doi.org/10.3390/ijms24032643

[84] Mitragotri, S. and Stayton, P. (2014) Organic Nanoparticles for Drug Delivery and Imaging. *MRS Bulletin*, **39**, 219-223. https://doi.org/10.1557/mrs.2014.11

[85] Barenholz, Y. (2012) Doxil®—The First FDA-Approved Nano-Drug: Lessons Learned. *Journal of Controlled Release*, **160**, 117-134. https://doi.org/10.1016/j.jconrel.2012.03.020

[86] Turnbull, I.C., Eltoukhy, A.A., Fish, K.M., Hajjar, R.J., Anderson, D.G. and Costa, K.D. (2013) Abstract 18088: Myocardial Delivery of Lipidoid Nanoparticle mRNA Designed for Tailored Expression of Cardiogenic Factors. *Circulation*, **128**, 128. https://doi.org/10.1161/circ.128.suppl_22.a18088

[87] Conway, A., Mendel, M., Kim, K., McGovern, K., Boyko, A., Zhang, L., *et al.* (2019) Non-Viral Delivery of Zinc Finger Nuclease mRNA Enables Highly Efficient *in Vivo* Genome Editing of Multiple Therapeutic Gene Targets. *Molecular Therapy*, **27**, 866-877. https://doi.org/10.1016/j.ymthe.2019.03.003

[88] Joo, S., Song, Y., Park, Y., Myung, E., Chung, C., Park, K., *et al.* (2012) Epigallocatechin-3-Gallate Inhibits LPS-Induced NF-κB and MAPK Signaling Pathways in Bone Marrow-Derived Macrophages. *Gut and Liver*, **6**, 188-196. https://doi.org/10.5009/gnl.2012.6.2.188

[89] He, Y., Hara, H. and Núñez, G. (2016) Mechanism and Regulation of NLRP3 Inflammasome Activation. *Trends in Biochemical Sciences*, **41**, 1012-1021. https://doi.org/10.1016/j.tibs.2016.09.002

[90] Duewell, P., Kono, H., Rayner, K.J., Sirois, C.M., Vladimer, G., Bauernfeind, F.G., *et al.* (2010) NLRP3 Inflammasomes Are Required for Atherogenesis and Activated by Cholesterol Crystals. *Nature*, **464**, 1357-1361. https://doi.org/10.1038/nature08938

[91] Zhang, M., Viennois, E., Prasad, M., Zhang, Y., Wang, L., Zhang, Z., *et al.* (2016) Edible Ginger-Derived Nanoparticles: A Novel Therapeutic Approach for the Prevention and Treatment of Inflammatory Bowel Disease and Colitis-Associated Cancer. *Biomaterials*, **101**, 321-340. https://doi.org/10.1016/j.biomaterials.2016.06.018

[92] Liu, B., Lu, Y., Chen, X., Muthuraj, P.G., Li, X., Pattabiraman, M., *et al.* (2020) Protective Role of Shiitake Mushroom-Derived Exosome-Like Nanoparticles in D-Ga-

lactosamine and Lipopolysaccharide-Induced Acute Liver Injury in Mice. *Nutrients*, **12**, Article 477. https://doi.org/10.3390/nu12020477

[93] Liu, B., Li, X., Yu, H., Shi, X., Zhou, Y., Alvarez, S., *et al.* (2021) Therapeutic Potential of Garlic Chive-Derived Vesicle-Like Nanoparticles in NLRP3 Inflammasome-Mediated Inflammatory Diseases. *Theranostics*, **11**, 9311-9330. https://doi.org/10.7150/thno.60265

[94] Levchenko, T.S., Hartner, W.C. and Torchilin, V.P. (2012) Liposomes in Diagnosis and Treatment of Cardiovascular Disorders. *Methodist DeBakey Cardiovascular Journal*, **8**, 36-41. https://doi.org/10.14797/mdcj-8-1-36

[95] Chen, J., Song, Y., Wang, Q., Li, Q., Tan, H., Gao, J., *et al.* (2022) Targeted Neutrophil-Mimetic Liposomes Promote Cardiac Repair by Adsorbing Proinflammatory Cytokines and Regulating the Immune Microenvironment. *Journal of Nanobiotechnology*, **20**, Article No. 218. https://doi.org/10.1186/s12951-022-01433-6

[96] Brito, L.A., Chandrasekhar, S., Little, S.R. and Amiji, M.M. (2010) Non-Viral Gene Delivery Using Self-Assembled Multi-Component (SAMC) Nanoparticles. *Journal of Biomedical Materials Research Part A*: *An Official Journal of the Society for Biomaterials*, *the Japanese Society for Biomaterials*, *and the Australian Society for Biomaterials and the Korean Society for Biomaterials*, **93**, 325-336.

[97] Bertrand, N., Bouvet, C., Moreau, P. and Leroux, J. (2010) Transmembrane pH-Gradient Liposomes to Treat Cardiovascular Drug Intoxication. *ACS Nano*, **4**, 7552-7558. https://doi.org/10.1021/nn101924a

[98] Wrobeln, A., Schlüter, K.D., Linders, J., Zähres, M., Mayer, C., Kirsch, M., *et al.* (2017) Functionality of Albumin-Derived Perfluorocarbon-Based Artificial Oxygen Carriers in the Langendorff-Heart. *Artificial Cells*, *Nanomedicine*, *and Biotechnology*, **45**, 723-730. https://doi.org/10.1080/21691401.2017.1284858

[99] Ayyagari, A.L., Zhang, X., Ghaghada, K.B., Annapragada, A., Hu, X. and Bellamkonda, R.V. (2006) Long-Circulating Liposomal Contrast Agents for Magnetic Resonance Imaging. *Magnetic Resonance in Medicine*: *An Official Journal of the International Society for Magnetic Resonance in Medicine*, **55**, 1023-1029. https://doi.org/10.1002/mrm.20846

[100] Zhang, S., Gao, C., Lü, S., He, J., Liu, M., Wu, C., *et al.* (2017) Synthesis of Pegylated Polyglutamic Acid Peptide Dendrimer and Its Application in Dissolving Thrombus. *Colloids and Surfaces B*: *Biointerfaces*, **159**, 284-292. https://doi.org/10.1016/j.colsurfb.2017.08.009

[101] Din, F.u., Aman, W., Ullah, I., Qureshi, O.S., Mustapha, O., Shafique, S., *et al.* (2017) Effective Use of Nanocarriers as Drug Delivery Systems for the Treatment of Selected Tumors. *International Journal of Nanomedicine*, **12**, 7291-7309. https://doi.org/10.2147/ijn.s146315

[102] Pinzaru, I., Coricovac, D., Dehelean, C., Moacă, E., Mioc, M., Baderca, F., *et al.* (2018) Stable Peg-Coated Silver Nanoparticles—A Comprehensive Toxicological Profile. *Food and Chemical Toxicology*, **111**, 546-556. https://doi.org/10.1016/j.fct.2017.11.051

[103] Corsi, I., Venditti, I., Trotta, F. and Punta, C. (2023) Environmental Safety of Nanotechnologies: The Eco-Design of Manufactured Nanomaterials for Environmental Remediation. *Science of The Total Environment*, **864**, Article ID: 161181. https://doi.org/10.1016/j.scitotenv.2022.161181

[104] Yoo-Iam, M., Chaichana, R. and Satapanajaru, T. (2014) Toxicity, Bioaccumulation and Biomagnification of Silver Nanoparticles in Green Algae (*Chlorella* sp.), Water Flea (*Moina macrocopa*), Blood Worm (*Chironomus* spp.) and Silver Barb (*Barbon-*

ymus gonionotus). *Chemical Speciation & Bioavailability*, **26**, 257-265. https://doi.org/10.3184/095422914x14144332205573

[105] Rani, V., Deep, G., Singh, R.K., Palle, K. and Yadav, U.C.S. (2016) Oxidative Stress and Metabolic Disorders: Pathogenesis and Therapeutic Strategies. *Life Sciences*, **148**, 183-193. https://doi.org/10.1016/j.lfs.2016.02.002

[106] Vyshnava, S.S., Kanderi, D.K., Panjala, S.P., Pandian, K., Bontha, R.R., Goukanapalle, P.K.R., *et al.* (2016) Effect of Silver Nanoparticles against the Formation of Biofilm by *Pseudomonas aeruginosa* an *in Silico* Approach. *Applied Biochemistry and Biotechnology*, **180**, 426-437. https://doi.org/10.1007/s12010-016-2107-7

[107] Atale, N., Saxena, S., Nirmala, J.G., Narendhirakannan, R., Mohanty, S. and Rani, V. (2016) Synthesis and Characterization of *Sygyzium Cumini* Nanoparticles for Its Protective Potential in High Glucose-Induced Cardiac Stress: A Green Approach. *Applied Biochemistry and Biotechnology*, **181**, 1140-1154. https://doi.org/10.1007/s12010-016-2274-6

[108] Veeresham, C. (2012) Natural Products Derived from Plants as a Source of Drugs. *Journal of Advanced Pharmaceutical Technology & Research*, **3**, 200-201. https://doi.org/10.4103/2231-4040.104709

[109] Atale, N., Gupta, K. and Rani, V. (2014) Protective Effect of *Syzygium cumini* against Pesticide-Induced Cardiotoxicity. *Environmental Science and Pollution Research*, **21**, 7956-7972. https://doi.org/10.1007/s11356-014-2684-3

[110] Yadi, M., Mostafavi, E., Saleh, B., Davaran, S., Aliyeva, I., Khalilov, R., *et al.* (2018) Current Developments in Green Synthesis of Metallic Nanoparticles Using Plant Extracts: A Review. *Artificial Cells, Nanomedicine, and Biotechnology*, **46**, 336-343. https://doi.org/10.1080/21691401.2018.1492931

[111] Rasheed, T., Bilal, M., Iqbal, H.M.N. and Li, C. (2017) Green Biosynthesis of Silver Nanoparticles Using Leaves Extract of Artemisia Vulgaris and Their Potential Biomedical Applications. *Colloids and Surfaces B: Biointerfaces*, **158**, 408-415. https://doi.org/10.1016/j.colsurfb.2017.07.020

[112] Zheng, M., Huang, Z., Ji, H., Qiu, F., Zhao, D., Bredar, A.R.C., *et al.* (2020) Simultaneous Control of Soil Erosion and Arsenic Leaching at Disturbed Land Using Polyacrylamide Modified Magnetite Nanoparticles. *Science of the Total Environment*, **702**, 134997. https://doi.org/10.1016/j.scitotenv.2019.134997

[113] Vickers, N.J. (2017) Animal Communication: When I'm Calling You, Will You Answer Too? *Current Biology*, **27**, R713-R715. https://doi.org/10.1016/j.cub.2017.05.064

[114] Xiu, J., Zhang, Y., Paray, B.A., Gulnaz, A. and War, M.U.D. (2022) Facile Preparation of Fe_2O_3 Nanoparticles Mediated by *Centaurea alba* Extract and Assessment of the Anti-Atherosclerotic Properties. *Arabian Journal of Chemistry*, **15**, Article ID: 103493. https://doi.org/10.1016/j.arabjc.2021.103493

[115] Mosaddegh, M., Tavakoli, M. and Behzad, S. (2018) Constituents of the Aerial Parts of *Centaurea behen*. *Chemistry of Natural Compounds*, **54**, 1015-1017. https://doi.org/10.1007/s10600-018-2539-0

[116] Öksüz, S. and Ayyildiz, H. (1986) Sesquiterpene Lactones from *Centaurea Coronopifolia*. *Phytochemistry*, **25**, 535-537. https://doi.org/10.1016/s0031-9422(00)85520-x

[117] Oksuz, S., Ulubelen, A., Aynechi, Y. and Wagner, H. (1982) A guaianolide from *Centaurea behen*. *Phytochemistry*, **21**, 2747-2749. https://doi.org/10.1016/0031-9422(82)83116-6

[118] Esmaeili, A., Mousavi, Z., Shokrollahi, M. and Shafaghat, A. (2012) Antioxidant Ac-

tivity and Isolation of Luteoline from *Centaurea behen* L. Grown in Iran. *Journal of Chemistry*, **2013**, Article ID: 620305. https://doi.org/10.1155/2013/620305

[119] Harper, D. (2002) Talking about Pictures: A Case for Photo Elicitation. *Visual Studies*, **17**, 13-26. https://doi.org/10.1080/14725860220137345

[120] Ghashghaii, A., Hashemnia, M., Nikousefat, Z., Zangeneh, M.M. and Zangeneh, A. (2017) Wound Healing Potential of Methanolic Extract of *Scrophularia striata* in Rats. *Pharmaceutical Sciences*, **23**, 256-263. https://doi.org/10.15171/ps.2017.38

[121] Adams, R.P. (2017) Identification of Essential Oil Components by Gas Chromatography/Mass Spectrometry (ed. 4.1). Allured Publ Crop.

[122] Akiyama, H., Ito, A., Sato, M., Kawabe, Y. and Kamihira, M. (2010) Construction of Cardiac Tissue Rings Using a Magnetic Tissue Fabrication Technique. *International Journal of Molecular Sciences*, **11**, 2910-2920. https://doi.org/10.3390/ijms11082910

[123] Mou, Y., Zhou, J., Xiong, F., Li, H., Sun, H., Han, Y., *et al.* (2015) Effects of 2,3-Dimercaptosuccinic Acid Modified Fe_2O_3 Nanoparticles on Microstructure and Biological Activity of Cardiomyocytes. *RSC Advances*, **5**, 19493-19501. https://doi.org/10.1039/c4ra11079j

[124] Sapir, Y., Cohen, S., Friedman, G. and Polyak, B. (2012) The Promotion of *in Vitro* Vessel-Like Organization of Endothelial Cells in Magnetically Responsive Alginate Scaffolds. *Biomaterials*, **33**, 4100-4109. https://doi.org/10.1016/j.biomaterials.2012.02.037

[125] Han, J., Kim, B., Shin, J., Ryu, S., Noh, M., Woo, J., *et al.* (2015) Iron Oxide Nanoparticle-Mediated Development of Cellular Gap Junction Crosstalk to Improve Mesenchymal Stem Cells' Therapeutic Efficacy for Myocardial Infarction. *ACS Nano*, **9**, 2805-2819. https://doi.org/10.1021/nn506732n

[126] Hussein, J., El-Banna, M., Razik, T.A. and El-Naggar, M.E. (2018) Biocompatible Zinc Oxide Nanocrystals Stabilized via Hydroxyethyl Cellulose for Mitigation of Diabetic Complications. *International Journal of Biological Macromolecules*, **107**, 748-754. https://doi.org/10.1016/j.ijbiomac.2017.09.056

[127] Teixeira, B.C., Lopes, A.L., Macedo, R.C.O., Correa, C.S., Ramis, T.R., Ribeiro, J.L., *et al.* (2014) Inflammatory Markers, Endothelial Function and Cardiovascular Risk. *Jornal Vascular Brasileiro*, **13**, 108-115. https://doi.org/10.1590/jvb.2014.054

[128] Alshehri, M.A. (2022) Cardioprotective Properties of Artemisia Herba Alba Nanoparticles against Heart Attack in Rats: A Study of the Antioxidant and Hypolipidemic Activities. *Saudi Journal of Biological Sciences*, **29**, 2336-2347. https://doi.org/10.1016/j.sjbs.2021.12.009

[129] Radulović, N.S., Randjelović, P.J., Stojanović, N.M., Blagojević, P.D., Stojanović-Radić, Z.Z., Ilić, I.R., *et al.* (2013) Toxic Essential Oils. Part II: Chemical, Toxicological, Pharmacological and Microbiological Profiles of *Artemisia annua* L. Volatiles. *Food and Chemical Toxicology*, **58**, 37-49. https://doi.org/10.1016/j.fct.2013.04.016

[130] Skowyra, M., Gallego, M., Segovia, F. and Almajano, M. (2014) Antioxidant Properties of *Artemisia annua* Extracts in Model Food Emulsions. *Antioxidants*, **3**, 116-128. https://doi.org/10.3390/antiox3010116

[131] Acikel, M., Buyukokuroglu, M.E., Erdogan, F., Aksoy, H., Bozkurt, E. and Senocak, H. (2005) Protective Effects of Dantrolene against Myocardial Injury Induced by Isoproterenol in Rats: Biochemical and Histological Findings. *International Journal of Cardiology*, **98**, 389-394. https://doi.org/10.1016/j.ijcard.2003.10.054

[132] Shalyapina, A.Y., Solovyova, A.Y., Zaporozhets, M.A., Khokhlov, E.M., Plotnichenko, V.G., Buslaeva, E.Y., Rustamova, E.G. and Gubin, S.P. (2012) Composite

Materials Based on Graphene and Zinc Oxide Nanoparticles. *Fine Chemical Technologies*, **7**, 80-84. (In Russian)

[133] El-Sayed, M.A. (2001) Some Interesting Properties of Metals Confined in Time and Nanometer Space of Different Shapes. *Accounts of Chemical Research*, **34**, 257-264. https://doi.org/10.1021/ar960016n

[134] Ibrar, M., Khan, M.A., Abdullah, and Imran, M. (2018) Evaluation of Paeonia Emodi and Its Gold Nanoparticles for Cardioprotective and Antihyperlipidemic Potentials. *Journal of Photochemistry and Photobiology B*: *Biology*, **189**, 5-13. https://doi.org/10.1016/j.jphotobiol.2018.09.018

[135] Dreaden, E.C., Austin, L.A., Mackey, M.A. and El-Sayed, M.A. (2012) Size Matters: Gold Nanoparticles in Targeted Cancer Drug Delivery. *Therapeutic Delivery*, **3**, 457-478. https://doi.org/10.4155/tde.12.21

[136] Zhang, T., Dang, M., Zhang, W. and Lin, X. (2020) Gold Nanoparticles Synthesized from *Euphorbia fischeriana* Root by Green Route Method Alleviates the Isoprenaline Hydrochloride Induced Myocardial Infarction in Rats. *Journal of Photochemistry and Photobiology B*: *Biology*, **202**, Article ID: 111705. https://doi.org/10.1016/j.jphotobiol.2019.111705

[137] Shiny, K.S., Kumar, S.H.S., Farvin, K.H.S., Anandan, R. and Devadasan, K. (2005) Protective Effect of Taurine on Myocardial Antioxidant Status in Isoprenaline-Induced Myocardial Infarction in Rats. *Journal of Pharmacy and Pharmacology*, **57**, 1313-1317. https://doi.org/10.1211/jpp.57.10.0010

[138] Vinodhini, A., Govindaraju, K., Singaravelu, G., Mohamed Sadiq, A. and Kumar, V.G. (2014) Cardioprotective Potential of Biobased Gold Nanoparticles. *Colloids and Surfaces B*: *Biointerfaces*, **117**, 480-486. https://doi.org/10.1016/j.colsurfb.2014.01.006

[139] Karthikeyan, K., Sarala Bai, B.R., Gauthaman, K., Sathish, K.S. and Devaraj, S.N. (2003) Cardioprotective Effect of the Alcoholic Extract of Terminalia Arjuna Bark in an *in Vivo* Model of Myocardial Ischemic Reperfusion Injury. *Life Sciences*, **73**, 2727-2739. https://doi.org/10.1016/s0024-3205(03)00671-4

[140] Liu, Y., Guo, J., Zhou, Z., Wu, Q., Jin, X. and Wang, T. (2023) Protective Properties of Nanoparticles Green-Synthesized by Plant on Myocardial Ischemia. *Inorganic Chemistry Communications*, **154**, Article ID: 110902. https://doi.org/10.1016/j.inoche.2023.110902

[141] Ritchie, R.H. and Abel, E.D. (2020) Basic Mechanisms of Diabetic Heart Disease. *Circulation Research*, **126**, 1501-1525. https://doi.org/10.1161/circresaha.120.315913

[142] Hao, W., Jia, Y., Wang, C. and Wang, X. (2022) Preparation, Chemical Characterization and Determination of the Antioxidant, Cytotoxicity and Therapeutic Effects of Gold Nanoparticles Green-Synthesized by Calendula Officinalis Flower Extract in Diabetes-Induced Cardiac Dysfunction in Rat. *Inorganic Chemistry Communications*, **144**, Article ID: 109931. https://doi.org/10.1016/j.inoche.2022.109931

[143] Yadid, M., Feiner, R. and Dvir, T. (2019) Gold Nanoparticle-Integrated Scaffolds for Tissue Engineering and Regenerative Medicine. *Nano Letters*, **19**, 2198-2206. https://doi.org/10.1021/acs.nanolett.9b00472

[144] Hassan, H., Sharma, P., Hasan, M.R., Singh, S., Thakur, D. and Narang, J. (2022) Gold Nanomaterials—The Golden Approach from Synthesis to Applications. *Materials Science for Energy Technologies*, **5**, 375-390. https://doi.org/10.1016/j.mset.2022.09.004

[145] Wei, X., Jiang, X. and Li, H. (2024) Fundamental Characteristics of Ultrasonic Green

Formulations Using *Avena sativa* L. Extract-Mediated Gold Nanoparticles and Electroconductive Nanofibers for Cardiovascular Nursing Care. *Heliyon*, **10**, e35018. https://doi.org/10.1016/j.heliyon.2024.e35018

[146] Bala, I., Bhardwaj, V., Hariharan, S. and Kumar, M.N.V.R. (2006) Analytical Methods for Assay of Ellagic Acid and Its Solubility Studies. *Journal of Pharmaceutical and Biomedical Analysis*, **40**, 206-210. https://doi.org/10.1016/j.jpba.2005.07.006

[147] Yu, X., Wang, J., Wang, T., Song, S., Su, H., Huang, H., *et al.* (2024) Ellagic Acid-Enhanced Biocompatibility and Bioactivity in Multilayer Core-Shell Gold Nanoparticles for Ameliorating Myocardial Infarction Injury. *Journal of Nanobiotechnology*, **22**, Article No. 554. https://doi.org/10.1186/s12951-024-02796-8

[148] Hao, T., Qian, M., Zhang, Y., Liu, Q., Midgley, A.C., Liu, Y., *et al.* (2022) An Injectable Dual-function Hydrogel Protects against Myocardial Ischemia/Reperfusion Injury by Modulating ROS/NO Disequilibrium. *Advanced Science*, **9**, Article ID: 2105408. https://doi.org/10.1002/advs.202105408

[149] Dong, F., Cui, Z., Teng, G., Shangguan, K., Zhang, Q. and Zhang, G. (2022) Green Synthesis of Gold Nanoparticles (AuNPs) as Potential Drug Carrier for Treatment and Care of Cardiac Hypertrophy Agents. *Journal of Cluster Science*, **33**, 1129-1137. https://doi.org/10.1007/s10876-021-02003-w

[150] Alyan, A., Abdel-Samad, S., Massoud, A. and Waly, S.A. (2019) Characterization and Thermal Conductivity Investigation of Copper-Polyaniline Nano Composite Synthesized by Gamma Radiolysis Method. *Heat and Mass Transfer*, **55**, 2409-2417. https://doi.org/10.1007/s00231-019-02588-z

[151] Jayakodi, S., Shanmugam, R., Almutairi, B.O., Almutairi, M.H., Mahboob, S., Kavipriya, M.R., *et al.* (2022) *Azadirachta indica*-Wrapped Copper Oxide Nanoparticles as a Novel Functional Material in Cardiomyocyte Cells: An Ecotoxicity Assessment on the Embryonic Development of Danio Rerio. *Environmental Research*, **212**, Article ID: 113153. https://doi.org/10.1016/j.envres.2022.113153

[152] Vinotha, V., Iswarya, A., Thaya, R., Govindarajan, M., Alharbi, N.S., Kadaikunnan, S., *et al.* (2019) Synthesis of ZnO Nanoparticles Using Insulin-Rich Leaf Extract: Anti-Diabetic, Antibiofilm and Anti-Oxidant Properties. *Journal of Photochemistry and Photobiology B*: *Biology*, **197**, Article ID: 111541. https://doi.org/10.1016/j.jphotobiol.2019.111541

[153] Sivaraj, R., Rahman, P.K.S.M., Rajiv, P., Narendhran, S. and Venckatesh, R. (2014) Biosynthesis and Characterization of *Acalypha indica* Mediated Copper Oxide Nanoparticles and Evaluation of Its Antimicrobial and Anticancer Activity. *Spectrochimica Acta Part A*: *Molecular and Biomolecular Spectroscopy*, **129**, 255-258. https://doi.org/10.1016/j.saa.2014.03.027

[154] Morgan, E.D. (2009) Azadirachtin, a Scientific Gold Mine. *Bioorganic & Medicinal Chemistry*, **17**, 4096-4105. https://doi.org/10.1016/j.bmc.2008.11.081

[155] Ganda, O.P. (2009) Dyslipidemia: Pathogenesis and Management. In: Poretsky, L., Ed., *Principles of Diabetes Mellitus*, Springer US, 435-456. https://doi.org/10.1007/978-0-387-09841-8_28

[156] Hajar, R. (2017) Risk Factors for Coronary Artery Disease: Historical Perspectives. *Heart Views*, **18**, 109-114. https://doi.org/10.4103/heartviews.heartviews_106_17

[157] Qu, S., Han, X. and Yu, Y. (2024) Protective Effects of Copper Nanoparticles Green-Formulated by *Ginkgo biloba* Leaf Extract on Cardiac Function in Obese Insulin-Resistant Rats. *Inorganic Chemistry Communications*, **162**, Article ID: 112204. https://doi.org/10.1016/j.inoche.2024.112204

[158] Swamy, A., Gulliaya, S., Thippeswamy, A., Koti, B. and Manjula, D. (2012) Cardioprotective Effect of Curcumin against Doxorubicin-Induced Myocardial Toxicity in Albino Rats. *Indian Journal of Pharmacology*, **44**, 73-77. https://doi.org/10.4103/0253-7613.91871

[159] Yadav, Y.C., Pattnaik, S. and Swain, K. (2019) Curcumin Loaded Mesoporous Silica Nanoparticles: Assessment of Bioavailability and Cardioprotective Effect. *Drug Development and Industrial Pharmacy*, **45**, 1889-1895. https://doi.org/10.1080/03639045.2019.1672717

[160] M Luisa, D.P., Griselda, R., Valentín, M., Carmina, O., Cristina, V., JJ, M., *et al.* (2020) Curcumin-Loaded Poly-ε-Caprolactone Nanoparticles Show Antioxidant and Cytoprotective Effects in the Presence of Reactive Oxygen Species. *Journal of Bioactive and Compatible Polymers*, **35**, 270-285. https://doi.org/10.1177/0883911520921499

[161] Cheng, J., Ding, Q., Wang, J., Deng, L., Yang, L., Tao, L., *et al.* (2016) 5-Azacytidine Delivered by Mesoporous Silica Nanoparticles Regulates the Differentiation of P19 Cells into Cardiomyocytes. *Nanoscale*, **8**, 2011-2021. https://doi.org/10.1039/c5nr08560h

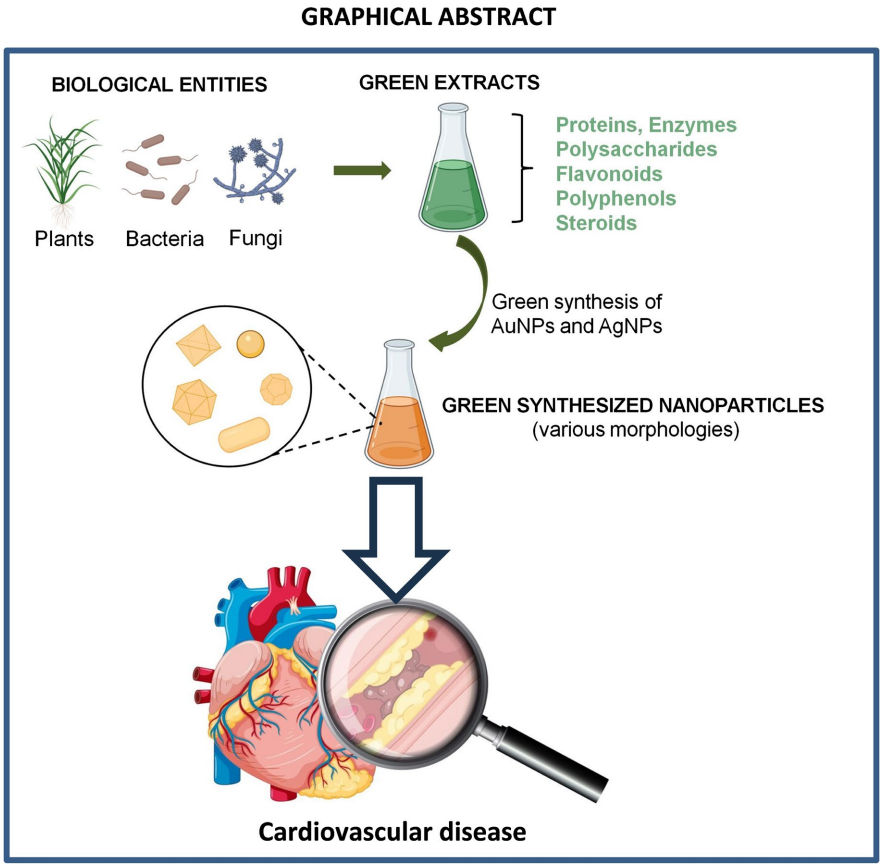
[162] Ren, M., Han, Z., Li, J., Feng, G. and Ouyang, S. (2015) Ascorbic Acid Delivered by Mesoporous Silica Nanoparticles Induces the Differentiation of Human Embryonic Stem Cells into Cardiomyocytes. *Materials Science and Engineering: C*, **56**, 348-355. https://doi.org/10.1016/j.msec.2015.06.048

[163] Ramezani Farani, M., Farsadrooh, M., Zare, I., Gholami, A. and Akhavan, O. (2023) Green Synthesis of Magnesium Oxide Nanoparticles and Nanocomposites for Photocatalytic Antimicrobial, Antibiofilm and Antifungal Applications. *Catalysts*, **13**, Article 642. https://doi.org/10.3390/catal13040642

[164] Nisa, F.Y., Rahman, M.A., Rafi, M.K.J., Khan, M.A.N., Sultana, F., Majid, M., *et al.* (2023) Biosynthesized Magnesium Oxide Nanoparticles from *Tamarindus indica* Seed Attenuate Doxorubicin-Induced Cardiotoxicity by Regulating Biochemical Indexes and Linked Genes. *Biomaterials Advances*, **146**, Article ID: 213291. https://doi.org/10.1016/j.bioadv.2023.213291

[165] Venkatappa, M.M., Udagani, C., Hanumegowda, S.M., Pramod, S.N., *et al.* (2022) Effect of Biofunctional Green Synthesized Mgo-Nanoparticles on Oxidative-Stress-Induced Tissue Damage and Thrombosis. *Molecules*, **27**, Article 5162. https://doi.org/10.3390/molecules27165162

Appendix


GRAPHICAL ABSTRACT
BIOLOGICAL ENTITIES
GREEN EXTRACTS
Plants
Bacteria
Fungi
Proteins, Enzymes
Polysaccharides
Flavonoids
Polyphenols
Steroids
Green synthesis of
AuNPs and AgNPs
GREEN SYNTHESIZED NANOPARTICLES
(various morphologies)
Cardiovascular disease