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Synthesis and Characterization of Wool Keratin/Hydroxyapatite/Alginate Composites

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Abstract

Interests in HA/polymer composites for bone tissue engineering have escalated due to their excellent biological response to damaged tissues. HA/polymer composites have been researched as potential implant in bone defects and voids. In this paper, HA was co-precipitated with two polymers including wool keratin and alginate. By changing the concentrations of wool keratin solution, alginate solution and Ca^{2+} and PO_4^{3-} solution, the ratios of inorganic and organic phase were changed. The final result shows that HA embedded in the organic phase well and HA nanoparticles grown on the surface of wool keratin and linear alginate macromolecules formed cross-linking around Ca^{2+} of HA nanoparticles.

Keywords: Hydroxyapatite; Wool keratin; Alginate; Nanocomposite; Biomimetic

1 Introduction

Bone takes an important role in the human body for protection, movement and support [1]. A natural bone is mainly composed of collagen and calcium phosphate. Collagen as microfibers provides a matrix with net-like mass structure, taking up 17%-20% of bones [2]. Calcium phosphate, accounting for 69%-80% of bones, is in the presence of crystallized hydroxyapatite (HA) and amorphous calcium phosphate (ACP)[18] [2]. HA crystals are parallel to the collagen fibres along the long axis [2]. Bone diseases such as osteoarthritis, osteomyelitis and osteoporosis have troubled patients for a long time, leading to bone defects or voids [1]. Bone defects with non-union and critical-sized defects must be treated by filling substitutionary materials, and mechanical fixation does not work [1]. Traditional approaches to treating bone defects are autogenous bone grafting and allograft, possibly contributing to complication or infections [1]. Based on demands for improving the treatment of bone defects and voids, bone tissue engineering was proposed to enhance the biological response to damaged tissues with engineering principles [1, 3]. Ideal implants used in the bone tissue engineering must mimic the natural environment to facilitate physiological responses [1]. For satisfying biomimetic requirements, implants used in bone tissue engineering should have following properties: proper mechanical support, bone cell migration facilitation, osteoconductivity, osteoinductivity, cellular activity enhancement, controllable

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degradability, non-toxic degradation, controllable drug delivery and no active chronic inflammatory response [1]. Thus, many biomaterials including ceramic, metals, polymers and composites have been studied. Among of these materials, ceramics especially HA and polymers especially natural polymers have become the most potential materials. HA/natural polymer composites due to its excellent properties emerged as ideal implants for treatments of bone defects [1]. HA with 1.67 Ca/P molar ratio is the most stable phase of calcium phosphate between pH 4.0 to pH 12.0 [4, 5]. HA can be easily obtained, extracted from cortical bovine bone or prepared by wet reaction or solid state reaction [2]. Synthetic nano-sized HA, with similar structures of biological apatite, is nearly identical as mineral HA of natural bones [5]. It has good biocompatibility and osteoconductivity [6, 7]. The presence of synthesis HA in the implant is the key for improving the biological response since it can simulate the Ca-P rich layer of natural bones for mineralization of ions [8]. Natural polymers are often collagen, alginate, chitosan and gelatine [9]. These natural polymers have good degradation property, biocompatibility and non-toxicity [1, 10]. Meanwhile, they can enhance cell attachment and provide an organic phase for simulating the 'ceramic-organic' system of natural bones [2, 9].

Most of papers researched natural HA/collagen composites for their similar compositions of natural bones. For instance, in vitro collagen mineralisation, thermally-triggered assembly of HA/collagen gels and vacuum infiltration of collagen into a HA matrix and etc. are common HA/collagen composites [11]. Collagen can be only extracted from natural extractions such as skin, tendon, and derivatives from human placenta and marine sources [11]. Isolation and purification of collagen require precise operation because collagen easily dissolves when covalent crosslink exists [12]. Due to its complex extraction and single source, collagen is high-priced [12]. What is more, it must be handled with in addition to removing antigenic sites, and its hydrophilicity contributes to swelling and releasing drug faster [12]. Although natural collagen can reduce risks of rejections and has very excellent biocompatibility and biodegradability, it is not quite suitable for applications in bone diseases due to high cost and antigenicity. Therefore, HA/collagen composites are hard to promote. Alginate is a linear non-repeating negatively charged copolymer belongs to polysaccharides [13]. Alginate usually exists as hydrogels, which are composed of hydrophilic polymers with 3D cross-linked networks, similar to the macromolecular-based components in the body [13]. So it is potential in drug delivery. In the presence of G blocks, divalent cations such as Ca^{2+}, Ba^{2+} or Sr^{2+} can interact with G monomers by ionic bridges [13]. Then the polymer chains form cross-links like a model of egg-box [13]. Usually, Ca^{2+} is used as the agent to form hydrogels because of nontoxicity. Alginate has a number of hydrophilic groups like —OH so that its gelation is not stabilised and cannot be controlled well [13]. Alginate has good biocompatibility but lacks enough mechanical properties for load bearing at the first stage of fixation [13]. For HA/alginate composites, the common way to combine HA and alginate is cross-linking method that mixing synthetic HA powders with aqueous sodium alginate solution [13, 15]. Due to the good ability of drug delivery of alginate, HA/alginate composites aim at delivering drugs. Organic materials combine with inorganic materials by electrostatic interactions and hydrogen bonding [16]. These reactions have been proved they can improve mechanical properties, degradation and swelling behaviour [16]. As for its limitations, the fundamental problem is there is no collagen or similar materials in this system, which reduces repair efficiency of HA/alginate composites.

Alginate and collagen are most selected to combine with HA as HA/natural polymer composites. Other HA/natural composites such as HA/chitosan composites and HA/gelatine composites have similar advantages and disadvantages. Although HA/chitosan composites are potential bone implant materials with good osteoconductivity, osteoinductivity and osteogenictity, issues with