Trace element-incorporating octacalcium phosphate porous beads via polypeptide-assisted nanocrystal self-assembly for potential applications in osteogenesis

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\textbf{A B S T R A C T}

The promising future of calcium phosphates (CaP) as a group of biomedical materials with a wide range of functions, might ultimately depend on tuning their composition and microstructure. However, the disorderly growth and aggregation of CaP nanocrystals limit their practical application. This paper reports a strategy for designing polypeptide/trace elements (TE), dual mediating the self-assembly of octacalcium phosphate (OCP) nanocrystals, with multilayered porous cross section and TE dilute doping. Intriguing advantages such as bead morphology, mesoporous structure, tunable diameter (20–1000 µm) and TE contents, biodegradability and bioactivity are obtained. The microcomputerized-tomography reconstruction reveals an interconnective macroporous architecture and a void volume of over 49.02% for the nearly close-packed bead scaffolds. The specific surface area and average mesopore size are 89.73 m\textsuperscript{2} g\textsuperscript{−1}, and 2.75 nm for the 180 µm diameter bead group, and those of 500 µm diameter beads are 130.17 m\textsuperscript{2} g\textsuperscript{−1} and 3.69 nm, respectively. It is demonstrated that the bead production mechanism is a multistep process including liquid-like precursor formation, nanocrystal nucleation and aggregation, aggregate combination and bead growth. Such a multilayer structure of TE–OCP porous beads would have adequate physical strength to maintain their shape, in contrast to the physical weakness of pure OCP hollow shell. The beads exhibit good biocompatibility and degradability and encourage bone mineralization in the early stage in vivo. This study demonstrates the feasibility of developing highly porous calcium phosphate giant beads via biomimetic self-assembly for direct application in reconstructive surgery and other widespread applications such as tissue engineering and drug delivery.

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1. Introduction

The use of dilute dopants or impurities to control the behavior of materials is at the heart of many technologies. Doping is widely critical for semiconductors [1], superconductors [2], new energy materials [3] and biomaterials [4–6], which would otherwise fall far below their performance requirements. The biogenic apatite is non-stoichiometric and contains relatively high levels of magnesium, sodium and carbon (in the form of carbonate groups, CO\textsubscript{3}\textsuperscript{2−}), and lower levels of trace elements (TE) [7]. These foreign TE ions at critical levels are considered to play pivotal roles on the process of biomineralization as well as other diverse effects on nanocrystal size, dissolubility and bioactivity of synthetic hydroxyapatite (HA) [8]. As a family of attractive materials with great chemical similarity to biological apatite, calcium phosphates (CaP) have been widely investigated in particle, ceramic, cement or film form in skeletal repair, drug delivery, cell scaffolds and interference coatings. Some investigations have demonstrated that the CaP ceramics could be endowed with ectopic osteoinductivity by changing the surface texture and microstructure [9–11], whereas a major drawback of the sparingly soluble CaP biomedical device is its low surface reactivity in orthotopic bone regeneration [12,13].

Systematic efforts to mediate stoichiometric CaP structure by impurity dilute doping can be dated back to the 1990s, when a variety of foreign TE ions were incorporated into CaP using sintering or solution-phase reactions [14,15]. The selection of TE as dopants was motivated by their pharmacologically beneficial and biologically properties in activating cell response, nuclei acid syn-