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Dense polycrystalline β-tricalcium phosphate for prosthetic applications

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A method is described for preparing dense, polycrystalline β-tricalcium phosphate. The compressive and flexural strengths of the polycrystalline bodies sintered at a temperature of 1150° C for 1 h were found to be 459 and 138 MPa, respectively. Observation of the fracture surfaces by scanning electron microscopy indicates a predomination of transgranular failures. The polycrystalline tricalcium phosphate is non-toxic in a cell culture system.

1. Introduction

Intense interest has been shown recently towards using calcium phosphate ceramics as bone and tooth implant materials, because of their close resemblance to bone and tooth minerals and their superior compatibility with these tissues. Hydroxyapatite [$Ca_{10}(PO_4)_6(OH)_2$] [1–4] and β-tricalcium phosphate [$Ca_3(PO_4)_2$] ceramics [5–8] have been investigated, although it has been difficult to obtain dense ceramic forms of tricalcium phosphate. Jarcho *et al.* [9] have described a method for the production of dense, polycrystalline β-tricalcium phosphate by doping with catalytic amounts of ammonium sulphate. In the present study, a simple method for preparing dense, sintered β-tricalcium phosphate is described and its mechanical properties estimated. The cytotoxicity is evaluated by cell culture techniques.

2. Experimental procedure

2.1. Preparation of sintered tricalcium phosphate

A suspension of $Ca(OH)_2$ (0.6 mol) in 1000 cm^3 distilled water was vigorously stirred at room temperature and a solution of H_3PO_4 (0.4 mol) in 1000 cm^3 distilled water was added in drops to produce a gelatinous precipitate. The pH was always kept above 6.0 by adding 3% ammonia (about 30 cm^3). The reaction mixture was stirred for a few hours. The resulting slurry was filtered. The filter cake was dried at 90° C and calcined at 800° C for 3 h. The product has a Ca/P ratio of 1.51 estimated by standard EDTA titration for Ca and phosphomolybdate techniques for PO_4. The finely ground powder, mixed with 1 wt% corn starch and a few drops of distilled water, was pressed in a mould with a pressure of 50–60 MPa. The compact was heated in air at 1100, 1150, 1200, 1250 and 1300° C for 1 h.

Phases of the precipitate, calcined product and sintered materials were identified by X-ray powder diffraction and infra-red spectroscopy. The phase composition of the sintered materials was determined by the X-ray diffraction method. Peaks used for calculation of the composition were (0210) for β-tricalcium phosphate and (300) for hydroxyapatite. The maximum sensitivity for detection was 2 wt% in these systems. The relative density values were calculated by assuming a theoretical density of 3.07 g cm^{-3}. The average grain sizes were estimated by the linear intercept method from scanning electron micrographs of the specimens after etching in 0.1 M acetic acid solution for 1–2 min. The thermal expansion coefficient

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TABLE I Phase composition, relative density and grain size for sintered β-tricalcium phosphate

Temperature (° C)	Phase composition (wt%)*		Relative density (%)	Grain size (μm)†
	β-tricalcium phosphate	Hydroxyapatite		
1100	100	0	85.7	0.67 ± 0.35
1150	100	0	98.6	1.17 ± 0.54
1200	100	0	99.4	1.59 ± 0.69
1250	95	5	–	2.23 ± 0.94
1300	93	7	–	3.64 ± 1.21

* By X-ray analysis.
† By the linear intercept method.

was measured by a dilatometer employing a bar of 5 mm square cross-section and 15 mm length.

2.2. Material testing

Test pieces of the sintered materials were cut from discs with a low-speed diamond saw and polished with 800-grit SiC before testing. Compression tests were made on a bar of 5 mm square cross-section and 10 mm length at a cross-head speed of 2.0 mm min^{-1}. Three-point bend tests were made on a 15 mm span of material with a 2 x 4 mm cross-section at a head speed of 0.5 mm min^{-1}. In all tests, 20 to 25 specimens were used. The displacement values in the compression and bending tests were measured by a differential transformer [10]. The fracture surfaces resulting from bending failures were examined by scanning electron microscopy (SEM).

2.3. Cytotoxicity test

L-cells [11] were grown in Eagle's minimum essential medium (MEM) [12] supplemented with 10% calf serum, and were harvested with 0.02% EDTA in Ca- and Mg-free balanced salt solution. Test samples of the β-tricalcium phosphate sintered at 1150° C and the dense polycrystalline hydroxyapatite prepared as in [10] were cut and polished as in Section 2.2. The test samples (10 mm x 4 mm x 0.3 mm), sterilized by exposure to ultraviolet light for 15 min, were placed in the bottom of short test-tubes. Empty test-tubes served as controls. The cells (7 x 10^4 in number) in 1.5 cm^3 of Eagle's MEM supplemented with 10% calf serum were added to the test-tubes and the cultures incubated at 37° C. Cell multiplication in the cultures was measured by counting the cells from five replicate cultures [13] at days 1, 2, 3 and 4.

The test samples were placed centrally in the bottom of Leighton tubes [14]. The cells (5 x 10^4) in 1 cm^3 of Eagle's MEM supplemented with 10% calf serum were grown in the Leighton tubes at 37° C. After 48 h incubation, the cell morphology around the test samples was observed under a phase-contrast microscope.

3. Results and discussion

3.1. Phase transformation and sintering

X-ray powder diffraction patterns of the gelatinous precipitate showed a few broad peaks of calcium-deficient hydroxyapatite, sometimes called "amorphous" calcium phosphate. On heating to 800° C, sharp peaks of β-tricalcium phosphate appeared indicating complete transformation to crystalline β-phase. The infra-red spectrum of the precipitate (KBr pellets) showed the apatite spectrum together with a sharp band at 1400 cm^{-1} [15]. The 1400 cm^{-1} band, most likely caused by NH_4 impurities [16], completely disappeared after heating to 1100° C. In the range from 1100 to 1200° C, α-tricalcium phosphate and hydroxyapatite phases were not detected by X-ray diffraction method. The secondary recrystallization of hydroxyapatite was observed at 1250 and 1300° C. The phase transformation is similar to the sulphate-doped β-tricalcium phosphate described by Jarcho *et al.* [9]. The optimal sintering temperature for β-tricalcium phosphate ceramics was between 1150 and 1200° C (Table I).

The linear thermal expansion coefficient was measured in the range from 100 to 700° C and found to be 10^{-5} ° C^{-1}. The coefficient is similar to that for sintered hydroxyapatite (11 x 10^{-6} ° C^{-1}) [17].

3.2. Microstructure

The microstructure of the sintered materials was examined by SEM techniques. The ceramics indicated as single-phase by the X-ray investigation and obtained at 1150 and 1200° C had a pore-free microstructure, as shown in Fig. 1. The mixed

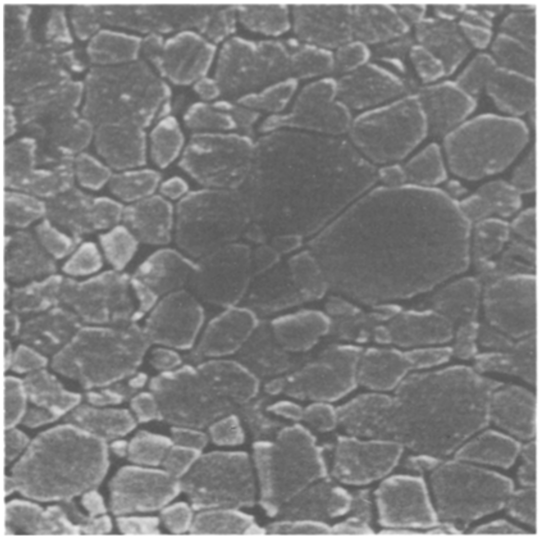

Figure 1 Scanning electron micrograph of etched surface of β-tricalcium phosphate sintered at 1150° C for 1 h (× 2400).

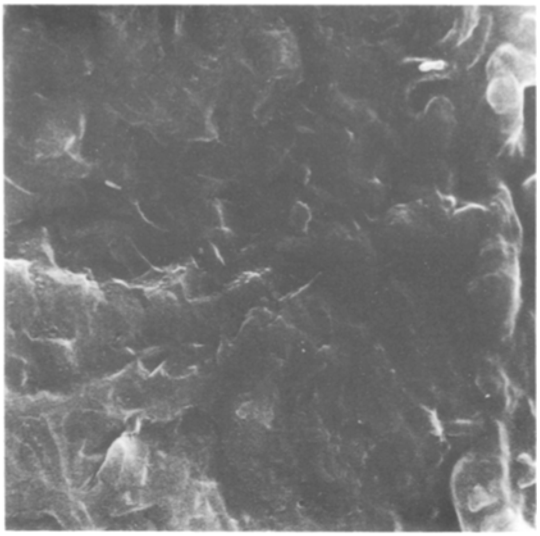

Figure 2 Scanning electron micrograph of fracture surface of β-tricalcium phosphate sintered at 1150° C for 1 h (× 4100), showning transgranular fracture. Crack has been propagated from right to left.

tricalcium phosphate–hydroxyapatite ceramics were also pore free. The microstructures were indicative of single-phase ceramics and the second ary recrystallization and grain-boundary deposits were not detected in the SEM micrographs.

3.3. Mechanical properties

The mechanical properties of tricalcium phosphate ceramics are summarized in Table II. The mechanical properties of the material sintered at 1100° C are not given because of its very low strength. The compressive and flexural strengths of the material sintered at 1150° C are greater than those of the material sintered at 1200° C because of the finer grain size. The mixed-phase ceramics show the greatest compressive and flexural strengths, probably due to the secondary recrystallization of hydroxyapatite.

Jarcho *et al.* [9] reported that the sulphate-doped β-tricalcium phosphate ceramics have a compressive strength of 687 MPa, a flexural strength of 154 MPa and a modulus of elasticity in tension of 33 GPa. The mechanical properties of the present materials are similar to those for sintered hydroxyapatite [10, 17, 18].

3.4. Fracture topography

SEM examination of the fracture surfaces produced by bending failures revealed that the fracture of the single-phase and mixed-phase ceramics is a transgranular process. Fig. 2 shows a fracture surface of a specimen sintered at 1150° C; transgranular fracture is predominant. Akao *et al.* [10] reported that the fracture surface of dense, sintered hydroxyapatite indicates predomination of transgranular failures. The origins of crack propagation detected in the SEM micrographs were large particles and surface flaws.

3.5. Cytotoxicity

Fig. 3 shows the cell multiplication in the presence of the sintered β-tricalcium phosphate and hydroxyapatite. Each point is the mean of five replicate cultures, the standard deviation being about 10%. A statistically significant reduction in cell numbers

TABLE II Compressive and flexural strengths, σ, and moduli of elasticity, E, in compression and bending for sintered β-tricalcium phosphate

Temperature (°C)	σ_C(MPa)	σ_F(MPa)	E_C(GPa)	E_B(GPa)
1150	459 ± 37	138 ± 11	82.6 ± 4.6	89.2 ± 5.3
1200	436 ± 35	119 ± 12	77.2 ± 3.6	72.7 ± 6.2
1250	599 ± 57	153 ± 10	79.4 ± 4.2	84.6 ± 6.1
1300	648 ± 38	137 ± 10	77.5 ± 4.4	83.5 ± 5.9

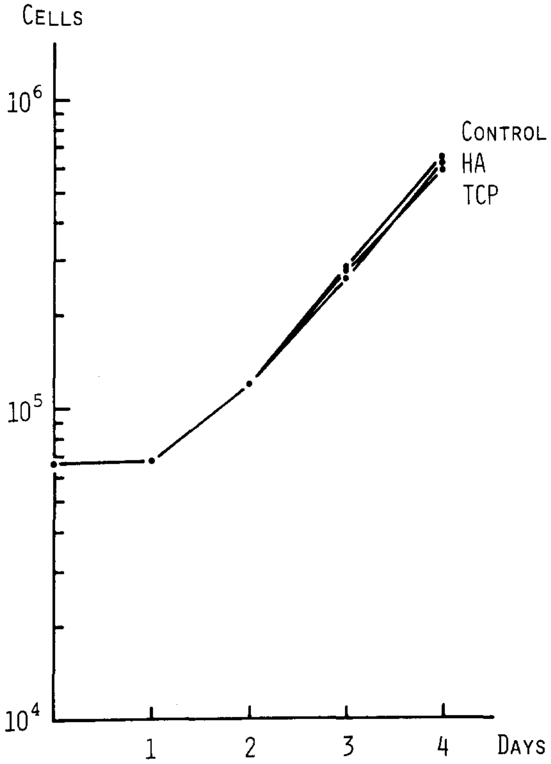

Figure 3 Growth of L-cells around plates of β-tricalcium phosphate (TCP) and hydroxyapatite (HA) ceramics, as measured by cell numbers.

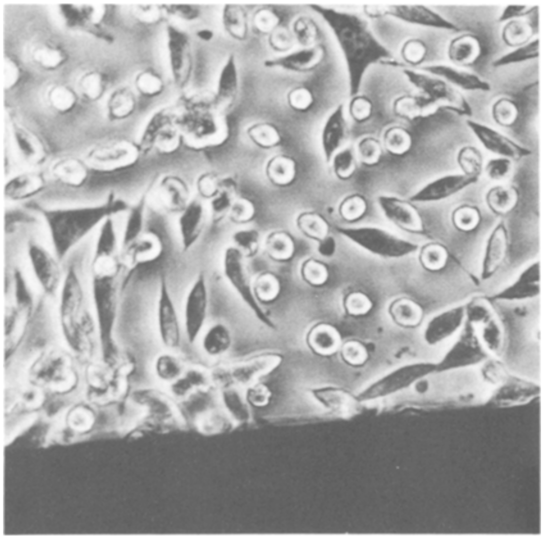

Figure 4 Phase-contrast micrograph of monolayer-cultured L-cells around a plate of dense polycrystalline β-tricalcium phosphate (X 135).

was not observed, compared with the controls. As shown in Fig. 4, spindle-shaped, polymorphic and mitotic cells were observed around the test samples. Vacuolar degeneration, debris of the cells and disruption of the cell membranes were not detected. Thus the dense polycrystalline β-tricalcium phosphate and hydroxyapatite did not exhibit cytotoxic effects.

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