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NATURAL POLYMERS AND BIOMATERIALS IN MYOCARDIAL REGENERATION

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Abstract

Cardiac tissue regeneration remains a significant challenge in treating myocardial infarction and heart failure, conditions leading to substantial morbidity and mortality worldwide. Biomaterials, particularly synthetic polymers and natural substances, have emerged promising tools for promoting myocardial repair. Synthetic polymers, such as polylactic acid (PLA) and polycaprolactone (PCL), offer customizable mechanical properties and controlled degradability, while natural biomaterials like collagen and fibrin closely mimic the extracellular matrix, enhancing biocompatibility and cellular integration. Scaffold-based structures, hydrogels, and nanotechnologies facilitate the delivery of stem cells, growth factors, and bioactive molecules, fostering angiogenesis and cardiomyocyte proliferation. Despite these advances, challenges persist. Synthetic materials may induce immune responses, and natural biomaterials face limitations in scalability and mechanical strength. High production costs and difficulties in complete tissue integration further hinder widespread application. Future research focuses on developing smart biomaterials responsive to biological stimuli, integrating genetic and cellular therapies, and leveraging nanotechnology for precise therapeutic delivery. These approaches aim to address current limitations, offering scalable and effective solutions for myocardial regeneration. This review highlights the advantages, limitations, and future directions of biomaterials in cardiac tissue engineering, emphasizing their potential to revolutionize regenerative medicine for cardiovascular diseases.

Keywords: cardiac regeneration, biomaterials, synthetic polymers, natural biomaterials, nanotechnology.

Introduction

Myocardial regeneration is one of the most important challenges of modern medicine, given the increasing prevalence of cardiovascular diseases, including myocardial infarction and heart failure. These conditions, which lead to permanent loss of cardiomyocytes and pathological remodeling of the heart, remain the leading causes of morbidity and mortality globally. Conventional therapeutic solutions, such as medication or heart transplantation, often provide temporary relief, without completely restoring the structure and function of the affected myocardium [1,2].

In this context, regenerative medicine offers new perspectives through the use of biomaterials and polymers, either synthetic or natural. These materials have the potential to create a favorable microenvironment for the regeneration of cardiac tissue, by stimulating cell proliferation, supporting angiogenesis, and protecting stem cells or growth factors used in treatment. In particular, natural biomaterials such as collagen, fibrin, and hyaluronic acid are intensively researched due to their high biocompatibility and ability to mimic the native extracellular matrix [1,3,4].

Synthetic polymers such as polylactate (PLA) and polyglycolate (PGA) also offer advantages such as adjustable mechanical strength, controlled degradability, and the ability to

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be combined with other materials to create customized solutions. The combination of polymers with advanced technologies such as 3D printing and tissue engineering opens up new avenues for the development of scaffolds and hydrogels that can be used in myocardial regeneration [2-4].

However, the use of these biomaterials is not without its challenges. Immunogenicity, degradation control, integration with native tissues, and high development costs are barriers that limit the widespread application of these technologies [3-6].

This review aims to explore the role of polymers and natural biomaterials in myocardial regeneration, with a focus on clinical applications, their advantages and limitations, as well as prospects. We will look at various types of biomaterials, including natural and synthetic, used to facilitate the regeneration of heart tissue and discuss emerging technologies, such as scaffolds and hydrogels, that improve the delivery of stem cells and growth factors into the affected myocardium.

We will also highlight the importance of a multidisciplinary approach in the research of these materials, combining expertise from areas such as tissue engineering, nanotechnology, and molecular biology to develop effective and safe therapies. This synthesis will provide a comprehensive perspective on the current state of knowledge in the field and will outline strategic directions for future research in biomaterial-based myocardial regeneration.

Types of natural polymers and biomaterials

Biomaterial-based myocardial regeneration involves the use of innovative structures capable of replacing or supporting damaged heart tissue. These materials are classified into two main categories: synthetic polymers and natural biomaterials, each with unique characteristics that determine their applicability in regenerative therapy [4-8].

Synthetic polymers are materials manufactured through controlled chemical processes, providing the possibility to adjust their mechanical, physical, and biological properties to suit the specific requirements of myocardial regeneration. Among the most widely used is polyglycolate (PGA), a biodegradable polymer used for scaffolds due to its rapid degradation rate, which allows for the formation of new tissues. However, it requires adjustments to reduce the acidity produced during degradation, which can damage cells. Another example is polylactate (PLA), which has a slower degradation rate than PGA and provides more durable mechanical support. It can be combined with other polymers to create hybrid materials. Polycaprolactone (PCL) is noted for its mechanical stability and very slow degradation rate, making it ideal for applications requiring prolonged structural support. Polyurethanes, known for their flexibility and excellent mechanical properties, are used in the creation of scaffolds that can withstand cardiac stresses [5-8].

These polymers are often customized by combining with other materials or through chemical modifications to improve biocompatibility and prevent inflammatory reactions [5-8].

Natural biomaterials have a significant advantage due to their high biocompatibility and ability to mimic the native extracellular matrix. These materials are derived from biological sources and are preferred for cardiovascular applications due to their reduced risks of immunogenicity. Collagen, the main component of the extracellular matrix, provides an ideal structural environment for tissue regeneration, promoting cell adhesion and proliferation. Fibrin, derived from blood plasma, is used to create temporary matrices that support the migration and proliferation of stem cells, being particularly useful for the delivery of growth factors [5-9].

Hyaluronic acid, a natural component of tissues, is used in hydrogels due to its moisturizing properties and ability to stimulate angiogenesis. Chitin and chitosan, derived from the exoskeletons of crustaceans, have antimicrobial properties and are biodegradable, being used to support vascular and myocardial regeneration [6-10].

Synthetic polymers and natural biomaterials can be used individually or combined to create hybrid solutions that take advantage of each type. In the following sections, we will explore how these materials are integrated into advanced technologies for myocardial regeneration (Table 1) [6-11].

Table 1. Comparative: synthetic polymers vs. natural biomaterials [6-11].

Characteristic	Synthetic polymers	Natural biomaterials
Biocompatibility	Moderate, often requiring chemical modifications to improve interaction with biological tissues.	High, due to their biological origin, with minimal risks of triggering immune responses.
Degradability control	Highly tunable through molecular adjustments, offering precise control over degradation rates.	Limited to their natural properties, often dependent on the source material and environmental factors.
Mechanical strength	It is adjustable and can be engineered to meet specific requirements, from soft to highly rigid structures.	Generally lower mechanical strength, but sufficient for applications that do not require load-bearing capacity.
Integration with tissues	Challenging, as synthetic materials may lack the signaling molecules required for seamless integration.	Excellent, as they mimic the native extracellular matrix (ECM), promoting cellular attachment and growth.
Customization potential	High, allowing for tailored physical, chemical, and biological properties.	Limited customization, but can be enhanced through modifications or combinations with other materials.
Risk of immunogenicity	Potentially moderate to high if not properly modified or coated.	Very low, particularly if derived from autologous or biocompatible sources.
Applications	Often used in creating scaffolds, hydrogels, and drug delivery systems for various medical purposes.	Primarily used for tissue regeneration, wound healing, and as carriers for cells and growth factors.

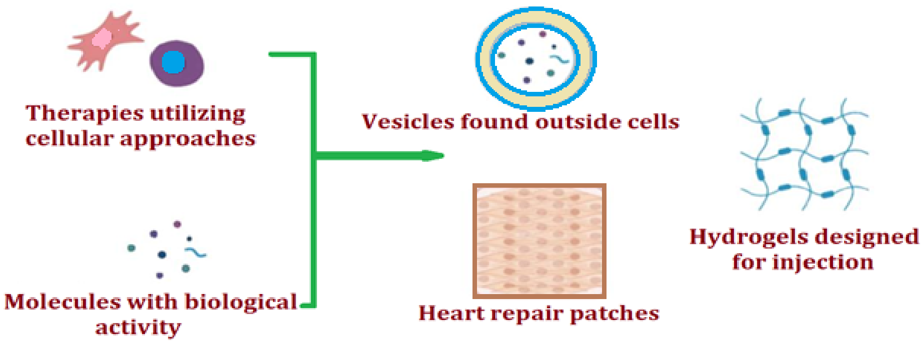

Fig. 1. Biomaterial approaches for cardiac repair [12].

Traditional methods, such as cell-based therapies and bioactive molecules, can be delivered directly to the heart. This review highlights three biomaterial-based strategies to enhance these and emerging therapies: extracellular vesicles, cardiac patches, and injectable hydrogels. Extracellular vesicles can also be incorporated into hydrogels or patches for improved delivery [12,13]

Tissue delivery and engineering techniques

Myocardial regeneration is based not only on the use of biocompatible materials but also on the development of effective techniques for the delivery of stem cells, growth factors, and other therapeutic agents. These techniques integrate biomaterials in the form of scaffolds, hydrogels, and nanostructures, using advanced tissue engineering methods. The main objective is to create a microenvironment that favors myocardial regeneration, improves cell survival, and stimulates angiogenesis [13-15].

Scaffolds are three-dimensional structures that provide mechanical and biological support for tissue regeneration. They are designed to mimic the native extracellular matrix (ECM), facilitating cell attachment, proliferation, and differentiation. The materials used to manufacture scaffolds include both synthetic polymers, such as PLA, PGA, and PCL, and natural biomaterials, such as collagen or fibrin [13-16].

Scaffold manufacturing methods have evolved significantly in recent decades. Electrospinning produces ultra-thin fibers that mimic the structure of ECM, having a large surface area for cell attachment. 3D printing allows the creation of customized scaffolds with complex architectures, adapted to the specific needs of myocardial tissue. Decellularization is another method, whereby natural scaffolds are created by removing cells from tissues or organs, preserving the ECM structure. Scaffolds can be loaded with stem cells, growth factors such as VEGF or FGF, or microRNAs to improve myocardial regeneration [14-17].

Hydrogels are hydrated polymer networks that provide a favorable environment for therapeutic delivery and tissue regeneration. They can be made from natural biomaterials, such as hyaluronic acid or chitosan, or from synthetic polymers, such as PEG. Their key properties include the ability to retain water, providing a moist environment that favors cell survival, mechanical flexibility, adaptability to cardiac tissues, and controlled delivery of stem cells or bioactive factors to the affected region [16-18].

Injectable hydrogels have become particularly popular because they allow the minimally invasive delivery of therapy directly into the affected myocardium. In addition, hydrogels responsible for stimuli, such as pH or temperature, allow the controlled release of therapeutic agents, increasing the effectiveness of the treatment [16-19].

Nanotechnologies are often combined with scaffolds or hydrogels to create hybrid systems that optimize tissue regeneration. These modern tissue delivery and engineering techniques contribute to integrating biomaterials into myocardial therapy, providing promising solutions for patients with heart conditions. They demonstrate the potential to regenerate complex tissues, improve heart function, and reduce complications associated with traditional treatments. In the following sections, we will look at the advantages and limitations of these methods [17-21].

Conclusions

Regarding advantages, limitations, and prospects in the use of biomaterials for myocardial regeneration we can state the following:

- The use of biomaterials in myocardial regeneration offers multiple advantages but also challenges that limit clinical applicability on a large scale. Among the major advantages is the high biocompatibility, especially of natural biomaterials, which reduces the risk of immunological reactions and facilitates integration with native tissues. Synthetic polymers, on the other hand, allow for the customization of mechanical and chemical properties, providing structural support and precise degradation control. These materials can be loaded with stem cells, growth factors, and microRNAs, optimizing myocardial regeneration by stimulating angiogenesis and cell proliferation [19-23].
- However, biomaterials have significant limitations. The potential immunogenicity of some synthetic polymers, the lack of biological signals in non-natural materials, and the high production costs are important challenges. Also, controlling the degradation of natural biomaterials remains difficult, and full integration with native cardiac tissues may be incomplete [20-24].
- Prospects include the development of smart materials, capable of responding to biological stimuli, such as pH or temperature, to ensure the controlled release of therapeutic agents. Integration with gene and cell therapies, as well as the use of nanotechnology to optimize therapeutic delivery, are promising directions. Research in

this area will continue to advance toward personalized, sustainable, and effective solutions for myocardial regeneration [20-25].

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