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NANOTECHNOLOGY IN CARDIOLOGY: A NEW ERA OF TARGETED THERAPIES AND ADVANCED DIAGNOSTICS- A REVIEW

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Abstract
Cardiovascular diseases (CVDs) are disorders related to heart, blood vessels and circulatory system. The disease category of CVDs continues to rank as the primary cause of death in the world while death cases rose from 12.1 million in 1990 to reach 20.5 million in 2021, approximately one-third of all global deaths i.e. 33% deaths. Currently, CVDs are not completely curable but they can be prevented. Diagnostic methods for the CVDs are computerized electrocardiography, echocardiography, coronary angiography, magnetic resonance imaging, molecular imaging and cardiac immunoassay. Different medicines to treat CVDs are aspirin, statins, warfarin and poly-pill etc. Other than these medicines, some enzyme inhibitors, such as angiotensin-converting enzyme (ACE) inhibitors, β-blockers, ivabradine etc., and anti-platelet therapy is also used for the treatment of CVDs. New pharmacotherapy and interventional strategies exist but patients still face ongoing problems with systemic toxicity and restricted drug distribution alongside medical procedure constraints. Nanotechnology provides cardiovascular medicine with transformative capabilities by enabling precise diagnostic methods and highly targeted treatment approaches. Pharmacological systems that incorporate nanoparticles as polymeric nanoparticles, liposomes, dendrimers and solid lipid nanoparticles improve drug distribution while controlling delivery timing and achieving specific targets for minimizing side effects. Significant molecular imaging with theranostics and regenerative cardiology progress has been achieved through nanomaterial usage of gold nanoparticles, carbon nanotubes and graphene derivatives. This review delves into the latest advancements in nanomedicine for CVD management, emphasizing its pivotal role in precision cardiology, targeted therapeutics, and next-generation cardiovascular diagnostics.

1. Introduction

Cardiovascular diseases (CVDs) are disorders related to heart, valvular, blood vessels, and circulatory system. As cardiovascular system functions for the normal blood circulation, any error related to this system can cause hypertension, atherosclerosis, heart failure, ischemic heart diseases, stroke, angina pectoris, aorta disease, peripheral vascular disease, myocardial infarction, and congestive heart failure etc., (J. Wang, Zhang, Wan, Yang, & Zhao, 2024). Heart diseases together with blood vessel disorders

comprise cardiovascular diseases (CVDs) which show different origins alongside several risk factors. The combination of high cholesterol with hypertension and smoking combined with diabetes and obesity causes atherosclerosis which leads to CAD then produces myocardial ischemia that may evolve to infarction (Sood, Baishnab, Lang, Kumar, & Sindhu, 2024). Extended exposure to hypertension causes left ventricular hypertrophy, arrhythmias and heart failure through hypertensive heart disease development. Heart failure occurs because of CAD, hypertension, cardiomyopathy or valvular disorders thus reducing blood circulation capacity in the heart. Arrhythmias develop because of four primary reasons: ischemic heart disease and electrolyte handling problems together with genetic and structural heart abnormalities. Stroke develops as either a blood vessel rupture or blood clot event that hypertension and atherosclerosis tend to worsen (X. Tang, Zhu, Guan, Zhou, & Wei, 2022). The artery disease known as PAD results from narrowed blood vessels due to smoking and diabetes and atherosclerosis and hypertension which interfere with limb blood circulation. Congenital heart defects exist from birth because of genetic mutations together with maternal infections and environmental factors that affect fetal development (Doa'a, Allen, Hiram, & Alrabadi, 2021). The presence of cardiomyopathies arises due to genetic origins or infections, alcohol abuse or disorders which weaken heart muscles and raise the probability of heart failure. Providing early diagnosis requires comprehensive knowledge about the conditions and their root causes alongside the necessary treatment strategies and prevention methods (Brida et al., 2023).

CVDs are considered to be the deadliest disorders. According to World Health Organization (WHO), CVDs are responsible for the deaths of 20.5 million people i.e. 33% of all the global deaths in 2021. It is estimated that in 2030, the death rate due to CVDs could be raised up to 25 million. In 2018, 20.28% of total deaths i.e. 251,200 deaths were caused by CVDs, in Pakistan (Samad & Hanif, 2023). According to the 2019 Global Burden of Disease study, Pakistan had an age-standardized CVD death rate of 357.88 per 100,000 individuals, which was higher than the global rate of 239.85 per 100,000 ahajournals.org. Given the global trend of increasing CVD cases and deaths from 34.74 million cases and 12.33 million deaths in 1990 to 66.81 million cases and 20.5 million deaths in 2021 pmc.ncbi.nlm.nih.gov, it is plausible that Pakistan's CVD mortality rate has also risen during this period. However, without specific data for 2021, precise figures cannot be provided (Y.-Y. Lee, Sriram, Wang, Kogularasu, & Chang-Chien, 2024).

The risk factors that contribute to cardiovascular diseases are sedentary lifestyles, smoking and alcohol consumption. Similarly high sugar level, cholesterol, fatty acids are also leading factors towards the advancement of CVDs. Other risk factors for developing cardiovascular diseases are age, family history, diabetes, obesity, physical inactivity, and stress etc., (Hussain, Rafi, Imran, Rehman, & Abbas, 2024). The methods to diagnose CVDs include electrocardiography ECG, echocardiography, magnetic resonance imaging (MRI), advanced molecular imaging (MI) and cardiac immunoassays (CIAs). They proved to be one of the effective methods for CVDs diagnosis with high accuracy (Sabir et al., 2021). Currently, CVDs cannot be cured completely but they can be controlled in many ways. They can be prevented by taking preventing measures such as diet control and exercise. There are mostly treated by taking medicinal drugs. Sometimes, medicinal drugs are taken in form of poly-pill that is combination of different drugs that help in treating CVDs (D. K. Wang, Rahimi, & Filgueira, 2021). In worst cases, patients have to go through different surgeries. But cardiac surgeries have some limitations such as physically weak patients or elderly, co-morbidity patients having other diseases such as diabetes mellitus and immunocompromised patients, are not compatible for surgeries (da Silva Bauer, Teixeira, Leão, & Rosa, 2023).

Nanotechnology allows scientists to conduct specific molecular and cellular level interventions. The use of precise pharmaceutical processes at molecular and cellular levels enables health providers to stop and treat CVDs before they

progress (Hu, Fang, Ge, & Li, 2022). Studies have shown that nanoparticles have capabilities for conducting both noninvasive imaging procedures and disease monitoring behaviors independently. The monitoring of therapeutic instances along with disease progression assessment occurs through nanoparticles in patients who suffer from atherosclerosis (J. Cheng, Huang, Chen, & Wu, 2023). The treatment employs biomaterial-based microparticles and nanoparticles to deliver therapy through encapsulation methods. The delivery system uses biomaterials to encapsulate therapeutic compounds while sustaining their activity which results in better treatment success (Z. Zheng, Zhu, Lv, Gu, & Hu, 2022). Thrombus treatment can be advanced through nanosystems which provide more effective therapeutic delivery methods and minimize drug side effects and improve target site engagement. Nanotechnology platforms extend drug half-life duration and minimize side effects which affect standard pharmaceutical agents of thrombolytic drugs. Research into combining nanoparticle-based treatments for therapeutic purposes is currently being carried out (Jha et al., 2024).

The therapeutic capabilities of agents through nanosystems are improved by at least three different methods including nucleic acids, small-molecule drugs and proteins, gas-signaling molecules and stem cells. These biomedical systems deliver these distinct therapeutic agents to the targeted region. Nanosystems serve as effective delivery methods because they provide both sustained release and local therapeutic benefits (Iravani & Varma, 2022). For instance, injectable Hydrogel, drug delivery systems that combine nanocomplexes alongside therapeutic agents result in better drug distribution to the targeted site. Nanoparticles defeat biological obstacles to deliver treatment better (Smith & Edelman, 2023). Improved drug targeting at specific locations enhances both drug effectiveness and reduces medical side effects and minimizing systemic side effects. Polymeric nanoparticles represent an investigated method for decreasing oxidative stress and muscle damage in cardiac myocytes (Song et al., 2021). The development of nanosystems established a method to pass through the blood-brain barrier effectively (BBB) for stroke treatment. Nanosystems provide a way to control drug delivery rates, such nanoparticles include liposomal amiodarone and platelet-like fusogenic liposomes that decrease drug side effects. The tactical utilization of nanosystems produces improved therapeutic results in cardiovascular medical scenarios (Yuying Liu, Li, Yang, Yang, & Fu, 2024).

Nanotechnology is going to play a big role in treatment of CVDs in near future by using nanoparticles and nanomaterials such as CNTs, organic nanoparticles, inorganic nanoparticles, metal nanoparticles and dendrimers etc., (Figure. 1) and can provide us with better medical instruments, therapeutic and diagnostic technologies. Studies are being done to develop nanomedicines and nano-carrier based drug delivery systems that can help in overcoming the conventional diagnostic systems (Hu et al., 2022). It will only target the affected tissues leaving the normal tissues ineffective, and preventing drug accumulation and sustained drug release and distribution over time to maximize the therapeutic effect and minimize the side effects. Nanomaterials can also be used for developing implants such as heart valves, defibrillators, vascular grafts, pace markers, and stents etc., (Nenna et al., 2021). The implementation of nanotechnology delivers precise drug distribution systems to erase abnormal heart muscle tissues together with methods to control arrhythmias and minimize post-operative atrial fibrillation, abnormal heart muscle cells, management of arrhythmias, and post-operative atrial fibrillation (Shariati et al., 2023). Abid et al. (2025) examined strategic business approaches necessary for the development, commercialization, and adoption of nanotechnology-based sunscreens, focusing on advancements in titanium dioxide and zinc oxide nanoparticles. Scientific studies have evaluated Sirolimus nanoparticles as a potential treatment method for reducing objects in this area. The combination of inflammation response management and restenosis prevention occurs when using balloon injury procedures on lower extremity arteries jury (Lankala et al., 2023). The antiproliferative substance-filled PLGA-coated

stents show promise as a clinically important medical device. Medical research indicates drug-containing nanoparticles might help treat severe and threatening conditions that could lead to death. Mesoporous silica nanoparticles MSNPs improve the therapeutic properties of honokiol for suppressing neointimal hyperplasia (Jawaid et al., 2025).

This article delves into the study of current diagnosis, treatments of cardiovascular diseases and all the advancements, challenges faced and future R&D in nanotechnology that will play a major role in CVDs treatment.

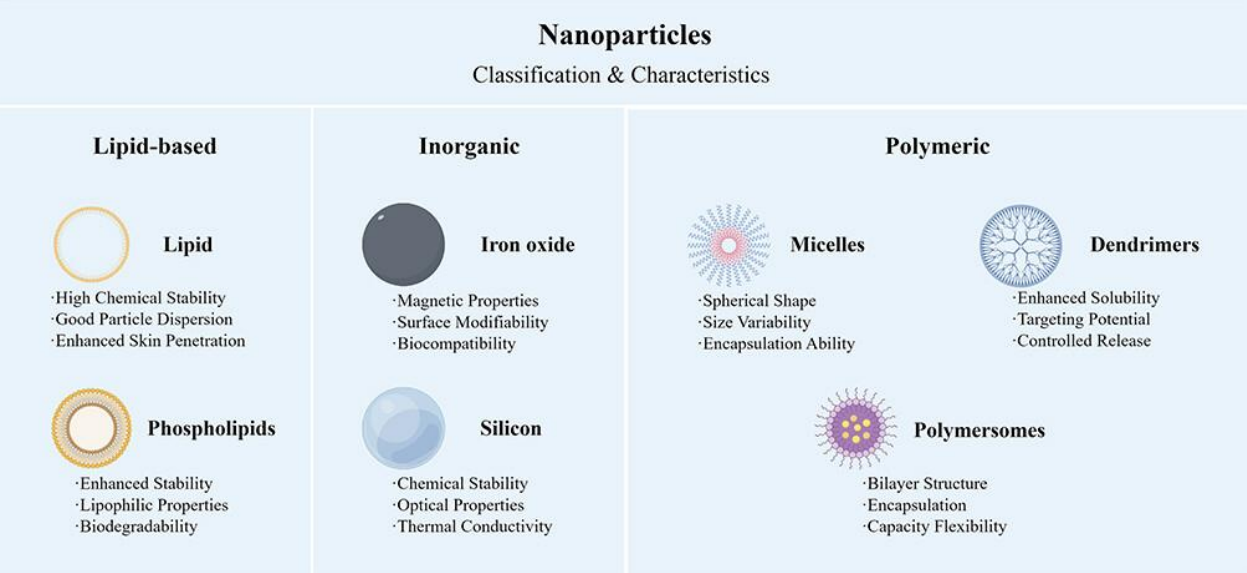

Fig. 1. Schematic diagram showing different type of nanomaterials, their classification and characteristic features (C. Tang, Zhou, Wu, & Zhu, 2024).

2. Conventional Procedures for Diagnosis of CVDs

Cardiovascular magnetic resonance imaging (MRI) is a clinically recognized, reliable and broad imaging modality for the wide spectrum diagnosis of cardiovascular diseases. Due to its outstanding reliability, cardiovascular MRI is the best technique for the evaluation of variations in ventricular constraints (Faizal, Thevarajah, Khor, & Chang, 2021). Its significant applications are in the assessment of left ventricular function in patients with poor echocardiographic inspections, RV evaluation, myocardial sustainability imaging, Evaluation of congenital heart, aorta, and valvular diseases (Solanki, Dhonnar, Shinde, Shelar, & Shirke, 2023). Another procedure used for the diagnosis of CVD is electrocardiography (ECG), which has a significant clinical effect on examining the severity of CVDs. The ECG signifies an electrical tracing of the heart and is recorded non-invasively. *ECG is used to detect myocardial damage, ischemia, earlier infarction and Rheumatic heart disease* (Moreno-Sánchez et al., 2024). It is also helpful for the evaluation of blunt cardiac trauma, in the diagnosis of congenital heart diseases, electrolyte imbalance and rhythm disorders, diagnosis tool in a sports physical exam to rule out cardiomyopathy (Sattar & Chhabra, 2021). Echocardiography is most commonly used method to assist the structural components of heart. It uses ultrasound that can provide a moving image of heart. Echocardiography delivers delicate cross-sections of heart structures this contains; left and right atrium, left and right ventricles, valves, and related valvular structures (Al-Assaf et al., 2024). Another technique used for CVD diagnosis is advanced molecular imaging, which is used to observe the inside of the body at molecular level. It is used for

diagnosis at cellular and subcellular level such as detection of specific tissue epitopes etc. It uses different imaging techniques and probe utilization to create variety of biomolecules (Sabir et al., 2021).

Cardiac immunoassay is an analytical procedure which has as its basis the principles of immunology- specifically the binding of drugs to antibodies. Commonly electrocardiography ECG is used to diagnose myocardial infarction but it has its limitation that it shows normal ECG result during emergency room cases (Denysyuk et al., 2023). This problem can be conquered by the measurement of biomarkers in blood which provides better diagnosis. Creatine kinase-MB, cardiac forms of troponin I (cTnI), cardiac troponin T (cTnT) and myoglobin are the crucial biomarkers for MI diagnosis (Radha, Shahzadi, & Al-Sayah, 2021). Another method that uses X-ray imaging technique is coronary angiography. This test is performed to observe if there is restriction in blood flow going to the heart. It can also be used to see detailed pictures of heart, brain and kidneys. It is also known as cardiac catheterizations. It is a Lumin gram because it provides only two dimensional images of the vessel (Candreva et al., 2022).

2.1. Conventional Procedures for Treatment of CVDs

There are many pharmaceutical drugs that are used for treatment of CVDs. Clopidogrel bisulfate irreversibly modifies the platelet and inhibits platelet aggregation. It involves adenosine diphosphate receptor and blocks its pro-aggregatory effects and contains different drug metabolizing enzymes (Danlos et al., 2021).Warfarin is an antagonist that is commonly used as an anticoagulant for treating patients with atrial fibrillation. The drug inhibits epoxide reductase enzyme that result in decreasing of vitamin K-dependent coagulation factor's activation (Dávila-Fajardo et al., 2019). Acenocoumarin is an anticoagulant working as vitamin k epoxide reductase inhibitor. It converts inactive oxidized vitamin k to active reduced form. It is used to avoid thromboembolic and hemorrhagic event. Research shows that fibrates decrease both death rates and disease severity during the first stage of cardiovascular disease prevention (Addissouky, El Sayed, Ali, Alubiady, & Wang, 2024). Higher levels of low-density lipoprotein represent the core danger factor when it comes to CVD development. Fibrates possess two essential therapeutic functions including atherogenic dyslipidemia modification and triglyceride serum reduction. Acetylsalicylic acid (Aspirin) works as an anti-inflammatory and antithrombotic medication that permanently blocks COX-1 by acetylating serine 520 in platelets thus reducing platelet production of prothrombotic thromboxane A2 (Bose, Ha, & McCarthy, 2021). Secondary prevention of CVD benefits more from aspirin's ability to prevent additional CV events than the risks of major bleeding therefore primary use of aspirin became standard for secondary CVD prevention. Daily doses between 75–100 mg help patients achieve complete antiplatelet effects while medical providers use this regimen to treat patients with cardiovascular diseases (Davidson et al., 2022). Medical use of statins as a hypercholesterolemia and atherosclerosis treatment relies on inhibition of 3-hydroxy methyl glutaryl-coenzyme A (HMG-CoA) reductase while decreasing plasma cholesterol levels. Competitive inhibition acts through which statins stop the enzyme from functioning. Mevalonate production stops when taking this medication because it blocks the action of HMG-CoA reductase which produces these compounds (X.-Z. Li et al., 2022).

A poly-pill is a fixed dose combination pill used for the prevention of cardiovascular diseases. It simplifies the treatment regimen and has reduced the cost and has prevented up to 88% of heart attacks and strokes (Li et al., 2023). Since the poly-pill's individual components are all very effective for secondary prevention of CVD it is estimated that the poly-pill will also be effective. The poly-pill that combines 3-4 pharmaceutical components having potential to reduce major cardiovascular risk factors includes "multi-purpose" or "cardiovascular" poly-pill (Jahangiri et al., 2022). ACE inhibitors are used in patients having hypertension, heart failure, coronary artery disease, chronic kidney disease and diabetes. ACE

inhibitors block the angiotensin II type 1 (AT1) and angiotensin II type 2 (AT2) receptor and inhibit the formation of angiotensin II. This results in blockage of vasoconstrictor actions of AT1 receptor (Strauss, Hall, & Narkiewicz, 2023). Beta blockers are also used to reduce major cardiovascular events such as stroke. Beta blockers inhibit renin angiotensin by inhibiting the release of renin from the kidney. Ivabradine is utilized in the cure of various cardiovascular diseases including coronary blood vessel disorder and heart malfunction. Ivabradine is a new and only offered HCN inhibitor, which can lower higher heart rate and also improves myocardial oxygen quantity by delaying diastole (Sripusanapan et al., 2024).

Table. 1. Medications among patients with coronary heart disease (Naessen, Bergsten, Lundmark, & Forslund, 2022).

Medications	*Proportion with treatment (%)*
Aspirin	*97*
Beta-blockers	*81*
ACE inhibitors	*38*
Angiotensin II blockers	*16*
Statins	*91*
Clopidogrel	*31*
Diuretics	*38*
Calcium channel blockers	*78*

2.2. Cardiac Surgeries

The first cardiac surgery was performed by Axel Cappelen on 4 September 1895. Since the different types of cardiac surgeries are now been performed for various types of heart issues. Balloon angioplasty is one of them which were first invented by Grüntzig on Sept 16, 1977. Although it is effective in treating coronary stenosis but the patient gone through it had high rate of abrupt vessel closure that resulted in repeat dilation or bypass surgery and the patient had high rate of restenosis that occurred in the treated vessel segment. Because of these limitations, it is usually combined with stent implantation (Van Veldhuisen et al., 2022). These devices have been revolutionized for the treatment of coronary artery diseases because they have biodegradability and excellent biocompatibility and also reduce the incidence of restenosis (Cho et al., 2021). Another surgery includes heart transplantation because of refractory heart failure and total artificial heart surgery is done by replacing patient's ventricles and valves by a pneumatically powered artificial heart because of biventricular heart failure (Naldemir et al., 2024). Although it improves the quality of life of the patients with end-stage heart failure but the scarcity of heart donors makes it difficult and it has many complications such as Primary graft failure, Right ventricle dysfunction, bleeding, thrombosis, renal failure, chronic anemia, infections and rejection (Overbey, Rajab, & Turek, 2024).

Coronary artery bypass grafting (CABG) is the most preferred surgical procedure for restoring obstructed coronary arteries worldwide with improving blood flow and oxygen supply. Aortic valve repair or valve replacement is a surgical method that is used to replace or repair the aortic valve that is dysfunctional (Krittanawong et al., 2024). It is a recognized method that showed excellent stability in patients with valve repair. This technique has led to the enhancement in the reproducibility and dissemination of AV repair (Gaudino et al., 2022). Implantable Cardioverter-Defibrillator (ICD) is a small electrical device for monitoring and regulating abnormal heart rhythms by sending electrical pulses and helps to prevent sudden cardiac death. But in some cases they can cause potential device infection and inappropriate shocks, worsening the quality of life So they aren't considered a high priority treatment

and secondary prevention of sudden cardiac death (Maron, Estes, Rowin, Maron, & Reynolds, 2023). Artificial cardiac pacemakers (PMs) are tiny electrical appliances that recognize intrinsic cardiac beat and convey electric signals, if suggested, to accelerate the heart and switch the malfunctioning pure pacemaker but, they are not preferred because they can cause blood clots and infections (Hung et al., 2024).

2.3. Single cell RNA Sequencing in CVDs

Both clinical professionals and scientific researchers maintain cardiovascular health promotion as an ongoing essential task. The contemporary method for studying RNA transcripts inside single cells uses Single-cell RNA sequencing technology which scientists call scrRNA-seq (S. U. Khan et al., 2024). The methodology delivers knowledge about cell composition together with cell-specific functions within highly structured tissue structures and body systems of organisms. Scientific research that embraces scRNA-seq techniques has generated extensive information across various fields leading to valuable discoveries about human and model organism and plant cell structures (Tehrani et al., 2024). The research developments based on this investigation led to the growth of cell numbers which created a new pathway for high-throughput RNA sequencing execution (Ke et al., 2022). The development of modern single-cell RNA sequencing tools including enhanced methods for sample collection as well as barcoded reverse transcription, cellular isolation, cDNA enhancement, library construction, sequencing and bioinformatics has been made possible. The new technological developments achieve both cost-reduction and automated workflow advancement and increased processing speed (Xu, Hua, Mo, Hu, & Song, 2023). The basic principle of scRNA-seq has endured unchanged while additional solutions have been established. This technological advancement will boost the clinical and personalized healthcare applications of this approach. Single-cell RNA-seq technologies have become extensively used for studying heart diseases as part of modern CVD research (S. U. Khan et al., 2024).

2.4. Cardiovascular Biomarkers

The field of cardiovascular diagnosis depends heavily on biomarkers especially cardiac troponins (cTnI and cTnT) alongside natriuretic peptides (BNP and NT-ProBNP). The regulatory proteins known as cardiac troponins prove vital for muscle contraction when myocardial injuries occur particularly during myocardial infarction (MI) (Tehrani et al., 2024). The detection of myocardial damage results in bloodstream liberation of these proteins as specialized detectors for diagnosing cardiac muscle injuries (Ouyang et al., 2021). Medical professionals heavily affirm the importance of this specific characteristic because it enables the detection of cardiac events while excluding other types of muscle tissue damage. The clinical significance of cardiac troponins exists in their ability to both identify heart attacks and analyze how troponins escape from cardiac cells and decay in the blood (Shlimon, Lindenberger, Welander, Dangardt, & Bjarnegård, 2022). The analytical data gives doctors essential knowledge to determine when and how much myocardial damage occurred. Doctors recognize elevated levels of cTnI and cTnT as the definitive methods to diagnose myocardial infarctions (Clerico, Zaninotto, & Plebani, 2024).

The two natriuretic peptides BNP and NTProBNP used together with cardiac troponins enable healthcare professionals to obtain important diagnostic and management information about HF. Blood cells produce these peptides as a reaction to increased ventricular stress and volume problems that characterize HF (Z. Li et al., 2022). The peptides participate actively in preserving cardiovascular stability by supporting natriuric and diuretic effects while dilating blood vessels (Su et al., 2023). The diagnostic value of HF is provided by BNP and NT-ProBNP tests which display elevated levels in conditions that increase intracardiac pressure and lead to ventricular dysfunction. NT-ProBNP stands out for its prolonged blood circulation duration and stable characteristics in bloodstream which makes it an ideal biomarker for chronic heart failure examinations (Goryacheva et al., 2022). The study by Bianucci investigates latest biomarkers for HF diagnosis beyond commonly used BNP. The

research discusses inflammation together with noncoding RNAs in HF development and their diagnostic and prognostic and personalized treatment applications. New protocols suggest that precise patient-centered medicine will adopt advanced "omics" tools along with extensive biomarkers to strengthen medical treatment for heart failure patients (Caro-Codón et al., 2021). Through their latest article that biomarker detection plays a critical role in CVD diagnosis as a worldwide major health issue. Modern research on biomarkers has gained speed because scientists use novel biomarkers identified by contemporary methods which include proteomics and biosensing along with microfluidics and troponin (Taghdiri, 2024). Their research showcases the combination between advanced optical sensors and their methods with advanced optical sensing technology through high-performance liquid chromatography and LASER/LED-induced fluorescence and Raman spectroscopy. Nanotechnology and microfluidic technologies boost the functionality of optical methods to detect patterns of multiple markers in whole blood and serum clinical specimens (Minhas et al., 2023).

The accurate CVD diagnosis depends primarily on detecting multiple biomarkers with high sensitivity along with specificity which leads to better therapeutic options and improved patient outcomes. The assessment of cardiovascular diseases benefits from two key markers which include C-reactive protein (CRP) and lipoprotein associated phospholipase A2 (Lp-PLA2) (Burger et al., 2023). Acute-phase reactant CRP has become a vital marker for measuring systemic inflammation because this inflammatory response is essential for atherosclerosis development along with other cardiovascular pathologies. Medical research confirms that coronary events increase when CRP levels become elevated so this indicator maintains its significance in cardiovascular risk assessments (Plebani, 2023). The advancement of high-sensitivity CRP tests allowed medical professionals to measure minimal but medically significant inflammation markers to identify cardiovascular risks within people who don't show obvious CVD symptoms (W. Zhang et al., 2021). Within atherosclerotic plaques the inflammatory process includes a participation from Lp-PLA2 which is an enzyme linked to low-density lipoproteins (LDL). Research indicates that Lp-PLA2 enzyme levels directly reflect the cardiovascular disease and stroke risks making it a possible biomarker to detect atherosclerosis. Lp-PLA2 takes a vital role in atherosclerosis development along with affecting cardiovascular event risks making it essential for CVD preventive diagnostics (Y. Lee, Sriram, & Wang, 2024).

Table. 2. The report mentions cardiac biomarkers together with their role in diagnosing heart failure pathophysiology (Berezin & Berezin, 2023).

	Influence on heart failure	*Biomarker Types*
1	Myocardial injury	*Troponin, H-FABP*
2	Inflammation	*IL-6, TNF-α, IL-1-Beta, CRP*
3	Remodeling	*sST-2, Galectin*
4	Fibrosis	*TGF-β*
5	Mechanical stretch	*BNP, GDF-15*
6	Neurohumoral	*Copeptin, Endothelin-1*
7	Oxidative stress	*Uric acid, Myeloperoxidase*
8	Micro RNA	*miR-18a-5p, miR-26b-5p, miR-27a-3p, miR-30e-5p, miR-106a-5p, miR-199a-3p, miR-652-3p, miR-30c, miR-221, miR-328, miR-375, miR-423, miR-34a, miR-21-3p, miR-199, miR-30a*

3. Use of Nanotechnology for the Diagnosis of CVDs

3.1. Molecular imaging of CVDs based on nanotechnology

Nanoparticles are perfect for imaging due to their flexibility, elevated surface to volume proportion, and excellent bioavailability increased the accuracy of clinical imaging purposes. AuNPs have effectively utilized in the cardiovascular field because of their necessary bioactivity and mobility (Sabir et al., 2021).

i. **Photoacoustic imaging** in which AuNPs can be involved depend on the temperature variations of nano agents when vibrated laser rays are absorbed (K. Wang et al., 2024).

ii. **Optical coherence tomography (OCT)** is an additional technique for CVD imaging utilizing AuNPs. In OCT, the infrared wave is directed to the target nerve from coherent beam supply and an image is constructed dependent on the back-dispersed beam. It demonstrated that specific cells held in biocompatible solutions can be recognized utilizing cardiovascular OCT (Abdiakhmetova, Momynzhanova, Temirbekova, Turken, & Dildabek, 2024).

iii. **MRI** is a non-invasive methodology that could deliver broad vasculature information that is crucial for the useful CVD analysis. Gd is frequently applied in MRI to generate a positive indicator because of its superior paramagnetic ability as a T1-based contrast media. Super magnetic iron oxide nanoparticles (SPIONs) are also frequently utilized as MRI contrast media. For enhanced accuracy and bioavailability, the Fe3O4/Gd2O3 NPs have been covered with harmless 3,4-dihydroxyhydrocinnamic acid (DHCA) (Turgut et al., 2025).

3.2. Superparamagnetic Nanoparticles

The sensitivity of magnetic resonance imaging (MRI) could be enhanced with contrast media like iron oxide nanoparticles (IONPs). Iron oxide nanoparticles have been broadly researched and used as imaging agents for analysis of cardiovascular (CVD) disorders. IONPs are also known as super magnetic IONPs (SPIONs) because they perform outstanding magnetic functions (Schumacher et al., 2025). The single effective IONPs presently being utilized as MRI contrast media for the CVD structure is ferumoxtran. SPIONs can change the basic contrast possessions of organic tissues precisely by altering the proton concentration of a tissue, and secondarily by changing the easing properties of nearby H protons, altering local magnetic field and thus its relaxation period T2 amounts (Vangijzegem et al., 2023). All of the IONPs created to aim the monocyte-macrophage, both passively and by actively aiming macrophages with dextran, D-mannose, and antibodies. IONPs could also be incorporated with ligands to aim for platelets, vascular smooth muscle cells, monocytes, fibrin, and macrophages (Berezin & Berezin, 2023). IONPs can be coupled with ligands to support position-specific communications and improve its supply to the target of our interest. The targeted IONPs effectively gather at target site and could increase MR images by stimulating contrast agent (Vazquez-Prada et al., 2021).

4. Use of Nanotechnology for the Treatment of CVDs

4.1. Targeted Drug Delivery System

A variety of delivery systems exists for treating CVDs. Drug carriers showing non-toxic attributes together with immune system evasion capacity and biodegradability with compatibility to biological conditions and immune system non-triggering ability and targeted drug delivery functions are considered the ideal properties. Different parameters such as PH, temperature, enzyme activity and stimuli and more enable the achievement of targeted drug delivery systems (X. Cheng, Xie, & Sun, 2023). Nanoparticles of polymeric and liposomal structures have diagnostic and therapeutic abilities by incorporating multiple drugs into their structures while other nanoparticles need to combine functional ligands before drug binding. The drug targeting process along with stability enhancement and improved surface ratio requires surface modification of nanoparticles through functional agents including peptides and aptamers and antibodies and so on (Pang et al., 2024).

4.2. Nanoparticles

4.2.1. Magnetic Nanoparticles

Due to distinct properties and diverse applications, improvement in synthesis strategies of metal nanoparticles emerged as a field of prime interest in material science (Abid EK et al. (2025). These particles created to target particular receptors in tissues are close to go through clinical trials for CVD purposes. Their biocompatibility, superparamagnetic, nonorange mass and surface covering properties allow selective attachment for site-specific delivery. Superparamagnetic iron oxide nanoparticles (SPIONs) are appropriate for in vivo observing of the stem cells due to their exceptional magnetic properties (Lapusan, Borlan, & Focsan, 2024). Modified SPIONs were injected into random sections of the preenacted region to transport the cells into the damaged portion of myocardium devoid of open chest surgical treatment. An FDA-approved SPION, ferumoxytol (which is an intravenous (IV) iron product substitute utilized to cure anemia) doubly conjugated with anti-CD45 and with antibodies located in damaged cardiomyocytes. The double antibody conjugated nanoparticles aided elevated affinity attachment of cells to damaged cardiomyocytes equally in vitro and in vivo. The attained outcomes report that this method can cure severe myocardial infarction (Konnova & Rozhina, 2024).

4.2.2. Gold Nanoparticles

Gold nanoparticles are usually inert materials that are made up of gold particles of the size of 1-100nm. They have their applications in drug delivery and molecular labelling because of their properties such as easy to synthesize, high Surface plasmon resonance (SPR), high absorption capability, low immunogenicity, low cytotoxicity, stability, biocompatibility and their ability to bind with targeted materials (Jayeoye et al., 2024). They decompose in proper environment once they reach targeted sites and are renally excreted through the body. They have efficient antioxidant properties that help them to deal with cardiovascular diseases. The photo thermal property of gold nanoparticles helps in the diagnosis of photo thermal revascularization of blocked arteries (Sabir et al., 2021).

The drug delivery effectiveness of clinical drugs leaps forward when gold nanoparticles come into play for conjugation purposes because Simdax shows enhanced coronary disease treatment along with Metoprolol becoming more effective for cardiac tissue delivery after coupling with gold nanoparticles. The diabetic cardiomyopathy therapeutic treatment involves miR155-AuNPs or gold nanoparticle antagonist (Iravani & Varma, 2022). Different target sites exist for gold particles that possess diverse dimensions. Gold nanoparticles measuring below 200 nm penetrate and accumulate within the ischemic muscle tissue using their enhanced permeability and retention effect that enables medication delivery to exogenous growth factors for recovering substantial volumes of ischemic tissue (Georgeous, AlSawaftah, Abuwatfa, & Husseini, 2024). The size reduction of infarcted hearts occurred through PEGylated gold nanoparticles (10 nm size) that prevented necrosis and apoptosis in cardiomyocytes because PEG coating increases hydrophilicity and stability in circulation time. Studies demonstrate that gold nanoparticles find medical applications in CVD including photo acoustic imaging that functions as optical or ultrasound imaging as well as electrochemical detection and diagnosis alongside photothermal therapy (Georgeous et al., 2024).

4.2.3. Solid Lipid Nanoparticles

These submicron solid lipid nanoparticles known as SLN include two main components: a solid lipid substance with sizes ranging from 10 to 1000 nm together with surfactants used for stabilization (Klein et al., 2022). The drug obtains uniform dispersion through surfactants that ensure stability within these carriers. They provide a space for encapsulating high drug doses of hydrophilic substances as well as lipophilic compounds and nucleic acids making them adaptable drug delivery platforms (Ly, Cordoba, Blackburn, & Shi, 2024). The bioavailability of hydrophobic molecules benefits from two successive drug release phases. The nanoparticles incorporate different chemical

groups for controlling delivery methods along with stimulus-triggered medication release. These nanoparticles demonstrate potency as drug carriers for both coronary ailment treatment and cancer therapies together with pulmonary and oral medication delivery (Dominiak, Czarnecka, Czylkowska, & Szymański, 2024).

Scientific research demonstrated clinical benefits of using solid lipid-based nanoparticles with carvedilol (β adrenergic receptor blocker) to enhance bioavailability for treating peripheral artery diseases through medicating hypertensive drugs (Dominiak et al., 2024). SLN nanoparticles that combine iron oxide nanoparticles with prostacyclin demonstrate platelet-aggregating reduction which makes them useful for atherosclerosis theranostics. A patent was registered for efficient treatment of coronary heart disease through traditional Chinese medicine combined with solid lipid nanoparticles (Gu et al., 2025).

4.2.4. Polymeric Nanoparticles

The fundamental goal of cardiovascular disease treatment focuses on the ability of polymeric nanoparticles (NPs) to show adjustable characteristics together with body absorption capacity. Polymeric NPs serve two functions by staying either attached or free as new substances (F. Yang, Xue, Wang, & Diao, 2022). Polymeric nanomaterials incorporating polyester with carbon nanotubes (CNTs) improved their electric conduction properties causing increased strength for enhanced cell-cell connection applications in CVD treatment (Gil-Cabrerizo, Simon-Yarza, Garbayo, & Blanco-Prieto, 2024). The nanodrug distribution system uses Polymeric Poly (lactic-co-glycolic acid) PLGA NPs to influence monocyte-derived irritation in atherosclerosis (figure 2). The effectiveness of Polymeric Poly (lactic-co-glycolic acid) PLGA NPs as drug delivery system is supported by the fact that they enfold pioglitazone while also significantly decreasing the amount of fibrous caps and enlarging fibrous caps (Sabir et al., 2021).

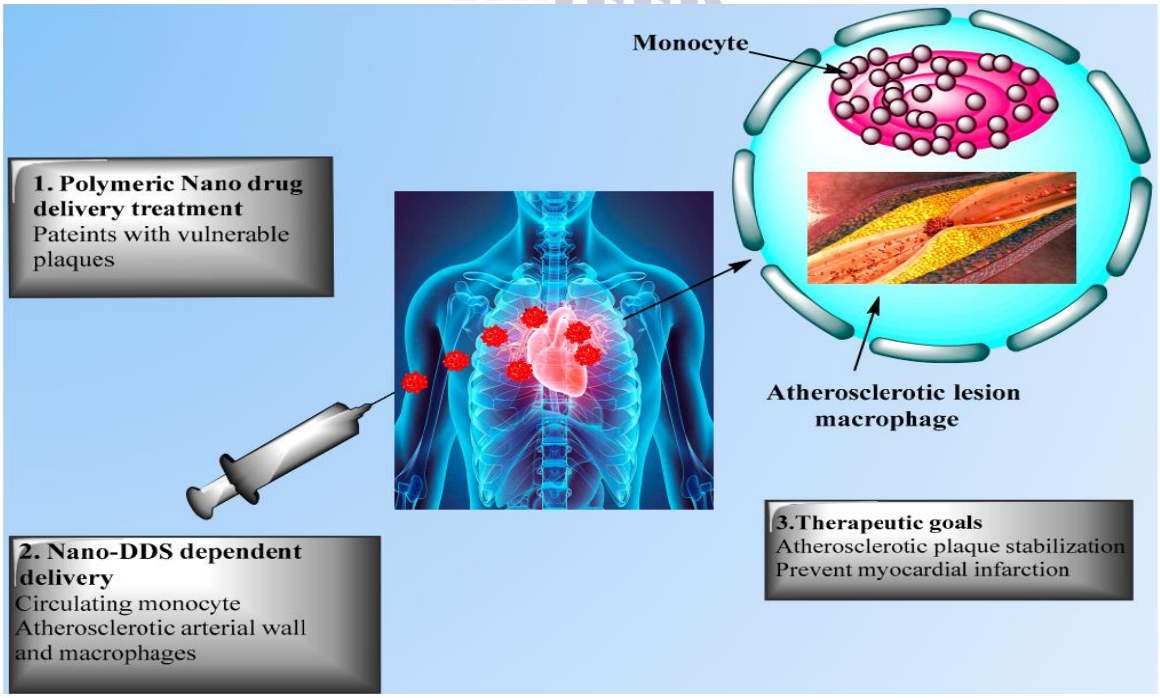

Figure. 2. Nanodrug delivery systems facilitated cure for severe coronary disorder. The Figure shows nanodrug delivery system facilitated cure for patients with unreliable plaque through (1) intravenous injection (IV) plus (2) distribution to mingling monocytes, with (3) healing aim consisting atherosclerotic plaque balance and inhibition of severe myocardial infarction (Sabir et al., 2021)

4.2.5. PEG-Based Nanoparticles

Polyethylene glycol (PEG) is a biocompatible material often coated on the surface of nanoparticles (NPs), which enhances circulatory lifetime of the drug delivery system. A smooth conductive hydrogel was manufactured comprising of a multiple armed PEGDA700-Melamine (PEG-MEL) crosslinker for cardiac repair (Krishnan, Poomalai, Ravichandran, Reddy, & Sureshkumar, 2024). The PEG-MEL could cross-linkage with thiol-altered hyaluronic acid to make an injectable hydrogel quickly. To enhance the therapeutic capability of the hydrogel, adipose tissue-developed stromal cells (ADSCs) were included (figure .3). After an infusion in the myocardial infarction region in a rat, general improvement of heart function was noted (Skourtis, Stavroulaki, Athanasiou, Fragouli, & Iatrou, 2020).

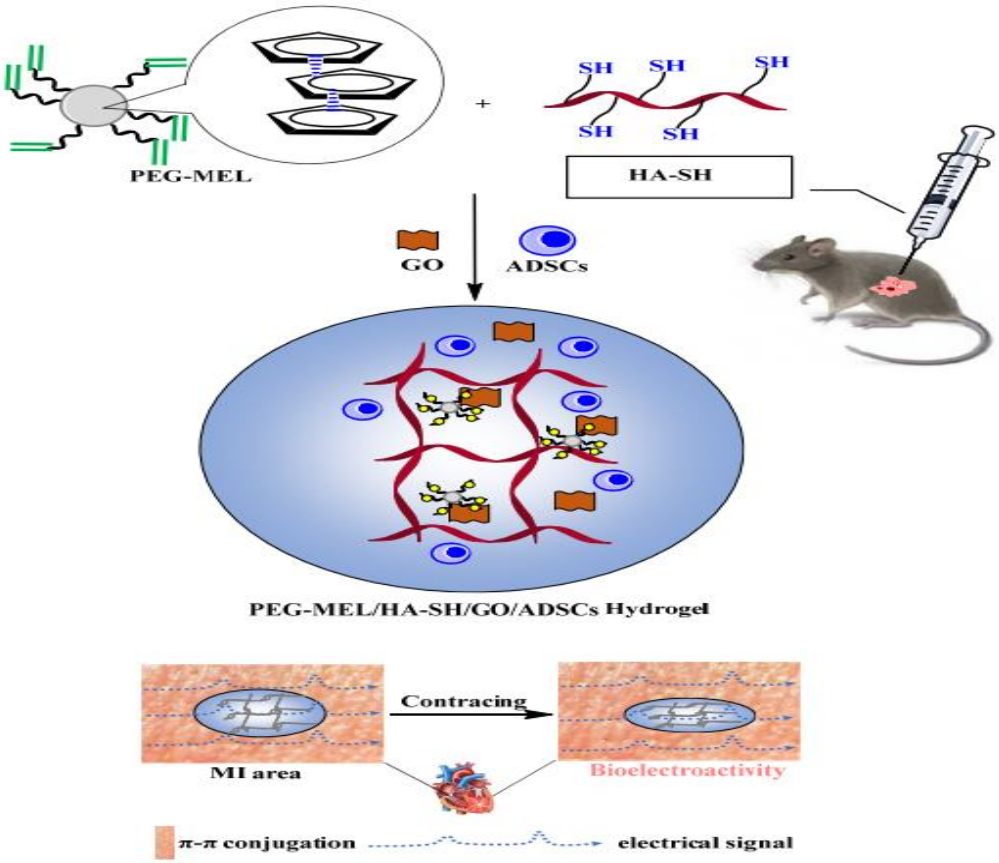

Figure. 3. Diagram showing the function of PEG-MEL/HASH/GO based nanoparticle hydrogel system including ADSCs for heart restoration by shot into the myocardial infarction region of rats, with the aim of improving the spread of automated and electric indicators to restore cardiac function (Skourtis et al., 2020).

4.3 Nanocarriers

4.3.1. Chitosan Nanoparticle & Hydroxypropyl Methyl Cellulose Nanoparticle

The linear polysaccharide called chitosan demonstrates biodegradability and biocompatibility as its main features. Controlling targeted medication delivery and drug release at specific locations is possible with this material. The usage of chitosan enhances drug stability because it protects medications from acid breakdown. The incorporation of chitosan strengthens the stability of drugs that have poor

solubility issues in antihypertensive medication. The drug release control at specific sites can be managed through the use of hydroxypropyl methyl cellulose as a non-ionic water soluble cellulose derivative (Yu, Liu, Jin, & Jiao, 2023).

4.3. 2. Liposomes

The vesicle structure of liposomes contains bilayer phospholipids with dimensions ranging from 50–200 nm. Research shows the vesicles can exist in different structural forms due to varying lipid molecule dimensions and chemical makeup and elasticity. Liposomes contain analogies of structure that have both hydrophobic and hydrophilic characteristics which enable them to serve as effective delivery systems (L. Yang, Mei, Qiao, Chen, & Xu, 2025). Scientific research has demonstrated that drug compounds embedded inside liposomes create a therapeutic approach which results in lower toxicity than typical free drug treatments for cardiovascular disorders. Surface modifications of liposomes can be achieved through PEG coating or targeted delivery through antibody or other targeting chains attachments for improved biological system residence (Rane et al., 2024). Liposomes have many therapeutic applications, function as therapeutic agents for peripheral artery disease patients and patients dealing with intermitted claudication. The systems show significant value but their short-term stability issues result in premature drug discharge. The technique requires using larger ratios of excipients to drug components leading to increased production costs which makes it less effective compared to polymer-based systems per study (X. Wang et al., 2024).

4.3.3. Micelles

The amphiphilic polymeric micelle structure forms aggregate solutions when their dimensions measure <100 nm in size. The drug encapsulation area inside micelles remains hydrophobic while the outer shell provides hydrophilic properties to increase circulation duration. The administration of therapeutic water-soluble compounds through micelles stands as the most promising treatment method for CVDs drug delivery systems according to (Y. Zheng et al., 2024). The dynamic structure of polymeric micelles represents an advanced drug delivery system because it supports multiple drug loading possibilities and targeted ligand attachment and reduces dissolution rates (Yuhao Liu, Chen, Liu, Guan, & Lu, 2023). An excellent drug delivery system which exhibited sensitivity to oxidative atherosclerotic plaque microenvironment was presented in 2018. Block co-polymer micelles composed of poly-ethylene glycol and poly-propylene-sulphide (PEG-PPS) served to solubilize andrographolide while decreasing both inflammatory response and reactive oxygen species levels for atherosclerosis therapy (Dizaj et al., 2019).

4.3.4. Dendrimer nanostructures

The dendrimer molecular structure features compartmentalized branching structure that exhibits exceptional solubility characteristics along with high precision distribution and minimal antigenic traits and enhanced durability properties. The size ranges of dendrimers are from 1–5 nm. A spherical form of synthetic dendrimers results from polymerization operations to create internal voids inside the molecular structure (Ahmadi Kamalabadi, Kazempour, Fatemidokht, Molazadeh, & Koosha, 2024). Their drug delivery function receives support from exceptional drug encapsulation capabilities. When used as a platform for conjugation with biocompatible compounds dendrimers enable the achievement of high permeability together with reduced toxicity. Doctors can implement various modification strategies to achieve higher therapeutic delivery accuracy of drugs (Zhuo, Zhao, & Zhang, 2024). Polyamide-amines represent the primary dendritic molecules which contain nitric oxide as a free radical variety. The drug delivery capability of vascular smooth muscle makes this compound useful for various CVDs applications. The storage of cardiac functions was enhanced by using siRNA-based oligo-arginine conjugated dendritic delivery systems to silence ATIR expression in cardiomyocytes through improved siRNA internalization in these cells (Y. Zhang & Tian, 2024). Dendrimers serve as adaptable nanocarriers which assist in anti-thrombotic protection and cardio-protection

through delivery of drug-resistant hormone mimetic compounds. The high number of surface branches on dendrimers generates toxicity risks due to their exceptionally cationic or anionic nature according to (Kashyap et al., 2023).

4.3.5. Carbon Nanotubes

High aspect ratio of CNTs is accountable for their effective drug loading capability and regulated drug delivery to the target area. CNTs are effective to stimulate neonatal rat ventricular cardiomyocyte (NRVM) spread, development, and enhanced electrical performance. Multi-walled carbon nanotubes (MWCNTs) created close connections with NRVM cell membranes are found by conducting transmission electron microscopy (figure. 4) (R Amin et al., 2020). This discovered the ability of CNTs as biocompatible probes for uses in cardiomyocyte study. Highly refined single walled CNTs had no lethal consequences on the H9c2(2-1) rat cell line as noticed by an assessment of cell increase and sustainability vs. programmed cell death and of structural variations under light microscopy, encouraging additional work for CVD diagnosis and therapy (Novikov et al., 2025).

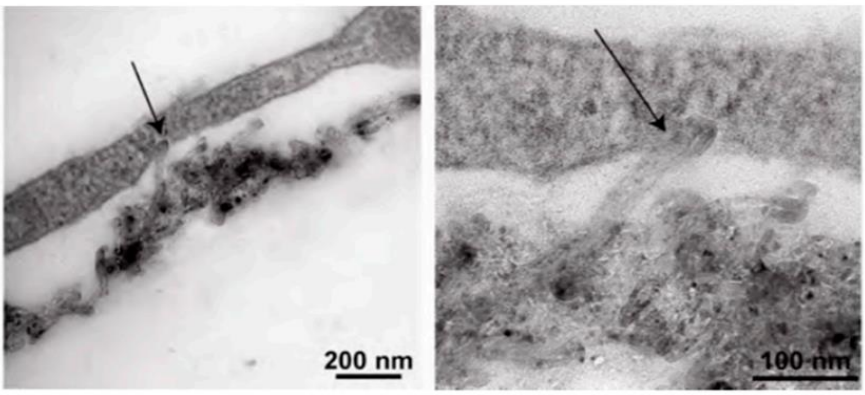

Figure. 4. Association of CNT with cardiac myocyte membranes (arrows). The figures exhibit a close interaction among the CNT and cardiomyocyte cell membrane (R Amin et al., 2020).

Table. 3. Nanocarriers studied for the Efficient Treatment of Cardiovascular Diseases.

Types of Nanocarriers	Drugs used in the treatment of CVDs	Biological Functions	Limitations of the Drugs	Advantages of Nanoplatforms	References
Liposomes					
Liposomal nanoparticles coated with PEG	Prednisolone phosphate	Best for atherosclerotic disease	Short half-life in circulation	Increase the drug's half-life to 45–63 hour in humans	(Shi et al., 2021)
Naked liposomes and water-soluble double emulsion polymer	Streptokinase (Streptase)	Plasminogen activators	Shows immunogenic effect and severe bleeding complications	Minimize reperfusion time, infarct size and less hemorrhage	(Koroleva, 2023)
PEGylated Liposomes, with a peptide sequence of	Recombinant tissue plasminogen activator (rtPA, (alteplase))	Plasminogen activators	Short half-life of rtPA	Improved thrombolytic activity	(Farrokhi & Gkikas, 2024)

fibrinogen gamma chain					
Metallic Nanoparticles					
Gold	Vascular endothelial growth factor (VEGF)	Severe hindlimb ischemia is treated	Short half-life of VEGF in circulation	Targeting rate is high	(Ceylan, Kırbay, Yazgan, & Elibol, 2024)
Gold	Mesenchymal stem cells (BMSCs) derived from bone marrow	Potentiates the cardiogenic differentiation of stem cells	Control ability to differentiate into multiple lineages	Enhanced cellular and functional effects on the regrowth of infarcted myocardium	(C. Xu et al., 2023)
Gold	Levosimendan (Simdax)	Inotropic agent Contraction of myocardial is increased in heart failure related patients.	Preferential targeting Simdax to the target heart tissue decreased	Having vital cardio protective effects in rats with doxorubicin-induced heart failure	(Susilo et al., 2024)
Silica Nanoparticles					
Polymeric superparamagnetic nano-silica	Quercetin	Antioxidant agent, quercetin is used to control atherosclerosis	Poor water stability	Allowing cell attachment, expansion, and circulation of heart proteins in local myocardium	(El Naggar, Soliman, Noor El-Din, Ramadan, & Youssef, 2022)
PEGylated mesoporous-silica	Puerarin	Best for the treatment of cardiovascular diseases	Short half-life in human High doses of puerarin.	Improved blood compatibility with low hemolysis	(Keshavarz, Taib, & Iravani, 2023)
Polymeric Nanoparticles					
Poly (lactide-co-glycolide) (PLGA)	Glutathione and Heparin	Antioxidant and anticoagulant agent used for vascular therapy	Systemic coagulopathy, toxicity and hemorrhage symptoms	Delivery to the area of an Ischemia/reperfusion injury	(Baek, Lee, & Kim, 2024)
Dendrimer	Hirudine	Antithrombotic and	Short plasma half-life, generates	Transfer gene to thrombosis and its treatment	(Xuechun Wang, Shukla, &

		anticoagulant agent	permanent hirudin-thrombin complex		Gupta, 2022)
Micellar	Hirudine	Natural thrombin inhibitor	Short plasma half-life	Stop the formation of fibrin clots after coronary artery occlusion	(Shariati et al., 2023)
Polymeric micelles	m-Tetra (hydroxyphenyl) chlorin (mTHPC)	Anti-inflammatory agent	Side effects and other off-target effects	Increased stability and thus allow accumulation of intact mTHPC- to macrophages of atherosclerotic lesions	(Udriṣte et al., 2024)

4.3.6. Graphene and Its Derivatives

Graphene derivatives feature both hydrophilic (water-loving) and hydrophobic (non-water loving) drug loading features alongside extensive surface areas and localized drug delivery capabilities. The drug loading capabilities of GO and rGO exceed other graphene-based biomaterials thus making them preferred as drug transporters. Blockages in blood vessels appear as an important warning sign that comes from atherosclerosis (Alanezi et al., 2024). Therapeutic angiogenesis stands as an effective treatment which enables new blood vessels to generate from previous blood vessels. The therapeutic effects of Vascular endothelial growth factor (VEGF) result from solvable component capabilities that drive new blood vessel formation in ischemic cardiac tissue (illustrated in figure. 5). Researchers used VEGF functionalization with GO to improve both the half-life duration and distribution of VEGF for boosting angiogenesis in ischemic muscle tissue (Ahmad et al., 2024).

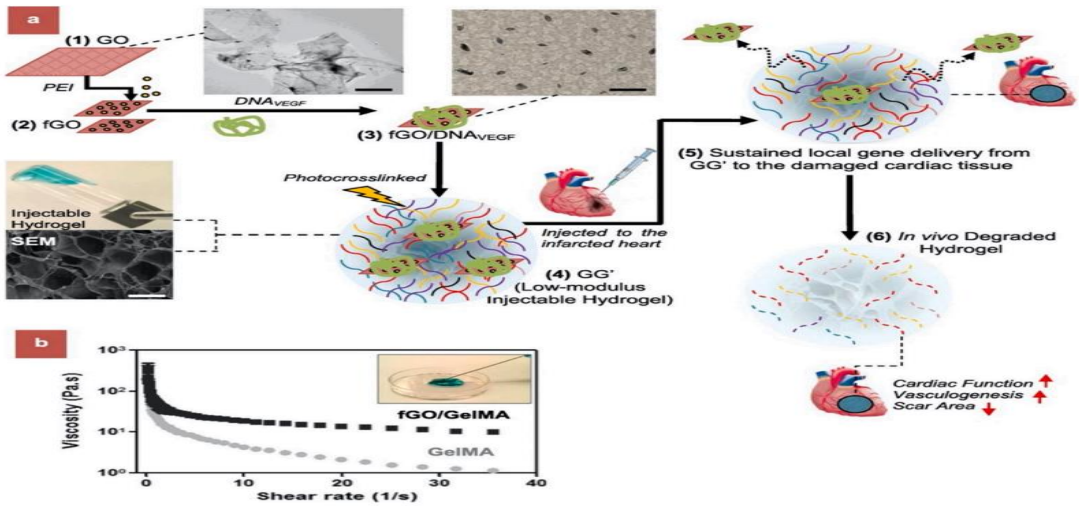

Figure. 5. Formulation of injectable hydrogel for severe myocardial infarction treatment. (1) The first procedure begins by applying Polyethyleneimine to GO nanosheets while forming cationic functionalized GO (fGO). (2) The fGO breakthrough stage leads to DNAVEGF anionic plasmid modification resulting in the formation of fGO/DNAVEGF products. (3) The UV cross-linking process creates Gel-MA hydrogel from the previously generated fusions. (4) The procedure involves the production of low modulus hydrogel

(GG′) with the combination of fGO/DNAVEGF that is operationally injectable. (5) The local gene administration of combined fGO/DNAVEGF nanocomplexes for the damaged cardiac tissue. Hydrogel degradation within the body promoted myocardial vasculo-genesis in order to reduce cardiac damage areas while enhancing cardiac functioning (Alagarsamy et al., 2021).

5. Self-Emulsifying Drug Delivery System

The development of lipid-based drug delivery systems tries to enhance absorption rates of lipophilic pharmaceuticals. The pharmaceutical formulation known as self-emulsifying drug delivery systems (SEEDS) represents one type among these formulations. SEEDS consist of natural as well as synthetic oils and solid/liquid surfactants or hydrophilic solvents that mix into isotropic solutions (Salawi, 2022). The absorption and availability increase for drugs due to SEEDS while they defend the drug against harmful conditions in the gut environment. The system produces nano-emulsion droplets inside the gut while following the lymphatic route to reach the target. SEEDS maintain prolonged stability throughout time while offering convenient handling properties (Hsieh, Yang, Putri, & Chen, 2023).

5.1. Nano Emulsions

Formulation of nano emulsions to enhance therapeutic effectiveness and protection of antihypertensive medications, many other formulations can be created utilizing nanotechnology. For instance, the formulation of curcumin in a nano emulsion structure with the objective of lowering its undesirable solubility and bioavailability (Yu et al., 2023). The curcumin nano emulsion demonstrated improved ACE retardation contrasted with natural curcumin. This discovery proves that the curcumin nano emulsion structure has enhanced bioavailability and solubility (Preeti et al., 2023). Preparation of protein filled Perfluorocarbons (PFCs) nano emulsions is used to deliver therapeutic proteins to heart for the therapy of cardiac disorders. Perfluorocarbons (PFCs) are inert substances with great biocompatibility and solubility (Davoodbasha et al., 2024). In vivo findings demonstrated that the protein filled Perfluorocarbons nano emulsions(PNEs) effectively supplied proteins to the myocardial muscle of mice and decreased ischemic myocardial damage produced by severe myocardial infarction (Qin et al., 2021).

5.2. Nanoparticle Drug Eluting Stents

The present stent technologies have some limitations such as formation of in-stent restenosis, which can be improved by using nanotechnology. It can be used for prevention of smooth muscle cell proliferation by anti-restenosis strategy and restoring functional endothelium by pro-healing strategy (Davoodbasha et al., 2024). Anti-restenosis strategy prevents in-stent neointima formation by nanoparticles assisted delivery of anti-proliferative and anti-inflammatory agents or by heat induced death of inflammatory cells using light/radiation activated nanoparticles (Islam et al., 2024). The pro-healing strategy involves reendothelialization, by using nanofibrous scaffold which act as extracellular matrix, enhancing the cells proliferation under the stent in presence of magnetic field by using magnetic nanoparticles. In order to achieve these strategies, stents are coated by biodegradable polymeric blends and nanoparticles to forms drug eluting stents, which can act as drug carriers (Senst, Goyal, Basit, & Borger, 2023).

5.3. Hydro gels

Hydro gels are Hydrophilic polymeric networks capable of absorbing large volumes of biological fluids that facilitate controlled drug-release. Because of their high biocompatibility they are used as attractive drug delivery vehicles (Filimon, Onofrei, Bargan, Stoica, & Dunca, 2023). They can bind with various moieties such as nanoparticles, slabs, microparticles, coatings and films. External stimuli such as hydrolytic, enzymatic or environmental stimuli are sufficient to control the hydrogels to release drug at the desirable site (Xinming Wang et al., 2023). The major issue in this includes toxicity which occurs

after the degradation of hydrogels by residual monomer, cross-linker and catalysts. There are distinct material-based hydrogels used in percutaneous coronary intervention (PCI). These strategies help in the recovery of damaged cardiac tissues while in some severe cases implantation of ventricular assist devices is required. Although hydrogels have shown their ability to be used in PCI but it still lack the required mechanical strength, enzymatic activity and bioactivity (Saxena & Pandey, 2020).

6. Applications

6.1. Application of Nanotechnology in CVD Diagnosis

AS exists as one of several heart and blood vessel diseases under CVDs because it causes arterial narrowing and hardening from buildup of lipid and inflammatory plaque material. The development of AS depends on macrophages together with tissue factors and platelets which make suitable targets for diagnostic imaging methods that avoid invasive procedures (Himasa, Singhal, Ojha, & Kumar, 2022). During early AS development the formation of foam cells made by macrophages after ox-LDL consumption stands vital for plaque development and tissue inflammation. Tissue factors along with platelets support local blood clotting which accelerates disease advancement (Ghosh, Chowdhury, & Patki, 2024). Platelets achieve stable plaques by releasing bioactive compounds that induce vascular inflammation and promote expansion of smooth muscle cells from the vessel wall (VSMCs). Researchers believe that targeting macrophages tissue factors and platelets with nanoparticles has the potential to boost diagnosis technologies for CVD (Tahir et al., 2024). The phagocytosis of SPION-based contrast agents makes arterial wall plaques easier to visualize because they cause signal loss in T2-weighted imaging (Filimon et al., 2023). SPIONs receive targeting fragments including dextran and osteo bridging protein (OPN) that allow them to bind precisely with macrophage surface epitopes while prompting vulnerable aortic and carotid artery plaques to cluster their macrophages (Kang, Tahir, Wang, & Chang, 2021). Research has shown that SPIONs targeting monocytes in plaques can be achieved by encapsulating MCP-1 motifs on their surfaces. Higher darkness levels appeared in Vivo tracking of aortic tissues after the researchers fed the subjects a high-fat diet demonstrating MCP-1 motif magnetic nanoparticles may serve as effective AS plaque targeting agents. The T1-weighted imaging contrast improvement with Gd-DTPA administration showed an increased proportional relationship to plaque-specified macrophage numbers. The medical application of Gd-DTPA remains uncertain because it demonstrates risk factors toward developing nephrogenic systemic fibrosis (Gastelum-Leyva et al., 2022). PET provides an outstanding technique to detect macro phage mediated CVD inflammation because it combines deep tissue penetration with high sensitivity as an examinational tool. The specificity problem of the 18F-FDG radiotracer being non-macrophage specific together with the false-positive signals caused by cardiomyocyte uptake can be solved with nanoparticles containing 18F-labeled polyglucans and 89Z-labeled nanoparticles (Himasa et al., 2022). PET with 68Ga-labeled nanoparticles detects the CVD biomarkers VCAM1 MMR and LOX1 at specific levels but remains unable to show anatomical imaging. The technique frequently operates jointly with CT or MRI as part of diagnostic procedures. Research by Tu et al showed the potential of their MMP2cNPs to function as PET-MRI contrast agents for detecting MMP-2 presence in AS plaques through their study (C. Tang et al., 2024).

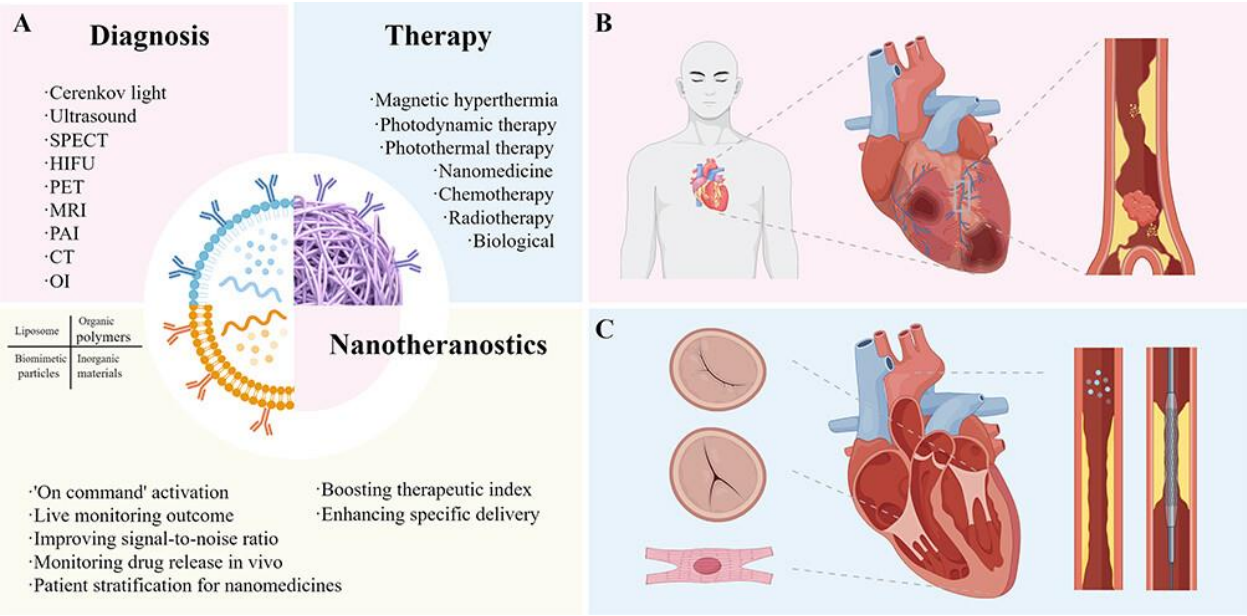

Figure. 6. Overview of nanotechnology in CVD.

Nano theranostics serves diagnostic along with therapeutic functions while being employed for CVD management. **(A)**Traditional diagnostic and treatment procedures merge with four types of nanocarriers including liposomes, organic polymers, biomimetic particles and inorganic materials. **(B)** Nanoparticles can directly enter the body to stop or reduce atherosclerosis development because this condition represents the main cardiovascular disease leading to death. **(C)** Heart valve, myocardial patch and vascular stent functionality can be enhanced through nanotechnological applications which can also be delivered directly to the body (C. Tang et al., 2024).

Abbreviations: SPECT is single photon emission computed tomography, **HIFU** is high-intensity focused ultrasound, **PET** stands for positron emission tomography, **MRI** describes magnetic resonance imaging, **PAI** is photoacoustic imaging, **CT** indicates computed tomography and **OI** signifies optical imaging.

6.2. Nanotechnology application in CVD Treatment

Three fundamental processes drive CVD progression starting from myocardial injury and inflammation and following valvular and structural problems and electrical problems. Research using nanomaterials allows scientists to develop heart patches along with heart valves and vascular grafts and stents through properties enhancement for efficiency and durability and extended service capability. Nanomaterials prove useful for treatment of ischemia-reperfusion injury through intravenous and intracardiac direct injections (D. K. Wang et al., 2021). The heart needs artificial repair after myocardial injury through implantable and injectable and nanofiber or nanopatterned stent cardiac repair materials. These materials enhance the healing process of tissues (Mohamed, Marei, Crovella, & Abou-Saleh, 2022). A perfect regenerative biomaterial should replicate native tissue functionality through combined properties that include electrical conduction capabilities with growth factor discharge and cell nestling functions along with non-immunogenicity features and structural strength and prolongevity rather than focusing on firmness maintenance alone (Hu et al., 2022). Existing biomaterials do not possess multiple necessary physicochemical and structural properties based on research findings according to existing research. Nanomaterials offer solutions to resolve these limitations when used for cardiac regenerative medical applications (Li et al., 2023).

Such materials serve to extend growth factor supply over time for stem cells and other cells while they address natural heart tissue stability needs and duplicate cardiac syncytia electrical properties (Nguyen, Iqbal, Block, & Mousa, 2023). The albumin electro spun fiber structure combines with gold nanorods to produce an infrared light absorption that generates heat to perform secure and safe heart tissue welding which enhances its conductivity abilities and promotes efficient electrical cell coupling without causing typical cardiac patch suturing adverse effects on myocardium. These days manufacturing and precision demand from CVD biomaterials makes 3D-printed CVD biomaterials very appealing (Smith & Edelman, 2023).

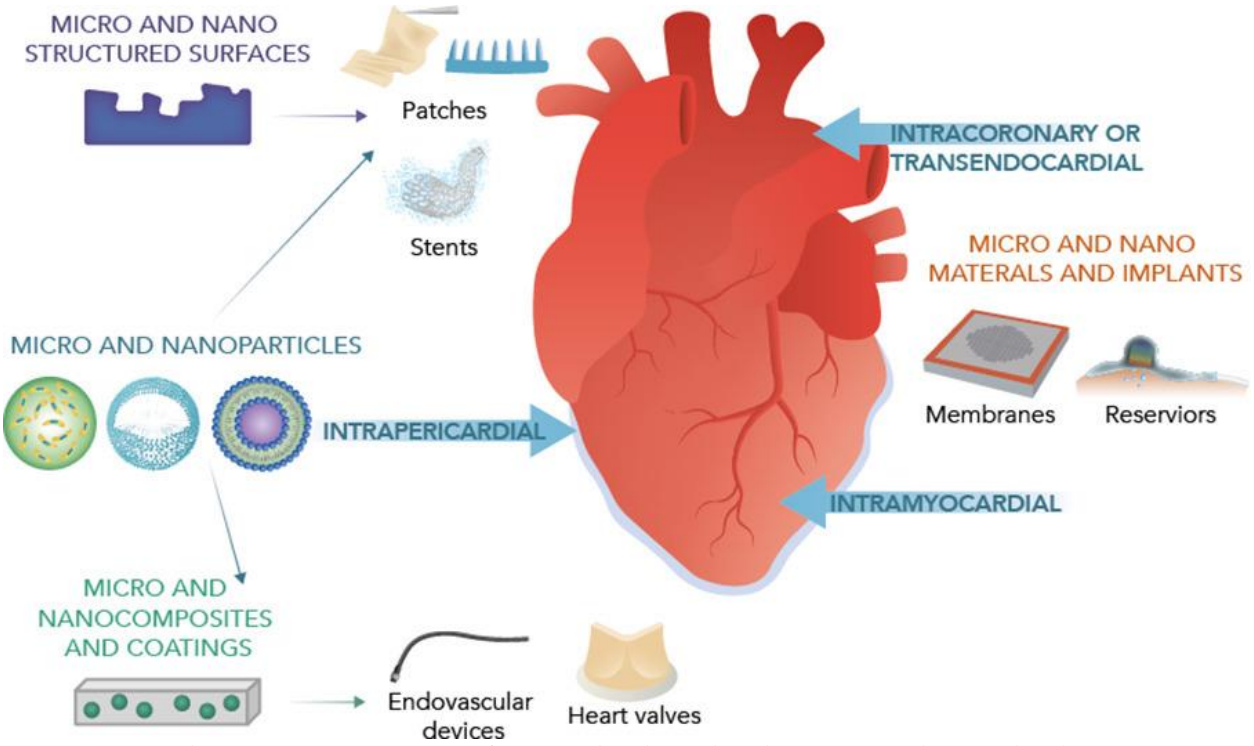

Figure. 7. Schematic representation of nanotechnological inclusion in cardiovascular disease (D. K. Wang et al., 2021).

Adding nanomaterials to 3D bioprinter inks enables the reproduction of human heart tissue with optimal functionality through simulation of three essential biological functions: contractility, conductivity and thermal regulation. The creation of functional heart valve implants remains a critical problem even though research has delivered notable advancement toward TEHV construct functionality (Tzounis & Bangeas, 2022). Nanomaterials supply several different solutions that can enhance both heart valve implants safety performance and their mechanical properties alongside longer product lifespan. The use of nanomaterials for valve surfaces efficiently blocks biomolecule interaction while sustaining drug release to decrease valve calcification and immune response (D. K. Wang et al., 2021). The valve surface receives biomimetic nanomaterials derived from erythrocyte membranes through chemical bonding for treating surfaces previously soaked with harmful glutaraldehyde that leads to valve degeneration and immunogenicity. The anticoagulant and anti-calcification effects improve after the valve surface receives nanocoating and the implant becomes deendothelialized. Jet spinning technology produces human-sized valves from polymeric gelatin nanofibers mixed with extracellular matrix

(ECM) to achieve both excellent biocompatibility and functionality (Ullah et al., 2024). The fabrication process uses fast-fabrication techniques.69 In addition to that the new nanotechnologies enable tissue-engineered valves to become more effective through creation of multi-scale porous structures. Natural heart valves possess properties that change directionally based on stress application (Z. Zheng et al., 2022). The creation of anisotropic nanostructures together with microstructures enables developers to construct necessary multidimensional biomimetic anisotropy needed for in vivo performance. Utilization of intravascular injection represents the primary administration method for nanomaterials involved in vascular diseases treatment (C. Tang et al., 2024).

7. Current Challenges

Biocompatibility together with potential cytotoxicity represents a main difficulty when implementing nanotechnology to treat cardiovascular diseases. Nanoparticles interact with cells and molecules through molecular-level processes thereby causing unexpected physiological effects on human health (Narkhede, Pardeshi, Bhagat, & Dharme, 2024). Research has proven that silver nanoparticles together with quantum dots produce reactive oxygen species (ROS) that create oxidative stress along with lipid peroxidation and mitochondrial dysfunction and apoptotic cell death in both cardiomyocytes and endothelial cells (C. Tang et al., 2024). The activation of macrophages together with the complement system during inflammatory responses initiated by nanoparticles contributes to tissue destruction instead of repair mechanisms. Academicians and researchers face an essential challenge to develop nanomaterials which can be safely broken down by the reticuloendothelial system (RES) through the liver and spleen while maintaining non-immunogenic properties (D. K. Wang et al., 2021). Nanoparticles that persist within liver tissues alongside kidneys and lungs threaten to create unexpected toxic results requiring detailed in vivo and clinical testing. The major obstacle in nanoparticle synthesis and functionalization lies in achieving reproducible uniform standards. Shot-term nanoparticle effectiveness depends strongly on four fundamental characteristics combining size, shape, surface charge and attached functional ligands (Hu et al., 2022). Kinds of nanoparticle synthesis methods including co-precipitation and sol-gel synthesis and emulsion polymerization create variations in physicochemical properties which leads to different drug release patterns and targeting precision among nanoparticles (N. Wang, Chen, Ren, & Dai, 2024). The absence of standardization makes it complicated to gain regulatory approval because Good Manufacturing Practice (GMP) must guarantee identical results between different production batches (Z. Zheng et al., 2022). Nanoparticle biodistribution in biological fluids becomes diminished because protein corona formation (plasma protein adsorption to NP surfaces) causes aggregation. The main barrier to overcome today involves creating trustworthy, efficient production techniques which preserve nanoparticle endurance and operation capabilities during conditions found in biological environments (Gonnah & Roberts, 2024).

The implementation of nanotechnology in cardiovascular medicine faces hurdles from ethical standards along with government regulations. The unpredictable biological system interactions of nanoparticles operating at nanoscale require extensive research of PK and PD effects including evaluations of ADME profiles (Syahputra et al., 2024). The U.S. Food and Drug Administration (FDA) together with European Medicines Agency (EMA) still need to develop common approval frameworks for nanomedicines which results in delayed clinical directives. The safety of patients and long-term observations of treated individuals along with the study of nanoparticle-induced DNA damage must be prioritized by addressing ethical concerns (Jawaid et al., 2025). The challenge of equal access to nanomedicine stands as a socioeconomic barrier because advanced treatments tend to be available mostly to high-income populations primarily. Widespread adoption of nanotechnology in CVD treatment faces great obstacles due to both its expensive nature and low scalability capabilities (J. Khan,

Yadav, & Alam, 2025). Liposomes and dendrimers along with polymeric nanoparticles and mesoporous silica nanoparticles (MSNPs) require advanced engineering processes which cost a lot of money and take considerable time for synthesis. The production of large quantities of targeted drug delivery systems necessitates both dedicated specialized infrastructure and specialized expertise to achieve cost affordability (Chen, Yu, Gong, & Shan, 2025). Economic feasibility of nanomedicine presents substantial hurdles to developing nations since they continue using conventional cardiovascular treatments including angioplasty and statins along with beta-blockers (Shariati et al., 2023). New medical infrastructure needs nanotechnology implementation together with nanotoxicology testing along with biosafety assessments and healthcare worker training enabling it to become operational but this necessitates major budget resources. Making nanoparticles less costly to create and improving biodegradable polymers specifically poly (lactic-co-glycolic acid) (PLGA) for efficient drug packaging combined with the development of nano diagnostic technology at patient access points will make nanomedicine more accessible and sustainable for cardiovascular disease management (P. Yang, Ren, & Yang, 2023).

The research on nanomaterial-based biosensors targeting heart failure biomarker NT-ProBNP encounters issues in repeatability along with sensor component development and molecule binding attachment methods (Omran et al., 2022). Nanomaterial biosensor performance depends heavily on the consistency of their synthesis process since variations in dimensions together with shape and surficial properties lead to performance changes. Appropriate biocompatible connection through antibodies or aptamers enables biosensors to maintain their selective binding capabilities (Addissouky et al., 2024). Biosensors need proper functionality in biological media such as blood or serum which requires effective handling of interferences and sample stability issues. The advancement of nano biosensors for clinical usage depends on multidisciplinary research that unites material scientific expertise with biochemistry and engineering fields to achieve proper accuracy and reliability (Y.-Y. Lee et al., 2024).

Addressing these challenges requires a multidisciplinary approach, combining expertise in biotechnology, materials science, pharmacology, and biomedical engineering. Continued research into surface modifications, functionalized nanocarriers, and personalized nanomedicine strategies will be essential in overcoming current limitations and ensuring the safe and effective application of nanotechnology in cardiovascular healthcare (Y.-Y. Lee et al., 2024).

8. Future perspectives

Nanomaterial-based biosensors represent an upcoming revolution in cardiovascular diagnostic technology since they provide exceptional detection capabilities for the essential heart failure biomarker NT-proBNP. Scientific advances will rely on deploying specific nanomaterial varieties including customized metallic nanoparticles and quantum dots alongside graphene derivatives because these materials demonstrate exceptional sensor properties which boost detection both sensitivity and selectivity (Panda, 2024). The nanomaterials demonstrate superior electric properties as well as optical functionality for detecting minimal levels of NT-proBNP biomarker through their sensitive detection mechanism. The next stage of development includes uniting these biosensors with wearable technology. The system intends to develop uninterrupted wearable monitoring of NT-proBNP that delivers vital cardiac data immediately for quick clinical choices (Batta, Patial, Sobti, & Agrawal, 2024). A rising priority exists to integrate sophisticated computational tools that include artificial intelligence alongside machine learning algorithms into sensor systems. The expected outcome from these techniques involves modernizing biosensor data analysis for more accurate diagnosis and discovering brand new biomarkers which indicate heart failure pathology (Parhi, Jena, Patra, & Jammula, 2025). Nanoparticle-based monitoring solutions need optimized biocompatible and stable materials for

their effective use in prolonged diagnostic applications (Y.-Y. Lee et al., 2024). The development of affordable biosensors for point-of-care diagnostics represents a critical need because it will expand sophisticated cardiac diagnostic technologies throughout underdeveloped healthcare facilities (Bargieł et al., 2021). Next-generation biosensors enabled by nanomaterials will revolutionize their operational potential which positions them as basic healthcare tools for individualized proactive cardiovascular care. Researchers achieved a major progress in cardiovascular medical diagnosis when they developed these advanced diagnostic tools using nanomaterial-based biosensors (Thupakula, Nimmala, Ravula, Chekuri, & Padiya, 2022).

Clinical medicine should focus mainly on CVD detection and treatment capabilities. The combination of nanotechnology with multifunctional agent generation permits simultaneous execution of detection and treatment capabilities. The advantages of this method include determining where agents go and how they work and release mechanisms within the body. The application of nanomedicine strategies shows clear potential to transform current medical practices for CVD treatment through diagnostics and therapy procedures (Netala, Teertam, Li, & Zhang, 2024). Current research has dedicated itself to illustrate diverse fabrication approaches and formulation methods for nanomedicine in this field. The majority of these reports use either preclinical small animal model in vivo research or in vitro experiments. Future clinical tests will determine the ability of this method to predict cardiovascular events (Narkhede et al., 2024).

Many of the preventable factors which contribute to CVD continue to produce rising CVD incidence numbers. The combination of dangerous eating patterns with saturated fats, trans fats, and cholesterol alongside inactive lifestyle patterns and alcohol and tobacco consumption leads to CVD development (Gonnah & Roberts, 2024). More attention from researchers needs to be focused on nanotechnological approaches that detect risk factors early because of increasing tobacco use rates. cation and treatment. Heart disease monitoring improvements through nanotech-enabled wearable trackers that provide continuous heart parameter measurements along with physical activity tracking and dietary intake monitoring while monitoring sleep activities (Elsaygh, Zaher, Parikh, Frishman, & Peterson, 2024). Nanotech-based handheld exam kits that help patients in heart sound examination for abnormalities or nanotech sensors supporting medication adherence can be other options to achieve this focus. Nanoscale structure manipulation enables this technology to develop fundamental applications for device enhancements and detection performance improvement (Li et al., 2023). Nanomaterial-based sensor technologies enable early identification and continuous tracking of symptoms while nanoscale switches and remote-control mechanisms strengthen disease prevention methodologies and heart tissue treatments benefit from nanotechnology-powered molecules and therapeutic agents that deliver specific interventions over time (Guo et al., 2023). New medical technologies must be developed to prevent and treat cardiovascular events because CVDs represent the more costly healthcare condition; this leads to enhanced life quality with increased years of healthy as well as healthcare equity for CVD (D. K. Wang et al., 2021).

Conclusions

The entire world faces Cardio vascular diseases (CVDs) as the top death-causing group thus demanding improvements to both diagnostic systems and treatment methods. Standard treatments including pharmacotherapy and surgery help manage CVDs yet these methods restrain management through medical side effects and drug tolerance and surgical invasiveness. Nanotechnology integration with cardiology reveals a new methodological approach because it enables precise drug delivery and improved imaging quality combined with real-time medical observation capabilities. The three components of nanomedicine exemplified by nanoparticles and nanocarriers together with biosensors deliver a superior diagnostic and therapeutic system that improves the accuracy and minimizes invasiveness for CVD care. The delivery of nanotechnology to

cardiovascular medicine encounters important hurdles which involve compatibility with biological tissues as well as safety issues and manufacturing consistency and government recognition and price affordability. Nanomaterial applications need multidisciplinary teamwork and controlled fabrication approaches together with clinical trial procedures for achieving successful and secure utilizations. Sensor development targeting cardiac biomarkers such as NT-ProBNP needs better technologies for nanomaterial production as well as biofunctionalization methods and stable sensing mechanisms in biological solutions.

Future cardiovascular healthcare will undergo revolution because nanotechnology-based therapeutics and diagnostics continue to receive dedicated research and innovation. Future research must prioritize advancements that improve safety standards and reduce costs and scale up applicability of nanomedicine for clinical adoption. Continuous development in technology enables nanotechnology-based solutions to advance patient recovery rates and minimize cardiovascular disease prevalence worldwide.

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