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The effects of temperature on the behaviour of an apatitic calcium phosphate cement

M.P. GINEBRA, E. FERNÁNDEZ, F.C.M. DRIESSENS, M.G. BOLTONG, J. MUNTASELL*, J. FONT*, J.A. PLANELL
*Departments of Materials Science and Metallurgy and *Physics and Nuclear Engineering, Universitat Politècnica de Catalunya, Av. Diagonal 647, 08028 Barcelona, Spain*

An apatitic calcium phosphate cement is obtained by mixing α-tricalcium phosphate (α-TCP) and precipitated hydroxyapatite into a cement powder, and by then mixing this powder with an aqueous solution of Na_2HPO_4 as an accelerator. Setting times were reduced by about 30% by increasing the temperature from 22 to 37 °C. Compressive strength reached higher intermediate and final values at 37 °C. Degrees of transformation of the α-TCP in the resulting calcium-deficient hydroxyapatite (CDHA) were much higher at 37 °C after 24 h of storage in Ringer's solution according to X-ray diffraction. Differential scanning calorimetry indicated that the rate of reaction increased by a factor of about 5 when the temperature was increased from 25 to 37 °C. Scanning electron microscopy showed that the microstructure was more homogeneous and that a more tight entanglement of the precipitated CDHA crystals occurred after storage at 37 °C than at room temperature.

1. Introduction

Brown and Chow [1] were the first to develop a calcium phosphate cement. They used a cement powder containing tetracalcium phosphate (TTCP) and dicalcium phosphate (DCP). They showed that a setting reaction occurred according to the following equation:

$$2Ca_4(PO_4)_2O + 2CaHPO_4 \rightarrow Ca_{10}(PO_4)_6(OH)_2$$

Brown *et al.* [2] showed that, if the reactants are put together in a 1:2 molar ratio, the first reaction occurring in the mixture is the same as that found by Brown and Chow [1], but then the reaction proceeds so that in a second step a calcium-deficient hydroxyapatite (CDHA) is formed:

$$3Ca_{10}(PO_4)_6(OH)_2 + 6CaHPO_4$$
$$\rightarrow 4Ca_9(HPO_4)(PO_4)_5OH + 2H_2O$$

Brown and Fulmer [3] investigated the effect of temperature on the kinetics of the setting reaction of this cement formulation. The rate of reaction was improved by a factor of about 2.5 when the temperature was increased from 25 to 38 °C.

In a previous paper [4] we described an apatitic cement, also consisting of a CDHA formed after a reaction, but this was obtained in one step from α-tricalcium phosphate (α-TCP):

$$3Ca_3(PO_4)_2 + H_2O \rightarrow Ca_9(HPO_4)(PO_4)_5OH$$

With this cement we found [5] that a compressive strength of 25 MPa was reached after soaking for about 7 h in Ringer's solution at 37 °C, when soaking was started immediately after setting. However, it took about 11 h in total to reach the same compressive strength when soaking at 37 °C was delayed by 2.5 h. This effect might primarily be due to the temperature, which was room temperature during the delay. Recently, we found [6] that the setting time of this cement decreased by about 30% when the temperature was increased from 22 to 37 °C. For these reasons it was decided to study the effect of temperature on the various properties of this calcium phosphate cement in more detail.

2. Materials and methods

An appropriate mixture of $CaHPO_4$ and $CaCO_3$ was heated in air at 1300 °C for 6 h and then quenched to room temperature in air. The product consisted of 85% α-TCP and 15% β-TCP according to quantitative X-ray diffraction analysis [7]. This intermediate product was milled in an agate ball mill for 1 h; 2% precipitated hydroxyapatite was added and homogenization of the cement powder was carried out by further milling for 7 min. The morphology of the starting powder is shown in Fig. 1.

For the cement liquid an aqueous solution of 2.5% Na_2HPO_4 was used at a liquid-to-powder ratio of $0.32\,ml\,g^{-1}$ [5]. Powder and liquid were mixed in a mortar for about 1 min. Initial and final setting times were determined with Gillmore needles according to the C266-ASTM standard at both 25 and 37 °C.

Cylindrical specimens, 12 mm high and 6 mm in diameter, were also prepared and stored for either 24 or 48 h in Ringer's solution at either 25 or 37 °C. These specimens were removed from the moulds and the compressive strength was determined with a cross-head speed of $1\,mm\,min^{-1}$. Afterwards the crushed

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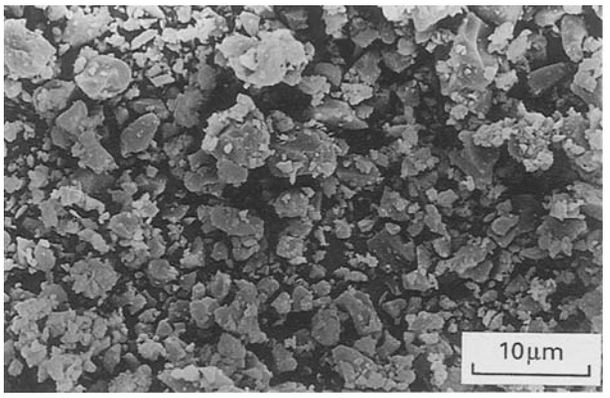

Figure 1 Scanning electron micrograph of the α-TCP starting powder used as the cement reactant.

specimens were subjected to X-ray diffraction (XRD) in order to follow the progress of reaction.

During the setting reaction differential scanning calorimetry (DSC) was carried out in a Setaram DSC92 calorimeter to estimate the rate of heat evolution at room and physiological temperatures.

The microstructures formed at 25 and 37 °C were examined by scanning electron microscopy (SEM).

TABLE I Initial setting time (I) and final setting time (F) as a function of the temperature

Temperature (°C)	I (min)	F (min)
22	9	19
37	6	15

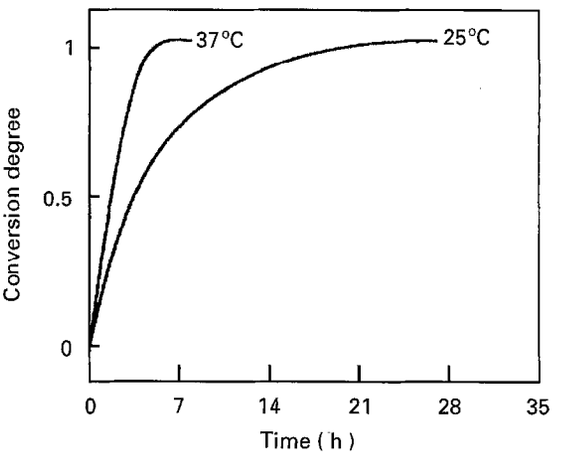

Figure 2 Normalized heat evolution of the cement at 25 and 37 °C.

3. Results and discussion

The values obtained for the initial setting time (I) and the final setting time (F) for both temperatures are given in Table I. As expected, setting was much faster at body temperature. As a consequence the surgical procedure can be resumed faster after implantation of the cement than might be thought on the basis of 'laboratory' data about the setting, which are generally determined at room temperature.

This increase in the setting velocity of the cement at physiological temperature was corroborated by obtaining the rates of heat liberation during the reaction by DSC. Fig. 2 gives the normalized integral heat evolution as a function of the reaction time. At 25 °C heat evolution is no longer measurable after about 28 h, while at 37 °C this point is reached within about 6 h. This indicates that the rate of reaction at 37 °C is about five times faster than at 25 °C.

On the other hand, parallel XRD analyses show the presence of α-TCP as well as apatite after 24 h of reaction, both at room and body temperatures. Nevertheless, as can be seen in Fig. 3, the degree of transformation of α-TCP in the resulting CDHA is much higher at 37 °C after 24 h of storage in Ringer's solution than at 25 °C. Further XRD analyses have shown that the transformation of α-TCP into CDHA at 37 °C proceeds after 24 h and even after 48 h, with a decreasing rate, until the α-TCP completely disappears. The final product contains only CDHA and the β-TCP that was already present in the initial powder, which does not take part in the reaction. This important decrease in the velocity of reaction may be the reason why, after the initial stage, it is not possible to detect further heat evolution using DSC.

The XRD data are also corroborated by the SEM pictures obtained from fracture surfaces of the strength specimens. Fig. 4a and b are two SEM pictures of a specimen stored for 24 h at room temperature. Granules of α-TCP are observed which are surrounded by small acicular apatite crystals. They precipitate between the α-TCP granules and cover the surface of the reactant, forming a shell-like morphology. The presence of such a feature is consistent with a reaction in which the product phase isolates the reactant. According to Brown *et al.* [2], who observed similar structures in the formation of hydroxyapatite and CDHA from different reactants, this type of reaction is comparable to the hydration of tricalcium silicate, which has been widely studied [8]. Following this model, the rate of hydroxyapatite formation would be controlled initially by the interfacial area of the reactant, and subsequently by the diffusion through the surrounding shell.

After 48 h of reaction at 25 °C, the microstructure has slightly evolved, as it can be observed in Fig. 4c and d. Much less granules of α-TCP are found; instead, some plate-like crystals, bigger than the acicular ones, can be seen inside the shells that were previously occupied by the α-TCP particles. Although the morphology and size of these crystals are different from the needle-like ones that had previously precipitated, the only phase that could be observed by XRD in addition to the reactants was CDHA. A similar evolution in the morphology of the apatite crystals is also referred to by Brown *et al.* [2], who claim that the microstructure of the forming apatite depends on the solution chemistry. Thus, the acicularity of the crystals increases with a decrease in the pH of the surrounding solution. In our case, after an initial precipitation of acicular crystals surrounding the α-TCP granules, the

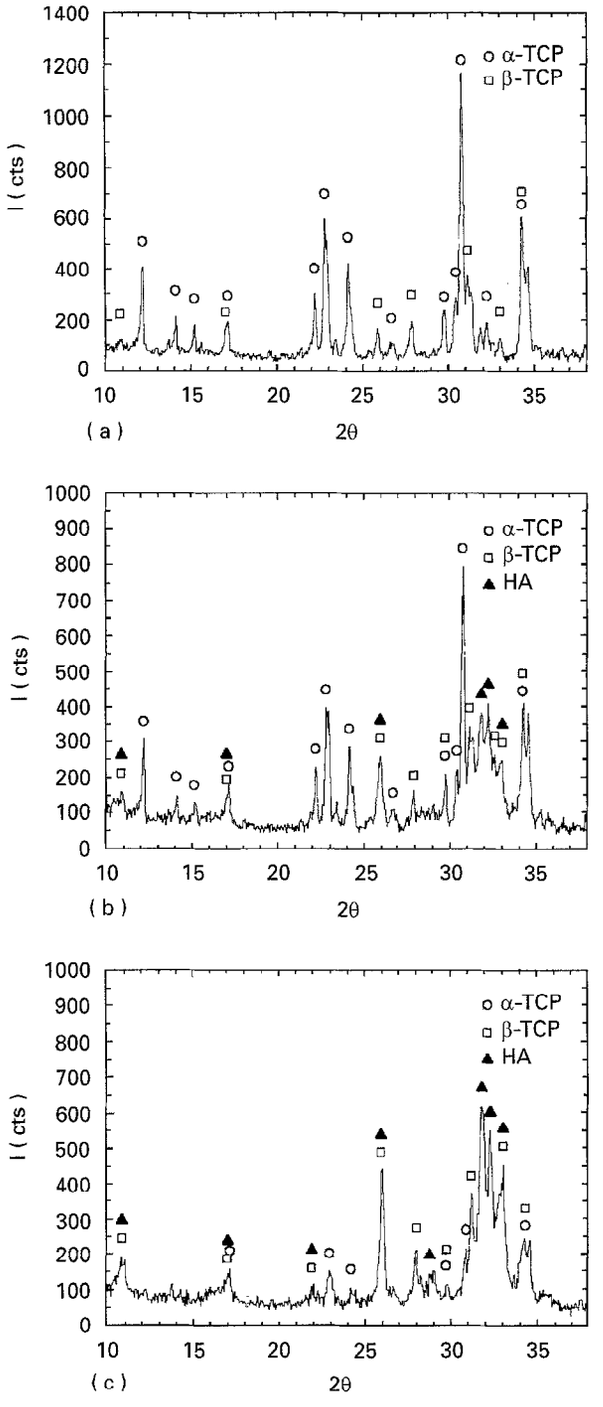

Figure 3 X-ray diffractogram of (a) the α-TCP starting powder (containing 15% β-TCP); (b) the cement after 24 h of reaction at 25 °C; and (c) the cement after 24 h of reaction at 37 °C.

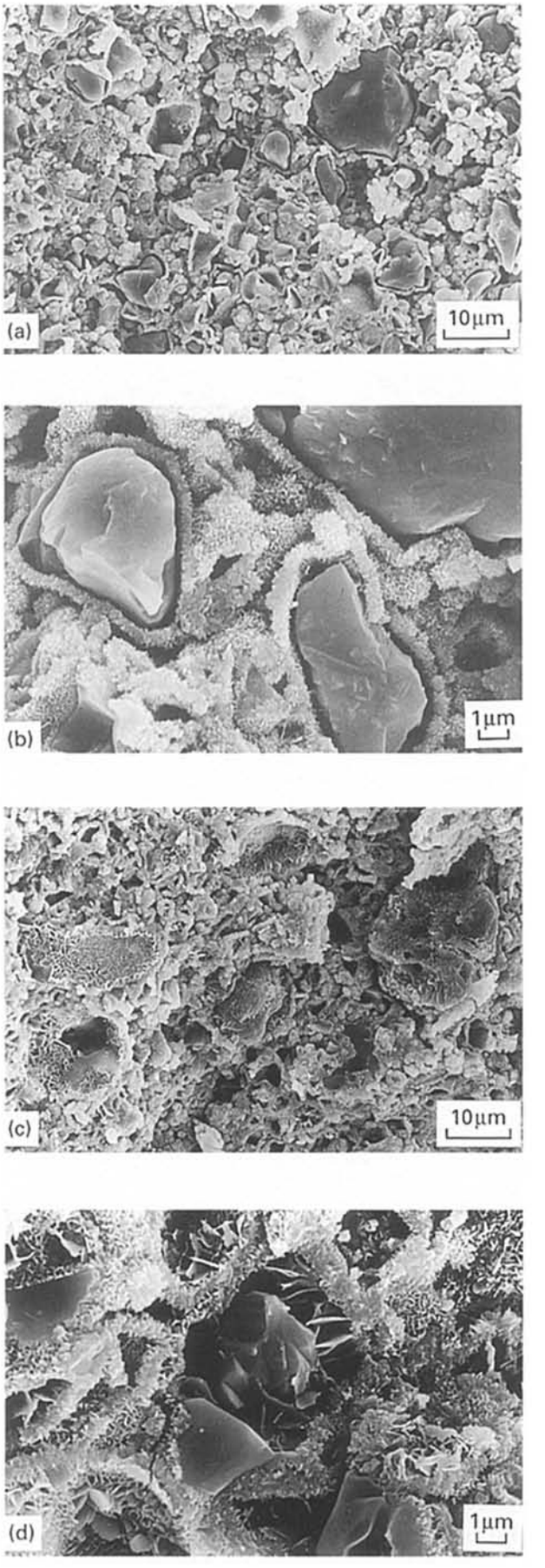

Figure 4 Microstructures of the samples stored at 25 °C obtained by SEM: (a) after 24 h of reaction – granules of α-TCP are clearly visible, surrounded by needle-like small apatite crystals; (b) the same sample at higher magnification – a rim of apatite surrounding three α-TCP particles can be observed; (c) after 48 h of reaction – fewer α-TCP granules are visible, and it is possible to observe some bigger plate-like crystals formed in the space originally occupied by α-TCP particles; and (d) the same sample at higher magnification.

local pH might increase inside the shells, encouraging the precipitation of new crystals with a plate-like structure. These changes in pH would cause also fluctuations in the Ca/P ratio of the precipitated hydroxyapatite.

In Fig. 5a and b the microstructure of a sample stored for 24 h at 37 °C is shown. When compared to Fig. 4a and b, it is clear that the degree of transformation of the α-TCP is higher, since fewer granules can be observed. However, the sample presents the same shell structure, and some plate-like crystals that appeared after 48 h at 25 °C are already present after 24 h at body temperature. After 48 h at physiological temperature (Fig. 5c and d) the changes observed are less important, consistent with a lower rate of transformation.

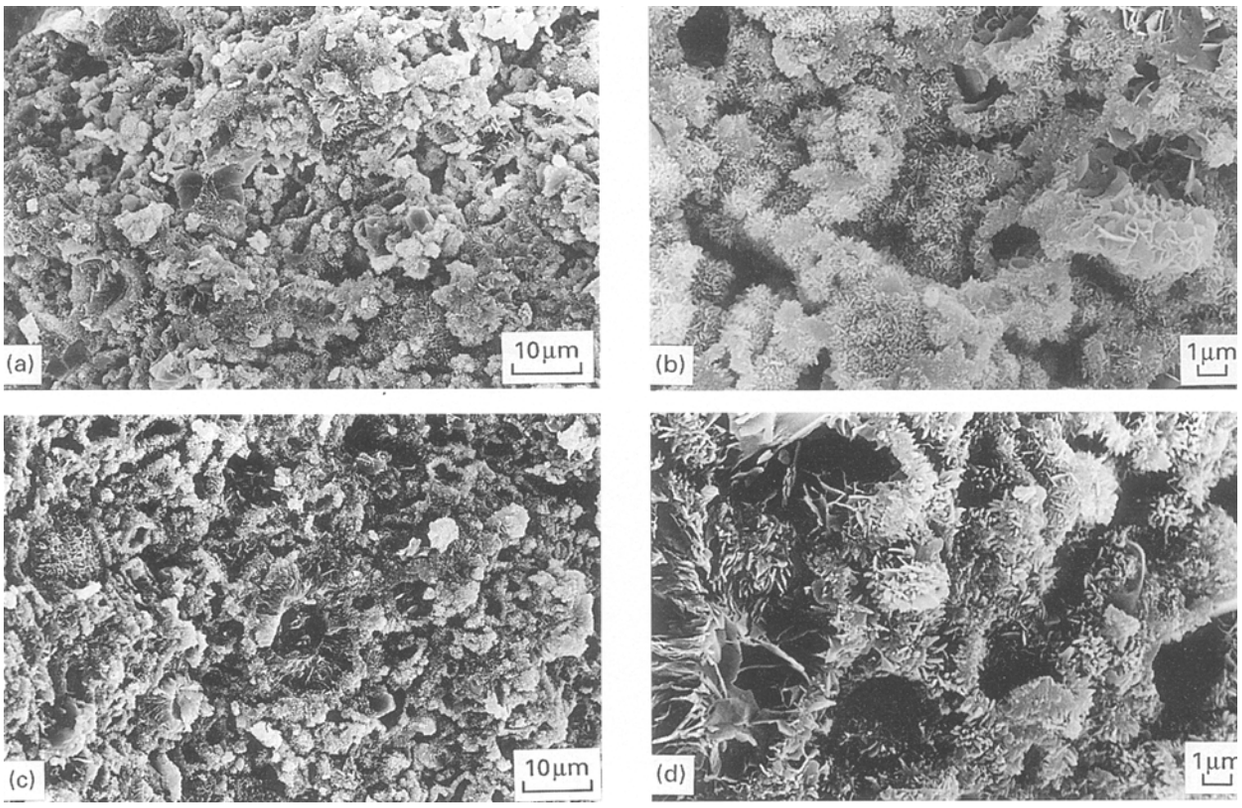

Figure 5 Microstructures of the samples stored at 37 °C obtained by SEM: (a) after 24 h of reaction – a more homogeneous microstructure is formed compared with Fig. 4a, less α-TCP granules are observed, corresponding to a higher degree of reaction, and again two types of precipitated crystals are visible, with different sizes and morphologies; (b) the same sample at higher magnification; (c) after 48 h of reaction – the microstructure is similar to Fig. 5a, but shows an even higher degree of reaction; α-TCP granules are hardly visible; and (d) the same sample at higher magnification.

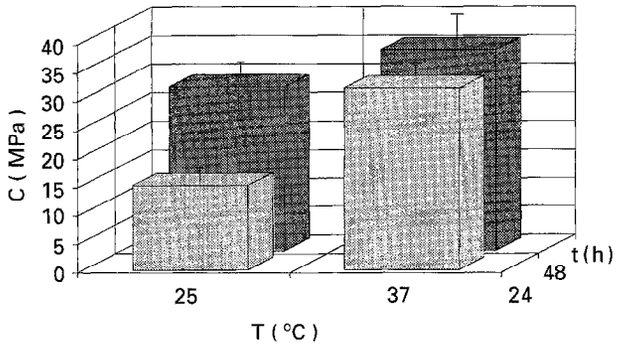

Figure 6 Compressive strength (C) of the cement stored in Ringer's solution at room and physiological temperature for 24 and 48 h.

On the other hand, the structure at 37 °C makes a much more homogeneous impression, with a higher degree of entanglement between the crystals.

Taking into account that the entanglement between the precipitated crystals is thought to be responsible for the mechanical strength of a cement, it is to be expected that the differences observed in the microstructure may have important consequences for the mechanical behaviour of the cement. The data for the compressive strength after 24 and 48 h in Ringer's solution either at 25 or 37 °C are in accordance with this hypothesis; they are shown in Fig. 6. At 37 °C the final compressive strength of 35 ± 5 MPa is reached practically within 24 h. However, at 25 °C the strength after 24 h is not even half of that obtained after 48 h. Moreover, at body temperature the final value after 48 h is significantly larger than that obtained at 25 °C.

Acknowledgements

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