

Development of an octocalcium phosphate cement

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From previous studies it is known that alpha-tertiary calcium phosphate and dicalcium phosphate form a cement upon mixing with water. In this study this cement was optimized in terms of the milling of the constituents, their molar ratio, the amount of hydroxyapatite added and the water/powder ratio. The optimum Ca/P molar ratio of the cement mixture was 1.36 ± 0.03 . X-ray diffraction showed the reaction product to be octocalcium phosphate. Addition of precipitated hydroxyapatite of over 3% diminished the final strength of the cement significantly. However, admixtures of only 2% of precipitated hydroxyapatite (a) kept the final compressive strength at 30 ± 5 MPa after soaking in Ringers solution at 37 °C, (b) diminished the initial setting time from 27.5 to 10 min and the final setting time from 65 to 40 min, (c) diminished the time in which the final strength was reached from 36 to less than 14 h. The tensile strength of this cement is $19 \pm 1\%$ of its compressive strength. The optimum water/powder ratio as found in this study was 0.30 g/g.

1. Introduction

The term 'calcium phosphate cements' has been introduced by Gruninger *et al.* [1]. Such a cement may be described as a powder or as a mixture of powders which, upon mixing with water or an aqueous solution to a paste, reacts around room or body temperature by the formation of a precipitate containing crystals of one or more calcium phosphates and sets by the entanglement of the crystals of that precipitate. One way to classify the different calcium phosphate cements is according to the type of calcium phosphate formed during the setting reaction. Brown and Chow [2] and later Fukase *et al.* [3] claimed that their powder mixture of dicalcium phosphate (DCP) and tetracalcium phosphate (TTCP) reacted upon mixing with water to stoichiometric hydroxyapatite. However, more recent investigations [4, 5] have shown that only the first nuclei consist of nearly stoichiometric hydroxyapatite whereas further growth of these nuclei occurs in the form of calcium deficient hydroxyapatite. Another hydroxyapatite cement was formed by Constantz *et al.* [6] who mixed water-free phosphoric acid with TTCP.

Lemaitre *et al.* [7–9] formed a brushite cement by mixing a powder of β -tertiary calcium phosphate with an aqueous solution of monocalcium phosphate monohydrate (MCPM). Another brushite cement was formed in our laboratory [10] as well as by Contantz *et al.* [11] by reaction of a mixture of MCPM and TTCP.

Monma *et al.* [12] reported that they obtained an octocalcium phosphate cement by reaction of alpha-tertiary calcium phosphate (α -TCP) with brushite. In our laboratory [10] several other octocalcium phosph-

phate cements have been developed. The purpose of the present work was to optimize one of these OCP cements with respect to setting times and mechanical strength. We selected the OCP cement formed by reaction of α -tertiary calcium phosphate with monetite.

2. Materials and methods

Alpha-tertiary calcium phosphate was prepared by heating the appropriate mixture of monetite and calcium carbonate for 6 h at 1300 °C and quenching in air to room temperature. The quenching procedure appeared to be so fast that the β -TCP content of the product was less than 5% according to X-ray diffraction. The product was milled in an agate ball mill to a particle size in the range from 2 to 20 μm with an average diameter of 5 μm as measured by laser diffraction. Monetite (Merck catalogue number 2144) was milled to a similar particle size.

Mixtures of α -TCP and monetite were prepared with varying Ca/P ratios. Pastes were prepared from the mixtures by addition of water at a water/powder ratio of 0.30 g/g. Initial setting time *I* and final setting time *F* were determined with Gilmore needles. Cylinders were prepared having a diameter of 6 mm and a height of 12 mm. They were soaked in Ringer's solution at 37 °C for 1 day. Their compressive strength *C* and their diametral tensile strength *T* were determined on an Instron electromechanic universal testing machine type 4507 at a crosshead speed of 1 mm min⁻¹. In this way the optimum Ca/P ratio of the mixture of reactants was found. At this value the product was investigated by X-ray diffraction.

The second series of experiments was carried out at the optimum Ca/P ratio so that various amounts of precipitated hydroxyapatite (PHA) were added to the mixture of reactants. Setting times and strengths were measured as before.

The third series of experiments was also carried out at the optimum Ca/P ratio but now the water/powder was varied.

In the fourth series of experiments the strengths C and T were determined as a function of the time of soaking in Ringer's solution at 37°C. This was done for a mixture of powders not containing any PHA as well as for a mixture containing 2% PHA.

Finally, the pH of the reacting cement was measured as a function of time.

3. Results

In the first series of experiments with mixtures of α -TCP and DCP the variation of setting times was very small. However, as observed from Fig. 1 the maximum in the strength is obtained at a Ca/P molar ratio of 1.36 ± 0.03 which equals the value of OCP within the limits of error. X-ray diffraction showed that the reaction product was OCP indeed. The value of the tensile strength was $19 \pm 1\%$ of the compressive strength.

The results of the second series of experiments are shown in Fig. 2. The strength decreases monotonously with the hydroxyapatite content whereas the setting times decrease by addition of up to about 6% of hydroxyapatite, after which the values level off.

Variations of the water/powder ratio of the cement in the range from 0.33 to 0.27 had no effect on the strength. After 1 day of soaking C remained 16 ± 3 MPa. As far as the workability of the cement paste was concerned a W/P ratio of 0.30 g/g appeared to be the optimum value.

The development of strength in the cement mass as a function of the soaking time in Ringer's solution is

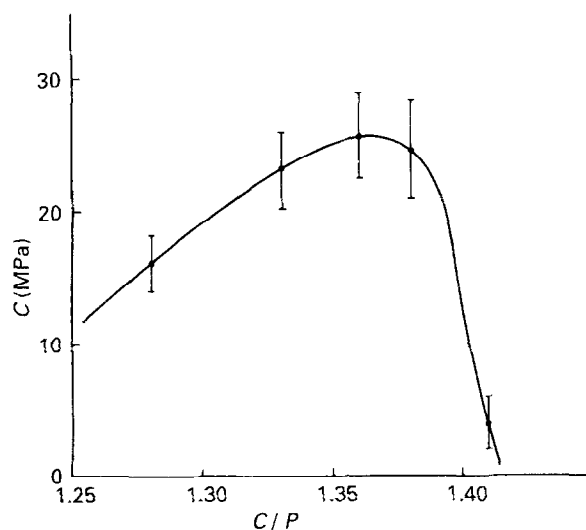


Figure 1 Compressive strength C of cements obtained from mixtures of α -TCP and DCP having varying Ca/P molar ratios and mixed with water into a paste at a water/powder ratio of 0.30 g/g after one day of soaking in Ringer's solution at 37°C.

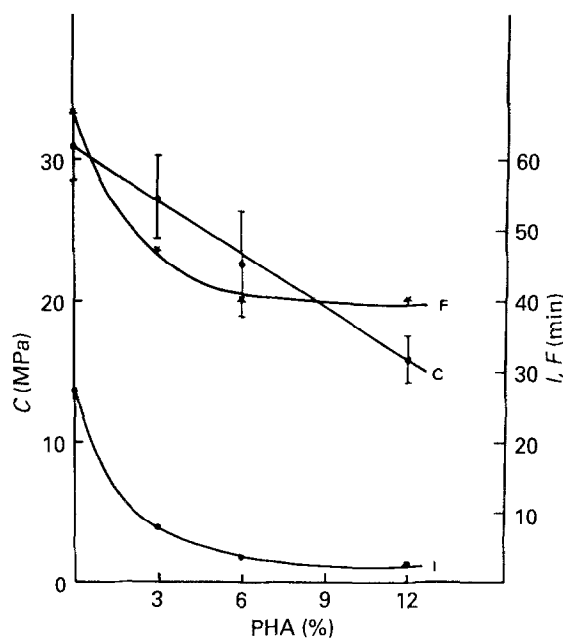


Figure 2 Compressive strength C , initial setting time I and final setting time F of cements obtained from a mixture of α -TCP and DCP (at Ca/P = 1.36) to which various amounts of precipitated hydroxyapatite PHA were added. The water/powder ratio was kept at 0.03 g/g. The strength was determined after 3 days of soaking in Ringer's solution at 37°C.

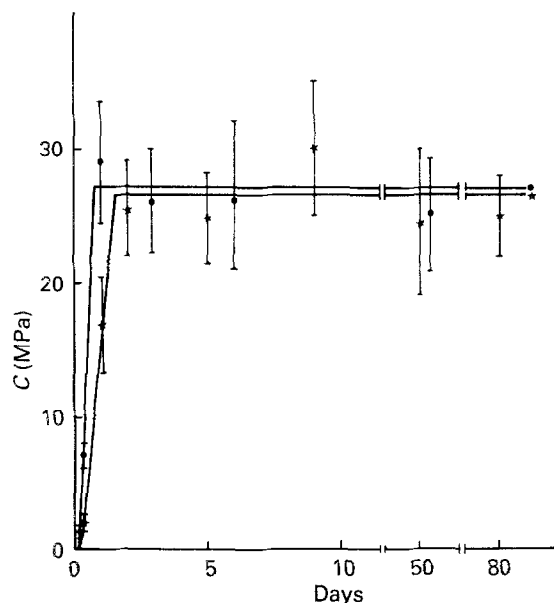


Figure 3 Compressive strength C of the cement obtained from a mixture of α -TCP and DCP having a Ca/P of 1.36 without addition of PHA and with addition of 2% PHA as a function of the time in soaking in Ringer's solution at 37°C (● F362; * F360).

seen in Fig. 3. The mixture without PHA reaches its maximum strength after about 36 h. However, by addition of 2% PHA the cement reaches its maximum strength within about 14 h.

The strength did not change significantly by the addition of 2% PHA. However, the initial setting time I was decreased from 28 to 10 min and the final setting time F from 65 to 40 min.

Finally, the initial pH of the cement paste right after mixing appeared to be 8.98. But soon it diminished to near 8 where it ended after completion of the setting reaction (see Fig. 4).

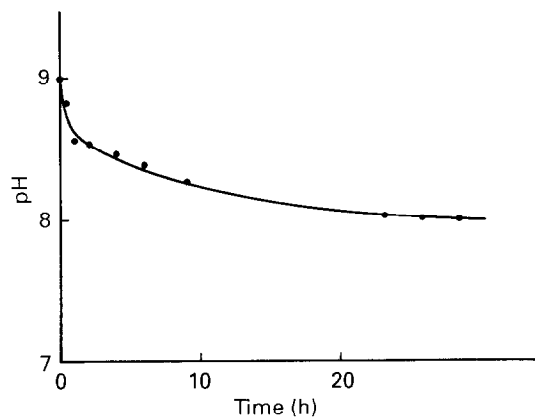


Figure 4 pH of the cement paste as a function of time as measured from the beginning of mixing of powder and water at room temperature. The powder was a mixture of α -TCP and DCP having a molar Ca/P ratio of 1.36.

4. Discussion

The setting times and strength values found for this cement formulation compare well with those reported for the hydroxyapatite cements from Brown and Chow [2] and from Constantz [6]. But they are much lower than those of PMMA bone cements or of bone [13].

It is expected that hydroxyapatite cements will be maintained in the body as they are implanted because the solubility of hydroxyapatite is very low. However, we know from other studies [14, 15] that octocalcium phosphate is the natural precursor mineral in the bone of vertebrates and that this is converted with a half-life of about 1 month into bone mineral apatite. As Nishimura *et al.* [16] have shown, such a transformation may be accompanied by an increase of strength and other mechanical properties. Therefore the next purpose of our research is to observe whether this cement is transformed and reinforced after implantation.

The pH of the cement paste as a function of time according to Fig. 4 is such that we do not expect an inflammatory response upon implantation.

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Received 5 January

and accepted 14 September 1993