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Review Article

Application of Chitosan-Based Polysaccharide Biomaterials in Tissue Engineering

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ABSTRACT

Chitosan-based polysaccharide biomaterials have gained interest as viable options in tissue engineering due to their distinctive properties and wide range of potential applications. Biomaterials play a crucial role in regenerative medicine because they foster an environment conducive to cell growth and tissue repair. The chitin-derived polysaccharide chitosan is superior than synthetic materials in several ways: it has a similar structure to the extracellular matrix, is biocompatible, biodegradable, antimicrobial, and can incorporate bioactive chemicals. In this article, check how chitosan can be used in tissue engineering as a scaffold for different types of tissue, a hydrogel for wound healing, and a carrier for gene therapy, stem cell culture, and drug delivery. Scaffolds made from chitosan have shown tremendous promise in tissue engineering for the neurological system, bone and cartilage transplantation, and skin regeneration. Hydrogels made from chitosan have been shown to be useful in treating wounds and stopping bleeding. Chitosan's medicinal potential in gene therapy, stem cell culture, and targeted medication administration is further enhanced by the addition of bioactive components such as growth factors, genes, or medicines. In addition, using chitosan in tissue engineering can pave the way for future developments in stem cell techniques, nanotechnology, biofabrication, and 3D bioprinting, among other areas of study. These advances may one day lead to individualized and highly effective therapies for tissue repair and regeneration. The use of chitosan in tissue engineering has the potential to advance regenerative medicine and address the growing demand for more effective techniques to heal damaged tissues. Tissue engineers can revolutionize the field of regenerative medicine and enhance patient outcomes by taking use of chitosan's adaptability and bioactivity to create cutting-edge biomaterials and therapeutic techniques.

INTRODUCTION

Overcoming the limitations of current therapy for tissue and organ injuries, tissue engineering has emerged as a potentially game-changing strategy in recent years. Tissue engineering, on the other hand, is at the forefront of modern interdisciplinary approaches since it draws on knowledge from biology, engineering, and materials sciences. This research aims to explore the immense potential given by polysaccharide biomaterials based on chitosan in the context of tissue engineering. We shall look into the various methods of chitosan processing, modification, and modification's effects on tissue regeneration [1]. It is because of advancements in tissue engineering that damaged individuals can now receive transplants of synthetic tissues designed just for them. According to this tissue technique the goal of this method is to create living tissues that can be used to restore, maintain, or improve the function of organs that have been damaged or killed due to illness, which is the most crucial

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component in determining whether or not tissue engineering is effective in the development and use of biomaterials that can foster optimal conditions for cellular proliferation, differentiation, and tissue regeneration [2].The unique properties and broad applications of chitosan-based polysaccharide biomaterials in tissue engineering have garnered considerable interest among the vast selection of biomaterials [3]. Polysaccharides like chitosan are synthesized from chitosan. Biomaterials are man-made compounds designed to interact with living organisms for medicinal or diagnostic purposes. Scaffolds for cell growth and tissue regeneration, drug delivery carriers, and wound dressings are just some of the many uses that tissue engineers have found for biomaterials based on chitosan [4]. The scale of these biological structures can extend from a single cell to a whole organ. Biomaterials' innovative contributions to fields like regenerative medicine, medical implants, drug delivery systems, and diagnostic equipment make it impossible to overstate their importance in modern medicine. Customization and the addition of new capabilities boost the material's use for targeted needs in tissue engineering. As previously stated, while creating biomaterials, one must take into account the biomaterial's biocompatibility, biodegradability, and mechanical properties in addition to its ability to support cell adhesion and proliferation [5]. This field has a lot of unrealized potential in terms of helping doctors to keep up with the rising demand for transplantable organs and tissues and giving patients more control over their care. Significant progress is expected to be made in organ transplantation, 3D bioprinting, stem cell methods, nanotechnology, and biofabrication as scientists continue to investigate innovative formulations and combinations of chitosan with bioactive chemicals [6]. The applications of these changes will be due to chitosan's prominence in tissue engineering attributed to its exceptional biocompatibility, biodegradability, non-toxicity, and antibacterial characteristics [7]. Chitosan is a polysaccharide that is made from chitin and occurs naturally. Since it is cost-effective and environmentally friendly, chitosan is frequently used in sustainable biomedical applications. The chitin from which chitosan is derived is a plentiful marine resource in and of itself [8]. Chitosan's lack of negative effects on the environment is an added bonus. Cell proliferation and tissue development are aided by chitosan because of the material's porous structure and high mechanical quality [9]. Recognizing the importance of biomaterials and then investigating the adaptability of chitosan in tissue engineering may pave the way for revolutionary advances that may one day make tissue and organ transplantation a safer and more accessible reality. Exciting possibilities for the development of regenerative medicine lie ahead for the use of chitosan-based biomaterials in tissue engineering. Furthermore, we discuss the various applications of chitosan in tissue engineering, highlighting the challenges faced and future prospects for enhancing its utilization.

The Chitosan Properties

Chitosan, a polysaccharide generated from chitin, is receiving a lot of interest for its useful characteristics in many different areas. The 1, 4 glycosidic linkages in this biopolymer connect N-acetylglucosamine and glucosamine units. The exoskeletons of crustaceans including crabs, shrimp, and insects, and the cell walls of fungi are rich in chitin, the precursor to chitosan.

Antibacterial Properties

Chitosan's potent antibacterial capabilities make it a promising substance for use in healthcare, food preservation, and even environmental safeguarding. Chitosan's chemical structure includes positively charged amino groups, which interact with the negatively charged membranes of bacteria, causing membrane breakdown, intracellular component leakage, and ultimately bacterial cell death [10]. Chitosan-based materials have been developed for use as wound dressings, medical implants, and food packaging because of its antibacterial qualities. These materials are a natural and environmentally friendly alternative to synthetic antimicrobial agents.

Anti-fungal properties

Chitosan, like other antibacterial compounds, is effective against numerous types of fungi. The antifungal effects of chitosan are due to its ability to disrupt the formation of the fungal cell wall, which in turn damages the cell membrane and stunts the growth of the fungus [11]. Chitosan-based formulations are used as environmentally benign fungicides to treat plant diseases and boost crop yields because of this feature.

Biodegradability

Chitosan decomposes rapidly in the presence of oxygen, and the byproducts are safe for organisms and the environment. Enzymatic breakdown of chitosan by microorganisms like bacteria and fungi yield simpler components like glucosamine that can enter natural metabolic pathways [12]. This property of chitosan makes it an eco-friendly material with many potentials uses in biomedicine and the environment, such as in drug delivery systems and water purification.

Biocompatibility

Biocompatibility is an important characteristic of chitosan. Chitosan's capacity to promote cell adhesion, proliferation, and differentiation has led to substantial research into its potential medical uses [13]. Its low cytotoxicity makes it a good choice for uses like medication delivery and tissue engineering. Furthermore, molecular weight, degree of

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deacetylation, and specialized applications all affect chitosan's biocompatibility and can be modified to improve its performance in different biological settings.

Bio-accessibility

Bioavailability of some medications and active chemicals can be increased by combining them with chitosan due to its special structure and characteristics. Chitosan's interaction with mucosal surfaces increases medication residence time and improves drug absorption [14]. This quality has been utilized in nasal formulations, mucosal delivery systems, and oral drug delivery systems.

Physical and Chemical Properties

Chitosan's many uses can be attributed to its unique combination of physical and chemical properties, such as its ability to form films, gel, and bind metal ions. Wound dressings, controlled medication release systems, and tissue engineering scaffolds are only some of the applications for chitosan films and gels [15]. Additionally, heavy metal removal from wastewater using chitosan has helped with environmental cleanup because of its capacity to chelate metal ions. In conclusion, chitosan is a promising biomaterial for a wide variety of applications in medicine, agriculture, and environmental sciences due to its wide range of properties, such as its antibacterial and antifungal activities, biodegradability, biocompatibility, bioavailability, and various physical and chemical attributes.

Application of Chitosan in Tissue Engineering and Wound Healing

The unusual features of chitosan, a biocompatible and biodegradable polymer generated from chitin, have piqued the interest of researchers in a number of biological fields. Because of its adaptability and potential for customization, it has many potential uses in different nuances of tissue engineering and wound healing.

Dressing Material for Wound Healing

Chitosan-based wound dressings have gained popularity as a powerful therapeutic technique for speeding up the healing process and regenerating damaged tissue. Because of its porous nature, chitosan is able to efficiently absorb wound exudates while still keeping the wound's surrounding area moist, which promotes cellular migration and proliferation. Chitosan's antibacterial and antifungal characteristics also aid in lowering infection risks associated with wounds [16]. Wounds, both acute and chronic, can be treated effectively with chitosan dressings because they are simple to apply and remove without damaging the healing tissue.

Scaffolds in Tissue Engineering

Supporting cell adhesion, development, and differentiation, chitosan scaffolds play a critical role in tissue engineering as a scaffolding material. Supporting tissue regeneration and directing the growth of new functional tissues, chitosan scaffolds replicate the Extra Cellular Matrix (ECM) environment [17]. Bone, cartilage, and nerve regeneration are only some of the tissue engineering applications that can benefit from these materials because of their adaptability in terms of mechanical characteristics, degradation rates, and surface alterations [18, 19].

Chitosan as a Bioactive Agent in Tissue Engineering

Chitosan can be coupled with bioactive substances like growth factors, peptides, or medicines to improve tissue regeneration beyond its role as an inert scaffold. Tissue repair and regeneration can be guided by the regulated release of these compounds from chitosan-based matrices [19]. This method may speed up the recovery time for wounds, bone growth, and cartilage damage [20].

Biodegradable Implants

Chitosan's biodegradability is useful in creating biodegradable implants that promote tissue healing and disintegrate over time as new tissue forms. Research into chitosan-based implants for use in orthopedics, dentistry, and cardiovascular devices has been conducted in recent years [21]. The mechanical strength and degradation rate of such implants can be tailored to meet the needs of tissue restoration in the early stages before they are resorbed by the body. Chitosan is a biomaterial with several potential uses in tissue engineering and wound healing due to its unique characteristics. It has the potential to solve a wide range of medical issues due to its versatility as a dressing material, scaffold, and biodegradable implant. Chitosan's function in regenerative medicine is predicted to expand as novel formulations and combinations of chitosan with bioactive substances are investigated, potentially leading to ground-breaking advances in tissue repair and regeneration.

Biofabrication of Chitosan

Processing Chitosan

Chitin, a natural biopolymer, is used to make chitosan. Chitosan is extracted from chitin-rich materials in numerous processes. These procedures eliminate calcium carbonate and protein contaminants through demineralization and deproteination [22]. After these procedures, chitosan is crude and can be bioleached to remove leftover protein and minerals [23]. The next crucial step is deacetylation, which removes acetyl groups from chitosan's glucosamine units to make it more water-soluble [24].

Biofabricating Chitosan

In biofabrication, chitosan can be mixed with other materials to boost its efficacy and suit certain applications. Adding chitosan to biopolymers like polyvinyl alcohol (PVA) is a typical method. PVA, a water-soluble and

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biocompatible synthetic polymer, can increase chitosan's mechanical characteristics and film-forming capabilities [25]. Chitosan-PVA composite materials improve biodegradability and mechanical strength in tissue engineering, wound dressings, and drug delivery systems. In bio fabrication, crosslinking stabilizes and controls chitosan breakdown. Polyethylene glycol (PEG) crosslinks chitosan chains with stable covalent connections [26]. Chitosan-based materials can be used for tissue engineering load-bearing applications by crosslinking with PEG [27]. Adding additional materials to chitosan improves its physical characteristics and controls bioactive agent release. For instance, chitosan-based hydrogels containing growth factors or medicines can be created to release these compounds at a specified rate for sustained therapeutic benefits [28]. Tissue regeneration and wound healing are expected to see promising advancement with this method. To produce a water-soluble biopolymer, chitosan must be extracted from chitin, demineralized, deproteinated, bioleached, and deacetylated. In bio fabrication, chitosan can be coupled with PVA and crosslinkers like PEG to boost its efficacy and modify its characteristics for biomedical purposes. Regenerative medicine and biomaterial development can benefit from these modified chitosan-based materials in tissue engineering, wound healing, and drug delivery.

Chitosan-Based Scaffold

Biocompatible and biodegradable chitosan, produced from chitin, is a promising scaffold material for tissue engineering. Its particular qualities make it perfect for skin, bone, and nerve tissue regeneration.

Chitosan Scaffold for Skin Regeneration

Chitosan scaffolds for skin regeneration and wound healing seem promising. Chitosan's porous structure promotes nutrition and oxygen passage, promoting cell adhesion, proliferation, and migration [29]. Chitosan's antibacterial capabilities prevent wound infections. Growth factors and bioactive compounds in chitosan scaffolds increase tissue regeneration and wound closure [30]. Chitosan-based dressings and films promote wound healing and scar reduction by keeping wounds moist.

Chitosan Scaffold for Bone Tissue Transplantation

Bone tissue engineering uses scaffolds that encourage osteogenic cell development and mineral deposition to regenerate bone defects and fractures. Due to their biocompatibility and osteogenic differentiation, chitosan-based scaffolds have been extensively studied for bone tissue engineering. Bioactive substances like hydroxyapatite or growth factors can boost osteogenic characteristics and bone regeneration in chitosan scaffolds [31]. Chitosan-based scaffolds are promising for orthopedic and bone tissue transplantation due to their osteoinductive and osteoconductive capabilities.

Nervous Tissue Engineering: Chitosan Scaffold

Nerve injuries are hard to treat because the central nervous system regenerates slowly. Chitosan-based scaffolds enable neural cell proliferation and axonal guidance in nervous tissue creation [32]. Chitosan's biocompatibility, neural cell adhesion, and neurite outgrowth make it appropriate for nerve repair and regeneration [33]. Functionalizing chitosan scaffolds with neurotrophic agents or conductive materials enhances nerve tissue regeneration [34]. Chitosan conduits improve nerve regeneration and function in peripheral nerve injury. Tissue engineering for skin, bone, and nerve tissue using chitosan scaffolds appears promising. Biocompatibility, biodegradability, and bioactive agent customization make them useful tissue regeneration platforms. Chitosan-based scaffolds will improve tissue transplantation, wound healing, and regenerative medicine with sustained research.

Chitosan-Based Hydrogel: Wound Dressing and Hemostatic Agents

Hydrogels are three-dimensional hydrophilic polymer networks that absorb and retain significant amounts of water. Due to its unique qualities and versatility, hydrogel formulations use chitosan, a biocompatible and biodegradable polymer produced from chitin. Chitosan-based hydrogels are promising wound dressings and hemostatic agents that are natural and effective.

Chitosan-Based Hydrogel in Wound Dressing:

Biocompatibility and wound healing have made chitosan-based hydrogels popular as advanced wound dressings. These hydrogels can absorb wound exudate because chitosan is hydrophilic [35]. Chitosan's antibacterial properties aid wound healing by avoiding infections [36]. Chitosan in hydrogel matrices increases mechanical strength and flexibility, enabling for facile application and wound shape conformability. Chitosan hydrogels can also be designed to release bioactive substances like growth factors or antimicrobials to stimulate tissue regeneration and prevent microbial colonization [37]. Chitosan-based hydrogels can treat chronic and hard-to-heal wounds better than standard dressings because of these qualities.

Chitosan-Based Hydrogel as a Hemostatic Agent

In emergencies, chitosan hydrogels can stop bleeding quickly and effectively. Chitosan's strong interactions with red blood cells and platelets create a stable wound clot [38] Chitosan-based hydrogels can manage hemorrhages in civilian and military contexts since this mechanism speeds up clotting and reduces blood loss. Chitosan-based hemostatic hydrogels are easy to prepare and activate and conform to varied wound geometries. They're ideal for difficult surroundings or emergency circumstances.

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Table 1: Summarizing the role of biomaterials in tissue engineering

Experiment	Drugs Used	Citation
Chitosan based polymers for tissue engineering	Chitosan and PEG	[25]
Interpretation of axonal guidance	Chitosan based scaffolds	[31]
Nerve tissue regeneration	Chitosan and neurotrophic	[33]
Chitosan based polymers for drug delivery for wound healing	Chitosan and Poly vinyl alcohol	[17]
Chitosan based biomaterials for tissue engineering	Chitosan, PVA and PEG	[26]
Efficacy of biomaterials for bone tissue regeneration	Chitosan scaffolds bioactive substances i.e., hydroxyapatite crystals	[17]

Tissue integration and functional repair are made possible by chitosan's biomimetic properties, which encourage cell adhesion, migration, and proliferation [39]. Additionally, chitosan-based polymers have shown low cytotoxicity and immunogenicity, making them safe and appropriate for tissue engineering applications. As new tissue forms, the biodegradable scaffold can gradually degrade, allowing for a more natural transition [40]. Chitosan's potential in regenerative medicine is still being investigated and expanded through innovations in chitosan-based formulations like composite scaffolds with other biopolymers, incorporation of growth factors or stem cells, and surface modifications to enhance cell-material interactions. Chitosan is a strong contender to change the area and satisfy the need for better treatments for tissue and organ injuries due to its promising capabilities and applications.

CONCLUSIONS

In conclusion, the applications for chitosan-based materials in tissue engineering and regenerative medicine are extensive. Research has shown that chitosan has several advantages over synthetic polymers, including structural resemblance to the extracellular matrix (ECM), biocompatibility, and the potential to act as a drug delivery scaffold.

Authors Contribution

Conceptualization: AA

Writing-review and editing: AA, SZ, AUMF, FA, HF, RB, AUR, AB

Author have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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