A Comparison of Natural and Synthetic Biomaterials in Their Ability to Restore Damaged Cardiac Tissue

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Abstract

Cardiac tissue damage from cardiovascular diseases is one of the most pressing issues in modern medicine due to the heart's limited ability to heal itself. Both natural and synthetic biomaterials have demonstrated promise in the regeneration of cardiac tissue. They must have five key properties— biocompatibility, biodegradability, mechanical characteristics, structural properties, and electrical characteristics—to properly restore this damaged tissue. Chitin and chitosan, cellulose, and hyaluronic acid are examples of natural biomaterials, which may be preferred due to their excellent biodegradability and biocompatibility with human cardiac tissue. Poly-vinyl alcohol, polyglycolic acid, and polyurethane are examples of synthetic biomaterials, which may be preferred due to their high customizability. Overall, due to the fulfillment of more desired characteristics of biomaterials used in cardiac tissue regeneration, natural biomaterials are preferred over synthetic biomaterials. However, insight to future research suggests that a combination of both, forming a hybrid biomaterial, may be the best solution.

Background

Cardiac tissue can be damaged by cardiovascular diseases (CVDs), and some of the CVDS include stroke, coronary heart disease, and cerebrovascular disease. They have high morbidity and mortality rates, mainly since cardiomyocytes, the muscle cells of the heart, cannot be easily regenerated by the body due to the limited healing capacity of the heart. Thus, cardiac tissue remains damaged after it suffers the CVD. Some existing methods of cardiac tissue restoration include bioactive molecules and cell-based therapies, but the challenge of their delivery prevents them from having great clinical impact. However, there have been recent advances in the development of natural and synthetic biomaterials for restoration of damaged cardiac tissue. It is important to research different natural and synthetic biomaterials and the differences in their ability to restore cardiac tissue to improve the quality of life for those with cardiac tissue damage and direct future research in cardiac tissue engineering.

Biomaterials provide a wide variety of functions in biomedical engineering, especially in wound healing and tissue engineering. Damaged tissue heals through processes involving different types of cells, and biomaterials can be applied to these wound sites to trigger cell responses—such as growth, migration, and differentiation—for optimized tissue restoration. The two broad categories for biomaterials are natural biomaterials and synthetic biomaterials. Natural biomaterials include chitin and chitosan, cellulose, and hyaluronic acid, and they are derived from living organisms, including plants, animals, and algae. In some cases, they may be favored for their high biocompatibility with human tissue as well as their biodegradability. Synthetic biomaterials include poly-vinyl alcohol (PVA), polyglycolic acid (PGA), and polyurethane (PU), and they are derived from biocompatible polymers. In some cases, they may be favored for their high customizability.

Overview of the Application

Biomaterials used in cardiac tissue engineering have five main properties that must be addressed: biocompatibility, biodegradability, mechanical characteristics, structural properties, and electrical characteristics. With high biocompatibility, the biomaterial can easily and properly interact with surrounding tissues and cells as well as avoid immune rejection by the body. A good level of biodegradability is favored in biomaterials as they can degrade inside the body without need of surgery to remove them. Biodegradable materials are also able to interact with the environment better, further encouraging cardiac tissue regeneration. Key mechanical characteristics are biological similarity, plasticity, and durability. These aspects ensure that the biomaterial will not be rejected by the body and will be able to endure the physiological and mechanical stress of a beating heart. Key structural properties include intrinsic porosity, which prevents hypoxia in the tissue site; stability, which supports the normal structure of the heart; and mimicking of cardiac tissue structure, which promotes compatibility with surrounding tissue. Electrical conductivity is necessary for stimulating electrical signal transmissions of intercellular electrical coupling and myocardial tissue, and without this aspect, there is risk of cardiac arrhythmia. However, in sites without inherent electrical conductivity, this aspect should be avoided.

Technological Challenges

Due to the many requirements of biomaterials used for cardiac tissue engineering as well as the many different types of biomaterials, both natural and synthetic, it is a challenge to determine which biomaterial to use. Even more, it is difficult to decide if it would be preferable to use natural or synthetic biomaterials due to their different properties.

Review of Current Technology

Natural biomaterials include chitin and chitosan, cellulose, and hyaluronic acid, among many others.

Chitosan is a copolymer formed through the partial deacetylation of chitin, which is the second most abundant biopolymer found in nature. They are mainly derived from the exoskeletons of arthropods and the cell walls of fungi. Although chitin is typically insoluble, it can be deacetylated to produce the soluble chitosan. Physical and chemical characteristics of chitosan include water solubility, biodegradability, and reactivity. The surface of red blood cells contains a variety of negatively charged proteins and glycolipids that interact with the amino groups in the chitosan. Increased blood viscosity, platelet adhesion, and major improvement in hemostatic function are all results of this interaction. Thus, these biopolymers are recommended to be used in biomaterials focusing on drug delivery services, tissue engineering scaffolds, and bioactive wound dressings. The most prominent qualities of chitin and chitosan are its nontoxicity and non-immunogenicity, acceleration of tissue regeneration, and antimicrobial properties. Due to their inherent characteristics and capacity to facilitate wound healing, these biopolymers are appealing to be used for biomaterials for cardiac tissue engineering.

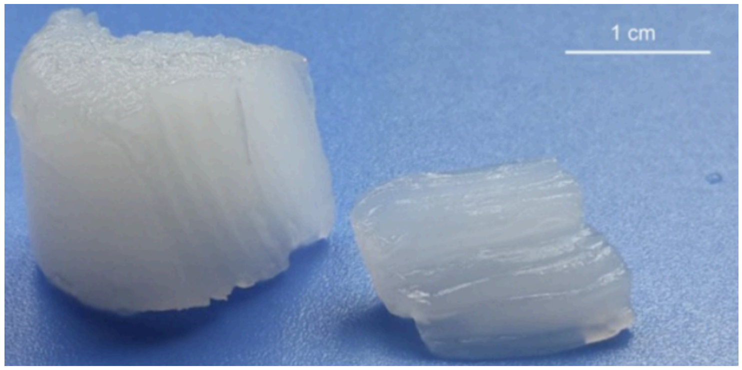

Figure 1: Chistosan Hydrogel

Cellulose is the most abundant biopolymer found in nature, and it is mainly derived from plants, bacteria, and algae. Due to its relatively high purity, bacterial cellulose is mainly derived for biomaterials. Bacterial cellulose exhibits great potential and promise as a biopolymer because of its capacity to regulate wound exudate and create a moist environment for tissue regeneration. However, because it lacks inherent antibacterial qualities, its application is limited. Nonetheless, cellulose's nanostructure offers high biocompatibility and biodegradability, along with beneficial physiochemical and mechanical traits. Numerous applications, other than biomaterials, including drug delivery, bioprinting, implants, artificial organs, are made possible using bacterial cellulose. It can also effectively be mixed with a variety of antimicrobial materials to account for its own lack in antimicrobial properties and fight infections at damaged tissue sites, including cardiac tissue sites.

Figure 2: Bacterial Cellulose Film

Hyaluronic acid (HA) is a natural and linear polysaccharide existing in all vertebrate species and humans, and it is the main component of the extracellular matrix. It has significant ability to retain water, making cell movement easier and enhancing cell migration. HA facilitates neo-angiogenesis by establishing an ideal microenvironment for fibroblast, endothelial, and keratinocyte development, replication, and migration. During the proliferative stage of tissue repair, granulation tissue forms as a result of the influence from HA, collagen, fibronectin, laminin, and other glycosaminoglycans. HA has drawn a lot of interest in usage for wound healing and tissue regeneration since it is naturally produced by the body during early stages of wound healing. By controlling inflammation at the site of the damaged tissue, it acts as a scavenger of free radicals, and it interacts with receptors on different cells associated with tissue restoration and repair. Thus, it plays a critical role in the angiogenic stage of wound healing. Because of its adaptability, researchers have also added different chemicals to HA's backbone to improve its mechanical and swelling properties, suitable for use in cardiac tissue regeneration.

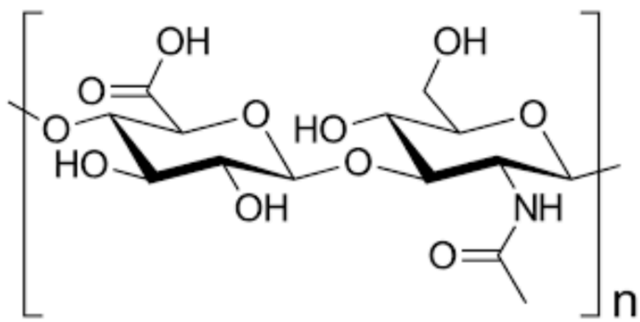

Figure 3: Chemical Structure of Hyaluronic Acid

Synthetic biomaterials include poly-vinyl alcohol (PVA), polyglycolic acid (PGA), and polyurethane (PU), among many others.

PVA is a water-soluble polymer and is made when polyvinyl acetate is hydrolyzed. It is a common polymer that has exceptional mechanical properties, high solubility, high degradability, and low toxicity. By exhibiting reduced in vitro toxicity and improved blood compatibility, PVA hydrogels promote cell proliferation and migration, which in turn promotes wound healing and tissue regeneration. Thus, PVA is compatible with biological systems, making it useful in biomedical fields and applications, especially biomaterials. However, unmodified PVA hydrogels lack flexibility, hemostatic qualities, and antimicrobial properties, but it can be synthesized with other polymers, such as chitosan, to make up for this lack and be used to restore damaged cardiac tissue.

Figure 4: PVA in Powdered Form

PGA is the simplest linear aliphatic polyester and a biodegradable thermoplastic polymer. It can be derived either through condensation or from the ring-opening polymerization of glycolic acid. Since 1954, PGA has been acknowledged as a polymer capable of producing strong fibers, but due to its hydrolytic instability, its use has been limited, especially in the medical field. In recent years, PGA has been used as a biomaterial to promote tissue regeneration since studies have shown that it is involved in inflammatory processes and the development of neo-epithelium. These factors, as well as its strong absorbency, though hydrolysis causes it to gradually degrade, make it a possible candidate as a biomaterial used to aid cardiac tissue regeneration, but it is not the best.

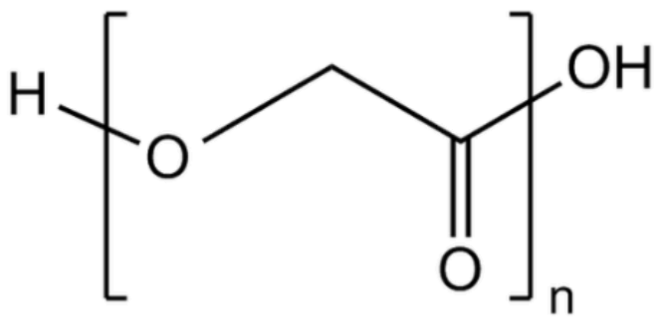

Figure 5: Chemical Structure of PGA

PU is a block copolymer derived from the reaction of a diisocyanate and a polyol. It is the most versatile polymer as its user can choose the structure and composition of its constituents under the appropriate reaction conditions, being able to be produced as a resin, plastic, elastomer, or adhesive. Because PU can maintain an ideal moist microenvironment for tissue healing, it is commonly used as a wound dressing in the form of a foam or film. Although they have shown clinical usefulness in wound treatment, traditional PU foams have been restricted to only bio-clinical applications due to their bioinert properties and the hazardous nature of petroleum-based products. However, a biocompatible PU material has recently been developed for biomedical applications, especially biomaterials in cardiac tissue engineering, to replace petroleum products.

Figure 6: PU film

Discussion of Emerging Technology

Natural biomaterials have a greater ability than synthetic biomaterials due to the multitude of traits that synthetic biomaterials often lack. Natural biomaterials are usually much more biocompatible, biodegradable, nontoxic, and antimicrobial than synthetic biomaterials, whose best trait seems to be their durability. However, within the past 5 years, researchers have discovered that a combination of natural and synthetic biomaterials, which are hybrid biomaterials, work better than the two individually. This is because hybrid biomaterials combine the attributes of both natural and synthetic biomaterials, making an ideal biomaterial that achieves all the desired characteristics to properly restore damaged cardiac tissue. Even more, researchers have also begun to add metal nanoparticles or graphene materials to biomaterials to strengthen their electrical characteristics, eradicating the risk of the heart developing arrhythmia or further tissue damage.

Technology Hope for the Future

Long term advances for more than five years away in the future can radically change cardiac tissue engineering. Smart biomaterials may be developed to respond to physiological and mechanical stresses of the heart in order to stimulate cell behavior in wound healing. Sticky “evolving” gels and biomaterials could also be made, synergizing strategies for rapid tissue repair. Scientists may also begin to move away from biomaterials, and use cardiac patches derived from the patient’s own stem cells. This would avoid immune rejection by the patient’s body, while also fulfilling the key properties that current biomaterials must fulfill to properly aid in cardiac tissue regeneration.

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