Ashdin Publishing
Journal of Drug and Alcohol Research
Vol. 13 (2024), Article ID 236416, 10 pages
DOI: 10.4303/JDAR/236416

Review Article

Bionanotissue Engineering in Cardiac Regeneration: Staying Young at Heart on Public

Bhaskar Rao Bollineni[1], Lakshmi Lalitha. D[1], Vemuri Praveen Kumar[2], P. Eshwar Rao[1], Sunjana Nelluri[1], Sahithi Kamepalli[3], M. Chetan[3], K. Seetha Reddy[3], N. Kanaka Durga Devi[3*]

[1]*Depatment of Pharmacy, Great Eastern Medical School and Hospital, India*
[2]*Department of Biotechnology, KL University, India*
[3]*Depatment of Pharmacy, KVSR Siddhartha College of Pharmaceutical Sciences, India*

[*]*Address Correspondence to N. Kanaka Durga Devi, E-mail: nelluriss@rediffmail.com*

Received: 30 October 2024; Manuscript No: JDAR-24-147715; **Editor assigned:** 01 November 2024; PreQC No: JDAR-24-147715 (PQ); **Reviewed:** 15 November 2024; QC No: JDAR-24-147715; **Revised:** 20 November 2024; Manuscript No: JDAR-24-147715 (R); **Published:** 27 November 2024; **DOI:** 10.4303/JDAR/236416

Abstract

Ischemic heart disease is the leading cause of morbidity and mortality worldwide for cardiovascular illnesses, which continue to be a major public health problem. The effectiveness of conventional therapy in promoting heart regeneration is limited. A rapidly developing technology called bionanomaterials has great potential to meet this unmet medical need. In this work, we assessed the use of bionanomaterials for heart regeneration, more especially tailored nanoparticles and nanofiber scaffolds. This study focused on specially created biocompatible nanoparticles loaded with heart growth agents and nanofiber scaffolds to offer structural support. Different drug delivery methods including nanoparticles for therapeutic medication delivery were discussed. According to our study, bionanomaterial-based treatments markedly improved cardiac function, decreased the size of the infarct, and increased the density of cardiomyocytes in the infarcted area. Endogenous heart repair was encouraged by the prolonged release of growth factors from nanoparticles and the three-dimensional structural support offered by nanofiber scaffolds. In treated hearts, histological investigation showed increased angiogenesis, decreased fibrosis, and improved cardiomyocyte alignment. With the potential to completely change the way that ischemic heart disease is treated, bionanomaterials provide a viable path for cardiac regeneration. Myocardial repair is facilitated by the combination of growth factor-loaded nanoparticles and nanofiber scaffolds, which increase angiogenesis, decrease fibrosis, and boost cardiomyocyte proliferation. These findings raise optimism for better outcomes for patients with heart illness by indicating that bionanomaterial-based therapies have a great deal of potential for therapeutic applications in cardiac regeneration in the future. For these discoveries to be translated into practical therapies for human patients, more investigation and clinical testing are required.

Keywords: Bionanomaterials; Bionanotechnology; Cardiac regeneration; Regenerative medicine; Tissue engineering

Introduction

The human heart is an incredibly complex organ that serves as life's rhythmic conductor. Its continuous, coordinated contractions guarantee that blood enriched with oxygen reaches every part of the body, allowing life to exist. Even yet, the heart is not immune to the damaging effects of ageing, illness, or trauma. Cardiovascular disorders, such as myocardial infarctions and heart failure, continue to pose enormous obstacles to the field of medicine. They take countless lives and impair the quality of life for a great number of people. Even though traditional treatments have significantly reduced the debilitating consequences of cardiac illnesses, they frequently are unable to return the heart to its ideal state. The use of bionanomaterials in heart regeneration has, however, risen to a remarkable level in the face of these obstacles [1]. Bio-nanomaterials are a novel class of materials that are shaped at the nanoscale to interact with biological systems in a seamless manner. This is the result of the merger of nanotechnology with the life sciences. With their remarkable qualities, these materials have sparked hope in the field of cardiovascular medicine by providing a means of overcoming long-standing barriers to cardiac regeneration. Bionanomaterials have the potential to revolutionise cardiac repair and rejuvenation by precisely delivering drugs and imitating the complex architecture of the heart's milieu. This introduction provides as a starting point for a journey through the most recent advancements, ground-breaking findings, and promising future directions in the field of bionanomaterials and heart regeneration. We take a deep dive into the various uses of bionanomaterials in scaffolding, cellular interactions, medicinal delivery, and tissue restoration in these pages. We present the cutting-edge techniques being used by scientists and researchers to fully utilise the potential of these tiny miracles, ultimately aiming to heal damaged hearts and enhance the quality of life for patients with cardiovascular conditions. As we explore this unexplored area, one thing becomes very evident: bionanomaterials have boundless potential for cardiac regeneration. They offer hope to those who are suffering from heart conditions and bring us one step closer to the profound accomplishment of healing even the most broken hearts. We will map out the path of innovation and discovery that has emerged at the nexus of bionanomaterials and heart regeneration in this extensive investigation. In this emerging discipline, scientists and doctors are charting a course towards the realisation of a future in which the heart's regenerative potential is unlocked, its resilience is increased, and the threat of heart disease is reduced with steadfast commitment and unrelenting curiosity. We have the opportunity to observe the beginning of a new age in cardiac medicine as we set out on this trip, one that will be characterised by the revolutionary potential of bionanomaterials in the admirable goal of cardiac regeneration.

Review of Literature

The integration of nanotechnology has led to substantial improvements in the field of cardiac tissue engineering and regeneration. The critical significance that nanomaterials play in improving our comprehension of cardiac tissue regeneration is examined in this chapter. We examine numerous research projects and discoveries from the last 10 years, providing insight into the ways in which nanomaterials can be used to treat heart conditions and restore damaged cardiac tissue. Nanotechnology presents interesting methods for treating cardiovascular problems, ranging from medication delivery to imaging and diagnosis. An important organ in the human body, the heart can sustain damage from a variety of illnesses and traumas, which can have serious repercussions. The effectiveness of traditional therapy procedures for regenerating heart tissue is limited. Recent studies, however, have demonstrated that heart tissue engineering and regeneration can be revolutionised by nanotechnology. The important studies that have influenced this developing topic are compiled and discussed in this chapter. Sundararaghavan and Burdick emphasised the potential of nanoparticles in cardiac tissue engineering in their 2011 paper that was published in Materials Today. They underlined how crucial it is to create nanoscale scaffolds that support the development and function of heart cells. A 2013 publication in Nanotechnology examined the potential of a range of nanomaterials for cardiac tissue engineering by Smith and Jiang. The utilisation of nanofibers and nanoparticles to improve tissue regeneration and cell adhesion was covered in their study. Rai et al. (2015) offered information on the uses of nanomaterials for controlling and regenerating cardiac tissues in the Journal of Nanoscience and Nanotechnology. They talked about how drug delivery systems based on nanomaterials can be used to treat heart conditions. An extensive review of nanomaterials for the treatment of myocardial infarction in Theranostics was provided by Yu et al. (2018). Their research included a range of nanotherapeutic strategies, such as medication administration via nanoparticles and imaging methods at the nanoscale. Zhang et al. (2018) published a paper in the Journal of Cardiovascular Translational Research that addressed the use of nanotechnology in cardiac tissue engineering. They talked about the potential for early diagnosis of cardiac problems using diagnostic instruments based on nanomaterials. A 2019 study by Kasar et al. (2019) examined current developments in nanotechnology for the treatment of cardiac conditions. Their work demonstrated the use of nanomaterials in medication distribution, imaging, and diagnostics and was published in the Journal of Cardiovascular Pharmacology and Therapeutics. Lykke-Hartmann and Banan Sadeghian (2020) in Nanomedicine gave information about the state of nanomaterials for heart repair at the moment. They emphasised the need for more research as they talked about the difficulties and potential directions in the sector. In the Journal of Nanobiotechnology, Bit et al. (2021) talked about new nanomaterials for cardiac tissue engineering. They emphasised current advancements as well as possible discoveries that may influence heart regeneration in the future. The substantial contributions of nanomaterials to cardiac tissue engineering and regeneration have been discussed in this chapter. Promising answers for heart disease can be found in nanotechnology, from creating nanoscale scaffolding to creating nanotherapeutic techniques. We expect many more cutting-edge uses of nanomaterials to enhance cardiac health and outcomes as this field of study develops.

Cardiac Regeneration: A Quest for Healing the Ailing Heart

A symbol of life and energy, the human heart is an amazing organ that pumps blood enriched with oxygen throughout the body. Its regular contractions supply the vital nutrients required for living and uphold the body's metabolic demands. The heart is vulnerable to a variety of illnesses, traumas, and the unavoidable consequences of ageing, despite its vital function. Heart failure, myocardial infarctions (heart attacks), and coronary artery disease are examples of cardiovascular illnesses (CVDs), which pose a serious threat to global health. When taken as a whole, these illnesses contribute significantly to global morbidity and mortality, making CVDs the world's biggest cause of death [2]. The heart's ability to regenerate itself is not as great as that of other bodily organs. The heart's capacity to regenerate tissue is comparatively limited, in contrast to the liver's capacity. The heart makes an effort to heal itself when cardiac tissue is damaged, usually as a result of ischemia (inadequate blood supply) after a heart attack or progressive deterioration in heart failure. However, these attempts are frequently insufficient to entirely restore lost function. Those who suffer from cardiac events therefore have impaired heart function, a lower quality of life, and a higher chance of having more cardiovascular events in the future. An overview on Importance of bionanomaterials in cardiac regeneration was shown in Figure 1.

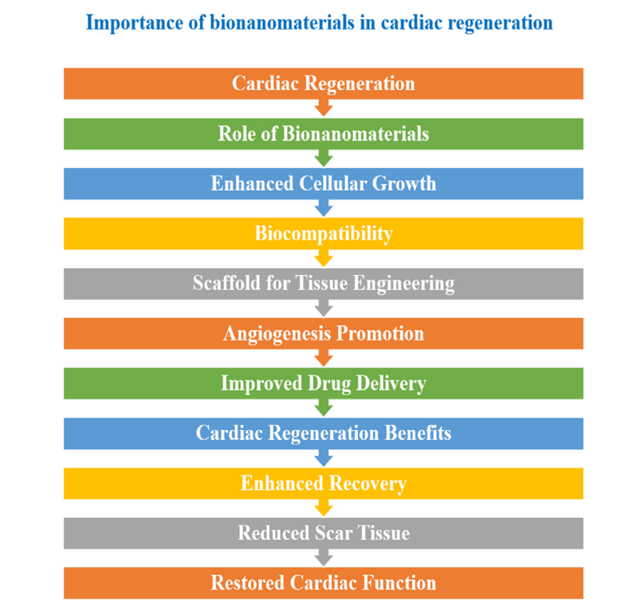

Figure 1: An overview on Importance of bio-nanomaterials in cardiac regeneration

In the past, palliative and symptom-relieving methods, like medication and lifestyle changes, were the mainstay of cardiac disease care. Even though these procedures have definitely helped many people live longer lives, they frequently fail to fully regenerate the heart-that is, to return damaged heart tissue to a healthy state. Due to this unfulfilled need, extensive research has been conducted, leading to the development of the discipline known as heart regeneration. By combining the fields of biology and engineering, tissue engineering allows for the creation of functional tissue analogues, such as artificial heart tissue, which can be used as a mechanical assistance or to replace an organ [3].

Early pursuits of cardiac regeneration

The idea of heart regeneration has been around for ages and is not a new one. Historical documents attest to the recognition of the heart's capacity for self-healing by early scientists and physicians. But it wasn't until the middle of the 20th century that scientists started to understand the complex biology behind heart regeneration. The field of cardiac regeneration has pursued its ultimate goals through a variety of approaches, such as applying chemical genetics, developing biomaterials and delivery systems that facilitate cell transplantation, and comprehending the developmental biology of cardiomyocytes and cardiac stem/progenitor cells [4]. The identification of cardiac stem cells seen in the adult heart was one significant finding. It has been shown that these specialised cells, sometimes known as cardiac progenitor cells, have the capacity to develop into diverse heart cell types and may even aid in tissue regeneration. Although this finding gave rise to optimism for regenerative treatments, it also brought up several concerns regarding the viability and efficiency of using these cells in therapeutic settings. An overview on the process of using bionanomaterials for cardiac regeneration was displayed in Figure 2.

Figure 2: An overview on the process of using bio-nanomaterials for cardiac regeneration

The Rise of Stem Cell Therapies

The development of stem cell technology in the late 20th and early 21st centuries became a major pathway towards the goal of heart regeneration. As potential sources for cardiac regeneration, researchers started looking at the use of different stem cell types, such as adult stem cells including Mesenchymal Stem Cells (MSCs) and cardiac progenitor cells, as well as Embryonic Stem Cells (ESCs) and induced Pluripotent Stem Cells (iPSCs). The potential for stem cell therapies to restore damaged heart tissue with functional, healthy cells held enormous hope. Experiments and clinical trials were started to evaluate the effectiveness and safety of various methods. The broad use of stem cell therapies for heart regeneration was constrained, despite positive early results, by issues with cell survival, integration, and long-term effects [5].

The Emergence of Tissue Engineering and Bionanomaterials

At the nexus of tissue engineering, nanotechnology, and regenerative medicine, disciplines began to collide as researchers looked for new approaches to cardiac regeneration. The idea of employing bionanomaterials which a class of materials with features customised to the nanoscale for the repair of heart tissue was first presented by this convergence. Biocompatibility, mechanical properties that can be tuned, and the capacity to replicate the natural cardiac milieu are just a few of the amazing qualities of bionanomaterials. By acting as scaffolds to encourage cell growth and differentiation, these materials can be used to create three-dimensional cardiac constructs that closely mimic real heart tissue. Furthermore, bionanomaterials enable precisely timed release of therapeutic drugs into the heart through controlled drug administration. The use of bionanomaterials into strategies for heart regeneration has created new opportunities to tackle the obstacles that impeded earlier methods. These materials are being investigated by researchers as potential tools for improving cell adhesion, proliferation, and maturation, which will ultimately aid in tissue regeneration and functional recovery. Cardiovascular regeneration is at a crossroads today, and bionanomaterials provide a potential new direction in the effort to treat failing hearts. We will investigate the novel uses of bionanomaterials in scaffolding, cellular interactions, drug delivery, and tissue restoration as we dig deeper into this exciting topic. We will see first-hand how these minuscule but potent materials have the potential to completely transform the field of cardiovascular medicine, giving those suffering from heart conditions newfound hope and bringing us one step closer to the important objective of regaining cardiac health and vigour [6].

Bionanomaterials in Regenerative Medicine: Pioneering the Future of Healing

Regenerative medicine is a cutting-edge field of medicine that attempts to return injured tissues and organs to their original state. It has the potential to revolutionise the way we treat a wide range of illnesses and injuries, including neurodegenerative diseases and cardiovascular ailments. The application of bionanomaterials, a novel class of materials designed at the nanoscale to interact with biological systems, is essential to the success of regenerative medicine. By improving targeted drug delivery, tissue engineering, cell treatments, and regenerative medicine, these materials have quickly developed into essential instruments [7].

A new era of biomedical innovation has been brought about by the combination of regenerative medicine and nanotechnology. Key issues in regenerative medicine, such as the development of biomimetic scaffolds, cellular response optimisation, and the regulated release of bioactive chemicals, are greatly aided by the use of bionanomaterials. The present study delves into the diverse applications of bionanomaterials in the field of regenerative medicine, emphasising their influence on tissue restoration, organ replacement, and the creation of innovative therapeutic approaches. Various bio-nanomaterials used for cardiac regeneration was enlisted in Table 1.

Table 1: Various bionanomaterials used for cardiac regeneration

Bio-nanomaterial	Description
Nanofibrous Scaffolds	These scaffolds, which provide a framework for cell attachment, proliferation, and differentiation, are frequently formed of biocompatible polymers like collagen, gelatin, or chitosan. They resemble the Extracellular Matrix (ECM) structure of heart tissue. Scaffolds made of nanofibers can aid in the regeneration and repair of heart tissue.
Nanoparticles	Liposomes, gold nanoparticles, and biodegradable polymeric nanoparticles are a few examples of the several types of nanoparticles that are employed in gene therapy, drug administration, and as carriers of growth factors or signalling molecules that promote cardiac cell regeneration. These medicinal substances can be released selectively and under control using nanoparticle engineering.
Extracellular Vesicles (EVs)	EVs, which are naturally occurring nanoparticles secreted by cells, are essential for intercellular communication. They can be separated and altered to transport particular substances, such as proteins or microRNAs, that improve cell signalling, lessen inflammation, and encourage the healing of damaged heart tissue.
Hydrogels	Three-dimensional networks of hydrophilic polymers, or hydrogels, can be designed to resemble the Extracellular Matrix (ECM) of the heart. They can be filled with medicinal substances and offer encapsulated cells a favourable environment, assisting in the regeneration of heart tissue.
Carbon Nanotubes (CNTs)	Because of their special mechanical and electrical qualities, CNTs can be used to create electroconductive nanomaterials. Materials based on Carbon Nanotubes (CNTs) can increase the injured heart tissue's electrical conductivity, promoting synchronised contractions and boosting regeneration.
Nanofibers	Angiogenesis, tissue healing, and cell attachment in the heart can be supported by patches and scaffolds formed of nanofibers, which come in a variety of materials. They frequently have the dual purposes of promoting the proliferation of heart cells and offering mechanical support.
Nanocrystals	Different material nanocrystals, including quantum dots, can be employed for diagnostic and imaging applications in heart regeneration. They can assist in real-time monitoring of the incorporation of nanomaterials and the development of regeneration.
Nanocarriers	Small chemicals, proteins, or genetic materials are among the therapeutic cargo that these specialised nanoparticles or nanoscale vesicles are intended to deliver to the site of heart damage. They can encourage tissue regeneration and improve medication administration.

Bionanomaterials in Tissue Engineering

Scaffolds for tissue regeneration

Tissue engineering is a key area of use for bionanomaterials in regenerative medicine. Nanoscale scaffold design and construction creates a biomimetic environment in which cells can attach, multiply, and differentiate. Tissue regeneration can be facilitated by customising these scaffolds to meet the unique mechanical and metabolic characteristics of target tissues. In vitro and in vivo, scaffolds are three-dimensional porous structures that can be used to encourage cell adhesion, migration, differentiation, and proliferation. They are made of biocompatible and bioactive materials. Because scaffolds are made to mimic the Extracellular Matrix (ECM), all of these qualities are conceivable. The Extracellular Matrix (ECM), which provides tissue structure organisation and intercellular signalling, is necessary for cells to join and communicate with one another [8].

Nanofibers and nanocomposites

Bionanomaterial-based nanofibers and nanocomposites have become essential components in tissue engineering. Their high surface area-to-volume ratios facilitate the development of tissue and allow for cellular connections. Nanomaterial-based scaffolds have great promise for skin grafts, cartilage repair, and bone regeneration. A study that examined the interaction between fibres and hydrogels employed the combination in a cardiomyocyte support system for cardiac tissue engineering [9].

Cellular interactions and tissue maturation

Bionanomaterials improve adhesion, proliferation, and differentiation, which in turn affects cellular behaviour. They have the ability to alter the fate of stem cells, promoting the development of particular cell types needed for tissue regeneration. Furthermore, by encouraging tissue maturation, these substances guarantee that the newly produced tissues perform as intended [10].

Therapeutic Delivery and Precision Medicine

Controlled drug delivery

One of the most important applications of bionanomaterials in regenerative medicine is precise and regulated medication delivery. Therapeutic compounds can be released selectively from nanoparticles or nanocarriers, reducing systemic negative effects. This method works especially well for cancer treatment since it allows for the localised delivery of drugs while protecting healthy tissues. Various treatment approaches for cardiac regeneration employing bionanomaterials were listed in Table 2.

Table 2: Various treatment approaches for cardiac regeneration employing bio-nanomaterials

Therapeutic option	Bio-nanomaterial used	Mechanism of action	Advantages	Challenges
Stem cell therapy	Nanoparticles	Enhanced cell delivery and retention Controlled release of growth factors Reduced immune response	Promotes tissue regeneration Improves cell survival	Ensuring precise nanoparticle targeting Long-term safety assessment
Tissue Engineering	Nanofibers, Hydrogels	Scaffold for cell attachment and growth Controlled drug/growth factor delivery	Mimics native tissue structure Promotes cell differentiation	Achieving mechanical strength Integration with host tissue
Drug Delivery Systems	Lipid Nanoparticles, Micelles	Targeted drug delivery to damaged areas Sustained release of therapeutic agents	Reduces systemic side effects Enhances drug bioavailability	Ensuring drug stability Potential toxicity of nanomaterials
Gene Therapy	Viral Nanoparticles, Liposomes	Efficient gene delivery to cardiac cells Precise targeting of genetic modifications	Potential to correct genetic defects Long-lasting therapeutic effect	Immune response to viral vectors Off-target effects
Nanoscale Imaging	Quantum Dots, Nanoparticles	High-resolution imaging of cardiac tissue Real-time monitoring of regeneration progress	Precise visualization of tissue Early detection of issues	Biocompatibility of imaging agents Long-term safety concerns
Extracellular Vesicles	Exosome-based Nanoparticles	Transfer of bioactive molecules Inter-cellular communication for regeneration	Low immunogenicity Minimal risk of tumorigenesis	Standardizing isolation and characterization Scalability issues

Gene therapy and personalized medicine

Gene treatments that treat hereditary diseases and genetic abnormalities are made possible by the transport of genetic material made easier by bionanomaterials. They play a key role in the creation of personalised medicine techniques that adjust therapies based on each patient's distinct genetic composition.

Clinical translation and challenges

It takes a lot of work to move bionanomaterial-based regenerative medicines from the laboratory to the patient. It is necessary to overcome obstacles like long-term biocompatibility, regulatory barriers, and scalability. But current studies and joint efforts by scientists, medical professionals, and business partners are moving these technologies quickly closer to clinical use. To sum up, bionanomaterials are at the forefront of regenerative medicine and present novel approaches to age-old medical problems. Their exceptional adaptability, accuracy, and capacity to communicate with biological systems provide them invaluable instruments for drug delivery, tissue engineering, and customised medicine. Bionanomaterials have the potential to revolutionise healthcare and bring about an era in which diseases may be conquered and regeneration becomes a reality, provided that research in this sector continues to thrive [11].

Types of nanomaterials for cardiac regeneration

Heart attacks and heart failure are examples of cardiovascular disorders that continue to be the world's top causes of morbidity and mortality. Researchers have turned to nanomaterials, a type of materials manufactured at the nanoscale, to meet the hurdles presented by these conditions and improve the science of heart regeneration.

Because of their special qualities, nanomaterials are useful resources for the regeneration and repair of injured heart tissue. This article examines several nanomaterials, such as nanoparticles, nanofibers, nanocomposites, nanogels, and nanoscale drug delivery systems, that show potential for use in heart regeneration [12].

Nanoparticles

Nanoparticles for therapeutic delivery

Due to their ability to distribute drugs precisely, nanoparticles, which normally have sizes between one and one hundred nanometers, have become more and more important in heart regeneration. Therapeutic medicines, such growth factors or tiny compounds, can be precisely delivered to injured heart tissue by means of their encapsulation. This focused strategy increases treatment efficacy and reduces systemic negative effects.

Gold nanoparticles for imaging and therapy

Because of their special optical characteristics, gold nanoparticles are used in both therapeutic and imaging applications. They can improve the accuracy of cardiac therapies through photothermal or photodynamic therapy, and they can act as contrast agents for imaging modalities such as photoacoustic imaging. Gold nanoparticles are attractive options for integrated imaging and therapeutic approaches because of these characteristics.

Nanofibers

Nanofibers in scaffold design

The perfect foundation for tissue engineering is provided by nanofibers, which are frequently created via electrospinning methods. They have a high surface area-to-volume ratio and resemble the Extracellular Matrix (ECM) seen in nature. Scaffolds based on nanofibers facilitate cell adhesion, proliferation, and differentiation, thereby establishing an environment that is favourable for the regeneration of heart tissue.

Polymeric nanofibers

Heart tissue engineering has made substantial use of polymeric nanofibers, such as those derived from biocompatible materials like Polycaprolactone (PCL) or Poly (Lactic-co-glycolic Acid) (PLGA). To further improve these materials' capacity for regeneration, bioactive compounds can be added to their functionalization.

Nanocomposites and Nanogels

Nanocomposites enhancing mechanical properties

Nanocomposites are materials with enhanced mechanical characteristics made of a polymer matrix and nanoscale fillers. Nanocomposites have the potential to improve the stability and durability of scaffolds in cardiac regeneration, which is important for preserving structural integrity in dynamic cardiac settings.

Nanogels for controlled drug release

Controlled drug release is a strong suit for nanogels, which are three-dimensional networks of hydrogel particles at the nanoscale. They have the ability to encapsulate medicinal substances and release them gradually over time, providing long-lasting therapeutic advantages. Additionally, injectable nanogels offer a less intrusive method of delivering medication to the heart.

Nanoscale Drug Delivery Systems

Lipid-based nanoparticles

Lipid-based nanoparticles have been used for cardiac medication delivery, such as liposomes and solid lipid nanoparticles. Drugs that are hydrophilic or hydrophobic can be encapsulated by them to increase their bioavailability and targeted specificity.

Polymeric nanoparticles

Polymeric nanoparticles, including polylactic acid nanoparticles, are adaptable delivery systems for cardiac treatments. Combination therapies catered to the specific requirements of each patient are made possible by their ability to co-deliver numerous therapeutic agents and provide exact control over drug release kinetics.

Exosomes and extracellular vesicles

The inherent ability of exosomes and extracellular vesicles, released by diverse cell types, to transport cargo, has drawn significant attention. They can be used to deliver regenerative factors to heart tissue that has been injured, encouraging regeneration and repair. To sum up, nanomaterials offer a variety of tools to help advance heart regeneration. Their adaptability, exact control over medication administration, and capacity to generate biomimetic conditions render them indispensable in the search for novel treatments for cardiac ailments. The future of heart regeneration appears increasingly bright as researchers continue to investigate and improve these nanomaterial-based techniques, providing hope to millions of people suffering from cardiovascular diseases [13].

Applications of Bionanomaterials in Cardiac Regeneration

Bionanomaterials have many uses in heart regeneration because they are designed at the nanoscale to interact with biological systems. These materials provide distinct benefits when it comes to tackling the intricate problems involved in the regeneration and repair of damaged heart tissue [14]. Applications of bionanomaterials in cardiac regeneration was summarized in Table 3. The following list includes some uses of bionanomaterials in the field of

Table 3: Applications of bio-nanomaterials in cardiac regeneration

Application	Description
Cardiac Tissue Engineering	Patches and scaffolds imitating the Extracellular Matrix (ECM) of the heart are made with bio-nanomaterials. The regeneration of heart tissue can be aided by these scaffolds, which can promote cell adhesion, proliferation, and differentiation.
Drug Delivery	Through controlled and targeted delivery of medications or growth factors to the injured cardiac tissue, bio-nanoparticles can be engineered to support tissue regeneration and repair.
Biomimetic Nanoparticles	The characteristics of extracellular vesicles, which are involved in intercellular communication, can be imitated by nanoparticle engineering. They can be applied to improve regeneration, lower inflammation in the heart, and modify cell signalling.
Myocardial Infarction Therapy	After a heart attack, bio-nanomaterials can be used to produce medicines that lessen fibrosis, scarring, and inflammation. They can enhance the vascular supply to the heart muscle by encouraging angiogenesis, or the growth of new blood vessels.
Electroconductive Nanomaterials	Electrically conductive nanomaterials can be integrated into cardiac tissue to improve electrical conductivity of injured heart tissue and augment contraction synchronisation.
Bioactive Nanoparticles	Bioactive substances, such as microRNAs, growth factors, or proteins, can be loaded onto nanoparticles to promote cardiac cell differentiation and proliferation, hence aiding in tissue regeneration and repair.
Regenerative Nanoscaffolds	With the help of specialised nanoscaffolds, damaged hearts can receive mechanical support, stimulate cell adhesion, and produce bioactive cues that drive myocardial tissue regeneration.
Diagnostic Nanosensors	Real-time monitoring of the healing process can be achieved by designing nano-sensors that are capable of detecting biomarkers linked to heart regeneration, process and guiding treatment strategies.

heart regeneration.

Scaffold design and tissue engineering

- Nanoscale scaffolds that imitate the natural Extracellular Matrix (ECM) of the heart can be created using bionanomaterials. These scaffolds give cardiac cells the structural support they need to attach, multiply, and differentiate.
- The utilisation of bionanomaterials in nanofibers, nanocomposites, and nanogels plays a crucial role in establishing three-dimensional environments that support tissue regeneration.

Cellular interactions and differentiation

- By encouraging cell adhesion, proliferation, and differentiation, bionanomaterials improve cellular interactions. They can be made functional by adding signalling cues and bioactive compounds that control biological reactions.
- By guiding stem cell differentiation into cardiac lineages, these materials are essential in producing cardiomyocytes and other cardiac cell types that are needed for tissue repair.

Controlled drug delivery

- Damaged cardiac tissue can receive precise and regulated medication delivery thanks to bionanomaterials. Small chemicals, growth factors, and medicinal substances can all be enclosed in them and released gradually at the intended location.
- By supplying vital components to the injured location, controlled drug release reduces systemic side effects, optimises therapeutic efficacy, and promotes tissue regeneration.

Gene therapy

- Small interfering RNA (siRNA) and plasmid DNA are 2 examples of genetic material that is delivered by bionanomaterials to modify gene expression in cardiac cells.
- The goals of gene therapy techniques are to improve cell survival, encourage tissue regeneration, and control cardiac fibrosis and inflammation.

Theranostics

- Bionanomaterials combine therapy and diagnostics as theranostic agents. They can be fitted with contrast materials or imaging probes to track the development of heart regeneration.
- Real-time evaluation of tissue healing and treatment effectiveness is made possible by multifunctional bio-nanomaterials.

Cardiac patch and implantable devices

- Bionanomaterials are integrated into cardiac patches and implantable devices that can be surgically placed over damaged cardiac regions. These patches provide mechanical support and deliver therapeutic agents to the injured area.
- Smart materials responsive to physiological cues can release drugs in a controlled manner based on the heart's needs.

Exosome delivery

- Bionanomaterials facilitate the delivery of cardiac-derived exosomes and extracellular vesicles, which carry regenerative cargo. Exosomes promote communication between cells and enhance tissue repair.

- Exosome-loaded bionanomaterials enable targeted delivery to the heart, offering a promising avenue for cardiac regeneration.

Personalized medicine

- Bionanomaterials are useful in personalised medicine because they allow medicines to be customised based on a patient's unique genetic profile and cardiac state.
- Customised treatments could entail tailoring nanomaterial-based delivery systems to meet the specific requirements of every patient.

Minimally invasive procedures

- Bionanomaterials are engineered to be delivered by minimally invasive techniques, like intravenous or intracoronary injections, which improve patient comfort and minimise procedural invasiveness.

Combination therapies

- Combination therapies, in which many therapeutic agents are administered simultaneously to address various elements of heart regeneration, are made possible by the invention of bionanomaterials.
- Therapeutic effects can be improved by combining anti-inflammatory drugs, growth factors, and stem cell therapy in nanomaterial-based systems.

All things considered, scaffold design, cellular interactions, controlled drug delivery, gene therapy, theranostics, and personalised medicine are only a few of the many uses for bionanomaterials in heart regeneration. These adaptable materials have enormous potential to advance the area of regenerative medicine and transform the way cardiovascular illnesses are treated.

Challenges and Future Directions for Using Bionanomaterials in Cardiac Regeneration

While there is a lot of potential for the application of bionanomaterials in cardiac regeneration, there are a number of obstacles that must be addressed with cooperation. We examine these difficulties here and suggest upcoming directions for the field's development.

Long-term biocompatibility

- Challenge: Maintaining bionanomaterials' long-term biocompatibility is still a major challenge. Immune reactions or unanticipated side effects may develop with time.
- Future direction: It is crucial to keep researching the immunomodulatory qualities of bionanomaterials and their biocompatibility. It is important to investigate methods like surface modification and encapsulation that reduce immunological reactions.

Clinical translation

- Challenge: Regulatory and safety barriers must be overcome before bionanomaterial-based therapeutics can be moved from preclinical research to clinical settings.
- Future direction: It is imperative that researchers, physicians, and regulatory bodies work together. Successful clinical translation requires careful consideration of regulatory requirements, robust preclinical testing, and well-designed clinical trials.

Scalability

- Challenge: A production barrier related to scalability may prevent bionanomaterials from being widely available for therapeutic application.
- Future direction: It is essential to develop scalable production procedures for bionanomaterials. To satisfy clinical want, industrial collaborations and advancements in producing methods ought to be investigated.

Targeted delivery and specificity

- Challenge: It is difficult to make sure that bionanomaterials are unique to cardiac tissue and arrive at the right place inside the heart.
- Future direction: The specificity of delivery can be enhanced by developments in targeting techniques, such as ligand-receptor interactions and surface functionalization. Furthermore, real-time navigation and imaging methods could improve accuracy.

Therapeutic efficacy

- Challenge: A major problem is maximising the therapeutic efficacy of bionanomaterials in heart regeneration, especially in complicated clinical settings.
- Future direction: Synergistic effects could be obtained from combination therapy utilising stem cells, bionanomaterials, genetic factors, and other regenerative techniques. Optimising results can be achieved by using precision medicine to customise treatments to the unique characteristics of each patient.

Safety and toxicity

- Challenge: Thorough assessment is necessary to determine the safety and possible toxicity of bionanomaterials, particularly in the event of prolonged exposure.
- Future direction: It is crucial to continuously analyse toxicity, including in vivo research. Safety problems can be reduced by developing materials that are biodegradable and biocompatible.

Regulatory approval

- Challenge: It can take a lot of effort and complexity to navigate regulatory channels for new bionanomaterial-based medicines.
- Future direction: It is essential that researchers and regulatory bodies work together. Approvals can be granted more quickly if efforts are made to simplify

regulatory procedures for regenerative medicine.

Cost-effectiveness

- Challenge: Adoption and accessibility of bionanomaterial-based therapeutics may be hampered by their cost.
- Future direction: To increase the accessibility of these medicines for patients, cost-effective production techniques and an assessment of the therapies' cost-benefit ratio are required.

Monitoring and assessment

- Challenge: It is still difficult to track the development and efficacy of bionanomaterial-based treatments in real time.
- Future direction: Improvements in non-invasive imaging methods, such ultrasound and MRI, can allow tissue regeneration to be tracked in real time. Research on biomarkers for heart repair is also necessary.

Ethical considerations

- Challenge: It is necessary to address the ethical issues surrounding the use of innovative medicines, particularly those incorporating genetic changes.
- Future direction: To develop ethical rules and assure responsible use, it is imperative that professionals, ethicists, and the public engage in honest and open conversations.

Discussion

In summary, even though bionanomaterials have a lot of promise for heart regeneration, resolving the issues around their use is crucial for a successful clinical trial. Bionanomaterial-based therapeutics for heart repair and regeneration will be shaped in part by future collaborative efforts, inventive research, and a multidisciplinary approach [15-17].

Conclusion

In conclusion, bionanomaterials have shown promise as a treatment for heart regeneration. These novel materials improve tissue repair, provide fine control over cell interactions, and raise the general efficacy of cardiac therapy. Bionanomaterials have considerable promise to address the problems associated with heart regeneration because of their capacity to replicate the natural cardiac milieu and deliver therapeutic medicines. We should expect major advancements in the treatment of cardiovascular diseases and, eventually, an improvement in the quality of life for patients with heart ailments as long as research in this field continues. The incorporation of bionanomaterials into techniques for cardiac regeneration is a significant advancement in the quest for better, functional hearts.

Acknowledgement

The authors are very much thankful to Management of Great Eastern Medical School and Hospital (GEMS), Srikakulam and KVSR Siddhartha College of Pharmaceutical Sciences, Vijayawada for their support and constant encouragement.

Conflict of Interest

The authors declare that they have no conflict of interest.

References

1. Arackal, K. Alsayouri, Histology heart, J Stat Pearls Publi Treasure Island, FL, USA: 2022.
2. R. Aziz, M. Falanga, J. Purenovic, S. Mancini, P. Lamberti, A review on the applications of natural biodegradable nano polymers in cardiac tissue engineering, J Nano Mtrls (Basel), 13(2023):1374.
3. N.F. Huang, V. Serpooshan, V.B. Morris, N. Sayed, G. Pardon, et al. Big bottlenecks in cardiovascular tissue engineering, J Commun Biol, 1(2018):199.
4. K. Kikuchi, K.D. Poss, Cardiac regenerative capacity and mechanisms, Annu Rev Cell Dev Biol, 28(2012):719-41.
5. J.M. Hare, S.V. Chaparro, Cardiac regeneration and stem cell therapy, J Curr Opin Organ Transplant, 13(2008):536-42.
6. P. Shankar, J. Jagtap, G. Sharma, J. Singh, A revolutionary breakthrough of bionanomaterials in tissue engineering and regenerative medicine, J Emer Appl Bio Nano Mtrls, 1(2022):399-441.
7. J. Whittam, Z.N. Maan, D. Duscher, V.W. Wong, J.A. Barrera Januszyk, Challenges and opportunities in drug delivery for wound healing, J Adv Wound Care, 5(2016):1089.
8. L. Li, M. Bao, Y. Nie, Extracellular matrix-based biomaterials for cardiac regeneration and repair, J Heart Fail Rev, 26(2021):1231–1248.
9. L. Ikonen, E. Kerkela, G. Metselaar, M.C. Stuart, M.R. De Jong, et al. 2D and 3D self-assembling nanofiber hydrogels for cardiomyocyte culture, Biomed Res Int, (2013):1.
10. M. Wei, S. Li, W. Le, Nanomaterials modulate stem cell differentiation: Biological interaction and underlying mechanisms, J Nanobiotechnology, 15(2017):75.
11. R. Pala, V.T. Anju, M. Dyavaia, S. Busi, S.M. Nauli, Nanoparticle-mediated drug delivery for the treatment of cardiovascular diseases, Int J Nanomedicine, 27(2020):3741-3769.
12. Cristallini, E. Vitale, C. Giachino, R. Rastaldo, Nanoengineering in cardiac regeneration: Looking back and going forward, J Nanomaterials (Basel), 10(2020):1587.
13. Zong, A. Bronckaers, G. Willems, H. He, M. Cadenas de Llano-Pérula, Nanomaterials for periodontal tissue regeneration: Progress, challenges and future perspectives, J Funct Biomtrls, 6(2023):290.
14. Cristallini, E. Vitale, C. Giachino, R. Rastaldo, Nanoengineering in cardiac regeneration: Looking

back and going forward, J Nanomaterials (Basel), 10(2020):1587.

15. R. Amin, E. Sink, S.P. Narayan, M. Abdel-Hafiz, L. Mestroni, Nanomaterials for cardiac tissue engineering, J Molecules,21(2020):5189.

16. T.J. Cahill, R.K. Kharbanda, Heart failure after myocardial infarction in the era of primary percutaneous coronary intervention: Mechanisms, incidence and identification of patients at risk, World J Cardiol, 9(2017):407.

17. Tzahor, K.D. Poss, Cardiac regeneration strategies: Staying young at heart, J Sci, 1039(2017):1035–1039.