Acta Biomaterialia 8 (2012) 1117–1124

Contents lists available at SciVerse ScienceDirect

Acta Biomaterialia

journal homepage: www.elsevier.com/locate/actabiomat

Mineral coatings modulate β-TCP stability and enable growth factor binding and release

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ARTICLE INFO

Article history:
Received 17 August 2011
Received in revised form 9 November 2011
Accepted 21 November 2011
Available online 2 December 2011

Keywords:
β-TCP
Bone morphogenetic protein 2
Vascular endothelial growth factor
Bone tissue engineering
Hydroxyapatite

ABSTRACT

β-Tricalcium phosphate (β-TCP) is an attractive ceramic for bone tissue repair because of its similar composition to bone mineral and its osteoconductivity. However, compared with other ceramics β-TCP has a rapid and uncontrolled rate of degradation. In the current study β-TCP granules were mineral coated with the aim of influencing the dissolution rate of β-TCP, and also to use the coating as a carrier for controlled release of the growth factors recombinant human vascular endothelial growth factor (rhVEGF), modular VEGF peptide (mVEGF), and modular bone morphogenetic protein 2 peptide (mBMP2). The biomineral coatings were formed by heterogeneous nucleation in aqueous solution using simulated body fluid solutions with varying concentrations of bicarbonate (HCO_3). Our results demonstrate that we could coat β-TCP granules with mineral layers possessing different dissolution properties. The presence of a biomineral coating delays the dissolution rate of the β-TCP granules. As the carbonate (CO_3^{2-}) content in the coating was increased the dissolution rate of the coated β-TCP also increased, but remained slower than the dissolution of uncoated β-TCP. In addition, we showed sustained release of multiple growth factors, with release kinetics that were controllable by varying the identity of the growth factor or the CO_3^{2-} content in the mineral coating. Released rhVEGF induced human umbilical vein endothelial cell (HUVEC) proliferation, and mVEGF enhanced migration of mouse embryonic endothelial cells in a scratch wound healing assay, indicating that each released growth factor was biologically active.

1. Introduction

Calcium phosphate bioceramics are attractive materials for bone tissue repair because of their similar composition to bone mineral, good osteoconductivity (e.g. ability of a material to promote bone formation directly on their surfaces), and osteointegration (e.g. the ability to physically and chemically bond to the surface of bone tissue) [1,2]. The most widely used bioceramics are hydroxyapatite (HAP) and β-tricalcium phosphate (β-TCP), and these bioceramics have different physico-chemical properties as a result of their different compositions and crystalline structures. Both materials have been used as bone replacement materials. However, dense HAP is resorbed very slowly, if at all [3], while β-TCP has a relatively fast rate of degradation [4]. Controlled dissolution of bioceramics is a critical parameter in the design of bone tissue engineering scaffolds, as ideally the scaffold is replaced by bone as it degrades. In this regard, β-TCP can be characterized by an adversely high dissolution rate in some applications, while stoichiometric HAP is characterized by adversely low dissolution, which can result in incomplete resorption [3]. In the current study β-TCP granules were mineral coated with the aim of enhancing and controlling the dissolution rate of β-TCP.

Calcium phosphate bioceramics can also serve as carriers for growth factors due to their high affinity for proteins [5–7]. Growth factors can be surface bound or added as a powder during the formation of low temperature calcium phosphate cements [8]. Additionally, proteins have been co-precipitated during "biomimetic" growth of HAP coatings in simulated body fluids (SBF) to achieve sustained release as the biomineral is resorbed [9]. Several growth factors that influence bone formation have been released from HAP, including BMP2, TGFβ1, IGF1, and FGF2. However, since some calcium phosphate materials are rapidly resorbed while others are only slowly resorbed, growth factor release kinetics from a given bioceramic material are difficult to control. In this study we

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doi:10.1016/j.actbio.2011.11.028