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Influence of Si substitution on the reactivity of α-tricalcium phosphate

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ABSTRACT

Silicon substituted calcium phosphates have been widely studied over the last ten years due to their enhanced osteogenic properties. Notwithstanding, the role of silicon on α-TCP reactivity is not clear yet. Therefore, the aim of this work was to evaluate the reactivity and the properties of Si-α-TCP in comparison to α-TCP. Precursor powders have similar properties regarding purity, particle size distribution and specific surface area, which allowed a better comparison of the Si effects on their reactivity and cements properties. Both Si-α-TCP and α-TCP hydrolyzed to a calcium-deficient hydroxyapatite when mixed with water but their conversion rates were different. Si-α-TCP exhibited a slower setting rate than α-TCP, i.e. k_{SSA} for Si-TCP ($0.021\ g \cdot m^{-2} \cdot h^{-1}$) was almost four times lower than for α-TCP ($0.072\ g \cdot m^{-2} \cdot h^{-1}$). On the other hand, the compressive strength of the CPC resulting from fully reacted Si-α-TCP was significantly higher (12.80 ± 0.38 MPa) than that of α-TCP (11.44 ± 0.54 MPa), due to the smaller size of the entangled precipitated apatite crystals.

1. Introduction

Calcium phosphate cements (CPCs) were discovered in the 1980's by Brown, Chown and LeGeros [1,2]. These materials are still actively studied nowadays since CPCs present attractive characteristics such as bioactivity, biocompatibility, osteoconductivity and resorbability [3,4]. Furthermore, CPCs consist on a moldable paste that can be injected into the bone defect using minimally invasive procedures [5–7], with in vivo self-setting after a few minutes.

The two most common types of CPCs have been called upon the end-product formed: apatite cement (precipitates at pH > 4.2) and brushite cement (precipitates at pH < 4.2). One of the most common main precursors of apatite cements is α-tricalcium phosphate (α-TCP) [8], which dissolves and precipitates into calcium deficient hydroxyapatite when mixed with water via a cementitious reaction.

Several studies have shown that it is not so easy to obtain a highly pure α-TCP [8–11]. The reason for that has been ascribed to the presence of magnesium impurities in most commercial reagents, a well-established stabilizer of β-TCP, a lower temperature isomorph of TCP [10,12–14]. When Mg^{2+} is present at ≥4.1 at% the temperature of β → α phase transformation can increase from ~1125 °C to 1485 °C [10,12,15–17]. The temperature of α-TCP synthesis can be reduced by using Mg-free reagents [8,11,18,19]. Cardoso et al. [11] and Motisuke et al. [18,19] succeeded in obtaining α-TCP using impurity-free reagent at a temperatures of 1165 °C and 1300 °C, respectively. On the other hand, Si has been shown to stabilize the α phase down to low temperatures [20,21]. Therefore, another path to reduce the temperature of α-TCP synthesis is by doping α-TCP with silicon (Si-α-TCP). The temperatures for synthesizing Si-α-TCP may vary from 700 °C to 1250° depending on the contents of Mg and/or other impurities [9,22–26].

Si-α-TCP can be obtained by treating at high temperatures a precipitate obtained after mixing calcium nitrate and ammonium phosphate solution at a proper ratio in the presence of ammonia and either colloidal silica or organic silicon compounds [23,27]. An alternative route consists in performing a solid state reaction of mixtures of 1) $CaCO_3$, $CaHPO_4$ or $(NH_4)_2PO_4$, and Ca_2SiO_4 or $CaSiO_3$ [9,28], or 2) β-$Ca_3(PO_4)_2$ and $CaSiO_3$ [29], or 3) HA and SiO_2 [26].

When calcium phosphate cements are prepared from a Si-α-TCP powder some cement properties are altered as compared to its pure counterpart. One example is powder solubility. According to Wei et al. [30], Si increases α-TCP solubility. Mestres et al. [26] verified a faster hydrolysis kinetics, the cement with Si present a similar resistance when compared with the pure, a decrease in cell proliferation and an increased in alkaline phosphatase (ALP) activity, which corresponds to

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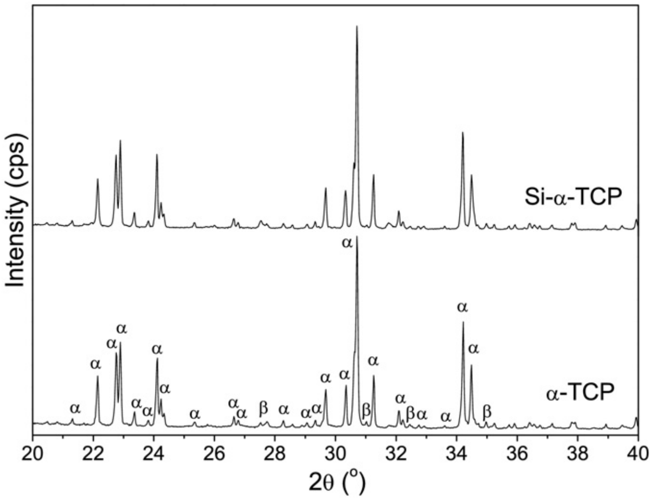

Fig. 1. XRD patterns of TCP powders. Legend: α = α-TCP, β = β-TCP.

an enhance of cell differentiation. On the other hand, Camiré et al. [28] observed a decrease on powder reactivity and cement mechanical strength and; an increased osteoclastic and osteoblastic activity.

Additionally to the stabilization of α-TCP phase, silicon has been shown to be beneficial for some biological properties such as bone calcification [32]. Si is essential for bone regeneration and therefore can stimulate certain cell activities such as proliferation and differentiation of osteoblasts [26]. Moreover, the bioactivity of a material can be improved by doping it with Si [33–35].

The role of silicon on the reactivity of α-TCP towards the formation of CPCs is not clear yet [19,26,28]. Thus, the aim of this work was: 1) to verify how silicon may influence on the setting reaction of α-TCP bone cement; and 2) to determine how the different reactivity affects the physico-chemical properties of CPCs. The novelty of this work relies on the use of Mg-free precursors for preparing α-TCP and Si-α-TCP [9] and on the attempt to employ feasible and large scale procedures to promote the production of more accessible bone cements.

2. Materials and methods

2.1. Preparation of TCP powders and bone cement

α-TCP and Si-α-TCP were synthesized by a solid state reaction from the appropriate mixture of lab made Mg-free $CaCO_3$ (Mg wt% < 0.0180), $CaHPO_4$ (Mg wt% < 0.0001) and $CaSiO_3$ (Mg wt% < 0.0001) as described elsewhere [9]. Briefly, $CaCO_3$ and $CaHPO_4$ were mixed to prepare α-TCP, and 2 wt% of $CaSiO_3$ was included in the mixture to prepare Si-TCP. The powders were calcined for 6 h at 1300 °C for α-TCP and 1200 °C for Si-TCP with a heating rate of 10 $°C \cdot min^{-1}$. Afterwards, samples were let to cool down inside the furnace without quenching. Finally, the powders were milled in a horizontal ball mill for 48 h using an alumina gridding media of Ø15 mm and ball to powder ratio of 20:1 w/w.

The mixing liquid used in cements was an aqueous solution of Na_2HPO_4 (2.5 wt%) and $C_6H_8O_7$ (citric acid) (1.5 wt%) in distilled water. Citric acid was employed as a liquid reducer agent and to promote a more homogeneous setting reaction due to its dispersant effect [36], and Na_2HPO_4 was added to accelerate the setting reaction due to the common-ion effect [37]. Cements were prepared by mixing the powder and liquid in a ratio (L/P) of 0.60 $mL \cdot g^{-1}$. The paste was introduced in Teflon molds (6 mm diameter × 12 mm height), and samples were immersed in 0.9 wt% of NaCl solution at 37 °C for setting.

Table 1
XRF results. Ca/P and Ca/P + Si ratios. Values are in at%.

Sample	Ca	P	Si	Ca/P or Ca/(P + Si)
Si-α-TCP	22.89	14.60	1.04	1.46
α-TCP	23.08	15.38	–	1.50

Table 2
Specific surface area (SSA), mean particle size (d_{Mean}) and particle size distribution (10% < d < 90%).

Sample	SSA ($m^2 \cdot g^{-1}$)	d_{Mean} (μm)	10% < d < 90% (μm)
α-TCP	0.5322 ± 0.0042	8.317	0.596 < d < 17.25
Si-α-TCP	0.6202 ± 0.0062	6.710	0.785 < d < 14.67

2.2. Characterization of physico-chemical properties

X-ray Fluorescence (XRF, Philips, MagiX Super Q Version 3.0) was used to evaluate the elemental composition (major and minor components), as well as Ca/P or Ca/(P + Si) ratios of the two TCP powders. X-ray Diffraction (XRD, Bruker D8 Advance, CuKα, Ni filter, 20 to 40° (2θ), 0.02° s^{-1}, 40 kV and 40 mA) was also used for qualitative and quantitative determination of the crystalline phases existing in the starting powders and set cements. JCPDS files used for phase identification were #09-0348 for α-TCP and #09-0169 for β-TCP. For quantitative determination of β-TCP on the starting powders the internal standard method was employed, in which a diffraction line from the phase quantified (β-TCP) was compared to a diffraction line from a standard (Al_2O_3) mixed with the sample in known proportions [38].

The density of the TCP powders was measured by helium picnometry (Micromeritics, AccuPyc 1330), the specific surface area (SSA) was measured by nitrogen adsorption (Micromeritics, ASAP 2020) according to Brunauer-Emmett-Teller theory and the granulometry of the powder was determined by laser diffraction particle size analysis (Coulter Counter LS 13 320).

The hardening kinetics was monitored by measuring the compressive strength (MTS, Test Star II) of wet samples after different time intervals (2, 4, 8, 24, 72, 120, 168, 360 h), at least 10 cylindrical specimens were tested per condition. After that, samples were immersed in acetone for 2 h to stop the setting reaction, and then dried at 100 °C overnight. The crystalline phase composition at each time point was assessed by XRD, (including a JCPDS file #46-0905 for CDHA). The conversion rate was determined by XRD following the procedure proposed by Ginebra et al. [39,40] and Rigo et al. [41]. It is known that the mass fraction of a crystalline material present in a given sample is proportional to their XRD lines intensities. To evaluate the evolution of the setting reaction of the cements studied, the rate of α-TCP conversion (α_t) was evaluated based on the evolution of its mass fraction with time as stated on Eq. (1).

$$\alpha_t = \frac{(w_0 - w_\infty) - (w_t - w_\infty)}{(w_0 - w_\infty)} \tag{1}$$

where w_0 is α-TCP mass fraction at initial time (t = 0 h), w_∞ is α-TCP mass fraction after the 168 h of setting reaction and w_t is α-TCP mass fraction at a determined time, t. At each time, α-TCP mass fraction was determined after its XRD lines (1 3 2), (1 1 3) and (1 0 7) integrated intensities (Eq. (2)) and an average value was established.

$$\frac{I_\alpha}{I_{\alpha,0}} = \frac{w_\alpha M_\alpha}{w_{\alpha,0}\left[(M_\alpha - M_{CDHA})(w_\alpha + w_\beta) + M_{CDHA}\right]} \tag{2}$$

where I_α is the integrated intensity of α-TCP (1 3 2), (1 1 3) or (1 0 7) XRD lines at a determined time, t; $I_{\alpha,0}$ is the integrated intensity of α-TCP (1 3 2), (1 1 3) or (1 0 7) XRD lines at initial time (t = 0 h); M_α is the is the mass absorption of α-TCP, 86.43 [40]; M_{CDHA} is the mass absorption of CDHA, 84.97 [40]; w_β is the mass fraction of β-TCP during setting reaction; w_α is the mass fraction of α-TCP at a determined time, t and; $w_{\alpha,0}$ is the mass fraction of α-TCP at initial time (t = 0 h).