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Characterization of α/β-TCP Based Injectable Calcium Phosphate Cement as a Potential Bone Substitute

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Abstract

Calcium phosphate cements (CPCs) can be a suitable scaffold material for bone tissue engineering because of their osteoconductivity and perfect fit with the surrounding tissue when injected *in situ*. However, the main disadvantage of hydroxyapatite (HA) forming CPC is its slow degradation rate, which hinders complete bone regeneration. A new approach is to use hydraulic apatite cement with mainly α/β-tricalciumphosphate (TCP) instead of α-TCP. After hydrolysis the α/β-TCP transforms in a partially non-absorbable HA and a completely resorbable β-TCP phase. Therefore, α-TCP material was thermally treated at several temperatures and times resulting in different α/β-TCP ratios. In this experiment, we developed and evaluated injectable biphasic calcium phosphate cements (BCPC) in vitro. Biphasic α/β-TCP powder was produced by heating α-TCP ranging from 1000-1125$0^0$C. Setting time and compressive strength of the CPCs were analyzed after soaking in PBS for 6 weeks.

Results demonstrated that the phase composition can be controlled by the sintering temperature. Heat treatment of α-TCP, resulted in 100%, 75% and 25% of α- to β-TCP transformation, respectively. Incorporation of these sintered BCP powder into the cement formulation increased the setting time of the CPC paste. Compressive strength decreased with increasing β-TCP content.

In this study, biphasic CPCs were produced and characterized in vitro. This injectable biphasic CPC presented comparable properties to an apatitic CPC.

Introduction

α-TCP based calcium phosphate cements (CPCs) have been widely used as a bone substitute biomaterial in the field of dentistry and orthopedics due to their similarity to the inorganic component of bone. They provide unique set of advantages such as injectability, malleability and self-setting that permits complete filling of irregular bone defects. They are osteo-conductive materials stimulating osseous apposition, allowing bone ingrowth within and around the implant, whereas the main disadvantage of this material is its slow degradation, which limit the active bone remodeling process [1]. Thus, it is of great interest designing an injectable scaffolds having a proper chemistry to induce degradability while maintaining its mechanical integrity.

The current method for bone reconstruction in dentistry and orthopedics is the use of biphasic implants (BCP) based on α- and β-TCP. Although having a similar chemical composition, they differ in solubility and biological response. In vivo studies showed that bone induction does occur in biphasic ceramics that degrading in a controlled manner and stimulating osteogenesis. Moreover, in contrast to α-TCP alone, as it has a lower biodegradability under psychological conditions, BCP implants are found to have better bone formation ability in terms of bony osseous apposition and bone ingrowth [2, 3]. Biphasic ceramics, however, are only produced in the forms of blocks or granules; they have not been applicable as an injectable system [4, 5]. The aim of this study was to develop biphasic calcium phosphate cement (BCPC). BCPC in this study is an intimate mixture of α- and β-TCP, in where the thermal treatment process can control α-TCP/β-TCP ratio.

Materials and Methods

Powder composition. α-tricalcium phosphate (α-TCP; CAM Implants BV, Leiden, the Netherlands) cement powder was sintered at different temperatures ranging from 1000-1125ºC for 6h. The powder X-ray diffraction ((XRD; PW3710 Philips, The Netherlands) was conducted to analyze the effect of the thermal treatment on the crystallographic composition of the α-TCP powders. The analyses were performed with a Cu Kα radiation source having a wavelength of 1.5405 Å and at a voltage of 40 kV and a current of 30 mA. Patterns were collected for 2θ values of 25º to 38º with a step size of 0.05° and a counting time of 20 seconds at each step. The change of α-TCP and β-TCP phase identifications in the samples obtained after treatment were calculated by the respective strongest lines of the two phases and compared with the standard mixtures of α- and β-TCP [6, 7].

CPC cement. The CPC powder mixture consisted of non-treated and thermally treated α-TCP (CAM Implants BV, Leiden, the Netherlands), while as a constant cement ingredient 18 wt% dicalcium phosphate anhydrous (DCPA, analytical grade; J.T. Baker Chemical Co., Phillipsburg, USA), 3 wt% precipitated hydroxyapatite (pHA; Biomet Merck, Darmstadt, Germany) and 4 wt% calcite ($CaCO_3$; Sigma-Aldrich Chemical Co., St. Louis, MO) were used (Tabel 1). CPC powders were ball milled in a sequential milling pathway according to a previously developed process [8].

Cement pastes were obtained by the homogeneous mixing of precursor powders with a 2% Na_2HPO_4 (Merck, Germany) solution at a liquid-to-powder ratio (L/P) of 0.35 ml/g (Fig. 1) [8].

After mixing, a paste was obtained and injected into Teflon® molds of 4.5 mm in diameter by 9 mm in height to obtain cylindrical samples. The samples in the mold were left to set at 37 °C. Cylinders of cement were removed from the mold and immersed in phosphate buffer saline (PBS) at 37 °C to allow hardening.

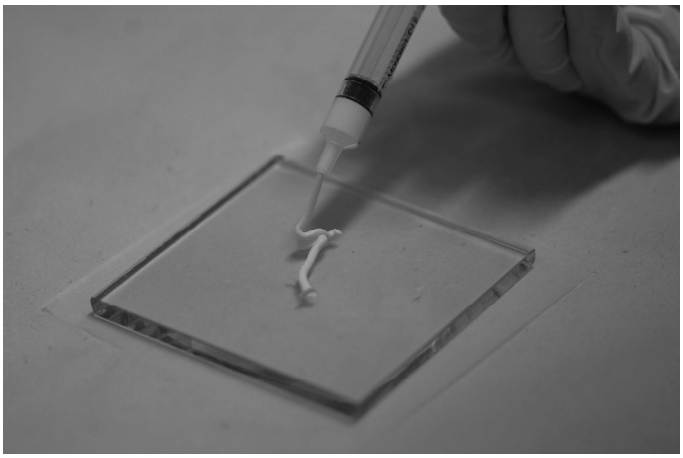

Fig. 1 Injection of the calcium phosphate cement from syringe

The initial and final setting times of the various cement pastes were assessed using Gilmore needles according to ASTM C266 [8].

The compressive strength of the samples were measured by using a mechanical testing bench (858 MiniBionixIIVR ,MTS, USA) at a cross-head speed of 0.5 $mm.min^{-1}$. Samples were tested before and after immersion in PBS solution at 37°C. The solution was renewed every week (n=3).

Results and discussion

From the XRD patterns the α- to β-TCP phases were determined. Sintering at elevated sintering temperatures (1000-1125^oC) resulted in partially or fully transformation of the α-TCP phase into a thermodynamically stable β-TCP phase. As a calcium phosphate cement ingredient, 75% of the non-treated and heat-treated TCP was used. The obtained transformation α- to β-TCP were 0% (CPC1), 25% (CPC2), 75% (CPC3) and 100% (CPC4), respectively.

CPC characteristics. The setting time of the cement pastes increased with increasing biphasic content. The shortest final setting time (4.5 ± 0.30 min.) was obtained with CPC1 group. For biphasic cements, however, the significant increases in the setting times were measured with increasing of β-TCP. Increasing the biphasic ratio increased the final setting time of CPC2, CPC3 and CPC4 up to 5.0 ± 0.30 min., 7.0± 0.30 min and 9.5 ± 1 min., respectively.

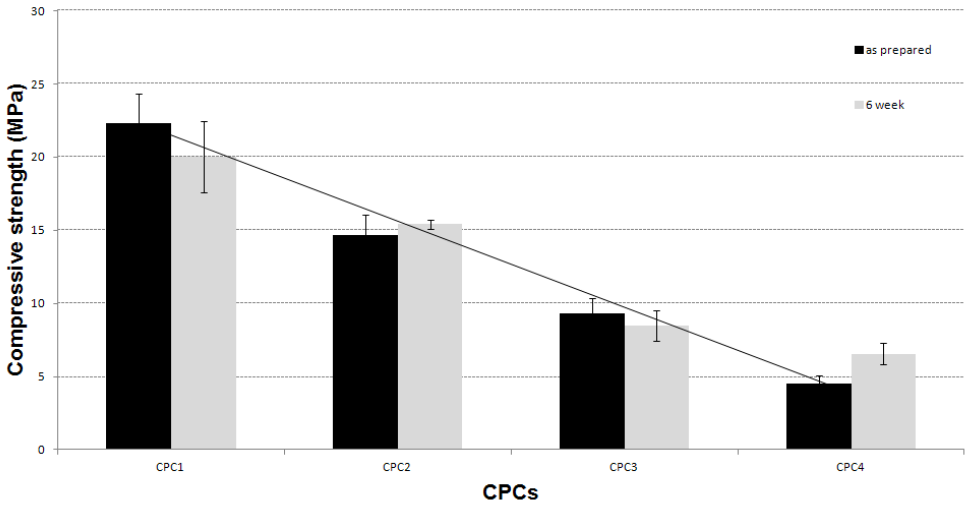

Fig. 2 Compressive strength of the cements before and after 6 weeks of incubation in PBS

The compression strength of the samples was demonstrated in Fig. 2. The strength of the injected and the set samples decreased with decreasing biphasic content in the present study. The results indicate that the setting and hardening process of the CPCs depend on the chemistry of the cement reactants. In comparison to β-TCP, α-TCP dissolves faster to provide calcium and phosphate ions and supersaturated the solution rapidly with respect to thermodynamically the most stable phase [9]. Additionally, the decrease in strength can be attributed to the less entangled crystalline structure due to the non-settable β-TCP remnants in the cement [10].

Conclusions

In this study, biphasic calcium phosphate cements were successfully produced. Due to the specific thermal treatment conditions, α- to β-TCP transformation occurred. When biphasic particles incorporated as a cement powder, setting time of the cements delayed and mechanical properties decreased. Biphasic particles seem to be a candidate for preparing biphasic cements which is favorable for biological conditions.

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