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SCIENCE DIRECT®
Biomaterials 26 (2005) 3395–3404
Biomaterials
www.elsevier.com/locate/biomaterials

Modulation of porosity in apatitic cements by the use of α-tricalcium phosphate—calcium sulphate dihydrate mixtures

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Received 22 July 2004; accepted 8 September 2004
Available online 22 October 2004

Abstract

Calcium phosphate bone cements are injectable biomaterials that are being used in dental and orthopaedic applications through minimally invasive surgery techniques. Nowadays, apatitic bone cements based on α-tricalcium phosphate (α-TCP) are of special interest due to their self-setting behaviour when mixed with an aqueous liquid phase. In this study, a new method to improve osteointegration of α-TCP-based cements is presented. This method consists in the modification of the cement's powder phase with different amounts of calcium sulphate dihydrate (CSD). The resulting hardening properties of the new biphasic cements are a combination between the progressive hardening due to the main α-TCP reactant and the progressive dissolution of the CSD phase, which render a porous material. It was observed that the maximum compressive strength of *Biocement-H*© (45 MPa) decreased as the amount of CSD increased in the cement powder mixture (≈30 MPa for 25 wt% of CSD). It was also observed that after complete dissolution of the CSD phase a porous apatitic structure appears with a mechanical compressive strength suitable for cancellous bone applications (10 MPa).

Keywords: Cement; Calcium phosphate; Calcium sulphate; Physico-chemical properties

1. Introduction

It is generally accepted that calcium phosphate bone cements need further improvements to broaden their potential clinical applications [1]. In fact, recent publications highlight the efforts made to improve the injectability [2], of use in spinal surgery applications [3,4], and/or the strength of these materials [5–8]. Unfortunately, these improvements are not enough for apatitic (i.e. the end setting product being hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$; HA) and/or calcium-deficient hydroxyapatite ($Ca_9HPO_4(PO_4)_5OH$; CDHA)) bone cements, which are so stable in vivo that bone cement's resorption takes a long time, i.e. 1–2 years [9,10]. In order to accelerate bone tissue colonisation and resorption of the cement implant, several authors have improved macroporosity, i.e. more and larger pores, of apatitic bone cements in several ways [11–17].

Sarda et al. [12] achieved a good compromise between suitable mechanical strength (porosity) and injectability by using surfactants in the cement's liquid phase as compared to other studies using oxygen peroxide [11] in the liquid phase and/or ice [14], sugar [15] and/or mannitol [16] crystals, as porogenic agents, in the

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doi:10.1016/j.biomaterials.2004.09.023

cement's powder phase and/or oil liquid-phase emulsions [17].

Barralet et al. [14] have applied pressure to mixtures of cement powder and ice crystals to form compacts with setting properties. Xu et al. [18] have tried to improve the strength by reinforcing the porous apatitic cement matrix with aramide fibres. However, none of these approaches are useful for minimally invasive surgery applications, where the main problem is still to assure cement's injectability [2].

In this study, we propose a new method to modulate the porosity (and so the strength) of an α-tricalcium phosphate (α-TCP; α-$Ca_3(PO_4)_2$) bone cement during hardening in a Ringer's solution. For that purpose, calcium sulphate dihydrate (CSD; $CaSO_4 \cdot 2H_2O$) particles are added into the cement paste. This method is related to that proposed by Fernández et al. [19] (later on by Lidgren et al. [20]), where α-TCP and calcium sulphate hemihydrate (CSH; $CaSO_4 \cdot 1/2H_2O$) were mixed together to form a biphasic cement that sets due to the hydration reactions of both main reactants, i.e. α-TCP into CDHA and CSH into CSD. Unfortunately, CSH crystals, which stayed partially unreacted within the cement matrix, increased the setting times and also reduced the strength of the cement [21,22]. Recently, Bohner et al. [23] showed interesting effects with various CSD amounts added to the liquid phase, such as better setting time control (faster setting times with more CSD) but more α-TCP left after 24 h of reaction, suggesting a complex effect of sulphate ions on the setting reaction. The present study adds more data for the whole comprehension of the setting of α-TCP and CSD cement mixtures.

2. Materials and methods

2.1. Cement preparation

Biocement-H© (by Merck GmbH; inlab preparation) [24] served as a basis for all experiments. The plain cement was used as control, whereas the experimental groups had variable amounts of CSD as addition. Biocement-H© is made of 98 wt% α-TCP (minor contents of β-TCP) and 2 wt% precipitated hydroxyapatite (PHA; Merck-2143), added as a seed in the powder phase. Its liquid phase is an aqueous solution of 2.5 wt% disodium hydrogen phosphate (Na_2HPO_4) DHP; Panreac-131679). The liquid to powder (L/P) ratio was 0.32 mL/g, which is its minimum L/P ratio to assure suitable mouldability and cohesive property [24]. This control cement presented the same setting properties as published in the literature [24,25], i.e. around 8 and 20 min for the initial and the final setting times, respectively. Biocement-H© was selected because it is ≈100 wt% α-TCP (up to 15 wt% of β-TCP). Thus, its modification with CSD should be of interest to other commercial α-TCP cements [25].

In this study, the powder phase of Biocement-H© was modified (α-TCP, by Mathys Medical, Switzerland) with 5, 10, 20 and 25 wt% CSD (Sigma-C3771). Samples were coded as BioCSD-5, BioCSD-10, BioCSD-20 and BioCSD-25, respectively. In addition, the liquid phase of all BioCSD samples was reduced from 2.5 to 2.0 wt% of DHP. This adjustment was necessary to keep the mouldability of BioCSD samples as similar to that of the control. In a previous study, Bohner [23] showed that CSD and DHP interact in the liquid phase as to control the cement setting (and so the workability) of α-TCP and CSD mixtures. In particular, the addition of CSD powder to α-TCP–water cement mixtures strongly decreased their setting time, particularly when the phosphate concentration was high [23]. For the same reason, in this study, it is expected that the DHP reduction was also dependent on the CSD content and could be further optimised. All the cements were mixed by hand in a mortar with a spatula.

2.2. Cement hardening

Biocement-H© and BioCSD samples were made at an aspect ratio of 2:1 (10 mm length × 5 mm diameter). The specimens, immersed in 200 mL Ringer's solution at 37 °C, were removed from the moulds after 30 min and stored again for 1, 2, 4, 8, 16 h and 1, 3, 5 and 14 days prior to testing. Moreover, BioCSD-20 and BioCSD-25 were kept in Ringer's solution for 28 and 35 days (in the 35 days group, the solution was renewed every day). The compressive strength C (MPa) ($n \geqslant 8$) was measured at the hardening times (HT) specified above at a crosshead speed of 1 mm/min using a mechanical testing machine Bionix-858 (MTS, Eden Prairie, MN, USA) with a 100 kN load cell.

2.3. Microstructural characterisation

The evolution of the cement microstructure was analysed, at different HTs, by scanning electron microscopy (SEM; JEOL JSM-6400) on the surface of two cylinders kept to this end and broken diametrically. These samples were quenched in acetone before fracture to stop the setting reaction. The fracture surfaces were gold covered previous to SEM observation.

2.4. Chemical characterisation

Immediately after the compressive strength testing, the broken samples were quenched in acetone, to stop the setting, dried and ground for X-ray diffraction (XRD; Siemens-D500, Germany). XRD data were collected from $2\theta = 4 - 45^\circ$ with a step size of 0.05° and a count time of 3 s/step. The phase composition was