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Development of some calcium phosphate cements from combinations of α-TCP, MCPM and CaO

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From previous studies it is known that alpha-tertiary calcium phosphate (α-TCP), monocalcium phosphate monohydrate (MCPM) and calcium oxide form cements upon mixing combinations of them with water. In this study some formulations were optimized with respect to the particle size of the constituents, their molar ratio, amounts of hydroxyapatite or beta-tertiary calcium phosphate (β-TCP) added and the water/powder ratio. Three suitable products were obtained. Product 1 had a relatively short setting time and might be suitable as a dental cavity liner or for filling parodontological pockets or for filling alveolar cavities to prevent alveolar ridge resorption. Products 2 and 3 may be more suitable for orthopaedic purposes. Their compressive strength being 35 and 12 MPa, respectively, after soaking for 1 day in Ringer's solution at 37 °C. Product 1 reaches its full strength within 4 h, whereas products 2 and 3 take about 12 h and 10 h, respectively.

1. Introduction

The term 'calcium phosphate cement' was introduced by Gruninger *et al.* [1]. Such a cement may be described as a powder or 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.

Lemaitre *et al.* [2–4] formed a brushite cement by mixing a powder of β-TCP with an aqueous solution of MCPM. Another brushite cement was formed in our laboratory [5] as well as by Constantz *et al.* [6] by reaction of mixture of MCPM and tetracalcium phosphate (TTCP). Monma *et al.* [7] reported that they obtained an octo calcium phosphate cement (OCP) by reaction of α-TCP with brushite. In our laboratory [5] several other OCP cements have been developed.

Brown and Chow [8] and later Fukase *et al.* [9] claimed that their powder mixture of dicalcium phosphate (DCP) and TTCP reacted upon mixing with water to stoichiometric hydroxyapatite. However, more recent investigations [10, 11] 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 with a Ca/P ratio near 1.5. Another hydroxyapatite cement was formed by Constantz *et al.* [12] who mixed water-free phosphoric acid with TTCP.

In a previous study [5] it was found that a cement was formed from a mixture of MCPM, α-TCP and CaO around a Ca/P ratio of 1.5. The purpose of the present study was to find out which useful cements might be derived from such combinations of ingredients.

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 followed by quenching in air to room temperature. The quenching procedure appeared to be so fast that the β-TCP content of the product was less then 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 of 5 μm as measured by laser diffraction. Calcium oxide was obtained from Merck, Darmstadt, Germany (catologue number 2109) and from Panreac, Barcelona, Spain (code number 151234). Both were crushed and milled to an average particle size of 5 μm. MCPM was used as such as obtained from Panreac (code number 141225).

Three series of mixtures of α-TCP, MCPM and CaO were made. Their molar contents are given in Table I. Their compositions represent straight lines in the ternary system $CaO–P_2O_5–H_2O$. All these mixtures were ball-milled for 15 min to homogenize them. Pastes were prepared from each mixture by addition of water up to a water/powder (W/P) ratio of 0.52 g/g with two exceptions. The W/P ratio for mixtures number 23 and 24 was 0.42 and 0.35, respectively.

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TABLE I Molar amounts in the mixtures of MCPM, α-TCP and CaO investigated in series 1, 2 and 3

Series	Number	MCPM	α-TCP	CaO	Ca/P	PHA(%)
1	1	0.180	0.320	0.155	1.29	–
	2	0.180	0.320	0.240	1.38	–
	3	0.180	0.320	0.325	1.47	–
	4	0.180	0.320	0.380	1.52	–
	5	0.180	0.320	0.415	1.55	–
	6	0.180	0.320	0.500	1.64	–
2	7	0.285	0.215	0.740	1.67	–
	8	0.250	0.250	0.620	1.62	–
	9	0.215	0.285	0.500	1.57	–
	10	0.180	0.320	0.380	1.52	
	11	0.170	0.330	0.340	1.50	–
	12	0.160	0.340	0.310	1.49	–
	13	0.145	0.355	0.260	1.47	–
5	14	1.0	0.0	2.0	1.50	2
	15	0.9	0.1	1.8	1.50	2
	16	0.8	0.2	1.6	1.50	2
	17	0.7	0.3	1.4	1.50	2
	18	0.6	0.4	1.2	1.50	2
	19	0.5	0.5	1.0	1.50	2
	20	0.4	0.6	0.8	1.50	2
	21	0.3	0.7	0.6	1.50	2
	22	0.2	0.8	0.4	1.50	2
	23	0.1	0.9	0.2	1.50	2
	24	0.0	1.0	0.0	1.50	2

Initial setting time I and final setting time F were determined with Gilmore needles. Cylinders were also 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 $1\ \mathrm{mm\ min^{-1}}$.

The maximum in the compressive strengths for series 1 and 2 was found for the point of intersection at a Ca/P molar ratio of 1.51 ± 0.01. Two series (series 3 and 4) were designed from this composition, series 3 with increasing amounts of β-TCP admixtures and series 4 with increasing amounts of precipitated hydroxyapatite (PHA). However, it appeared to be necessary as well to carry out series 5 at a constant Ca/P molar ratio of 1.50 and the optimum PHA content of 2% because the reaction product in this system appeared to be calcium-deficient hydroxyapatite $Ca_9(HPO_4)_5(OH)$. From series 5 two products appeared to be suitable: number 15 because of its very short setting time and number 24 because of its relatively high strength. A third product (an octocalcium phosphate cement) was obtained by mixing MCPM and α-TCP at a Ca/P molar ratio of 1.33.

3. Results

The final setting times F and the compressive strengths C for series 1 are given in Fig. 1. F shows a minimum and C a maximum for a Ca/P molar ratio of 1.51 ± 0.01. The results of series 2 are given in Fig. 2. They show a gradual change of F and only a slight maximum in C.

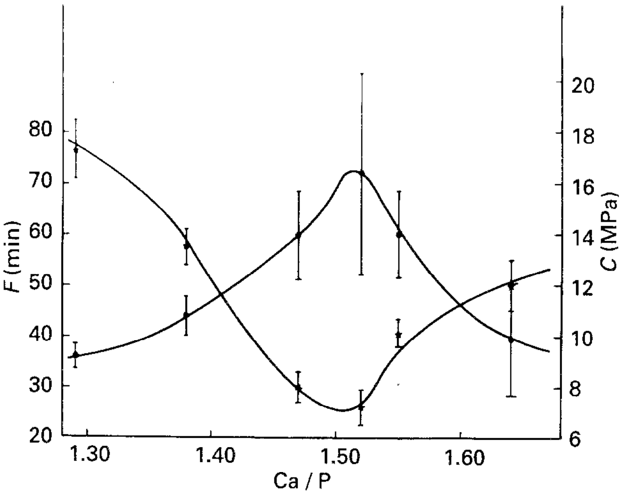

Figure 1 Final setting times F(✱) and 1-day compressive strength C(●) of cements prepared from the mixtures of series 1 (see Table I).

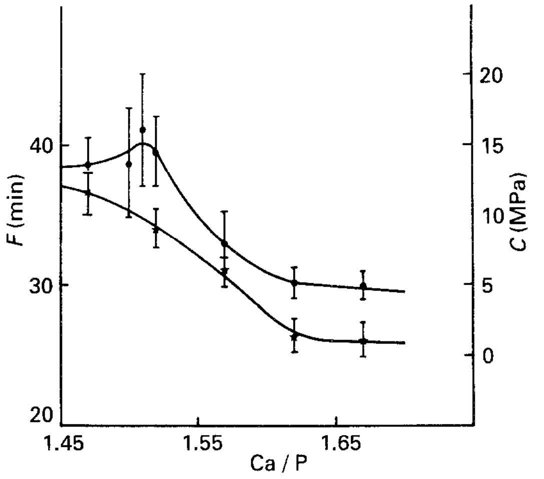

Figure 2 Final setting times F(✱) and 1-day compressive strength C(●) of cements prepared from the mixtures of series 2 (see Table I).

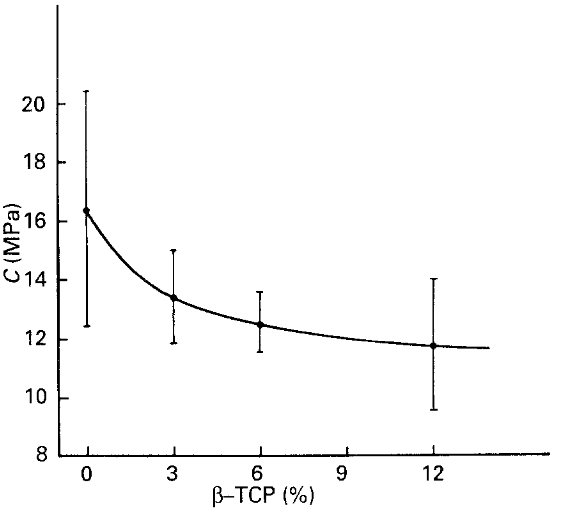

Figure 3 Compressive strength C (after 1 day) of cements prepared from the optimum composition of series 1 and 2 by addition of increasing amount of β-TCP.

According to Fig. 3 additions of β-TCP weaken cements of this type. Not shown is the fact that these additions also caused a tremendous delay in the setting. From Fig. 4 it is observed that additions up to 2% of PHA reinforce these cements and decrease the setting time. Therefore in series 5 an addition of 2%

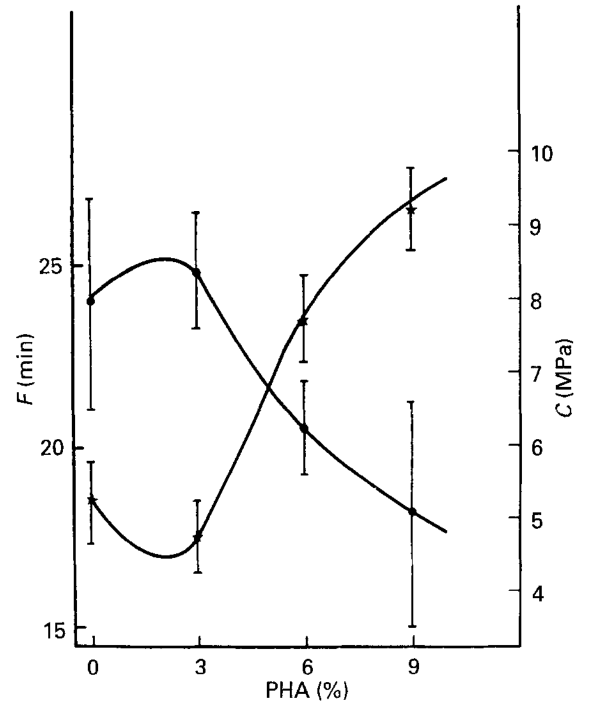

Figure 4 Final setting times $F(*)$ and 1-day compressive strength $C(\bullet)$ of cements prepared from the optimum composition of series 1 and 2 by addition of increasing amounts of precipitated hydroxyapatiate PHA.

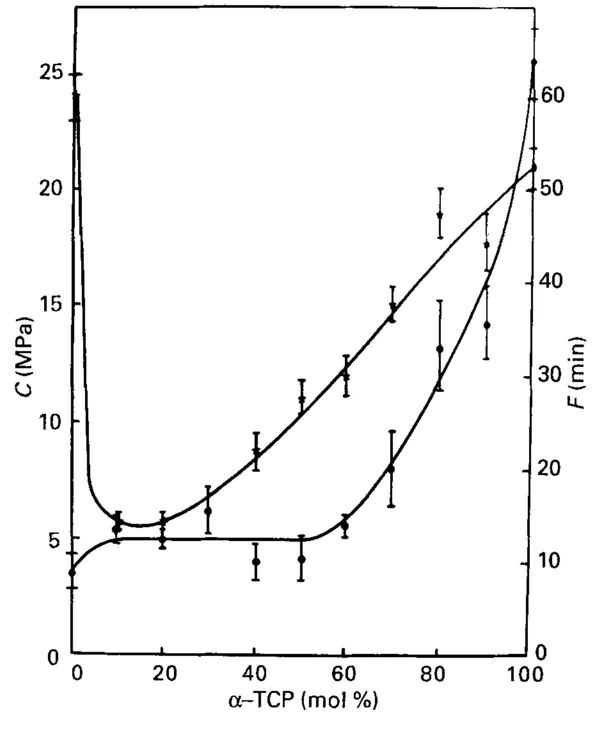

Figure 5 Final setting times $F(*)$ and 1-day compressive strength $C(\bullet)$ of cements prepared from the mixtures of series 3 (see Table I).

PHA was used. The results of that series are given in Fig. 5. They show a minimum in F at 14 min for a content of 15 ± 5% α-TCP in the reacting mixtures (product 1). A maximum in the compressive strength C was observed at 0% (MCPM + CaO). Hence, the latter product might be called an α-TCP cement, because the α-TCP is the sole reacting calcium phosphate in this cement (product 2).

This α-TCP cement was optimized further for PHA content and CaO content with respect to the final setting time F (Table II) and compressive strength C (Table III). No further improvements could be obtained. CaO appeared to be detrimental, but PHA essential for the strength of the final product, which reached a maximum value of 30 ± 5 MPa. The tensile strength was 8 ± 1 MPa.

Finally, in this system another cement was developed (product 3) by mixing MCPM and α-TCP in

TABLE II Final setting time F of the α-TCP cement as a function of its PHA content and its CaO content (water/powder ratio 0.35). Standard deviations in parenthesis.

	PHA (%)		
CaO (%)	0	2	4
0	58 (3)	53 (2)	41 (2)
1.5	40 (2)	42 (2)	55 (3)
3	60 (2)	54 (2)	54 (2)

TABLE III Compressive strength C (MPa) of the α-TCP cement as a function of its PHA content and its CaO content (W/P ratio 0.35). Standard deviations in parentheses.

	PHA (%)		
CaO (%)	0	2	4
0	5 (1)	26 (2)	29 (5)
1.5	13 (2)	23 (3)	15 (2)
3	0.5 (0.1)	0.3 (0.1)	0.3 (0.1)

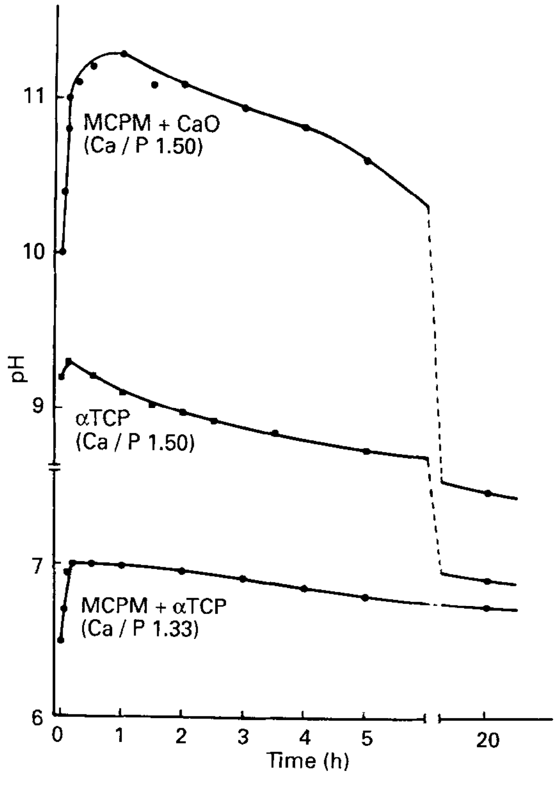

Figure 6 pH of the cement mixtures of the three optimized products as a function of time, measured from the beginning of the mixing with water.

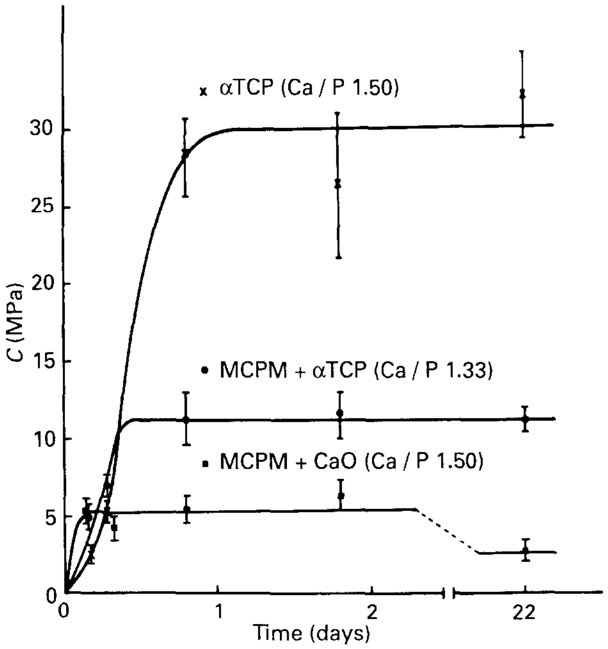

Figure 7 Compressive strength *C* of the three optimized products as a function of the time of soaking in Ringer's solution 37 °C.

a Ca/P molar ratio of 1.33 and an admixture of 4% PHA as a nucleator. The compressive strength of this product was about 12 ± 2 MPa.

Fig. 6 shows the pH of the cement mix as a function of the time starting from the mixing with water. Fig. 7 shows the compressive strength of the three products as a function of the time of soaking in Ringer's solution at 37 °C. Product 1 reaches its full strength within 4 h, product 2 after about 12 h and product 3 after about 10 h.

X-ray diffraction showed that products 1 and 2 consist of apatite after the setting reaction, whereas product 3 is octocalcium phosphate.

4. Discussion

Product 1 has the property that the setting reaction is in the range of most dental filling materials. Initially the pH of the cement mix might seem to be very high for *in vivo* application, but it returns to neutral within 20 h. For dental applications this seems acceptable, certainly in comparison with calcium hydroxide products which have a wide application in dentistry and which retain a high pH during a much longer time. The compressive strength of product 1 is about 5 MPa within 4 h, which is certainly enough as an application as a pulpa protector under a composite filling. But other applications like filling of periodontal pockets or even of alveolar pockets, in order to inhibit alveolar ridge resorption, might be envisaged.

Products 2 and 3 have a longer setting time and might be used as bone cements for orthopaedic purposes. We expect that they can be applied as they are in a press-fit procedure, in which they may function better than a plasma-sprayed HA coating, because such a coating needs much time to result in complete ongrowth of bone. In contrast, these cements result in a tight fit between the calcium phosphate and the bone right away. Animal experiments will be necessary to evaluate the biomechanical stability of structures obtained by implanting different metal endoprostheses in bones in which fixation is obtained or enhanced by the use of these new bone cements.

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