Original Article

Carbohydrate-Based Polymers For Cartilage Regeneration

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Abstract

This paper intends to accomplish the following objectives: The goals of this review are threefold: The goals of this review are threefold: first, to evaluate the current state of cartilage substitution and regeneration; second, to analyse the patented biomaterials currently used in preclinical and clinical stages; and third, to investigate the potential of polymeric hydrogels for some of these applications and the factors that hamper their clinical success. Hydrogels are a biomaterial that has been the subject of several studies and is of particular interest for this inquiry. Here's what each of these two groups looks like: First, there's the use of cellular-free biomaterials, and second, there's the use of cellular-filled biomaterials. Below, we also cover the methods of preparation and the final hydrogel characteristics. Recent approaches to enhance these materials by combining many distinct polymers in a process known as hybridization are also analysed and discussed in this article. The ideas here are quite novel. scaffolds (cellular solids), matrices (based on hydrogels), growth factors, as well as mechanical stimulation are all required for tissue formation, cartilage regeneration, and therapeutic use. It's possible that a combination of cellular solid scaffolds, hydrogel-based matrices, growth factors, and mechanical stimulation will accomplish this. This is crucial in order to optimise the quality of the critical materials to attain the best possible performance. The most interesting and potentially useful materials for this purpose are polymer mixtures and hybrids. The formation of cartilage-like tissue with biomimetic characteristics might potentially enhance the amount of cell proliferation and local tissue integration achieved by hybrid scaffolds.

Keywords— Cartilage Engineering, Carbohydrate and Polysaccharides, Skin Regeneration, Natural Biomaterials

I. INTRODUCTION

Carbohydrates are the most widely distributed natural biomaterial and may be found almost everywhere. They participate in basic biological processes such network connections, inflammation, the initiation of infections, and even the progression of diseases via their extensive cellular interactions. Glycoconjugates including glycolipids, glycosaminoglycans (GAGs), glycoproteins, and proteoglycans mediate these multifaceted interactions between carbohydrates and cells. Carbohydrates are continually sought after as biomaterials due to the crucial roles they play in biological systems. Depending on the intended purpose, these molecules' many functions may be combined or separated to produce the desired reactions. The fields of genomics and proteomics were founded with the intention of decoding the data encoded in the genetic blueprints of different species and, more narrowly, in the sequences of amino acids that make up proteins. The major goal of glycemic research is to increase our understanding of glycans to the level at which we understand other natural chemicals. Researchers in the area of glycemia in particular believe that polysaccharides have a better potential than other molecules to preserve biological information. This is presumably the case due to the wide variety of glycosidic linkages and interactions between saccharides seen in polysaccharides, in addition to a variety of conformational structures that they can take on. (Huang et al., 2019)

II. OBJECTIVE

The research aimed to fulfill the following objectives:

- To study the carbohydrate and polysaccharides as biomaterials
- Skin regeneration and wound healing applications
- Surgical uses of cartilage engineering

- Future Trends: From Combination of Materials to Hybrid Hydrogels

III. METHODOLOGY

One of the primary objectives of the field of glycemic is to decipher the intricate interactions that take place between certain polysaccharide sequences and other biomolecules. This knowledge would be immensely helpful in the development of creative solutions to the biological and chemical difficulties that are currently being faced. The domains of biochemistry, medicine, and materials science might all stand to benefit tremendously from developments in glycemic research. The rational design of biomaterial platforms targeted compounds, and therapies will be made possible once it is determined how polysaccharides participate in cell–cell interactions, inflammatory signaling, and the development of many illnesses. Furthermore, there are an infinite number of possible uses for this information in the fields of tissue engineering and medication delivery. In light of this, this viewpoint will explore some of the existing uses of polysaccharides in various sectors as well as future directions in the study of polysaccharide biomaterials.

IV. CARBOHYDRATES AND POLYSACCHARIDES AS BIOMATERIALS

Carbohydrates have a role in cell adhesion and differentiation by interacting with both other carbohydrates and proteins. Particularly, it has been shown that interactions between carbohydrates influence cellular recognition and adhesion. To a similar extent, a mountain of evidence suggests that carbohydrate-protein interactions control infection, inflammation, and cellular adhesion. Despite the fragility of carbohydrate bonds, the contact is bolstered by multivalent interactions between polysaccharides. Multivalent polysaccharide connections are strengthened by the ligand-induced clustering of proteins and the chelate effect, in which a single connection is followed by multiple contacts. Carbohydrates are adaptable biomaterials because of their ability to interact with a wide variety of polysaccharides and biological components.

Chitosan, hyaluronic acid, and alginates were all employed as biomaterials in the past. There are several advantages to using these materials, including their ability to drive cell growth, their superior mechanical properties, their capability to form hydrogels, and their biocompatibility. Several biomaterials have been used for specialized applications in medication delivery and tissue engineering research. Polysaccharide polymers have been studied for their potential as transporters, targeting agents, and targeted ligands in the administration of drugs. Polysaccharide biomaterials have been used in tissue engineering as scaffolds for directed tissue creation and to mimic the biological extracellular matrix. Tissue engineers have also studied how polysaccharides may be altered to serve as specific cellular matrices. We'll go into more detail on the applications of chitosan, hyaluronic acid, and alginate after providing a brief overview of each. (Park et al., 2017)

- **Chitosan**

Chitosan is a linear polymer derived from de-acetylated chitin, consisting of (1-4) connected d-glucosamine and N-acetyl-glucosamine. It has a semi-crystalline structure and may potentially hydrogel at a pH over 6.5. Chitosan is positively charged and has a molecular weight that may range from 50 to 1000 Kad. The central amine groups are amenable to easy modification, including conjugation with sulfate groups, which results in a negatively charged molecule. Forms vary in their biodegradability, biocompatibility, and solubility in water. (Chan, 2021)

- **Acid hyaluronic**

Naturally occurring hyaluronic acid is a kind of glycosaminoglycan (GAG) found in extracellular matrices. In contrast to immunogenic chitosan, hyaluronic acid occurs naturally in human tissue. It is composed of d-glucuronic acid and N-acetyl-d-glucosamine in alternating units. Hyaluronic acid is a very hydrated, negatively charged, and large-molecular-weight polymer. Hydrophobicity and biological activity are two properties that may be engineered into hyaluronic acid by chemical modification, much as they are with chitosan. Biocompatibility, biodegradability, and wound healing properties have all been shown for hyaluronic acid. (Nneka Alaribe et al., 2019)

- **Alginates**

Brown algae produce alginates, which are made up of (1-4)-linked -d-mannuronic acid and -l-guluronic acid residues. Both a sequential and a cyclical arrangement of these two sets is possible. Depending on the specifics of their makeup and structure, these remnants may exhibit a wide range of mechanical and physical properties. Compared to hyaluronic acid, the molecular weight ranges from 32 to 400 Kad. Whether ionically or covalently, alginates may be cross-linked. Alginates can degrade and are biocompatible under certain conditions, albeit this depends on their specific makeup.

It's important to stress that not all polysaccharides can be used as biomaterials. Commonly used as a food additive, carrageenan is a polymer extracted from red seaweed that has been shown to have detrimental effects when utilized as a biomaterial.

Accordingly, comprehensive in vitro and in vivo biocompatibility testing is required for all new biomaterials. A variety of systems, however, have included glycans or glycoproteins that trigger immune responses when inflammation or antigenic signals are beneficial.

V. UTILIZATIONS OF SKIN REGENERATION AND WOUND HEALING TECHNOLOGY

The fact that serious illness may manifest itself after significant portions of the skin has been damaged exemplifies how important it is for the skin to fulfill its role as a barrier between the internal environment and the outside world. Patients whose skin has been injured as a result of burns or other deep injuries may need skin grafts if the loss of full-thickness skin is more than 4 centimeters in diameter. Skin transplants might also be necessary for patients whose skin has been damaged as a result of other superficial injuries. On the other hand, people whose injuries are not as serious could just need wound dressings to be treated for their injuries. It has been difficult to produce replacement skin for these individuals, in part because there are appendages that protrude through the various layers of the skin. This has made the process more difficult. One of the techniques for wound healing and skin regeneration that is now receiving the most interest from researchers is the use of tissue-generated skin substitutes. In point of fact, skin replacements were the very first tissue-engineered products that were made available to patients. This is because of the complexity of the skin's structure. One of the most significant qualities of these materials is that, in addition to reducing pain and promoting healing, they also have the ability to protect the surrounding environment while still allowing water to travel through them. (Hardingham)

The regeneration of skin and the healing of wounds are two examples of applications that have made use of materials that are based on polysaccharides. In comparison to the standard of care, the researchers Azad and colleagues showed that the use of chitosan membranes as wound dressings led to an increase in re-epithelialization. Other research employed membranes comprised of both chitosan as well as alginate as medical applications; chitosan-based hydrogels were also utilized as joint wound dressings with drug delivery systems with promising results. Other studies used chitosan-based hydrogels as joint wound dressings and drug delivery systems. Chitosan is a kind of polymer that is derived from the outermost layer of the chitosan molecule. This layer is referred to as the chitosan shell. A number of other replacement skin treatments that make use of carbohydrates are already on the market. These solutions are already accessible. When it comes to the manufacture of cultured skin substitutes, hyaluronic acid is often used as a component of the scaffold. Keratinocytes and fibroblasts are cultivated on this scaffold before the transplant is actually implanted into the patient's body. Despite the fact that these skin replacements have enjoyed some level of commercial success, they still require ongoing research and development in order to shorten the amount of time that must pass before grafting can take place, improve their vascularization and mechanical integrity, and boost their production capacity. (Sousa Segundo et al., 2019)

Surgical uses of cartilage engineering

Articular cartilage is not well supplied with blood vessels, which slows the body's ability to mend itself. Chondrocytes and the extracellular matrix they produce make up articular cartilage. Key components of cartilage's extracellular matrix (ECM) incorporate GAGs including hyaluronic acid, chondroitin sulphate, dermatan sulphate, keratan sulphate, and heparan sulphate into type II collagen. Chemical composition of ECM secreted by chondrocytes is determined by their phenotype. It is essential to maintain expression of the necessary ECM components to create healthy articular cartilage. There is more information available on the challenges of cartilage healing.

In tissue engineering, influencing chondrocyte phenotype and encouraging chondrocyte proliferation are two goals that have been suggested utilising bioactive scaffolds. Both native chondrocytes and transplanted chondrocytes may be encased in scaffolds to facilitate their proliferation and survival. Because of the potential for their chemical and mechanical qualities to influence chondrocyte expression and, in turn, the resulting cartilage, the materials utilised to create these scaffolds need careful consideration. Considering that GAGs are a crucial part of the chondrocyte extracellular matrix, they are often mimicked or materials comparable to them are used when building chondrocyte scaffolds. Chondrocyte scaffolding is a relatively new field of study, and many polysaccharide-based biomaterials have been investigated. (Hyder Haq et al., 2019)

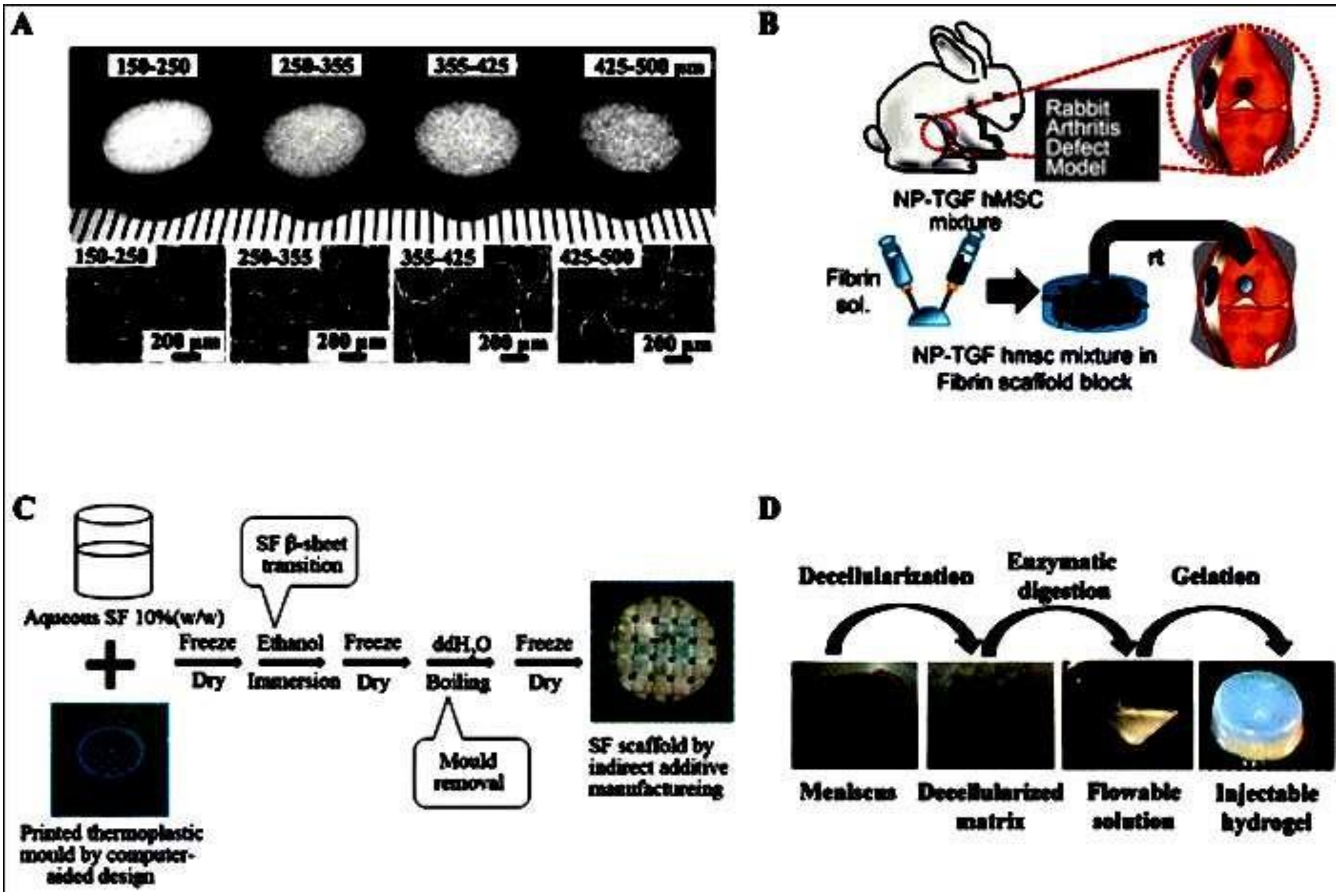

FIGURE 1. CARTILAGE REGENERATION

VI. Future Trends: From Combination of Materials to Hybrid Hydrogels

Because of its mechanical instability, hydrogel cannot integrate with the patient's natural cartilage after implantation. Several methods have been developed to create hydrogels with improved mechanical characteristics and greater mechanical stability. shown the need of certain mixtures of materials in the creation of matrices. Covalent bonding was used to graft two materials together, which increased the binding strength and the work's reinforced hydrogel maintains its mechanical properties. One was a gelatin meth acrylamide hydrogel containing chondrocytes, and the other was a thermoplastic polymer scaffold containing methacrylate groups, made in a three-dimensional printer. Numerous in vitro and in vivo studies have shown the presence of cartilage-specific matrix in chondrocytes cultured in hydrogel. A two-phased scaffold may be able to regenerate cartilage and bone tissue simultaneously due to the superior integration of ceramic-to-bone contacts over hydrogel-to-cartilage interfaces. Enhanced mechanical stability would be the effect of this. Bone will integrate within two weeks after a transplant, and cartilage will do so within twenty-four weeks.

It is possible to utilize subchondral bone fixation to stabilize a cartilage scaffold. Articular cartilage heals more quickly after implantation thanks to the osteochondral scaffold's ability to fixate and integrate with neighboring cartilage tissue. In order to aid in the regeneration of cartilage tissue, bone scaffolds must be robust enough to prevent excessive displacement or delamination of cartilage tissue in vivo. Following this line of thinking, we reinforced osteochondral scaffolds made from a combination of hydrogel and ceramic scaffolds. The scaffolds were press-fit into the defects in the rabbit knee joints' osteochondral tissue to allow for in vivo testing. Comparative study of hydrogel and hybrid scaffolds In vivo studies showed that after 12 weeks, mixed scaffolds were more effective than hydrogel scaffolds in regenerating osteochondral tissue, especially articular cartilage. The usage of ceramic scaffolds in combination with other kinds of scaffolds was required to give mechanical stability due to the instability of hydrogel scaffolds. found that physiological and physical parameters of mixed hydrogels may be altered to provide a spectrum of cell responses, suggesting therapeutic potential for treating chondral or osteochondral diseases. (Hyder Haq et al., 2019)

This strategy led to the establishment of a 3D plotting approach that enabled the development of a biphasic transplant of cartilage and subchondral bone, which proved effective in the treatment of osteochondral diseases. The combination of PLGH and alginate was employed to keep a transplanted osteochondral graft in its mature state. Human foetalis cartilage-derived progenitor cells were plated on alginate that had been mixed with either cartilage-derived extracellular matrix (ECM) or hydroxyapatite. In the shown biphasic osteochondral graft, cartilage and bone tissue predominated throughout the differentiation experiment, resulting in good integration across layers. The preponderance of bone and cartilage formation allowed for this. As a result of endochondral ossification, the final differentiation of MSCs derived from bone marrow used in the osteochondral approach is problematic. Because of this issue, chondrogenesis may stall at a phenotypic similar to that of stable cartilage hyaline. So, you'll need a proven inducer of chondrogenic differentiation and a hypertrophic suppressor to go along with a chondrogenic stimulator like the newly discovered karyogenic, which regulates.

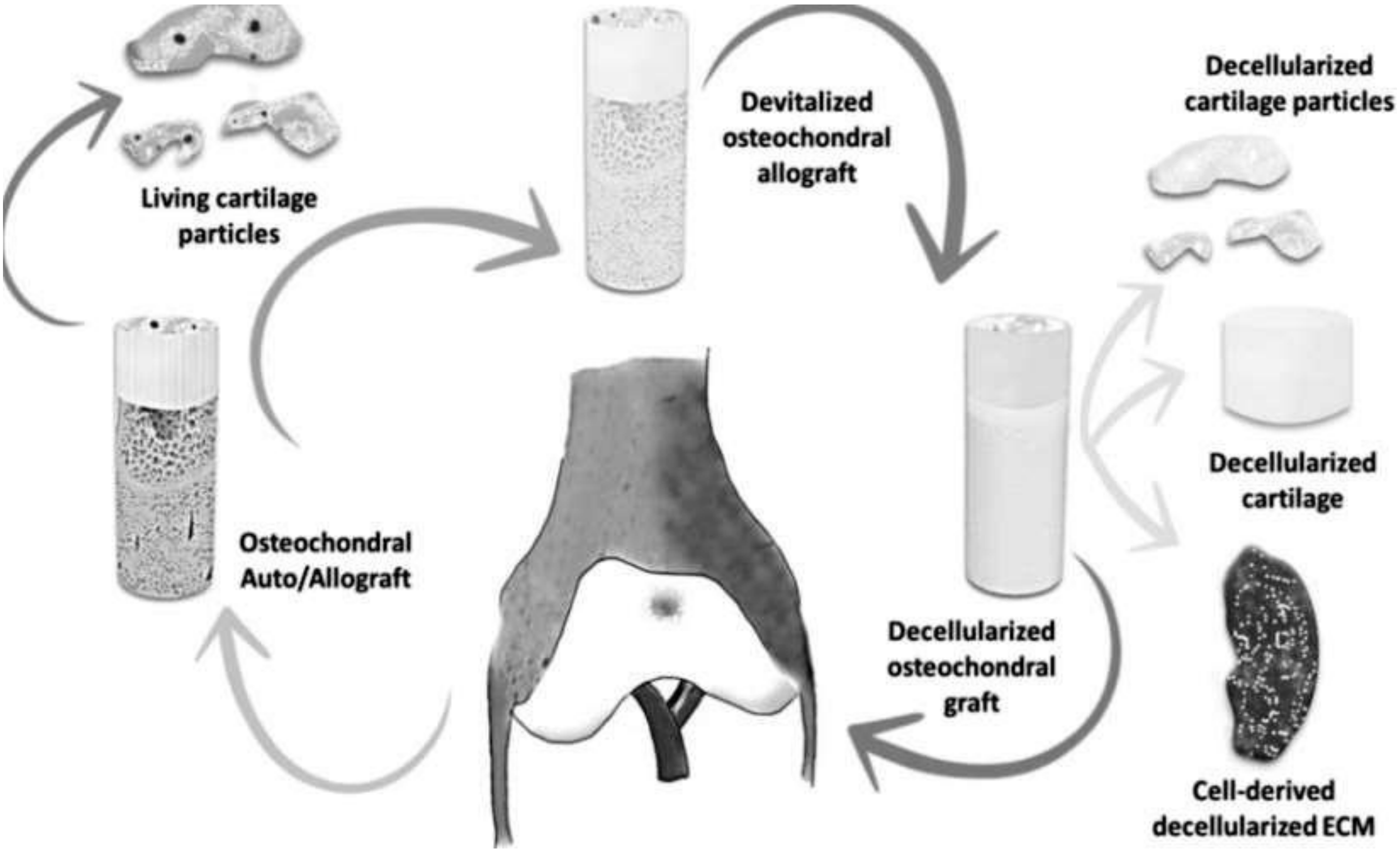

FIGURE 2: - HYDROGEL CARTILAGE REGENERATION

CONCLUSION

In the medication delivery process, polysaccharides have been employed as platforms, targeting moieties, and in the selection of active agents. Polysaccharides have furthermore been used in tissue engineering. Alginates, hyaluronic acid, and chitosan have all been extensively studied as potential protein drug delivery vehicles, while chitosan has been employed for oral gene administration. Scaffolds derived from tissue engineering that are constructed of polysaccharide materials have been used in the process of mending cartilage, cardiovascular tissue, brain tissue, and liver tissue. In the rapidly developing field of glycemic, new methods with increased throughput are being developed for synthesizing and analyzing man-made and naturally occurring polysaccharides. These technologies are also being used in the study of other polysaccharides. Antimicrobials, antivirals, anti-inflammatory medications, cancer treatments, cellular adhesion mechanisms, and drug delivery systems are just few of the exciting areas within which these approaches have led to discoveries. This puts them in an ideal position to make a major contribution to biomaterials science. Extensive work is now being put into the creation of new composite materials and synthetic polysaccharides. There is a lot of potential in biomedical research to create biomaterials that can sense biological stimuli. In this case, these hybrids will prove to be rather useful. Synthesizing polysaccharides containing high modulus and enhanced mechanical characteristics will have far-reaching effects on the development of novel tools and implants. Consequences of this magnitude are inevitable. Glycemic will bring about a sea change in the biomaterials that are now in use thanks to the discovery of these unique polysaccharides.

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