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Processing and *in vivo* evaluation of multiphasic calcium phosphate cements with dual tricalcium phosphate phases

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ABSTRACT

Calcium phosphate cements (CPCs) use the simultaneous presence of several calcium phosphates phases. This is done to generate specific bulk and *in vivo* properties. This work has processed and evaluated novel multiphasic CPCs containing dual tricalcium phosphate (TCPs) phases. Dual TCPs containing α- and β-TCP phases were obtained by thermal treatment. Standard CPC (S-CPC) was composed of α-TCP, anhydrous dicalcium phosphate and precipitated hydroxyapatite, while modified CPC (DT-CPC) included both α- and β-TCP. Physicochemical characterization of these CPCs was based on scanning electron microscopy, X-ray diffraction, specific surface area (SSA) and particle size (PS) analysis and mechanical properties. This characterization allowed the selection of one DT-CPC for setting time, cohesion and biological assessment compared with S-CPC. Biological assessment was carried out using a tibial intramedullary cavity model and subcutaneous pouches in guinea pigs. Differences in the surface morphology and crystalline phases of the treated TCPs were detected, although PS analysis of the milled CPC powders produced similar results. SSA analysis was significantly higher for DT-CPC with α-TCP treated at 1100 °C for 5 h. Poorer mechanical properties were found for DT-CPC with α-TCP treated at 1000 °C. Setting time and cohesion, as well as the *in vivo* performance, were similar in the selected DT-CPC and the S-CPC. Both CPCs created the desired host reactions *in vivo*.

1. Introduction

Calcium phosphate (CaP) ceramics have been used in dentistry and orthopaedics for more than a century [1,2]. CaPs are synthetic, available off-the-shelf and they do not have the drawbacks of autologous bone regarding graft harvest, donor site morbidity and increased time of surgery. In addition, CaPs possess a composition close to that of the mineral phase of bone, which can provide them with an intrinsic capacity to form bone [3]. Therefore, CaPs are ideal candidates to be used as bone substitutes. CaPs are available in different phase compositions, such as hydroxyapatite (HA) and tricalcium phosphate (TCP). These different phases present different properties, i.e. solubility, density, crystallinity, etc., which means that they engender different reactions *in vivo* [4]. Hence, the percentages of these CaP phases present in the implanted CaP material affect the solubility, reactivity, resorption and bonding of these materials to bone tissue [5]. CaPs are available as granules, pre-shaped blocks or as injectable cement-like materials. However, only injectable cement-like materials can be used in minimal invasive surgical procedures [6–8]. Hydraulic calcium phosphate cements (CPCs) combine CaP powders and an aqueous solution, often containing calcium or phosphate ions. Hardening of these CPCs takes place by nucleation and growth of one or more calcium phosphate compounds. In addition, CPCs can provide a good initial contact with the surrounding bone tissue, which is important in obtaining good integration of the biomaterial and adequate bone remodelling [9]. Several CPCs are commercially available and, depending on the number of CaP phases in their composition, these CPCs can be considered biphasic, triphasic or multiphasic [10]. α-TCP is ubiquitously found in these commercially available products, while multiphasic compositions are not.

CPCs with an appropriate CaP composition allow the adhesion of cells and their differentiation into osteoblasts, while osteoclast activity is influenced by the solubility of the ceramic [6,11]. Moreover, if provided with a suitable structure, CPCs are not only able to attract cells and induce their differentiation but also to create desired host responses leading to their remodelling into bone [12,13]. In addition, CPCs are able to provide strong initial mechanical properties compared with non-hardening materials [7,14].

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