IJARSCT
International Journal of Advanced Research in Science, Communication and Technology
International Open-Access, Double-Blind, Peer-Reviewed, Refereed, Multidisciplinary Online Journal
ISSN: 2581-9429
Volume 6, Issue 4, January 2026
Impact Factor: 7.67

Biodegradable Polymeric Nanoparticles for Targeted Therapy in Cardiovascular Diseases- A Comprehensive Review

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Abstract: *Cardiovascular diseases remain the leading cause of global mortality, driven largely by atherosclerosis and modifiable risk factors such as hypertension, dyslipidemia, diabetes, and lifestyle behaviors. Despite advances in pharmacological therapies, there is a growing need for improved drug delivery and continuous monitoring strategies. Recent developments in biodegradable polymeric nanoparticles offer targeted, sustained, and biocompatible drug delivery, while biodegradable materials also enable innovative cardiac tissue engineering and implantable devices. This review highlights current CVD pathology and management, and introduces a biodegradable, multifunctional cardiac monitoring system capable of sensing pressure, pH, lactate, and volatile organic compounds. Integrated with AI-driven analytics and wireless communication, this platform enables personalized, real-time cardiovascular assessment, representing a promising direction for next-generation cardiovascular care.*

Keywords: Biodegradable Nanoparticles, Targeted Therapy, Cardiovascular Diseases

I. INTRODUCTION

The cardiovascular system comprises the heart and blood vessels, and a variety of conditions can affect it, including endocarditis, rheumatic heart disease, and conduction system abnormalities. Cardiovascular disease (CVD), or heart disease, generally refers to four main categories:

Coronary artery disease (CAD): Also known as coronary heart disease (CHD), this occurs when reduced blood flow to the heart muscle leads to angina, myocardial infarction (heart attack), or heart failure. CAD accounts for roughly one-third to one-half of all CVD cases.

Cerebrovascular disease: Encompasses conditions such as stroke and transient ischemic attack (TIA).

Peripheral artery disease (PAD): Involves arterial narrowing in the limbs, often causing pain with walking (claudication).

Aortic atherosclerosis: Encompasses aneurysm development in the thoracic and abdominal segments of the aorta[1].

EPIDEMIOLOGY:

Cardiovascular diseases (CVDs) remain the foremost cause of death globally. In 2022, they were responsible for an estimated 19.8 million deaths, accounting for about 32% of all global deaths, with heart attacks and strokes making up 85% of these cases. Low- and middle-income countries account for over three-quarters of all CVD deaths. Among the 18 million premature deaths from non-communicable diseases in 2021 (those occurring before age 70), at least 38% were due to CVDs.

DOI: 10.48175/IJARSCT-31054

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Most cardiovascular diseases are preventable by addressing behavioral and environmental risk factors, including tobacco use, unhealthy diets high in salt, sugar, and fats, obesity, physical inactivity, harmful alcohol consumption, and exposure to air pollution. Early detection of CVD is crucial, as timely counselling and medical treatment can significantly improve outcomes [2].

RISK FACTORS:

A higher probability of developing cardiovascular disorders, such as:

- High blood pressure (hypertension)
- High cholesterol (hyperlipidemia)
- Tobacco use
- Type 2 diabetes
- A genetic predisposition due to family heart disease[3][4]
- Physical inactivity
- Hyperhomocysteinaemia
- Stressful behavioral pattern
- Heavy alcohol use
- Misuse of medicinal or recreational drugs
- A history of preeclampsia or toxemia
- Environmental influences
- Persistent inflammatory or autoimmune conditions
- Homocystinuria [3] [5].

PATHOPHYSIOLOGY

Coronary artery disease (CAD) is primarily driven by the development of atherosclerotic plaques within the coronary arteries, leading to progressive luminal narrowing and impaired myocardial perfusion. Plaque formation begins with endothelial injury, which permits the migration of circulating monocytes into the subendothelial space. These monocytes differentiate into macrophages that ingest oxidized low-density lipoprotein (LDL), forming lipid-laden foam cells and creating fatty streaks—the earliest visible lesion of atherosclerosis[6][7].

Sustained inflammation promotes the activation of T lymphocytes and the release of cytokines, stimulating vascular smooth muscle cell (SMC) migration and proliferation. SMCs contribute to extracellular matrix deposition and lipid accumulation, resulting in plaque growth and fibrous cap formation. Over time, plaques may undergo calcification, influencing their stability[6][8].

Hemodynamically significant stenosis typically develops when luminal narrowing exceeds 70%, producing exertional angina due to reduced coronary blood flow. Severe narrowing or plaque rupture with superimposed thrombosis can cause acute coronary syndromes, including unstable angina, non-ST elevation myocardial infarction (NSTEMI), and ST-elevation myocardial infarction (STEMI).

Plaque stability is closely associated with calcification patterns. Stable plaques generally exhibit thick fibrous caps and macrocalcifications, whereas unstable plaques are characterized by thin caps and microcalcifications, which increase mechanical stress and the risk of rupture, leading to myocardial infarction [6][9].

MANAGEMENT

Recent advances in cardiovascular pharmacology in 2022 include the approval of several first-in-class drugs that open new therapeutic pathways, such as mavacamten for obstructive hypertrophic cardiomyopathy, tirzepatide for type 2 diabetes mellitus, and sodium–glucose cotransporter 2 inhibitors for heart failure regardless of ejection fraction[5][10].Progress was also made with fixed-dose combination therapies that repurpose established medications—such as acetazolamide plus loop diuretics for acute decompensated heart failure, moderate-dose statins plus ezetimibe for atherosclerotic disease, angiotensin receptor blockers plus β-blockers for Marfan syndrome, and low-dose aspirin,

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ramipril, and atorvastatin for secondary prevention—addressing knowledge gaps and expanding treatment options. Additional clinical trials reinforced the benefits of dapagliflozin in heart failure with mildly reduced or preserved ejection fraction, long-term evolocumab for reducing cardiovascular events, vitamin K antagonists for stroke prevention in rheumatic heart disease–associated atrial fibrillation, antibiotic prophylaxis before invasive dental procedures for high-risk patients, and vutrisiran for hereditary transthyretin amyloidosis with polyneuropathy. Finally, emerging evidence indicates that FXIa inhibitors may decouple thrombosis from hemostasis,offering protection against thromboembolic events with minimal bleeding risk.[10][11]

BIODEGRADABLE DRUG DELIVERY SYSTEM

Biodegradable polymeric nanoparticles have emerged as valuable platforms for controlled drug delivery. Through surface functionalization, they enable precise targeting of specific cells or tissues, reducing off-target effects. These systems can also provide sustained drug release, helping maintain therapeutic concentrations at the desired site. Encapsulating drugs within nanoparticles improves their solubility, stability, and overall bioavailability—particularly useful for compounds with poor water solubility. In addition, the nanoparticles protect the drug from premature degradation, preserving its activity until it reaches its target. Because the polymers used are biocompatible and degrade into non-toxic byproducts, they offer a safe delivery option. Their design flexibility further allows customization to meet the requirements of different drugs and clinical applications. Overall, biodegradable polymeric nanoparticles represent an auspicious, promising approach for controlled drug delivery, combining targeted delivery, sustained release, enhanced bioavailability, and safety. Ongoing research is expected to expand their potential across a range of biomedical fields[12].

The advantageous properties of biodegradable polymers— including tunable degradation rates, controlled porosity, excellent biocompatibility, and elastomeric behavior capable of withstanding the contractile forces of cardiac tissue—have made them highly attractive for cardiac tissue engineering. These materials allow scaffolds to preserve critical mechanical integrity during tissue development, gradually degrade into non-toxic byproducts, and efficiently incorporate cells, growth factors, and other bioactive agents.

Biodegradable polymers can be broadly classified into natural and synthetic categories. Natural polymers originate from biological sources, while synthetic polymers are manufactured through human-engineered processes, often using petroleum-derived materials. Each type presents unique advantages and limitations in cardiac tissue engineering. To capitalize on their complementary properties, composite scaffolds combining natural and synthetic polymers are widely used across a range of cardiac tissue applications.

Natural polymers, valued for their biodegradability, renewability, and broad availability, have been widely applied in tissue engineering. In cardiac tissue engineering specifically, commonly used natural biodegradable materials include fibrin gel, collagen, gelatin, chitosan, alginate, and Matrigel [13].

Under normal physiological conditions, blood pH is maintained within a narrow range of 7.35–7.45. Values rising above 7.55–7.80 or falling below 6.80 can signal life-threatening disturbances. Such deviations may lead to metabolic alkalosis or acidosis, contributing to a range of disorders, including arrhythmias, cardiac dysfunction, muscular complications, and even certain cancers. Another critical biosensing parameter is lactate, a key biomarker associated with muscle inflammation and various cardiac diseases. Elevated lactate concentrations—typically exceeding 1.5–2.0 mmol/L—are strongly correlated with an increased risk of heart attacks, heart failure, and other cardiovascular complications.

In this review, we present a novel strategy for developing a multifunctional, biodegradable, and biocompatible cardiac monitoring system. The platform is designed to detect pressure, lactic acid, pH, and volatile organic compounds (VOCs). An AI-driven predictive model integrates these sensor readings to generate a personalized “health barcode,” providing a comprehensive overview of an individual’s cardiac condition. Owing to the fully biocompatible and biodegradable nature of its components, the device offers a safe and effective solution for both clinical evaluation and long-term monitoring.

The sensor array is highly flexible, straightforward to fabricate, and accurately calibrated to detect cardiac abnormalities by monitoring multiple physiological parameters. To validate its practical utility, ex vivo experiments

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were conducted using a 3D-printed silicone heart model and 3D-printed cardiac tissue patches, simulating realistic physiological conditions. Furthermore, the system was integrated with IoT and wireless communication technologies, such as Bluetooth and RFID facilitate seamless data transmission to computers or smartphones. [14]

Cardiovascular diseases remain a significant global health challenge. Despite steady progress in cardiovascular biomedical implant technologies, continued innovation is essential to improve therapeutic outcomes. Integrating Nano particulates drug carriers into implantable stent systems offers a promising approach for enhancing treatment effectiveness. [15]

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