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Chitosan: A BriefReview on Structure and Tissue Engineering Application

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Abstract:

Tissueengineering is an important therapeutic strategy for present and future medicine. Recently, functional biomaterial researches have been directed towards the development of improved scaffolds for regenerative medicine. Chitosan is a natural polymer from renewable resources, obtained from shell of shellfish, and the wastes of the seafood industry. Many researchers have focused on chitosan as a potential source of bioactive materials in the past few decades. It has novel properties such as biocompatibility, biodegradability, antibacterial, and wound-healing activity. Furthermore, recent studies suggested that chitosan and its derivatives are promising candidates as a supporting material for tissueengineering applications owing to their porous structure, gel forming properties, ease of chemical modification, high affinity to in vivo macromolecules, and so on. In this review, we focus on the skin and bone tissueengineering applications of chitosan.

Key Words: Chitosan, Bone tissue engineering, Scaffold, Natural polymer, Skin tissue engineering.

Introduction

Tissue engineering is a developing science technology and can be applied to improve the numerous clinical situations, including spinal fusion, joint replacement, and fracture nonunion and pathological loss of bones [1]. The tissue engineering applications from synthetic and natural polymer scaffolds have been comprehensively examined for the bone tissue replacement in lab and clinic. The polymer materials are more beneficial than others because of their biocompatibility, mechanical properties, micro-structure and the degradation rate, and these properties can even be precisely controlled by composition and fabrication of scaffold polymer materials. The basic idea in all of these accessions is to seed or grow the cell on thebiodegradable polymer scaffold to promote tissues growth and remodeling. During the bone tissue regeneration, cell cannot be directly entrapped, because the environment which is used to create them is brutal for the cells to inhabit [2, 3]. Tissue-engineering systems have attempted to mimic the function of ECMs by placing cells along with growth factors in synthetic scaffolds that act as temporary ECMs. As the new bone is formed, the temporary scaffold will degrade and be absorbed by the body [4, 5]. In last 15 years bone tissue engineering research has increased dramatically. The design and development of the bone scaffolds depend upon the porosity that provides inter-connected pores, suitable mechanical strength, and sufficient micro chemistry of surface. It is friendly to the cell behaviors like proliferation, migration, adhesion, and differentiation [6]. There are many factors for the bone tissue engineering, but all connected one are more of the fol-lowing key ingredients, (a) harvested cells, (b) recombinant signaling molecules, and (c) three dimensional (3D) matrices [7, 8]. During the tissue regeneration, all of these factors play very important roles in the healing process. In the field of bone tissue engineering three dimensional scaffolds facilitate the cells, the guilds, augment and then regenerate three dimensional tissues. After implanted into the defect sites, the scaffolds are

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expected to promote and direct the growth of new bone cells and make the new cells attach to intrinsic tissues nearby by degrading slowly and grow together afterwards. This article focuses on chitosan as natural polymer for skin and bone tissue engineering application.

Chitosan structure and properties

Chitosan, the amino polysaccharide copolymer of 1,4 D-glucosamine and N-acetyl glucosamine (Figure 1) is derived from chitin by alkaline or enzymatic deacetylation[9-12]. Therefore, chitin and chitosan are essentially the same polymer but with arbitrarily defined degrees of deacetylation(DD). Generally, if the DD is more than 40%, the term chitosan is used [13]. Chitosan's biodegradation process is dependent on two main factors; the DD and the distribution of NAG units. This was elucidated in the works of Lee et al. who showed that biodegradation declines sharply when the DD is more than 70% [14], and Aiba et al. who found that chitosans with randomly distributed NAG units are less susceptible to lysozymic degradation than chitosans which have repeated blocks of three consecutive NAG units [15].

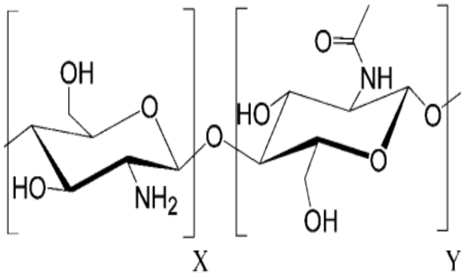

Figure 1.Molecular structure of chitosan.

In vitro hydrolysis kinetics of chitosan by lysozymes follows the typical Michaelis-Menten kinetics, where km and Vmax are 15 µg/ml and 0.083x10-3 g/L/min, respectively [16]. However, in vivo degradation of chitosan, which in theory parallels the rate of tissue regeneration, is variable. Tomihata et al. reported that only 10% of a chitosan film was degraded after 50 h of exposure to lysozymes and 80% of the dry film weight was retained afte r 12 week implantation in Wistar rats [16]. In addition to being biodegradable, chitosan is a biocompatible polymer. This stems from chitosan's distinct structural similarities to the mammalian glycosaminoglycans (GAGs), which are a family of heteropolysaccharides in mammals that are located primarily on the surface of cells and in the extracellular matrix (ECM) [17]. These molecules are long unbranched polysaccharides which contain repeating disaccharide units. Each disaccharide unit contains either one of two modified sugars; N-acetyl galactosamine or N-acetyl glucosamine and uronic acid such as glucuronate or iduronate [17].

Chitosan has wide applications in medical fields, such as wound dressing, hypocholesterolemic agents, blood anticoagulant, antithrombogenic and drug delivery systems, in addition to other fields such as waste-water treatment, food and feed additives, wound-healing materials, cosmetic preparations and textile, paper and film technologies [18, 20].

Tissue engineering applications of chitosan

Skin

Wound healing is a specific biological process related to the general phenomenon of growth and tissue regeneration. Wound healing progresses through a series of interdependent and overlapping stages in which a variety of cellular and matrix components act together to re-establish the integrity of damaged tissue and replacement of lost tissue [21]. The wound-healing process has been described as comprising five overlapping stages, which involve complex biochemical and cellular processes. These are described as hemostasis, inflammation, migration, proliferation and maturation phases. Many studies have been reported on the use of chitosan as a wound-healing accelerator, and in fact there is good evidence that chitosan can beneficially influence every separate stage of wound healing. Chitosan and its derivatives could accelerate wound healing by enhancing the functions of inflammatory cells, such as polymorphonuclear leukocytes (PMN) [22, 24], macrophages and fibroblasts or osteolasts [25, 30]. It has also been reported that chitosan could increase the tensile strength of wounds [31]. The wound-healing effects of chitosan could be affected by the factors of molecular weight deacetylation degree as well as the state of chitosan[32].

Bone

In bone tissue engineering, the biodegradable substitutes act as a temporary skeleton inserted into the defective sites of skeleton or lost bone sites, in order to support and stimulate bone tissue regeneration while they gradually degrade and are replaced by new bone tissue. Also, for being suitable for use in treating vertebral fracture or related conditions, bone cements must possess: proper injectability, a rapid setting time, appropriate stiffness, bioactivity, low setting temperature, and radio-pacity [33]. Composite materials are now playing predominant role as scaffolds in bone tissue engineering. Chitosan has numerous advantageous properties for orthopedic applications, as described above and elsewhere [34], which make it ideal as a bone graft substituent. Chitosan scaffolds are flexible and their mechanical properties are inferior to those of normal bone, as it is unable to support load bearing bone implants. Moreover, chitosan itself is not osteoconductive, although addition of ceramic materials improves its osteoconductivity and mechanical strength. Chitosan scaffolds alone cannot imitate all the properties of natural bone. The substantial development of composite materials with chitosan mimics all th e properties of bone. As proven, calcium phosphate materials are osteoconductive to mimic the inorganic portion of natural bone, while chitosan/HAp composite materials show promise in mimicking the organic portion as well as the inorganic portion of natural bone. Several studies have been conducted with chitosan/HAp composite materials for bone tissue engineering [34, 45]. Calcium phosphate compounds are of great interest in the field of bone tissue engineering. Hydroxyapatite [$Ca_{10}(PO_4)_6(OH)_2$] is one of the most stable forms of calcium phosphate and it occurs in the bone as a major component (60 to 65%) [46]. HAp also possesses a variety of uses, including orthopedic, dental and maxillofacial applications. Therefore, HAp has recently emerged as an important compound for artificial bone preparation. It stimulates osteoconduction being gradually replaced by the host bone after implantation. It is being used for orthopedic replacements, especially in bone regeneration and dental implant treatment. The mechanical properties of HAp are poor, though, so it cannot be used for load bearing bone tissues. Polymers have been used to improve the mechanical properties of HAp (compressive strength, Young's modulus, fracture toughness) [47].

Conclusion

Tissue engineering as termed Regenerative Medicine is regarded as an ultimately ideal medical treatment for diseases that have been too difficult to be cured by existing methods. This biomedical engineering is designed to repair injured body parts and restore their functions by using laboratory-grown tissues, materials and artificial implants. For regeneration of failed issues, this biomedical engineering utilizes three fundamental tools: living cell, signal molecules, and scaffold. Chitosanis one of the most promising biomaterials in tissue engineering because it offers a distinct set of advantageous physicochemical and biological properties that qualify them for a variety of tissue regeneration. In this review, we presented the examples of the chitosan applications in bone and skin tissue engineering. However, further improvements in the structure and function of this system, such as optimization of chitosan (molecular weight or DDA), chemical modification using functional groups, and formation of ternary complexes, are still necessary.

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