AN ASSESSMENT OF ALGINATE COMPOSITES FOR BONE TISSUE ENGINEERING

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ABSTRACT

Immune system is a complex and hierarchical structure made up mostly of nano hydroxyapatite and collagen. There have been many efforts to create artificial bone to replace auto graft and allograft therapy. Tissue engineering is a potential method for addressing a variety of problems, and it may also be used to create artificial bone using materials such as polymer, ceramics, metals, cells, and growth hormones. Polymer-ceramic composites are the best at mimicking bone's inherent activities. Because of its biocompatibility and gel-forming characteristics, alginate, an anionic polymer with many biomedical uses, is gaining popularity in bone tissue engineering. Too far, many composites have been explored, including alginate-polymer, alginate-protein alginate-ceramic, alginate-biogas, alginate-bio silica, alginate-bone morphogenetic protein-2, and RGD peptides composite. Pore size distribution, mechanical strength, cell adhesion, biocompatibility, proliferation and differentiation, alkaline phosphatase rise, good mineralization, and differentiation potential are all improved in these alginate composites. As a result, alginate-based composite biomaterials for bone tissue regeneration will prove promising. The purpose of this study is to provide a comprehensive overview of alginate manufacture and its uses in bone tissue engineering.

KEYWORDS: *Alginate, Bone Tissue, Chitosan, Hydroxyapatite, Immune System.*

1. INTRODUCTION

Bone is an involved in supply chain tissue with a hierarchical structure that is made up of about 70% nano hydroxyapatite and 30% collagen by composition. Furthermore, water is the third primary component, and the volume and weight fractions of hydroxyapatite, collagen, and water are not consistent. It is age-dependent as well as species-dependent. At a scale of several hundred nanometers, wet collagen and HA mineral crystal agglomerations interpenetrate each other, producing the mineralized fibril(1). Bone's primary function is to provide structural support, mechanical strength, blood pH control, and calcium and phosphate balance for metabolic activities. Trauma, neoplasia, congenital abnormalities, motor vehicle accidents, osteoporosis, and arthritis, among other things, may cause bone deformities or fractures. Auto graft, allograft, and xenograft are some of the therapeutic methods available to address bone abnormalities. The main drawbacks of auto graft and allograft methods are limited donor locations and the risk of transmissible illness, respectively(2–5).

As a result, researchers and orthopedicians have given tissue engineering materials a lot of thought in order to address the issues with the current treatment regime. Researchers are experimenting with polymers, ceramics, metals, cells, and growth hormones to create an artificial bone. Tissue engineering scaffolds are used to repair a function that has been lost or a bone that has been injured. A well prepared artificial scaffold should have the same structural, functional, and mechanical properties as healthy bone. For bone tissue regeneration, scaffolds should also promote cell adhesion, proliferation, and differentiation(6). In the future, regenerative composite biomaterials will be a viable alternative to traditional auto graft and allograft implants.

Chitin, chitosan, alginate, carrageenan, and chondroitin sulfate are examples of natural-derived polysaccharides that are extensively utilized in bone tissue engineering applications. Furthermore, chemical and physical changes to these polysaccharides may result in novel characteristics that can be used in biological applications. Natural polymers are better since they are biocompatible, biodegradable, nontoxic, and plentiful(7,8). Biopolymers have been proven to be structural materials, such as cellulose, which supports the structure of higher plants, chitin, which forms the exoskeleton of several mollusks, keratin, which provides thermo insulation to hair, collagen, which provides mechanical support in connective tissues, and silk, which provides strength to spider webs. As a result of their remarkable biological characteristics, we may speculate that polymers may play a critical role in the creation of artificial organs.

Alginate, like chitin and chitosan, is a popular biomaterial for bone tissue engineering among natural polysaccharides. Alginate is a well-known substance that has excellent scaffolding properties and may be used to treat organ loss or failure. Alginate is a biocompatible, non-toxic, non-immunogenic, and biodegradable substance made up of gluconic acid and mannuronic acid. It has been extensively utilized in the food business as a thickening, emulsifying agent, and tissue engineering material, in addition to its biocompatibility, availability of sources, and cheap costs. The use of alginate-based biomaterials in orthopedic applications has received a lot of attention.

1.1 Alginate formulation:

Brown algae such as Laminariahyperborea, Laminariadigitata, Laminaria japonica, Ascophyllumnodosum, and Macrocystispyrifera produce alginate, which is a biopolymer found in seaweeds treatment with aqueous alkali solutions, most often NaOH to precipitate alginate, the extract is filtered and calcium chloride is added to the filtrate. After that, dilute hydrochloric acid may be used to convert the alginate salt to alginic acid (HCl). Water-soluble sodium alginate is generated after purification. The chemistry behind the methods that produce sodium alginate from seaweed is straightforward.

The process for making sodium alginate from seaweed. Alginate may be made into hydrogels, microspheres, microcapsules, sponges, foams, and fibers with ease. This feature may expand the range of uses for alginate in areas like tissue engineering and medication delivery. Various techniques of preparation have been discussed. Alginate may be chemically and physically modified to tailor its characteristics and functions, such as biodegradability, mechanical strength, gelation property, and cell affinity, to specific applications. For bone tissue regeneration, additional substances such as growth factors and peptides may be combined to make physical and chemical modifications(9).

1.2 Alginate-polymer nanocomposites:

i. Chitosan composites

There are numerous study papers on the use of alginate polymer nanocomposites for bone tissue regeneration. One of the most researched materials is alginate-chitosan composite for bone tissue healing. The most common cationic polysaccharide is chitosan. Chitosan's cationic nature makes it easy to form polyelectrolyte complexes with a variety of anionic polysaccharides. Biomaterials such as chitosan and its composites have been widely researched for bone tissue engineering. The chitosan-alginate scaffold was produced using a simple mixing and freeze drying technique, and the scaffold exhibits mechanical characteristics and cell growth. Uniform The acetic acid and alginate concentrations in the composite scaffold are found to be directly related to the pore size of the alginate-chitosan scaffold. In comparison to greater viscosity samples, chitosan alginate polyelectrolyte with viscosities below 300Pas had good pore structure and improved cell proliferation.

ii. Composites of collagen or gelatin:

Preosteoblast spreading and proliferation, as well as osteogenic differentiation, were found to be supported by chemically modified methacrylate alginate coupled with collagen. Methacrylate is a chemical modification of alginate that allows it to be controlled in terms of physical characteristics including degradation rate, swelling, and tensile capabilities(10–12). In comparison to the pure methacrylate alginate hydrogel, collagen-added hydrogels showed greater mechanical moduli, fast cell proliferation, osteogenic differentiation, and reduced swelling ratios. Cell proliferation, mineral nodule development, and type 1 collagen expression have all been studied in vivo using sodium alginate/gelatin scaffolds for bone tissue creation. Gelatin is an irreversibly hydrolyzed form of collagen that is widely utilized as a gelling agent in the pharmaceutical, culinary, and cosmetic industries.

iii. Composites made of synthetic polymers:

The addition of synthetic polymer to alginate often improves the composite material's mechanical strength. Thermo sensitive copolymer was created by grafting poly-COOH with a single carboxyl end group onto active alginate through amide bond connections, and the composite was shown to be biocompatible with mesenchymal stem cells. The lyophilization technique was used to make alginate hydrogels from several synthetic polymers (poly (ethylene glycol) monomethacrylate (PEGmM), poly (propylene glycol) monomethacrylate (PPGmM), and methacrylic alginate (MA). Both nanopores and micropores were found in the hydrogels. Because of the rise in charge density, hydrophobicity, and pore size, increasing the mass fractions of MA and PPGmM in the microporous hydrogel encouraged the development of apatite layers.

1.3 Alginate was used as a delivery medium for stem cells, BMP-2, and RGD peptides:

Chemical alteration of the scaffold has led to the development of several bio composite materials, including the immobilization of functional cell-adhesive ligands and bioactive molecules like as enzymes, medicines, and cytokines. When a bone fracture occurs, the human body naturally generates numerous cytokines to heal the damage; these substances are known as growth factors. The big defect, on the other hand, is essential for the human body to heal and rejuvenate.

1.4 Interaction of stem cells with alginate scaffolds:

Mesenchymal stem cells can develop into a variety of cell types, including osteogenic, adipogenic, and chrondrogenic cells, making this a potential and new method to creating artificial organs. Delivering mesenchymal stem cells to the defective region is a crucial step in regenerating bone tissue in a variety of situations. Alginate is a popular biomaterial for stem cell encapsulation because it distributes stem cells to particular tissues. The cellular survival and osteogenic differentiation of periodontal ligament and gingival mesenchymal stem cells encapsulated in oxidized alginate micro beads were extensively studied. In vitro, the produced system was nontoxic scaffolds with superior osteogenic and adipogenic stem cell differentiation than the control group(13).

1.5 Delivery of growth factors:

Several medicinal substances, including as antibiotics, enzymes, growth factors, and DNA, have been effectively integrated and delivered into the targeted region using alginate. Alginate hydrogels have been extensively researched as scaffolds and carriers for physiologically active chemicals or cells in cartilage and bone repair. Bone Morphogenetic Proteins (BMPs) are a kind of growth factor that has been widely utilized due to its beneficial effects on bone development. Recombinant human BMPs, in addition to natural BMPs, are frequently utilized for orthopedic therapy.

1.6 RGD delivery for bone tissue regeneration:

L-arginine, glycine, and L-aspartic acid try to compensate the tripeptide RGD. RGD-peptides have been linked to cellular attachment and may be utilized to coat synthetic scaffolds to improve cellular adhesion in tissue engineering. The physical and biological properties of alginate hydrogels with low and high molecular weights were investigated when they were combined with RGD peptide. RGD-modified alginate microspheres showed more intense mineralization staining and greater levels of ALP and osteocalcin secretion than unmodified alginate microspheres(14–17). The cellular survival of human mesenchymal stem cells immobilized in RGD linked alginate microspheres was increased by more than 90%, resulting in increased alkaline phosphatase activity and upregulation of collagen type I and Runx. Furthermore, osteogenic stimulation immobilized cell microspheres exhibit significant mineralization, and cell immobilized alginate microspheres promote endothelial cell tube formation. To enhance cell proliferation, osteoblast cells were co-transplanted on alginate hydrogels modified with an RGD-containing peptide.

1.7 Tissue Engineering:

One of the most severe and expensive problems in human health care is tissue and organ failure caused by abnormalities, traumas, or other kinds of damage. The transplanted tissue does not perform all of the activities of the original tissue and may lead to complications at the donor location. As a result, stem cells, tissue engineering (TE), and organogenesis have emerged as promising and important fields of study, with the potential to provide not only tissues and organs for transplantation but also new avenues for disease treatment; TE aims to develop functional substitutes for damaged tissues and organs(18–21). The aim of TE is to overcome the constraints of traditional organ transplantation and biomaterial implantation therapies. In tissue engineering, a basic idea is to mix a scaffold or matrix with viable cells to create a cell–biomaterial construct that may be utilized to promote tissue repair and regeneration.

1.8 TE Bone:

Bone is a living tissue that is constantly regenerating its structure. Bone deficiencies may be caused by trauma or illness, and bone replacement materials are utilized to repair and rebuild them. Bone grafting, in which bone from another part of the patient's body is removed or bone from a human donor is utilized to replace the deficiency, is a common therapeutic method. Bone TE's ultimate aim is to create a construct that mimics the physical and biological characteristics of real bone tissue while avoiding the disadvantages of autologous or allogenic bone transplants(22). Applications for bone TE include bone regeneration following tissue loss due to degenerative, surgical, or traumatic events, as well as spinal arthrodesis. In addition, there is a need to hasten the healing from bone fractures and to treat nonunion fractures that have already occurred. Through the integration of scaffold structures with cells and bioactive chemicals, Bone TE provides novel treatment methods to assist musculoskeletal repair(23).

2. DISCUSSION

The objective of this review was to go over how alginate is used in bone TE. It aimed to provide an overview of the many kinds of materials available as well as their distinct characteristics, enabling the reader to choose the material that best suited the bone TE application. To summarize, alginates have quickly extended into the biomedical sector, adding substantially to the toolkit of biomaterial and TE scientists. They are no longer simply low-cost commodities for technical applications. Current alginate, on the other hand, is still unable to satisfy all of the design requirements at the same time. Alginate's Function in Bone Tissue Engineering Controlling these characteristics may be accomplished in future research by making chemical or physical changes to the polysaccharide or the gels made from alginate, allowing for the creation of more natural and functioning tissues. Despite all of the progress achieved in these areas, clinical usage is still restricted owing to certain unresolved issues. In many instances, it is a requirement that the scaffolds be biodegradable bone substitutes. Despite the fact that some of them have been used to clinical situations, no scaffolds that are clinically complete have been created. It is necessary to develop a more functioning scaffold so that it can be used more extensively. Close cooperation between biological and engineering disciplines is required to overcome these constraints.

3. CONCLUSION

Because of its biocompatibility, degradability, gel-forming ability, encapsulating characteristics, and ease of molding in different geometries, alginate has been demonstrated to be a potential biomaterial for bone tissue engineering. Alginate, on the other hand, falls short in terms of cell adhesive and mechanical characteristics. To address this problem, alginate-based scaffolds will be used more often with the inclusion of HA, calcium phosphate cements, biogas, and other natural and synthetic polymers. The inclusion of scaffold may not interfere with the development of bone, which happens in multiple stages in most cases. The use of Nano hydroxyapatite and other calcium phosphate cements in combination with alginate significantly aids in the creation of scaffolds for bone tissue regeneration. Hydroxyapatite and calcium phosphate cements are effective materials for bone tissue regeneration and transfer of growth factors and genetic materials to the bone. Outstanding biocompatibility, homogeneous dispersion of ceramic particles, and rapid cell proliferation are only a few of the benefits of using the HA in situ technique. For improved bone tissue regeneration, many researchers have created alginate composites incorporating bone growth factors such as BMP-2 and RGD. Alginate encapsulation of stem cells with administration of BMP-2 and RGD peptides is a potential method for bone tissue repair and regeneration. Alginate is unquestionably beneficial to bone tissue engineering.

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