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Nanotechnological approaches in treatments of cardiovascular diseases.

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Abstract
The majority of research in cardiovascular nanomedicine has been devoted to creating designer nanoparticles for better targeting in order to get beyond biological obstacles. Designer micro- or nanoparticles are frequently injected into the vasculature or a specific vessel for cardiac-related illnesses such atherosclerosis, hypertension, and myocardial infarction in an effort to prevent issues. difficulties with traditional drug delivery, such as detrimental systemic side effects. Additionally, as new nano-drug carriers circulate, they can be preferentially picked up by immune cells with the goal of conversations about the direction that the field of research should go. Additionally, we suggest that researchers pay more attention to nanotechnological techniques for risk factor treatment to aid in the early detection and treatment of cardiovascular diseases (CVD) as the condition is claiming a growing number of lives globally. modifying inflammatory processes before migrating to the plaque to deliver the therapeutic payload. For a number of heart disease indications, the discipline has improved thanks to creative design in nanoparticle composition, formulation, and functionalization. This opinion intends to speak about these developments and give fresh perspectives on how nanotechnology might be used to help treat cardiovascular disease. We provide our outlook on novel applications of nanotechnology inclusion and integration, such as in vascular, implantable, or wearable device technologies, as well as in nanocomposites and nanocoating's, in an effort to stimulate

Keyword-
Cardiovascular disease, Nanotechnology, Liposome.

I. INTRODUCTION

Cardiovascular diseases (CVDs) are one of the major causes of human death worldwide and responsible for more than 17.7 million deaths in 2015, according to world health organization [1]. CVDs are also a major health concern in the United States of America. It has affected the lives of 85.6 million Americans [2]. In 2011, CVDs led to more than 596 thousand deaths and was the top cause of death in the United States of America [3]. Due to the high incidence of CVDs, the need for developing effective treatments for CVDs is urgent; and motivates the research and development of biomaterials for cardiovascular applications. The application of About 560,000 surgeries for placing coronary arteries stents were performed in the U.S. [4]. A broad range of applications in CVDs is now investigated and translated within the field of cardiovascular engineering and regenerative improved the treatments for heart attack by providing mechanical support to the narrowed vessels. In the year of 2007 artery stent, a device mostly made of medical grade metallic alloys, significantly cardiovascular biomaterials have gained great success in the past. Such examples indicate a few of many successful biomaterials for example, coronary medicine, and much of their success is heavily rooted in advancements in biomaterials science. Such applications include, but are not limit to the targeted drug delivery, CVD diagnosis, and the repair and regeneration of the cardiac tissues. It is clear that biomaterials are at the core of further progress for CVD treatments [5].

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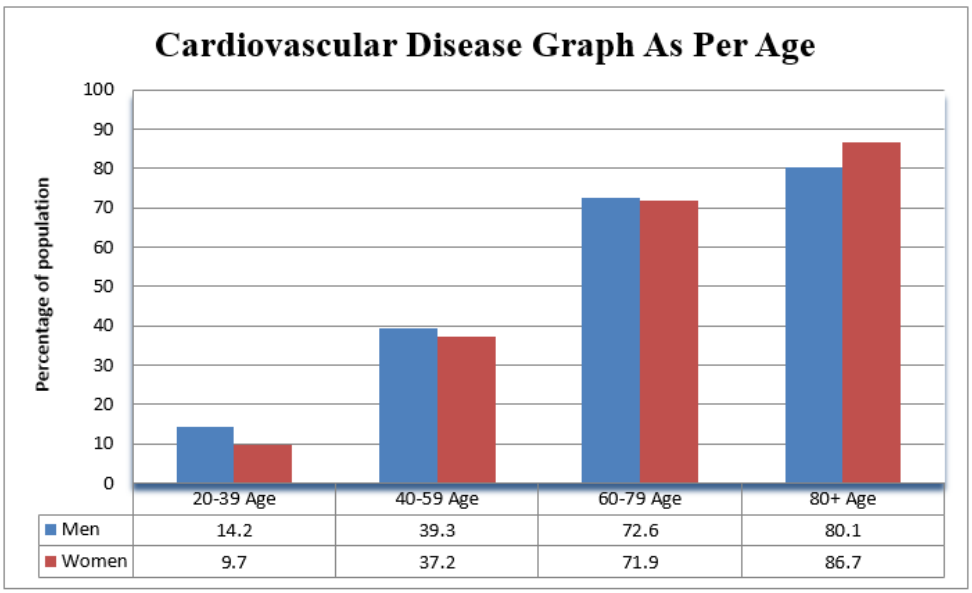
II. Cardiovascular-diseases

Cardiovascular Disease Types	Explanation	Indications	Risk Factors
1.Coronary heart diseases	The most prevalent type of heart disease is ischemia	(i) Heart attack; (ii) Angina at chronic condition	High blood pressure, high blood sugar, smoking, eating poorly, not exercising, diabetes, ageing, and a genetic predisposition are all contributing factors.
2.Stroke	Three categories and a common kind of CVD: (1) Ischemic stroke (2) Haemorrhagic stroke (3) Transient ischemic attack	Damage to the brain that causes sudden deficits and weakness, frequently on one side of the body	Diabetes, a high BC, tobacco use, a poor diet, inactivity, and advancing age
3.Rheumatic heart disease and Rheumatic fever	Rheumatic fever (streptococcal bacteria) causes health problems of the heart valves and heart muscle; it starts as a sore. in children, tonsillitis or the throat	(i) Chest pain, dizziness, fatigue, shortness of breath, and irregular heartbeats. (ii) Vomiting, stomach cramps, nausea, fever, and joint pain and swelling	-
4. Congenital heart disease	A hole in the heart, abnormal valves, or abnormal heart chambers are examples of heart abnormalities that can occur at birth or during pregnancy.	Breathing difficulties or a failure to meet standards for growth and development	Maternal drug and alcohol use; maternal illness (like rubella); poor maternal nutrition; and genetic defects, which is a close blood relationship between parents.
5.Peripheral vascular disease	Two significant forms of peripheral arterial disease (i) Abdominal aortic aneurysm (ii) Atherosclerosis	-	Chronic high blood pressure, Marfan syndrome, tangential heart conditions, syphilis, and other infectious and Inflammatory diseases
6.Deepvenous thrombosis (DVT) and pulmonary embolism	Leg vein blood clots may become dislodged and travel to the heart and lungs.	-	Obesity, recent childbirth, use of contraceptives and hormone replacement therapy, long periods of immortality, and previous DV episodes
7.Other cardiovascular diseases	Heart tumours, brain vascular tumours, heart valve diseases, cardiomyopathies, and heart muscle disorders. [6]	-	-



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III. DIAGNOSIS, TREATMENT, AND DRUG DELIVERY OF CARDIOVASCULAR DISEASES

There is a critical need to create more effective ways addressing early diagnosis, treatment options, and outcomes in individuals suffering from heart failure because demographic trends are predicted to double the at-risk generation over the next 30 years. Peacock studied the diagnosis, treatments, and management techniques for heart failure and recommended that the observation area of the emergency room use the best methods. [7] Coronaryartery disease, complications of MI, sustained cardiac arrhythmia/tachycardia, poorly controlled hypertension, valvular rupture or disease, myocarditis, idiopathic cardiomyopathy, postpartum cardiomyopathy, acute pulmonary emboli, pericardial disease/tamponade, and hyperkinetic states are just a few of the pathologies that may ultimately result in the clinical presentation of heart failure.

According to reports, up to 30% to 50% of people with heart failure suffer circulatory congestion as a result of diastolic dysfunction.[7] Systolic dysfunction and preserved systolic function (PSF) kinds of heart failure are separated. There are various reasons of systolic dysfunction, but ischemic heart disease is the most frequent. The ventricle struggles to expel blood mechanically. Increased intracardiac volumes, pressure, and afterload sensitivity are all results of impaired contractility. Because these patients are more susceptible to hypertension, it is crucial to keep their blood pressure (BP) as low as is tolerable. Systolic contractile function is preserved in heart failure, which shows up as the condition. The primary pathophysiology is poor ventricular relaxation, which results in an aberrant pressure/volume diastolic relationship. Processes associated with cardiovascular disease, such as atherosclerosis, restenosis, and inflammation, are frequently confined to specific areas of the vasculature, providing excellent opportunity for pharmacological treatment that is both specific and effective.[8] When it comes to such intravascular applications, liposomes may be advantageous targeted drug carriers. Lestini et al. [8]took into account three aspects of liposome design to make it easier for them to be used as drug delivery vehicles:

1] Identification of potential cell surface receptors for targeting;

2] Identification of legends that maintain binding specificity and affinity; and

3] Prevention of rapid nonspecific clearance of liposomes into the reticuloendothelial organs.

Even though there have been significant improvements in the detection and treatment of several CVDs, the mortality rate associated with these diseases is still substantially greater than that of cancer globally. Controlling and treating cardiovascular disorders can be done in a number of ways. Control of blood pressure, cholesterol, diabetes, weight, and physical activity; depression; and the choice of the best drugs are some of the treatment approaches for CVDs. The World Health Organization (WHO) has advised population-wide and individual-level smart actions to lessen the burden of CVDs. The population interventions include measures to reduce alcohol consumption, increase physical activity, implement tobacco control legislation, apply levies to reduce the consumption of high-fat, sugar- and salt-filled foods, build cycle lanes, and create walking areas (Figure 1).[9]

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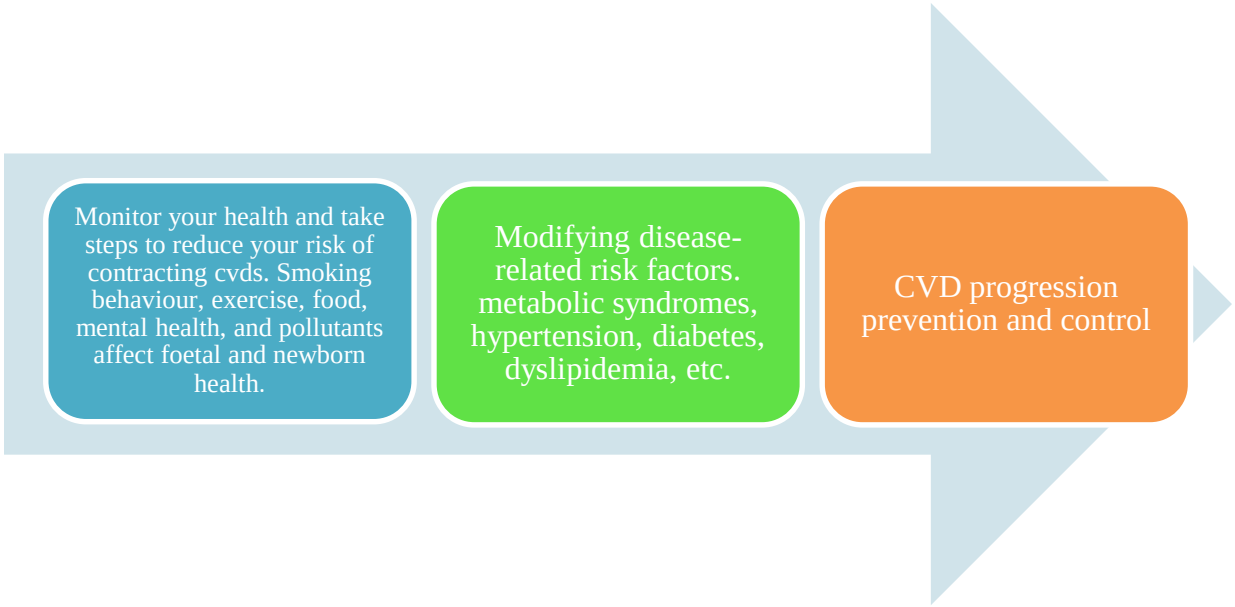

Fig 1: Current strategies included in CVD interventions.

IV. DEVELOPMENT OF NANOMEDICINE FOR CVDS: -

In the fields of communication, information, biology, medical technology, biotechnology, and medicine, nanoscience and nanotechnology are a developing field. Nanoscience is the study of the creation, manipulation, manufacturing, and use of materials that are smaller than 100 nm in size. Numerous medical treatments, including targeted medication delivery, gene delivery systems, and tissue engineering scaffolds, have been made possible by the use of nanotechnology, including imaging, diagnosis, and therapy techniques.[10] Due to their physicochemical characteristics (reactivity, roughness, high surface energy, and high surface to volume ratio) that enhance biological function, nanoparticles have attracted a lot of interest in medicine. In order to better people's quality of life and health, nanomedicine enables the detection, management, and control of diseases and disorders. The use of nanoparticles in medicine has many benefits over both conventional and cutting-edge medical procedures. These benefits include extended medication half-lives, decreased toxicity, improved biocompatibility of nanoparticles, and decreased pharmacological adverse effects by modifying the characteristics of nanoparticles (Figure 2).

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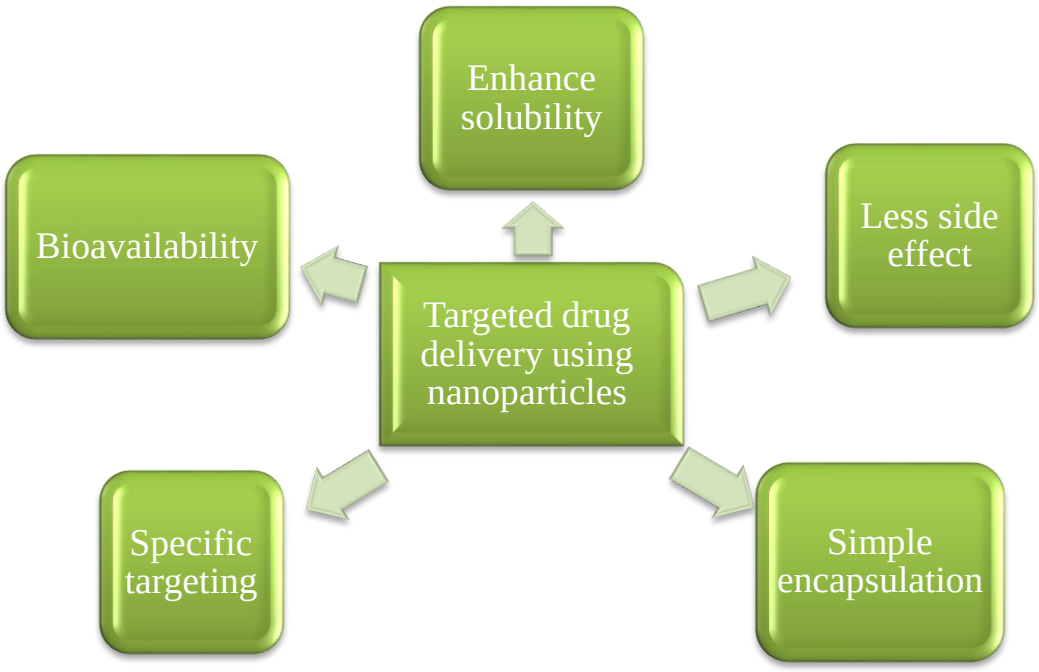

Fig 2: Benefit of medication delivery using nanoparticles

Additionally, tailored medication delivery employing nanocarriers via active or passive targeting appears to be a viable therapeutic approach. Drug conjugation to the cell-specific ligand linked to the nanoparticle is necessary for active drug targeting. A high molecular weight polymer has been used in passive targeting to deliver drugs that can infiltrate and remain in tissue for improved results.[10] Compared to their larger relatives, nanoparticles between 1 and 100 nm in size possess special properties. They can move between cells, tissues, and biological membranes.[11] Nano size, their particular quantum size, high surface to volume ratio, and shape are the characteristic properties. To emphasize the physical characteristics of nanoparticles, their surfaces can be altered. By manipulating the particle's size, shape, and aggregation, monodispersed nanoparticles have been created that can be internalized by cells. Due to their distinctive features, nanomaterials have been used in a variety of biomedical applications as theranostic, diagnostic, drug carrier, and therapeutic agents. For instance, because nanoparticles have a high surface to volume ratio, chemicals can be coupled, absorbed, or enclosed for distribution to the target site.[12] Vehicles that transport drugs are employed because of their capacity to deliver toxic or poorly soluble medications to the intended locations. The field of nanotechnology has experienced rapid expansion, which has provided solutions to all the issues related to CVD treatment options. The burden on the healthcare system is decreased by the early detection and successful treatment of CVDs made possible by nanotechnology. Drugs can be effectively removed from blood and tissue after being delivered there by nanoparticles as well. [13] Through the construction of effective cardiovascular molecular imaging probes based on nanotechnology in personalised cardio-medicine, quick advancements in the field of nanotechnology improve the imaging of CVDs. Figure 3 illustrates the special qualities of nanoparticles that make them ideal agents for cardiovascular imaging. The ability of nanoparticles to penetrate biological barriers and accumulate at the target site accounts for the promising applications of these imaging probes in CVD medicine.[14] Cardiology uses nanoimaging as a comprehensive method for diagnosis and real-time monitoring during procedures and treatments. Cardiovascular imaging using nanotechnology is connected to numerous areas of treatment, surgery, and diagnostics.

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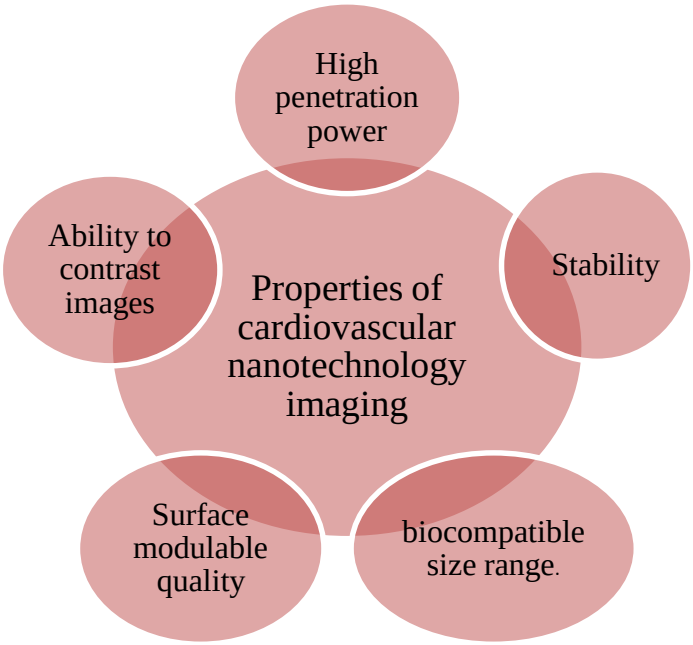

Fig 3: Unique properties of nanoparticles made nanomaterials essential for cardiovascular imaging

Accordingly, thrombus imaging, stem cell imaging, graft imaging, and theragnostic imaging have all been grouped under the umbrella term of nano-based cardiovascular imaging.[15] illustrates various imaging modalities and techniques utilised in cardiology.

Nanoparticles used theranostically in CVDs close the gap between experimental data and extensive clinical trials. Theragnostic in cardiology enables image-based therapeutic drug delivery systems, integrating medicines with imaging. For drug delivery, diagnostic imaging, and further drug efficacy testing, a variety of nanoparticles are used. To reduce local and systemic effects, light, an external magnetic field, or ultrasound are used to manage nanoparticle-based drug delivery and its action at the target region.[16] For vascular intervention, site-specific magnetic resonance imaging has been used. Atherosclerotic plaques' inflammatory activities have been found to be recognised and slowed down by magnetically attracted metallic nanoparticles.[17] The imaging of CVDs is effectively done using magnetic nanoparticles coated in natural chemicals. An arterial thrombus was imaged molecularly using magnetic resonance imaging (MRI) using ultra-small superparamagnetic iron oxide nanoparticles coated with fucoidan (a polysaccharide).

In a rat model of elastase-induced vascular injury, this contrasting agent was able to image P-selection, an adhesion molecule identified as the molecular component of atherothrombotic illness.[18] Researchers created gold nanorods that were utilised in photodynamic treatment to identify and weaken macrophages. [19,20] Nano theragnostic are often divided into three separate stages. Nanoparticle-based imaging agents are employed in stage I to assess the efficacy of conventional therapy. In Stage II, imaging agents are included to examine the effectiveness of nanoparticle-mediated therapy. Stage III, nanoparticle-based imaging Nanomedicine in cardiology typically focuses on four key areas that help manage or control CVDs. Targeted drug delivery, tissue engineering, diagnostics, and molecular imaging are some of these applications of nanotechnology. Targeted medication delivery, increased bioavailability of therapeutic agents, and regulated drug release are just a few benefits that nanocarriers offer. There are various drug delivery methods and equipment available for the treatment of CVDs. Liposomes, polymeric nanoparticles, micelles, dendrimers, and other potential and extensively researched drug carriers are a few. A drug carrier is said to be optimal if it is non-toxic, immune-system-escape-capable, biodegradable, biocompatible, non-immunogenic, and possesses drug-targeting capabilities.[21] Additionally, because to their small size, nanoparticles can carry medications to specific areas of the body by

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slipping past blood-brain barriers or cell membranes.

Optimizing a number of variables, including temperature, enzyme activity, pH, and stimuli (ultrasound, magnetic field, infrared, etc.), has enabled controlled and targeted drug delivery.[22] For a therapeutic or diagnostic approach, various nanoparticles, like polymeric nanoparticles and liposomes, can be loaded with a large number of medicines. For other nanoparticles to conjugate the medicines, more functional legends are needed. Due to their high surface ratio and ability to modify their surface, nanoparticles have been used as multifunctional agents for the detection and treatment of CVDs. It was possible to control the biodistribution and targeted administration of nanoparticles by surface-modifying them with various functional moieties, including small molecules, peptides, aptamers, and antibodies.[23] Liposomal platforms are versatile nanomaterials that can be employed as effective molecular imaging probes and drug carriers. Cardiovascular imaging uses ligand-bound liposomes.[24] Through the use of nanocarriers, medications can be conjugated or encapsulated, increasing their solubility and lowering their systemic toxicity while also shielding them from metabolism and excretion.[25] multi-criteria design is a factor in the development of nanocarriers for cardiovascular therapy. This multi-criteria for the design and development of nanocarriers includes the product's physiochemistry, the quality of the ingredient, such as safety, pyrogen content, and serializability, as well as the process cost and cost of goods. It also includes stability, biocompatibility, toxicity, efficacy, pharmacokinetics, biodistribution, stability, and stability. Finally, it includes clinical acceptability.[26] Before delving into specific views, this section will highlight some of the nanocarriers created for the treatment of cardiovascular illnesses. The most effective nanodevices for targeted medication delivery are polymeric nanoparticles, which are among nanocarriers.[27] When the medications are released over a longer period of time to the target region, these smaller particles show better absorption in the arterial walls. The features of medications, such as their molecular weight, cross-linking, and monomer ratio, have been used to predict their sustained release. The most popular type of biodegradable polymer nanoparticle is poly (lactic-co-glycolic acid, or PLGA). Once the medicine has reached the desired location, this polymer nanoparticle begins to break down. Gelatine-treated PLGA nanoparticles that carried sirolimus remained in the body for 50 days. Due to the pressure, administering drugs-coated nanoparticles via catheter aids in their penetration of the artery wall. As soon as the pressure is removed, the nanoparticle becomes trapped in the wall and serves as the treatment's drug reservoir. The use of a catheter for drug delivery provides an advantage over drug-eluting stents. It's because, when the medicine has been used up, the reaming polymer scaffold causes an inflammatory response inside the body. For the distribution of medications from polymer or stents, drug-eluting stents have been used.[28]

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V. STUDIES ON NANOCARRIERS FOR THE SUCCESSFUL THERAPY OF CARDIOVASCULAR DISEASE

1]Liposome

Types of Nanocarriers	Medications for the Administration of CVDs	Biological Purposes	Developed Model Organisms	Limitations of Drug	Benefits of Nanoplatforms
Polyethylene glycol conjugated liposomal nanoparticles	[Pyr1]-apelin-13 polypeptide	Controls cardiac hypertrophy and hypertrophy-induced heart failure	Murine model of transverse aortic constriction	Short half-life in circulation	Prolonged apelin stability in the blood circulation Potentiated beneficial effects in cardiac function
Liposomal nanoparticles coated with polyethylene glycol	prednisolone phosphate	Ideal for atherosclerotic disease	Clinical trials in humans	Short half-life in circulation	Prolonged the drug's half-life to 45–63 hour in human
Naked liposomes and water-soluble double emulsion polymer	Streptokinase (Streptase)	Plasminogen activator	Rabbits model of autologous carotid artery thrombosis	Shows immunogenic effect and severe bleeding complications	Reduced infarct size and reperfusion time and less haemorrhage
PEGylated Liposomes, with a peptide sequence of fibrinogen gamma chain	Recombinant tissue plasminogen activator (rtPA, (alteplase)	Plasminogen activator	Rats model of inferior venacava thrombosis	Short half-life of rtP	Enhanced thrombolytic activity

2]Metallic Nanoparticles: -

Gold	Vascular endothelial growth factor (VEGF	severe hindlimb ischemia must be treated.	Murine ischemic hindlimb model	Short half-life of VEGF in circulation Less specific targeting	Highest targeting
Gold	Conjugated with miR15	For the treatment of cardiovascular conditions in diabetic postmenopausal individuals	Ovariectomized diabetic mouse model	Inefficient targeting of miR155 to macrophages	MiR155 is effectively delivered into macrophages through phagocytosis, which in turn restores cardiac function.
Gold	Bone-marrow derived mesenchymal stem cells (BMSCs)	enhances the cardiogenic differentiation of stem cells for the repair of infarcted myocardium	Nil	Decreased ability to differentiate into multiple lineages	superior differentiation of the cardiomyogenic type Effects on the regeneration of infarcted myocardium that are more enhanced biologically and functionally
Gold	Levosimendan (Simdax)	Efficient inotrope that improves cardiac contractility in heart failure patients	Heart failure Wistar rat model	Decreased preferential targeting Simdax to the target heart tissue	demonstrated substantial cardioprotective benefits in rats with heart failure brought on by doxorubicin.

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3] Silica Nanoparticles: -

Mesoporous silica	Hydrogen sulphide (H2S)	a fresh organ-preserving substance in the transplantation field	Blab/c mice aged	due to the cytotoxic effects, limited use	Treatment of cardiac allograft vasculopathy (CAV), the main cause of death in recipients of heart transplants
Biodegradable porous silicon	Atrial natriuretic peptide	Myocardial injury in people with ischemic heart disease should be treated	Ischemic Wistar rat mode	less peptides produced inside the body are targeted	Increased colloidal stability and stronger cellular interactions with \cardiomyocytes and non-myocytes \ with little toxicity
Polymeric superparamagnetic nano-silica	Quercetin	Quercetin, an antioxidant, is used to prevent atherosclerosis and other related cardiovascular diseases.	Mice	Poor water Solubility	allowing for the recruitment, attachment, growth, and assembly of cardiac proteins in the local myocardium
PEGylated mesoporous silica	Puerarin	Chinese medicine used for the treatment of cardiovascular diseases	Male Sprague Dawley rat	Humans have a short elimination half-life. Puerarin must be administered intravenously in high doses. immediate side effects that are severe.	Less haemolysis and improved blood compatibility make this a strong candidate for intravascular medication administration.

4] Polymeric Nanoparticles

Poly (lactide-coglycolide) (PLGA)	Heparin and glutathione	Anticoagulant and antioxidant agent used for vascular therapy	Nil	Systemic toxicity, Systemic coagulopathy and haemorrhage symptoms	Effective delivery to the site of an Ischemia/reperfusion injury
Dendrimer	Hirudine	Antithrombotic and anticoagulant agent	Antithrombotic effect evaluated in venous thrombosis model of Wistar rat	Short plasma half-life, generates irreversible hirudin thrombin complex	Gene transfer to thrombosis and thrombosis treatment
Micellar	Hirudine	Natural thrombin inhibitor	ApoE-null mice fed a high-fat diet	Short plasma half-life	Increased delivery of hirudine to the plaques and inhibited the formation of fibrin clots after coronary artery occlusion
Polymeric micelles	m-Tetra (hydroxyphenyl) chlorine	Anti-inflammatory agent	Female Balb/c nude mic	Side effects and other off-target effects	Increased stability and thus allow accumulation of intact mTHPC-to macrophages of atherosclerotic lesion [29]

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Advantages:

- Delivery to the site of cardiovascular damage with accuracy
- Improved drug/dose effectiveness
- Lack of side effects and systemic toxicity

Disadvantages:

- Lack of information on clinical trials and safety
- Various techniques for purification and characterization analysis
- Scale-up production cost
- Stability of drugs for long term.

Fig 4: Advantages and Disadvantages of using nanoparticles to deliver drugs for cardiovascular disorders.

Examples of Nanocarriers

A good drug carrier must be able to demonstrate efficient delivery of a therapy to a damaged organ or tissue, and nanoparticles' tunability makes this possible as weight vehicles, appealing To increase plasma circulation lifetimes or hit a specific target in models of cardiovascular disease, various nanocomposite materials have been created and delivered intra-luminally.[5 Liposomes are a widely studied nano-carrier because they are nanometric vesicles made of concentric lipid bilayers that can be ligand-conjugated to make them "heart-homing by CRPPR conjugation to target the heart Cysteine-rich receptor protein, version 216] The expression of collagen, integrins, selectins, and cell adhesion molecules (CAMs) like intercellular adhesion molecule-1 (I CAMI), vascular cell adhesion molecule-1 (VCAM-1) platelet endothelial cell adhesion molecule (PECAM-1), and endothelial leucocyte adhesion molecule-1 (ELAM-1) on the surfaces of endothelial and smooth muscle can also be modified with antibodies for vascular [30] ICAM-1, 10AM-2 VCAM-1, E-Selectin, and P-Selectin are examples of cell adhesion molecules and chemokines that are expressed more frequently in inflamed endothelial cells that line atherosclerotic plaques. [S] The benefits of using liposomes include their low immunogenicity and capacity to cross the blood-brain barrier, which enables them to be used to deliver medications for the treatment of strokes [31]Co-polymers such as poly(ethyleneimine) (PEL)[32], poly(cyclohexane-1,4 diacyl-acetone ketone)[33], and polylactic- co-glycolic acid) (PLGA), [34] have all demonstrated applicability for siRNAs, proteins and stem cells in the treatment of cardiovascular inflammatory disorders Block copolymers, which have segments of one polymer composition alternated with segments of another have amphiphilic characteristics that allow them to self-assemble into supramolecular core-shell structures. Furthermore, reactive terminal groups enable the linking of legends or antibodies to aid in cell-specific docking. In addition to these platforms, protein-based polymer substrates that have been employed to transport growth factors include collagen [35] or fibria peptides for improving neovascularization, proliferating more, and speeding up the recovery of cala sicers and wounds.[36] [37]

Nanocarrier Vascular Target

Since atherosclerotic plaques, the underlying causes of atherosclerotic disease, and thrombosis are typically found in distinct vascular regions [38] Targeting particles with antithrombotic or anti-inflammatory payloads at diseases that are close to vessel walls should, in theory, be useful for treatment. Targeting the process of angiogenesis is another therapeutic approach used in cardiovascular nanomedicine in addition to the process of inflammation. The vitronectin integrin a283.It is expressed in angiogenic vessels in response to hypoxia [39] and offers another target used in cardiovascular disease research. It may be used to image myocardial angiogenesis or to inhibit angiogenesis in plaques. [40] Since the integrin a283 is only expressed in angiogenic vasculature, it serves as a marker for active angiogenesis associated with plaques that can rupture and cause myocardial infarction and stroke. Anti-angiogenesis therapy is being used to manipulate [381-a263 integrin-targeted nanoparticles in order to normalize atherosclerotic plaque vasculature and promote plaque stabilization through site-specific delivery of antiangiogenic drugs. In addition to selectively binding to a subset of integrin receptors on activated platelets, cyclic arginine-glycine-aspartic acid (CRGD) peptides also bind to glycoprotein IIb/IIIa (GPIIb/IIIa) receptors. To deliver the blood thinner urokinase, these peptides have been coupled to nanoparticles like liposomes specific thrombolysis treatment The clots cannot be targeted by urokinase alone, and it has a short half-life. Researchers sought to dissolve the thrombi that obstruct blood flow and can cause acute myocardial infarction, acute cerebral infarction, and pulmonary embolisms in this nanoparticle formulation [41]

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Nanocarrier Cardiac Targets:

The clot-binding peptide cysteine-arginine-glutamic acid-lysine-alanine (CREKA) has also been identified as a tumour-homing peptide and has been used in cardiovascular nanomedicine. Thymosin beta + (T4), a peptide that starts myocardial and vascular regeneration, is carried by PEG-PLA nanoparticles with CREKA attached as a targeting moiety. To produce mesenchymal stem cells modified with CREKA [42] liposomes were also modified. [43] Targeting fibrin and cardiac repair were two areas where these delivery systems were investigated. Fibrin can be used as a homing agent for targeted cardiac regeneration therapy because it is uncommon in a healthy myocardium and abundant in an infarct zone where it forms right away after cardiac myocyte necrosis as a result of myocardial injury [44] Since the formation of a fibrin matrix in a damaged heart is temporary, timing of delivery important for optimised repair Other targets in an infarcted heart include myosin, which is exposed in irreversibly damaged cardiomyocytes by an ischemic event [45], angiotensin II type 1 receptor (ATI), which is overexpressed in cardiomyocytes after myocardial infarction (MI) due to hypoxia.[46], and phosphatidylserine, which is expressed on the surface of cardiomyocytes in response to stress, such as ischemia [47] A therapeutic payload-carrying ATI targeting peptide was used to functionalize nano-sized PEGylated liposomes with AT1 [48] PEGylated liposomes were proposed as drag and imaging agent carriers to an infarcted myocardium and were covalently coupled to anti- navosin antibodies [49] In order to recognize and bind phosphatidylserine for the identification of early apoptotic cells following ischemia-reperfusion injury annexin V has been conjugated on the surface of iron oxide nanoparticles [50] The lack of blood supply to the MI region, where nonspecific carriers are unable to accumulate makes it crucial to identify and validate cardiac targets that are overexpressed on the surface of heart cells after injury.

Different Nanotechnological Advances:

There are numerous other nanotechnological developments poised to advance the field further aside from the systemic administration of targeting nanoparticles Technologies now allow for intramyocardial and intrapericardial delivery of cells and therapeutics to the heart in addition to intravenous injection [51] Other technologies involve therapeutic tools, such as the implantable epicardial reservoir known as "Therepi." created by Whyte et al for continuous administration of molecules or cells. The researchers customized their rate of therapy close to the infarct border zone by adjusting the semipermeable membrane's porosity. Implantable nanochannel membrane devices, which can be passively or actively modulated to release cardiovascular drugs for timed intervention demonstrate a similar method of tunable drug release [52,53,54,55]. An expanded polytetrafluoroethylene (ePTFE)-based drug delivery device locally infused heparin and improved graft patency in a primate arterial graft model to test the viability of human application [56]-[58] Additionally, the combination of medication and stem cells in microneedle patches that can be applied to a damaged heart has shown promise for therapeutic heart regeneration 1614 Finally functionalizing endovascular interventional devices with magnetic nanoparticles like superparamagnetic iron oxide can create MRI visible devices suitable for interventional cardiovascular magnetic resonance (CMR) [59] which can direct interventions with real-time imaging in multiple planes for treatments of the peripheral arteries and heart.

VI. CONCLUSION

Nanotechnology provides a special platform for innovative methods of cardiovascular imaging and drug delivery, as well as enhancing vascular tissue. The extensive work being done in the field of nanomedicine and the encouraging outcomes of animal studies give reason for optimism that soon, nanoparticle assemblies combining a carrier system, a targeting modality, and an active drug will be authorised for the diagnosis and treatment of cardiovascular diseases. Additionally, the shortcomings of the current surgical and interventional techniques used to treat atherosclerosis should soon be overcome thanks to the emerging nanotechnological approaches to revascularization procedures.

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