Review Article

RECENT ADVANCES IN NANOMATERIALS FOR THERAPY AND DIAGNOSIS IN CARDIOVASCULAR DISEASE

ABSTRACT

Cardiovascular diseases (CVDs) are among the world's widely affected disorders, including ischemia and stroke. Acute Myocardial ischemia (AMI) is a deadly disease caused by irreversible damage to the left ventricular heart tissues. The thromboembolic plaque occlusion, the main blood vessels which provide the oxygen to working ventricles, stopped. During chronic inflammation, myocardial infarction and free radicals damage stable myocardium, smooth muscles cell, and epithelial cells caused by Outer membrane loss and ventricular wall smoothing and dilation. Specially constructed scaffolds made of biological and nanoparticles have been created to shield the left ventricle from further injury and recover ischemic endothelial cells. Preclinical experiments have demonstrated that scaffolds containing growth factors and cells will regenerate ischemic tissue into a stable pericardium in good working order. Various medicinal approaches that treat cardiovascular disease conditions at different stages are discussed in this review article, with biomaterials receiving special attention. This paper further addresses the manipulation and manufacturing of biomedical implantable devices using nanomedicine methods and drug delivery principles. The use of graphene and exosomal nanovesicle in cardiovascular therapeutics recently progressed in research studies.

Keywords: CVDs, nanoparticles, cardiovascular therapeutics, myocardial infarction, biomedical implantable devices

1. INTRODUCTION

Cardiovascular disorders (CVDs) damage the heart and blood vessels. It encompasses both circulatory and respiratory system disorders, including peripheral artery disease. In the United States, Coronary heart disease and stroke are two of the most common causes of death. Cardiovascular disorders are one of the leading causes of disease worldwide, according to the World Health Organization (WHO)[1-2]. As a result, more successful therapies for CVDs are needed. Nanotechnology, described as the study of materials at the atomic, molecular, and supramolecular levels, has shown promise in the field of CVDs. Nanotechnology is known as the application of nanotechnology to biological structures to prevent, identify, heal, or restore injured cells [3-7]. It is becoming increasingly important in the treatment of cardiovascular diseases. Nanoparticles, or nanometric particles, have shown significant promise in various cardiovascular applications. Nanoparticles, or nanometric particles, have shown significant promise in various cardiovascular applications [8-10]. Nanoparticles are mobile in intravascular and extravascular environments. It is suitable for delivering therapeutics and imaging agents to particular sites. Because of their unusual multi-functionality, it has demonstrated considerable potential and provided a medium for targeted drug delivery [11]. Nano-coatings are nanotechnology developments that improve the bioavailability of surgical devices and their integration with the surrounding

tissues. This technique can be used in orthodontic treatment, cardiac stent coating, and orthopedic joint repair implants [12-13].

2. STRATEGIES FOR BIOMATERIALS

The advent of next-generation nanomaterials has revolutionized cardiovascular therapies at the preclinical stage, going to treat vascular ischemia as well as coronary artery stenosis. About 125,000 surgical devices were made at the molecular level and tested during clinical trials [14]. Physical interactions in the physiological environment can differ significantly based on the bioresorbable polymer's chemistry. Various polyesters, such as poly-(lactic acid), poly-(lactic-co-glycolic acid), and poly-(tyrosine)-derived polycarbonates, have been approved by the Food and Drug Administration for use in the manufacture of vascular scaffolds [15]. Thrombus clotting is the main coronary artery. A significant activation step contributes to pathological disorders such as hypoxia, CM necrosis, left ventricular wall thinning, and cardiac remodeling. Thus, in turn, it results in an asthma attack or a heart attack in chronic patients. Furthermore, applying the patch from xenogeneic origin may result in an extreme inflammatory response; the immune system then rejects the reaction [16]. Earlier, Stainless steel, titanium alloys, and cobalt-chromium alloys dominated the first wave of cardiovascular materials. As a result, synthetic polymers such as polyesters, polyurethanes, polyamides, and poly tetra fluoroethylenes have progressively replaced metal alloys over time. Novel polymers for cardiovascular applications are increasingly developed and have outstanding based nano characteristics [17]. Nature's inertia in the face of biotechnology of synthetic polymers, on the other hand, not only protects them from adverse biochemical functions but also prohibits them from promoting bio-responsive reactions [18]. For building a uniform surface layer of a polymeric cardiovascular scaffold, microbial substances may be mechanically immobilized or conjugated by organic compounds. Biological materials for the bio-responsive property include development factors, extracellular matrix (ECM) molecules, anti-coagulant heparin, and thrombomodulin [19-20].

Vascular endothelial growth factor (VEGF), essential fibroblast growth factor (bFGF), hepatocyte growth factor (HGF), stromal cell-derived factor-1 (SDF-1), insulin-like growth factor1 (IGF-1), platelet-derived growth factor, granulocyte-colony stimulating factor (G-CSF), angiopoietin, periostin, and neuregulin are growth factors enhanced the bio-responsive properties of scaffold [21-25]. Collagens, elastins, fibronectins, fibrillins, lamellins, and nephronectin are ECM molecules shown to aid bio-responsive properties. There is a need to have a deeper understanding of cardiac tissue changes during physiological and pathological conditions such as cardiac ischemia and heart failure [26-27].

2.1 Clinic-based therapeutic recovery methods and their drawbacks

To a certain extent, pharmacological treatments strategies can help decrease the pathological load of cardiovascular diseases. However, they prevent the healing or regeneration of weakened myocardial tissue. Myocardial tissue is a type of tissue found in the heart. Currently, repairing patches originating from small intestinal tissue is an advanced treatment procedure used in hospitals to treat left ventricle (LV) dilation and aneurysm involved with heart failure. Bovine/porcine pericardium covers the ischemic region [28]. The protected patch acts as a functional shield to prevent further LV thinning and preserves cardiac function. Furthermore, the xenogeneic nature and biodegradability of such patches in-vivo systems pose significant difficulties. This review covers a broad range of biological and non-biological biomaterials employed in the management and treatment of CVDs, summarized in Table 1.

Table 1. Biomaterials for cardiac tissue engineering (recently updated) cardiac tissue engineering biomaterials

Biomaterials	Utilized Technology	Outcomes
Heparin-based coacervate fibrin gel • Polycation: poly(ethylene argininylaspartate diglyceride) • Polyanion: Heparin Proteins: TIMP-3 or FGF-2 and SDF-1a are some of the proteins that have been identified.	Coacervate-gel composite system	Cardiomyocyte revascularization, stem cell preservation and homing [29]
3D collagen gel Cells: • Human cardiac microvascular endothelial cells • Human MSCs.	Collagen carrier acquired from the market (Viscofan Bioengineering, Weinheim, Germany).	Creation of a new blood vessel and regeneration of new cardiomyocytes [30]
Fibrin patch - fibrinogen with thrombin Cells: Iron oxide nanoparticles labeled bone marrow-derived mesenchymal stem cell	thrombin-fibrinogen mask	The epicardially implanted cells lasted 21 days after being implanted. The effectiveness is dependent on the paracrine function of bone marrow mesenchymal stem cells (BMMSC) [31]
Chitosan film or polyaniline doped with phytic acid.	Surface adsorption and film casting	The patch's electroactivity was attributed to phytic acid's heavy chelation behaviour with chitosan. Surface resistivity is reduced (35.85 6 9.40 kX/sq.) [32].
Mesoporous nanoparticles tagged with H_2O_2- sensitive probe Therapeutic drug: Captopril	Nanoparticles are small objects with a high surface area.	Enhancement of the drug carrier's clinical potency Captopril release from nanoparticles according to a predetermined schedule [33].
PLA Proteins: G-CSF	Electrospinning is the process of spinning metal with electricity.	Vimentin 1 cell colonization has increased. Inflammatory resistance is reduced. ECM remodeling and the construction of new blood vessels [34].
Neuregulin encapsulated PLGA microparticles Collagen Cells: • Human adipose derived stem cells	The water/oil/water emulsion process was used to make PLGA microparticles.	Neuregulin shrinks infarcts while also encouraging cardiomyocyte proliferation. Arterioles and capillaries regrowth are supported by this supplement [35].
Multi-armed crosslinker poly ethylene glycol diacrylate (PEGDA)700-Melamine (PEG-MEL) Thiol-modified hyaluronic acid (HA-SH) hydrogel	Hydrogel with PEG-MEL/HA-SH/graphene oxide	Mechanical and conductive properties that were anti-fatigue. Mechanical and electrical signals are effectively transmitted by hydrogel [36].
Collagen scaffold Cells: • Cardiomyocytes • Smooth-muscle cells • Endothelial cells from human iPSCs	3D printing with multiphoton excitation	Cellular synchrony improved heart efficiency, reduces apoptosis and infarction size [37].

oly(E-caprolactone) fiber	Electrospinning	Scaffolds resemble with the well-organized ECM of a healthy human heart [38].

3. NANOTECHNOLOGY AIDED: MYOCARDIAL SCAFFOLDING MANUFACTURING

The use of nanotechnology to fabricate scaffolds results in a unique nano-topography closely resembles that of Endothelial natural tissues. These nano-enriched scaffolds can revolutionize cardiac tissue engineering when combined with stem cells. The electrospinning technique allows for mixing biological and synthetic polymers to create nanofibrous structures [39]. Electrospinning poly-(lactide-co-caprolactone) and poly-(ethyl oxazoline) to build a nanofibrous scaffold results in a heterogeneous fiber distribution with an average diameter (500 to 700 nm and 50 to 200 nm) [40]. The microscopic observation of collagen fibrils observed in the left ventricle myocardium tissues of foetal and newborn rats matched this unique nano-architecture perfectly. When comparing the cardiac performance of the simultaneous development factor scaffolds inserted group to the non-loaded and polytetrafluoroethylene groups, echocardiography and ECG analyses revealed better cardiac function in the double growth factor scaffolds transplanted organizations. Smooth muscle actin staining was also used to validate molecular proof of neovascularization in the implanted area [41], the treatment hierarchy overlay for CVDs, represented in Fig. 1.

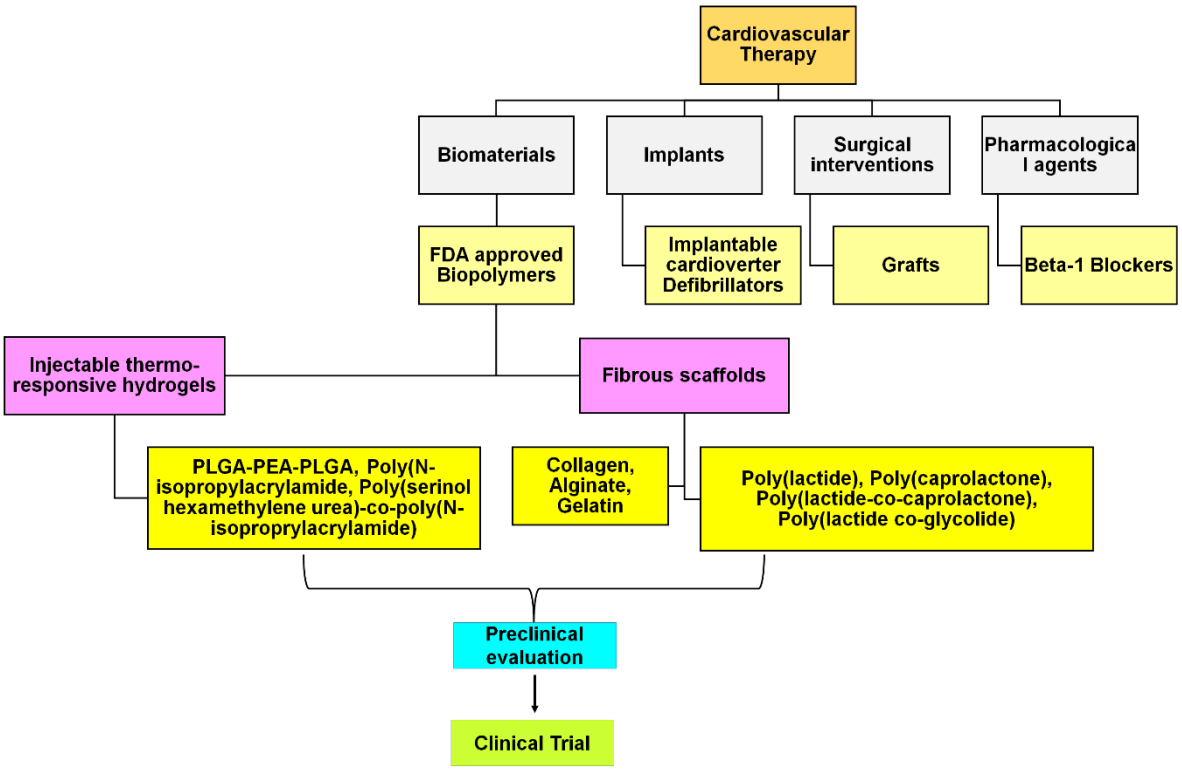

Fig. 1: The overall hierarchy of treatment modalities currently available to cure cardiovascular disorders.

4. SYSTEMS OF NANOPARTICULATES FOR THE TREATMENT AND DIAGNOSIS OF CVDs

Because of their unusual multi-functionality, nanoparticles have shown great promise in providing a medium for selective drug delivery. Nanoparticles' most significant properties are their ability to deliver and target drugs to their targeted sites.

4.1. Nanomaterials with targeted drug delivery to treat cardiovascular diseases (CVDs)

Biodegradable polymers including poly(lactide), copolymers (PLGA), poly(-caprolactone) (PCL), poly(lactide-coglycolide) and poly(amino acids) have been used to make a variety of polymeric nanomaterials for drug delivery [42]. CVDs have also been stated to use these types of nanoparticles as a delivery mechanism. In an ex-vivo arterial model, Labhasetwar et al. investigated the efficacy of nanopolymeric drug delivery systems for the treatment of venous thrombosis in 1997 [43]. A cationic agent was used to modify the surfaces of the poly (lactide-coglycolide) (PLGA) polymeric nanoparticles. The arterial absorption of surface coated nanoparticles was found to be ten times greater (10-fold) than that of non-coated nanoparticles in this study. They discovered that arterial uptake was size dependent, with small diameter particles (ca.100 nm) penetrating the ex-vivo model of the dog carotid artery better than large diameter particles (200 nm). When the artery was not cleaned, they found that 26% of the nanoparticles were retained; moreover, washing with Ringer's solution resulted in a 6% reduction in retaining nanoparticles, showing that the stent surface nanoparticles can be washed away through vascular flow [44].

Quercetin, as an antioxidant, has been shown to protect against cardiovascular disease. According to a recent study by Giannouli et al., PLGA loaded with quercetin showed promising efficacy for atherosclerosis prevention, with strong encapsulation efficiencies and appropriate drug release results, suggesting their potential to defend against CVDs. Their team is investigating the ability of these particles in vitro and in vivo [45].

4.2 Cardiovascular diseases management with Traditional formulation vs. new Nanomedicine.

This study discovered a large number of nanomedicine products (Table 2) that have been licensed for use in humans with CVDs. Since medical industries are so closely regulated, it's impossible to extrapolate these figures explicitly. Swings in the economy and regulatory mechanisms have an impact. There are, however, few clear developments in nanomedicine's potential. The field's relative adolescence is a recurring theme throughout. The issue of persistence is one of the main questions about the application of nanotechnology in the body. Traditional therapeutics are usually ingested by the body and the residues are excreted immediately after delivery. Although some nanoparticles have demonstrated persistent in vivo deposits that can last months or years.

Table 2. Nanomaterials and Conventional formulations for CVD treatment [46].

Type of drug	Drug	Conventional formulation	Nanomaterials
Lipid increasing	Isosorbide monohydrate	40 mg Monoket retard pill (Adeka, Turkey) Monodur 60 mg pill (Astra Zeneca, Canada)	Monisolmicropellet capsule 60 mg (Zorka, Russia) -Monitanmicropellet capsule 60 mg (Wyeth, Canada)-Mono corax micropellet capsule 60 mg (corax,

			Germany)
Anti-hypertensive	Diltiazem hydrochloride	Diltiazem ampoule 25 mg (Mustafa Nevzat, Turkey).	60 mg Altiazem SR micropellet (Nobel, Turkey) - 60 mg Dilatam SR micropellet (Abic, Israel) - 60 mg Coramil SR micropellet (Sanofi, Sweden)
Lipid increasing	Phenofibrate	Lipidil tablet 200 mg (Fournier, Germany, Canada) Lipofene tablet 200 mg (Teofarma, Italy)	Lipofene SR micropellet 250 mg (Nobel, Turkey) Feno-micro micropellet 250 mg (Apotex, Hungary

4.3 Diagnostics of CVDs using nanomaterials:

Nanoparticles can be used in CVD diagnostics (Fig. 2) because they target specific dangerous sites for detection. One example is the use of nanoparticles in the early identification of atherosclerosis. Nahrendorf and colleagues achieved this aim by using mono-crystalline magnetic nanoparticles (MNPs) for the noninvasive detection of vascular cell adhesion molecule-1 (VCAM-1), an indication of inflammation. The multivalent MNPs functionalized with a peptide to target VCAM-1-expressing cells in their research. The MNPs can detect the presence and severity of inflammation, offering valuable information, the ability to diagnose atherosclerosis in its early stages [46].

Magnetic resonance imaging (MRI) diagnosis has also been improved using nanoparticles. They can be used as ideal contrast agents for MRI because of their targeting capacity. Imaging the rejection site during rat cardiac allogeneic transplantation is effective for this technique [47]. The signal produced by macrophages successfully labeled with magnetic particles indicated the degree and position of rejection. Some analogous technologies are used to determine inflammatory and foreign body reactions in various other cardiovascular-related disorders in the future to identify macrophages [48-51].

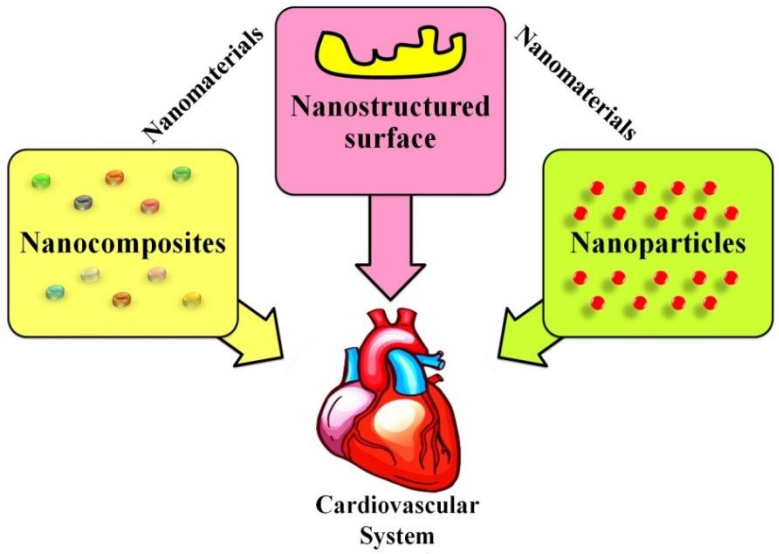

Fig. 2: Nanomaterials used for CVDs treatment.

5. NANOMATERIALS FOR CVDs DEVICES

In recent decades, nanotechnology-based systems have opened up new possibilities for developing new devices to handle CVDs. A stent is a tubular tube that protects a part of a blood vessel or some other anatomical lumen while preserving its patency. Balloon angioplasty was the most popular option for bypassing blocked artery arteries until the advent of coronary stents as bare metallic stents [52]. However, platelet aggregation, vascular smooth muscle cell migration, elastic recoil, and, finally, thrombus formation can all occur due to balloon angioplasty and stent placement [53]. It can be resolved by modifying the stent surface and adding medicinal agents to the mix. Different instruments used in the cardiovascular sector. A special combination of nanomaterial ensures cost-effective design, efficient operation, and long-term degradability without adverse effects. There are two basic approaches for the use of nanomaterials in CVD-related applications. The first method is nano-coating, which improves the biocompatibility and integration of medical implants with surrounding tissues. Another factor that enhances implants' electrical, electronic, and biological characteristics is nanostructured materials to replicate naturally occurring structures.

6. NANOMATERIAL TOXICITY

Nanoparticle toxicity may be more critical than other materials due to their mobility in the body. Where well-known stable, biocompatible materials are used as the matrix for nanocomposites. Despite an increasing body of literature focusing on the role of nanoparticles in cardiovascular applications, several reports have indicated that various types of nanoparticles have cytotoxic properties [54-55]. For example, ultra-small superparamagnetic iron oxide nanoparticles can cause thrombosis in-vivo, platelet aggregation, nucleic acid injury, and formed cardiac reactive oxygen species [56]. Pulmonary and coronary injuries were observed following the application of zerovalent iron nanoparticles. The enhance in oxidative danger in human A549 alveolar epithelial cells and EA. hy926 vascular endothelial cells were dead after exposure to nanostructured zerovalent iron in-vitro. This is also true for carbon nanoparticles and nanotubes (CNT), which are associated with many adverse side effects as used in biological applications. After being treated with single-wall CNT (SWCNT) or double-wall CNT, aortic endothelial cells showed a reduction in viability (DWCNT). After administration of either SWCNTs or DWCNTs to mice, increased direct monocyte adhesion to endothelial cells and initiated atherosclerosis. Other coronary conditions may be triggered by atherosclerotic plaque. After treatment with multi-walled carbon nanotubes (MWCNTs), plasma levels of acute-phase protein, a marker of cardiovascular disease, increased [57].

The toxicity profile of a nanomaterial that would be used in regenerative medicine or tissue engineering is critical. An excellent example of toxicity that could occur in extracellular and intracellular levels results in a broad spectrum of disruption in signaling cascades. Before any biomedical use, regardless of the excellent properties of any synthesized nanomaterial, a thorough assessment of its potential toxicity is needed. The field's newness should be considered, including the confirmed toxic effects of nanomaterials that act as novel incorporations of cardiovascular regenerative therapy. Further study is needed to comprehensively analyze the toxicity, especially chemotoxicity and inflammatory responses. In addition, future work should plan to introduce novel ways to reduce toxicity, represented in Table 3 [58-66] and Table 4 [67-70].

Table 3. Nanotechnologies and nanodrugs used to treat CVDs.

Drug Delivery	Nanoparticles System	Process involved	Therapeutics	Techniques utilized	Investigation

Targeted drug delivery	Iron hydroxyapatite nanoparticles in superparamagnetic properties	Oxidative process	A model medicine is ibuprofen.	Acute stimulation of isolated adult cardiomyocytes, used in rats to determine the biological effects. Involvement of electromagnetic radiation on the cardiac system in vitro and in vivo.	In both cases, no changes in cardiac electrophysiological properties, suggesting hierarchy of treatment low frequency combination of FeHAs and magnetic activation is an auspicious way for controlled release drug delivery to the failing heart [58].
Targeted drug delivery	Porous silicon NPs functionalized with atrial natriuretic peptide	Electrochemical anodization	Trisubsituted3,4,5-isoxazole	For cardiac repair in the ischemic heart, targeted drug penetration into left ventricle (epicardial surface).	In ischemic heart, increased ANP-PSi nanoparticle aggregation, especially in left ventricle (endocardial layer) results in enhanced colloidal stability and cellular interactions. Non-myocytes and Cardiomyocytes with low nanoparticle toxicity [59].
Targeted drug delivery	PLGA NPs is conjugated with anti-CD31 antibodies.	Evaporation with a paired emulsion solvent	4- hydroxyl tamoxifen	Tissue-specific antibodies allow targeted drug delivery into endothelial cells.	Increased ability to transmit targeted messages and increased uptake by endothelial cells [60].
Targeted drug delivery	Lipid nanocarriers updated with atrial natriuretic peptide.	Solvent evaporation	Prodrug of oleate adenosine	After intravenous infusion, in vivo inhibition action on infarct duration, tissue distribution, and pharmacokinetics in rats with heart muscles.	NPs have longer circulated properties than free drugs and can be targeted into the infarcted myocardium in a receptor-dependent process [61].
Diagnosis	PET-labeled magneto-fluorescent NPs that have been dextran and DTPA-modified.	Reduction of metal	-	Macrophage PET-CT imaging of inflammatory atherosclerosis.	Specificity and cellular transmission have both improved [62].
Nano structured device	Paclitaxel-eluting stent with a nanoporous matrix that is free of polymers	-	Paclitaxel is a drug that is used to treat diseases.	Endothelization and tumour cell metaplasia reduction in a porcine system	Desirable drug elution properties and targeted penetration into a nearby coronary artery [63].
Nano Coating	Magnetizable iron–platinum (FePt) alloy nanoparticles are used to coat stents.	Reduction of chemical substances	-	The magnetic stent's ability to trap stem cells for reendothelialization in vitro	High-performance capture of progenitor stem cells [64].

Nano Coating	stents with g PLA NPs coating	Electrospi nning	Dipyridam ole	Tissue engineering	Deal with artery thrombosis, an effective drug-eluting coating on stents has been developed [65].
Nano Coating	MMSNs and CNTs are used to coat stents.	Coprecipit ation	Anti-restenotic treatments	A drug-eluting two-layered polymer free-composite coating with outstanding network nano-topologies that is crack-free.	In contrast to commercial polymer-coated DES, the in vivo analysis reveals that this composite coating has the apparent benefit of rapid endothelization due to its unusual 3D nanostructured topology [66].

Table 4. Advantages nanoparticles in cardiovascular implantable systems [67-70].

Implantable devices for the cardiovascular system	Advantages
Biomedical instruments coated with nanoparticles	• Providing sustained release of drugs to reduce improvements in local opioid toxicity. • Their sub-micron and sub-cellular size accounts for their high tissue absorption. • By avoiding the use of polymers, we will achieve higher biocompatibility and lower toxicity. • Chemically labile drugs are protected by an inert shell.
Biomedical instruments with nanostructure	• Enhances biomaterial-blood or organ compatibility by simulating the sub-micron topography of internal tissue. • Endothelial cell proliferation is boosted. • The production of vascular smooth muscle cells is inhibited.

7. ATHEROSCLEROSIS LEADS TO CARDIOVASCULAR DISEASE

Marchand first used atherosclerosis to describe the association of fatty degeneration and arterial stiffness [71] and was characterized by subintima's patch intramural thickening. Fatty streaks cause clinical events causes Unstable and fibrous plaques.

Atheromas, patchy intimal plaques are signs of atherosclerosis. The lumen of medium- and large-sized arteries is the most prevalent site. Furthermore, the inflammatory and smooth muscle cells (MSCs), fibrous connective tissue, and a fat component of lipids make plaque cellular components. Hypertens3on, diabetes, dyslipidemia, obesity, sedentary living, family history, and smoking are all significant risk factors that need to be considered beforehand while treating CVD patients. Symptoms can be caused by intraplaque rupture, haemorrhage, thrombosis, or stenosis [72, 73]. Clinical diagnosis and imaging studies were used to confirm. Medications employed to treat cardiovascular disorders are antiplatelet pharmaceuticals and antiatherogenic drugs. Furthermore, the management strategy includes behavioural changes like a low-calorie diet and regular physical activity.

It is the primary cause of illness and death in the United States and the Western world. Cardiovascular disease (CVD) is still the lead mortality in the modern world and claimed the lives of 17 million people in 2008. However, more than 3 million fatalities occurred in persons under 60 years [74]. Further, in addition to this, there are rising disparities in the prevalence and outcome of CVD in socioeconomic classes.

7.1 Pathophysiology of Atherosclerosis:

Atherosclerosis is a long-term inflammatory condition. The fatty streak causes aggregation of lipid-laden foam cells in the intimal layer of the artery and characterizes it as the first sign of atherosclerosis [75]. During, initial stages of atherosclerosis, lipid retention causes persistent inflammation around arteries walls, resulting in fatty streaks, which eventually proceed to fibrous fibroatheromas (Table 5) [76,77].

Atherosclerosis is a disease that progresses over time. Fatty streaks appear nearly 11-12 years of age, and fibrous plaques appear around 15-30 years. Fig. 3 illustrates the development of the Fibrous plaque from fatty streaks [78]. The fatty streaks appear at the exact anatomic locations, indicating fibrous plaques. Further, in addition to this, the intimal thickening causes fatty streaks and fibrous cap atheromas and eventually abrupt cardiac death [79,80].

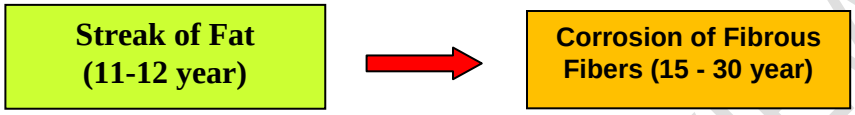

Figure 3: Fibrous plaques develop from fatty streaks.

Fatty streaks develop into atherosclerotic plaques and are made up of three parts; inflammatory cells, smooth muscle cells, a fibrous component of connective tissue, and a lipid fat component [81]. The triggering factor is endothelial injury. Endothelial dysfunction is caused by turbulent blood flow, which limits the synthesis of NO, a potent vasodilator, and promotes the creation of adhesion molecules, attracting inflammatory cells. Further, the Monocytes and T cells attach to endothelial cells and move to the subendothelial area. LDL and VLDL, two lipids found in the blood, attach to endothelial cells and oxidize in the subendothelial region (Fig. 4). Monocytes consume oxidized LDL and convert to foam cells in the subendothelial area. This is the initial step, causes fatty streak formation. Next, smooth muscle cells are recruited by proinflammatory cytokines and produced by macrophages. After this, the multiplication of smooth muscle cells occurs, which increases and thickens the extracellular matrix. The outcome is a subendothelial fibrous plaque (Fig. 4-6) with a lipid core surrounded by smooth muscle cells and connective tissue fibers [82].

The arterial layers, intima, and media are the substantial steps all involved in the study. Finally, adventitia is mentioned in the media, causing core lesions in arterial walls. An inflammatory reaction encircles a cholesterol-rich lipid core. Therefore, lipid buildup and inflammation are present in every lesson. Plaque increases arterial lumen diameter, distorts media/adventitia, and shrinks simultaneously. Vasa Vasorum is a new species that has invaded Vasa Vasorum and hemorrhage within the artery wall, caused by sick intima. Increased fibrous tissue and intramural bleeding caused thrombosis splitting, and healing occurs during the formation of thin fibrous caps. Clinically silent ruptures and repair cyclically result in many layers of recovered tissue and unexpected cardiac death. Finally, the calcium deposits as tiny aggregates in the wall and subsequently transform into prominent nodules. Thrombosis is caused by endothelial erosion, and increased plaque mass results in stenosis, leading to fatal ischemia [83].

Plaques are classified as either stable or unstable [84]. Stable plaques are regressed, remain static, and develop slowly. Further, the erosions, fissures, and tissue ruptures complicate the unstable plaques, resulting in stenosis, thrombosis, and infarction. Activated macrophages release enzymes that cause plaques to break. Further, the plaque contents are revealed during thrombosis is the consequence of blood clotting in the circulation. The thrombosis that occurs due to this alters the plaque form, obstructs the lumen, and embolizes arteries. In addition to this, the fibrous composition of low-risk plaques is higher and unstable. They contain low lipids and do not induce 100% blockage, and

plaques become dense. The fibrous top is thin, with a small lumen of 50%, and has an unexpectedly rupturing tendency [85-89].

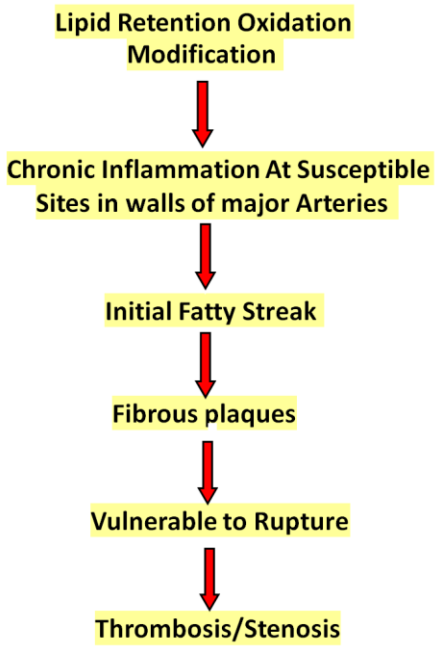

Fig. 4: Stages of Atherosclerosis

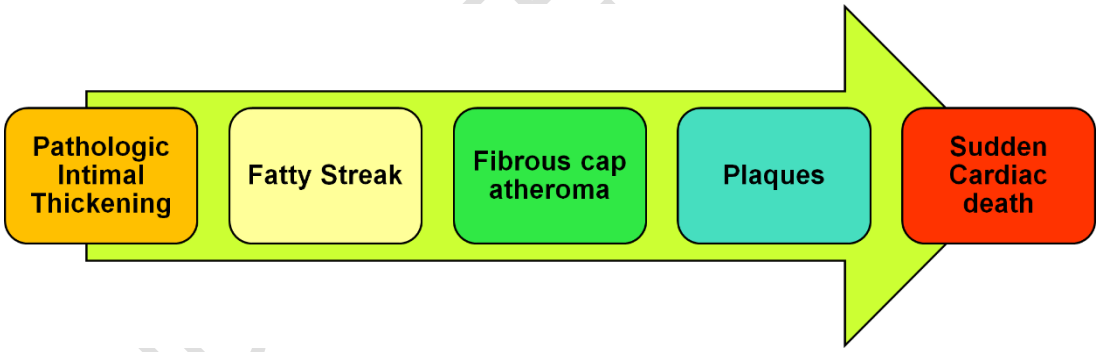

Fig. 5: Steps in terminal events.

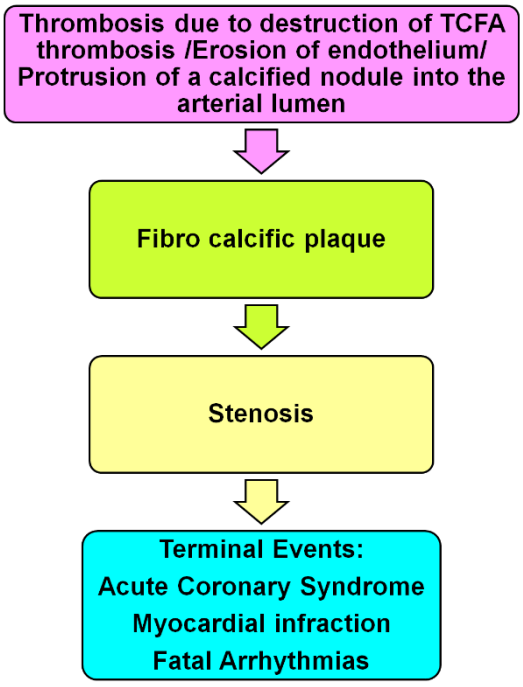

Fig. 6: Terminal events that arise due to stenosis.

8. CONCLUSION

Nanotechnology holds potential in the management of life-threatening diseases like CVD. The promising approach provides infrastructure for clinicians, scientists, and researchers to develop newer therapies that positively impact the lives of patients globally and improve health and well-being. Nanotherapeutics, nanomaterial devices are more geared towards personalized medicines and provide patient-tailored treatment to disease and individual patients. Newer strategies and techniques are coming into the market with advancements in nanomedicines. The treatment approaches can significantly improve and promise to provide alternatives for existing surgical and pharmacological medication. The nanosensor and biosensor engineering devices are becoming popular and helpful in diagnosing diseases. Furthermore, marker detection provides a patient-centric and accurate, cost-effective diagnosis of heart disease. In the future, Nanomaterials need combination approaches of an automated algorithm and computational methods for further research to target, enhancing the accuracy and efficacy of CVD diagnosis.

COMPETING INTERESTS DISCLAIMER

Authors have no competing and conflict of interest.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an

avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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