Specific roles of sodium for the formation process of manganese-substituted octacalcium phosphate

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ABSTRACT

In the field of biomaterials, octacalcium phosphate (OCP) and biocompatible elements doped with OCP-based materials are attractive materials for new bone substitution because they could be used to control the bone remodeling process in patients with bone diseases. Manganese (Mn) might be a good substitutional element candidate because of its regulation process of bone remodeling for controlling osteo-cellular activities. However, Mn strongly inhibits OCP formation. This study demonstrates that the sodium (Na)-induced OCP formation enhancing the HPO\(_4^{-}\)-OH layer structure of the OCP can overcome this Mn inhibition effect. The Mn-substituted OCP can be fabricated from the coexisting solutions of Na and Mn. The results show that the Mn-substituted OCP-induced Na (OCP-Mn,Na) showed a 4.7° peak in the X-ray diffraction pattern. The sub-peaks at 9.2° and 9.7° of the OCP disappeared, but an extra peak at 9.3° was observed. The thermal stability of the OCP-Mn,Na was significantly lower than that of the conventional OCP because the layer structure of the OCP-Mn,Na decomposed above ~70 °C. This ionic conjugation to Mn is a unique phenomenon for Na, unlike other cations.

Keywords: Mn, octacalcium phosphate, ion substitution, Na, ion conjugation

INTRODUCTION

Octacalcium phosphate [OCP: Ca\(_8\)(PO\(_4\))\(_6\)(HPO\(_4\))\(_2\)·5H\(_2\)O] is not only a main component of an immature bone but is also an attractive material for the centerpiece of new biomaterials because of its excellent biocompatibility and components of Ca and PO\(_4\)\(_3\), which universally exist in biological beings (Brown et al. 1962; Davies et al. 2014; Dorozhkin and Epple 2002; Habraken et al. 2016). Its excellent bone-replacing ability is valuable for new bone substitutes (Kamakura et al. 2002; Sugiura et al. 2018; Suzuki 2010). Various studies have investigated the enhancement of its biocompatibilities by additives (Bracci et al. 2009; Gentleman et al. 2010; Mladenovic et al. 2014; Myrissa et al. 2016; Obata et al. 2009).

Biomaterial biocompatibilities are mainly dominated by their tissue and cellular responses. In the case of bone substitutes, osteo-cells, such as osteoblasts, osteoclasts, and osteocytes, play essential roles in the bone remodeling process. In addition, their viability, cytokine generation, and differentiation are closely controlled by biocompatible trace elements and molecules, such as Sr, Mg, Zn, and SiO\(_2\) (Beattie and Avenell 1992; Boanini et al. 2012; Bracci et al. 2009; Mourino et al. 2010; Valanenzhad et al. 2010). Accordingly, various studies have presented the control-releasing process of these biocompatible trace elements from biomaterials, such as calcium phosphate, alloys, and glasses, or immobilized them onto the surface of biomaterials to control cell viability and differentiation (Myrissa et al. 2016; Obata et al. 2009; Saugo et al. 2018; Valanenzhad et al. 2010; Wei et al. 2019; Sugiura et al. 2021). Both in vitro and in vivo studies have indicated that trace elements, such as Sr-, Mg-, and Zn-substituted calcium phosphates, might control and improve the bone remodeling process (Bracci et al. 2009; Forte et al. 2019; Matsunaga and Murata 2009; Mourino et al. 2012; Parra et al. 2017).

Manganese (Mn) is an important candidate because it influences the regulation of bone remodeling and increases the ligand-binding affinity of integrins, which mediate cellular interactions with extracellular matrix and activate cell adhesion (Luthen et al. 2007; Miola et al. 2014; Pabbruwe et al. 2004). Therefore, an Mn-doped OCP might be an attractive material for bone substitution. However, Mn inhibits OCP formation but induces the formation of other calcium phosphate phases such as dicalcium phosphate hydrogen dihydrate (DCPD: CaHPO\(_4\)·2H\(_2\)O) and amorphous calcium phosphate (ACP) (Boanini et al. 2010). So far, no studies have investigated how Mn-substituted calcium phosphate (including OCP) affects the bone remodeling process, especially its cellular effects (Armullik et al. 2000; Boanini et al. 2010; Medvecky et al. 2006). Thus, a fabrication process of Mn doping to OCP was needed for evaluation of whether Mn-doped OCP (and Mn-doped calcium phosphates) is a valuable candidate for a new biomaterial or not.

We have been investigating how cations affect OCP formation. During the research, we discovered that the cationic conjugation process dominates a particular cation substitution into the OCP unit lattice (Sugiura and Makita 2018, 2019; Sugiura et al. 2019). Na strongly induced OCP formation by enhancing the OCP layer structure due to the similar ionic radii of Ca\(^{2+}\) (Sugiura and Makita 2018, 2019; Sugiura et al. 2019). Therefore, we investigate herein whether or not the inducing property of Na could overcome the Mn inhibition of OCP to fabricate an Mn-substituted OCP.