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A functional polymer designed for bone tissue engineering

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ABSTRACT

Most synthetic polymers lack biological and chemical functionalities. This lack of functionality restricts the polymer properties and prevents them from controlling specific cell–material interactions. Polymers with free functional groups allow facile modifications, which can be used to control the biointerface. Here we created a functionalizable polymer, poly(fumaroyl bioxirane) maleate (PFM), with three free functional groups – hydroxyl, carboxyl and alkenyl – for bone tissue engineering. PFM was readily synthesized in two steps. PFM showed strain-dependent moduli with mechanical strength approaching native bones. PFM supported the adhesion, spreading, proliferation, and maturity of rat calvarial osteoblasts. The alkaline phosphatase activity of osteoblasts on PFM was significantly higher than that on tissue-culture-treated polystyrene in vitro. The physical, mechanical, and biological properties of PFM can be modulated by various functionalizations to explore methods to improve bone tissue engineering and regenerative medicine in general.

1. Introduction

Bone defect due to trauma, tumor and other diseases is an important health care problem that presents a significant clinical challenge [1]. Autograft transplantation is the gold standard for bone reconstruction. However, the harvest of graft tissue leads to donor site morbidity. Allograft transplantation is clinically limited due to high incidence of immune rejection and lack of donor sources [2]. Recently, tissue engineering approaches have demonstrated potential solutions for bone tissue regeneration. Polymeric biomaterials play an important role in bone tissue engineering [2,3]. Ideally, polymers used in bone tissue engineering should have good biocompatibility, controlled biodegradability, excellent mechanical strength, and defined bioactivity. Synthetic polymers can be easily fabricated and designed to have tunable properties with low batch variation. Thus synthetic polymers have been widely used in bone tissue engineering. However, most synthetic polymers including poly(urethane)s [4–6], polylactide, poly(propylene fumarate) [7], and their derivates are hydrophobic, biologically inert, lack modification sites, and, consequently, have a relatively limited scope of properties [2,8,9]. To address these drawbacks, hydroxyl and carboxyl functional groups can be added to polyesters.

Introduction of functional groups can modulate macroscopic properties of materials such as hydrophilicity, charge, degradation rate, and thermal properties. Additionally, it can affect cell behaviors including attachment, proliferation, and differentiation [10–13]. More importantly, functional groups enable diverse post-polymerization modifications, which can easily alter the material's mechanical, physical, chemical, and biological properties [8,9]. However, efficient synthesis of functionalized polyesters is still a significant challenge in polymer science [8,9]. Both pre-functionalization via polymerization of functionalized monomer and post-functionalization via modification of non-functionalized polyester require complicated procedures with a low overall yield. Furthermore, modification after polymerization may cause polymer degradation [14–17]. Thus developing functionalized polyesters with facile preparation and controlled properties is highly desired for bone tissue engineering and regenerative medicine in general.

Accordingly, we designed a new functionalizable polyester, poly(fumaroyl bioxirane) maleate (PFM), for bone tissue engineering (Fig. 1). The design is based on the following criteria.

(1) Osteocompatibility: the extensive hydroxyl and carboxyl groups may promote cell adhesion, proliferation and differentiation, which are potentially beneficial for facilitating tissue formation and growth [11–13]. The free carboxyl groups should mimic the protein matrix of bone and provide mineralization sites to induce ossification [13,18,19]. In addition, carboxyl groups make the polymer negatively charged, which may increase attachment and viability of osteoblastic cells [20].

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