

# Effect of $\beta$ -TCP granularity on setting time and strength of calcium phosphate hydraulic cements

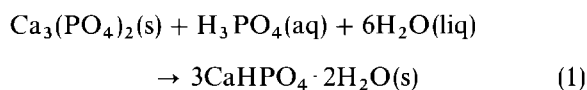
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The effects of  $\beta$ -tricalcium phosphate ( $\beta$ -TCP) granularity on the properties of calcium phosphate hydraulic cements (CPHC) have been investigated. A model system based on mixtures of ( $\beta$ -TCP) and aqueous solution of orthophosphoric acid has been used. Powders with different shapes (irregular agglomerates or spheres) and sizes ( $d_{50} = 7$  to  $130 \mu\text{m}$ ) were prepared from two different calcium phosphate sources: Ca-deficient hydroxyapatite (DAP) or hydroxyapatite dicalcium phosphate mixtures (HAP-DCP). The cements exhibited setting times (ST) ranging from 65 to 510 s; they are mainly affected by the specific surface area ( $S_{\text{BET}}$ ) of the  $\beta$ -TCP powders, longer ST corresponding to lower  $S_{\text{BET}}$ . In general, lower  $S_{\text{BET}}$  and shorter ST values were obtained with HAP-DCP powders. Diametral tensile strengths (DTS) ranging from 3.5 to 10.4 MPa were obtained. The results show that DTS is affected in a complex way by the experimental variables. In general, DTS is higher with irregular agglomerates compared to spheres (+ 1.2 MPa), while better results are obtained with HAP-DCP powders (+ 0.9 MPa). The dependence of DTS on particle size is variable according to powder source and shape. The highest DTS (10.4 MPa) was obtained with irregular agglomerates prepared from HAP-DCP mixtures ( $d_{50} = 16 \mu\text{m}$ ), and the lowest (3.5 MPa), with irregular agglomerates prepared with DAP ( $d_{50} = 123 \mu\text{m}$ ). It can be concluded from this work that specific CPHC formulations can give quite different cement properties, such as setting time and ultimate mechanical strength, depending on the characteristics of the raw materials used. In the case of  $\beta$ -TCP based cements, the granularity of the starting cement powder, including particle size, shape and specific surface area, is of crucial importance and should be specified when the performances of different formulations are to be compared.

## 1. Introduction

Calcium phosphate hydraulic cements (CPHC) are very promising materials for bone grafting, as they are perfectly biocompatible, resorbable, and can stimulate new bone formation [1–3]. A large variety of cement formulations are possible, which exhibit a broad range of setting times and mechanical strengths [4, 5]. Although variations in CPHC behaviours are certainly related to chemical differences [1], the effects of non-chemical factors have not yet been the object of systematic investigation. The aim of this work is to study the influence of granularity of raw materials on the behaviour of CPHCs. For this purpose, the  $\beta$ -tricalcium phosphate–orthophosphoric acid ( $\beta$ -TCP-OPA) cement has been used as a model. In this system, brushite (DCPD) is produced according to the following reaction [6]:



The effects of various factors such as solid/liquid ratio, OPA concentration in the mixing liquid, nature and concentration of additives on the setting time,

mechanical strength and porosity of these cements have been studied thoroughly in previous papers [3, 6, 7].

The present work investigates the effects of  $\beta$ -TCP granularity (i.e. grain size, shape and specific surface area) on the setting time and strength of a typical TCP-OPA cement formulation.

## 2. Experimental procedures

### 2.1. Materials

Two different methods were used for preparing the  $\beta$ -TCP powders: (i) the pyrolysis of Ca-deficient hydroxyapatite (DAP); and (ii) the reactive sintering of mixtures of hydroxyapatite (HAP) and anhydrous dicalcium phosphate (DCP,  $\text{CaHPO}_4$ ). The following raw materials were used without further purification:

DAP (Ca/P = 1.5): Merck, cat. no 2143  
 HAP: Merck, cat no 2194  
 DCP: Merck, cat no 2144.

After thorough homogenization by ball milling, the powders were converted into  $\beta$ -TCP by calcining in air for 1 h at  $900^\circ\text{C}$ .

From this point on, the powders were processed either as irregular agglomerates or spherical particles:

*Irregular agglomerates* were obtained by grinding and sieving the calcined cake obtained above, and sintering the size fractions for 4 h at 1150 °C in air.

*Spherical particles* were obtained as follows: the calcined cake was deagglomerated by ball-milling; the powder was suspended in water, containing 0.5 wt % ammonium polyacrylate (Aldrich cat. no 19203-1) as a deflocculant, and granulated by spray-drying (Büchi 190 mini spray-dryer). After sieving, different size fractions were sintered as above.

All the sintered powders were found by X-ray diffraction (Siemens D500,  $\text{CuK}_\alpha$  radiation) to consist of pure  $\beta$ -TCP.

The cement specimens were prepared by mixing thoroughly for 30 s 1.5 g of dry  $\beta$ -TCP powder with 1.0 ml of an aqueous solution containing 4.0 mol/l  $\text{H}_3\text{PO}_4$  (Merck, p.a.), 0.25 mol/l  $\text{H}_2\text{SO}_4$  (Merck, p.a.), and 0.20 mol/l  $\text{Na}_4\text{P}_2\text{O}_7$  (Fluka, purum; > 98%).

## 2.2. Characterization techniques

*Electron microscopy.* Scanning electron micrographs were obtained on a JEOL SM6300F apparatus in the secondary electron detection mode.

*Particle size distribution.* The particle size distributions of the different size fractions were determined using a Mastersizer (Malvern) apparatus, in the direct Fourier transformation mode.

*Specific surface area.* The measurements were performed by nitrogen adsorption at liquid nitrogen temperature (BET method), with a Gemini 2360 Surface Area Analyser (Micromeritics), using 3–4 g of powder per measurement.

*Liquid limit.* The liquid limit (LL) of a powder is the minimum volume of mixing liquid needed to confer a liquid behaviour to the mixture: thus, 1.0 g of dry powder was first mixed with 200  $\mu\text{l}$  of an ammoniated aqueous solution of PAA (0.5 wt %, Aldrich cat. no 19203-1); then, successive, 20  $\mu\text{l}$  aliquots of the same solution were added, the mixture being shaken vigorously for 30 s between two additions (REAX 200 vibrator, Heidolph), until the mixture could flow under its own weight.

*Setting time.* The setting times were measured using a variation of the Vicat needle technique previously described [6].

*Mechanical strength.* The diametral tensile strengths were determined on dry cylindrical specimens ( $\text{Ø} \times h = 9 \pm 0.2 \times 15 \pm 1$  mm) 12 days after their preparation, using a Lhomargy DY31 testing machine (displacement rate = 1 mm/min).

## 2.3. Statistics

The experiments were organized in a  $2^2 \times 4$  statistical factorial design [8]. The definitions and levels of the factors are presented in Table I. The complete set of experimental conditions (treatments) is presented in Table II. The data were analysed using the ANOVA technique.

TABLE I Experimental design: factor definitions

Factor	Definition	Levels			
		Low		High	
A	Particle shape	Spheres		Agglomerates	
B	Source	DAP		HAP + DCP	
		1	2	3	4
X	Nominal size ( $\mu\text{m}$ )	< 20	20–50	50–100	100–200

\* For effective size distributions, see Table III.

TABLE II Experimental design: list of experiments

Test	Treatment	Factors		
		Shape	Source	Nominal size ( $\mu\text{m}$ )
1	'1'	Spheres	DAP	< 20
2	a	Agglomerates	DAP	< 20
3	b	Spheres	HAP + DCP	< 20
4	ab	Agglomerates	HAP + DCP	< 20
5	'2'	Spheres	DAP	20–50
6	2a	Agglomerates	DAP	20–50
7	2b	Spheres	HAP + DCP	20–50
8	2ab	Agglomerates	HAP + DCP	20–50
9	'3'	Spheres	DAP	50–100
10	3a	Agglomerates	DAP	50–100
11	3b	Spheres	HAP + DCP	50–100
12	3ab	Agglomerates	HAP + DCP	50–100
13	'4'	Spheres	DAP	100–200
14	4a	Agglomerates	DAP	100–200
15	4b	Spheres	HAP + DCP	100–200
16	4ab	Agglomerates	HAP + DCP	100–200

## 3. Results and discussion

### 3.1. Particle size distributions and microstructures

Table III summarizes the results of particle size analyses of the  $\beta$ -TCP powders used in the experiments, expressed as  $d_{10}$ ,  $d_{50}$  and  $d_{90}$ , the particle sizes corresponding respectively, to the first decile, median and ninth decile of the cumulated volume distribution ( $d_v$  means that  $V$  vol % of the powder consists of particles with a diameter <  $d_v$ ).

The results show that, despite the great care exerted in sieving, the selected powders exhibit fairly broad particle size distributions, and still contain significant amounts of fines.

The microstructures of the powders are illustrated by the SEM micrographs presented in Fig. 1. Fig. 1a shows the microstructure of an irregular agglomerate prepared by reactive sintering of the HAP-DCP mixture, which is representative of the other irregular agglomerate powders. The particles consist of porous aggregates of elemental crystallites, with sizes in the 1–10  $\mu\text{m}$  range (0.1–1  $\mu\text{m}$  for DAP powders). Fig. 1b shows a typical microstructure of the  $\beta$ -TCP spheres prepared with the HAP-DCP mixture: the spheres consist of mosaic assemblies of elemental crystallites;

TABLE III Size distributions of the selected powders

Nominal size ( $\mu\text{m}$ )	Source	Shape	Size distribution*		
			$d_{10}$ ( $\mu\text{m}$ )	$d_{50}$ ( $\mu\text{m}$ )	$d_{90}$ ( $\mu\text{m}$ )
< 20	DAP	Spheres	0.4	15	33
		Agglomerates	0.6	7	22
	HAP + DCP	Spheres	0.7	18	45
		Agglomerates	1.4	16	35
20–50	DAP	Spheres	19	29	48
		Agglomerates	20	36	63
	HAP + DCP	Spheres	23	44	87
		Agglomerates	21	39	70
50–100	DAP	Spheres	45	63	101
		Agglomerates	17	67	113
	HAP + DCP	Spheres	47	67	107
		Agglomerates	48	77	123
100–200	DAP	Spheres	89	129	196
		Agglomerates	13	123	226
	HAP + DCP	Spheres	59	118	237
		Agglomerates	84	127	194

\* $d_v$  means that  $V$  % of the powder volume consists of particles with a diameter  $< d_v$ .

most of the spheres exhibit a hole communicating with an inner pore, which has been evidenced on broken particles (not shown). Spheres prepared with DAP are shown in Fig. 1c; the main difference with the HAP-DCP spheres is the much smaller size of the elemental

crystallites: 0.1–2  $\mu\text{m}$  versus 2–10  $\mu\text{m}$  for HAP-DCP sphere.

### 3.2. Specific surface area ( $S_{\text{BET}}$ )

The specific surface areas of the powders are presented in Table IV. The results are presented in Fig. 2, together with the adjusted values calculated with the statistical model retaining only the significant regression coefficient ( $p < 0.05$ , meaning that the risk of accepting by mistake a coefficient as significant is lower than 5%).

The figure shows that the powders prepared with DAP (treatments '1' to 4a) exhibit in general higher specific surfaces: DAP agglomerates exhibit the highest surfaces (treatments a to 4a), which are about twice as large as DAP spheres (treatments '1' to '4'); the smallest surfaces (0.1–0.3  $\text{m}^2/\text{g}$ ) are obtained with HAP-DCP mixtures, with little difference between spheres and agglomerates. In general, the observed surfaces are much higher than expected on the basis of the corresponding size distributions of dense smooth spheres. The discrepancy probably has three origins, the relative contributions of which might vary according to the raw material used and the shape of the particles: (i) the particle surfaces are not smooth, even for spherical particles; (ii) an important contribution to the specific surface is given by the fines, even though their volume fraction is small; and (iii) the particles

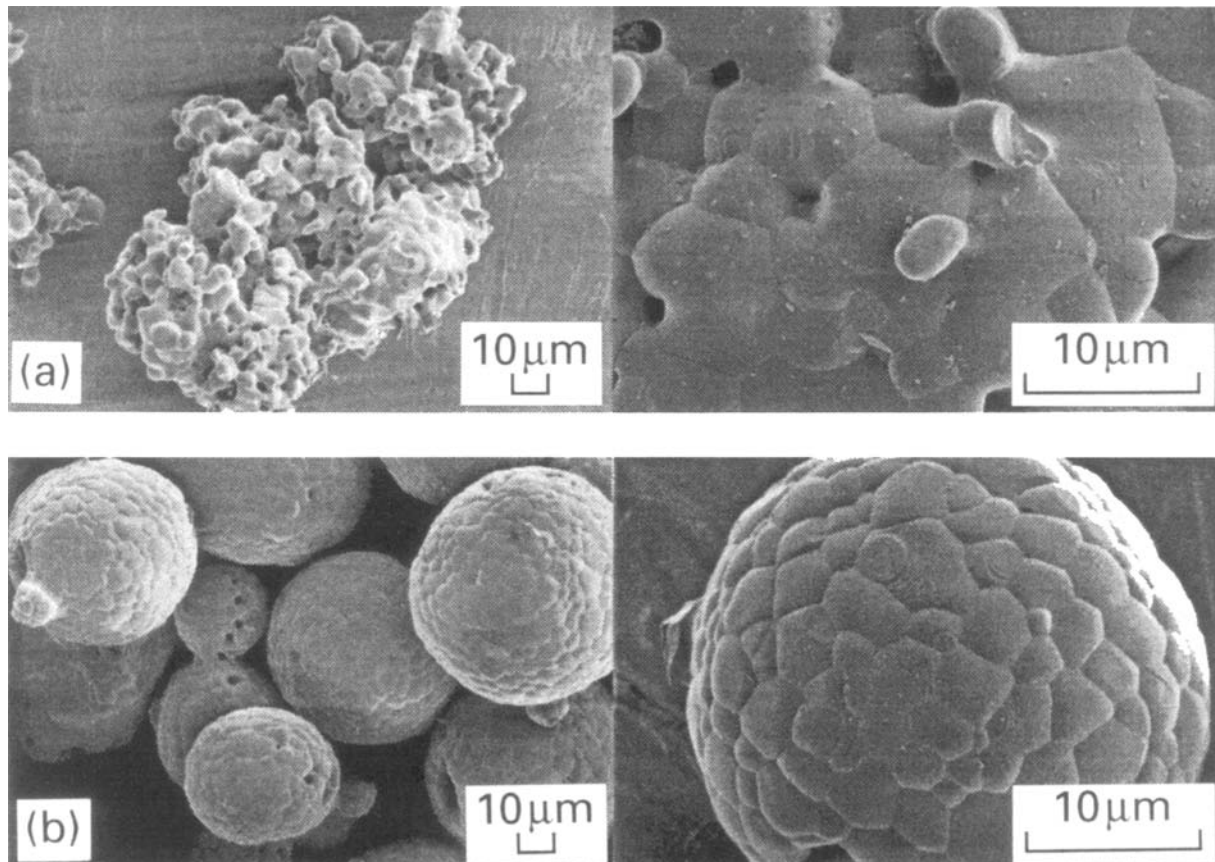


Figure 1 SEM micrographs of  $\beta$ -TCP powders ( $50 < d < 100 \mu\text{m}$ ): (a) HAP-DCP agglomerates; (b) TCP granules from HAP-DCP source, prepared by spray-drying (the spheres are composed of larger crystallites); (c) TCP granules from DAP source, prepared by spray-drying (the porosity of the spheres looks higher).

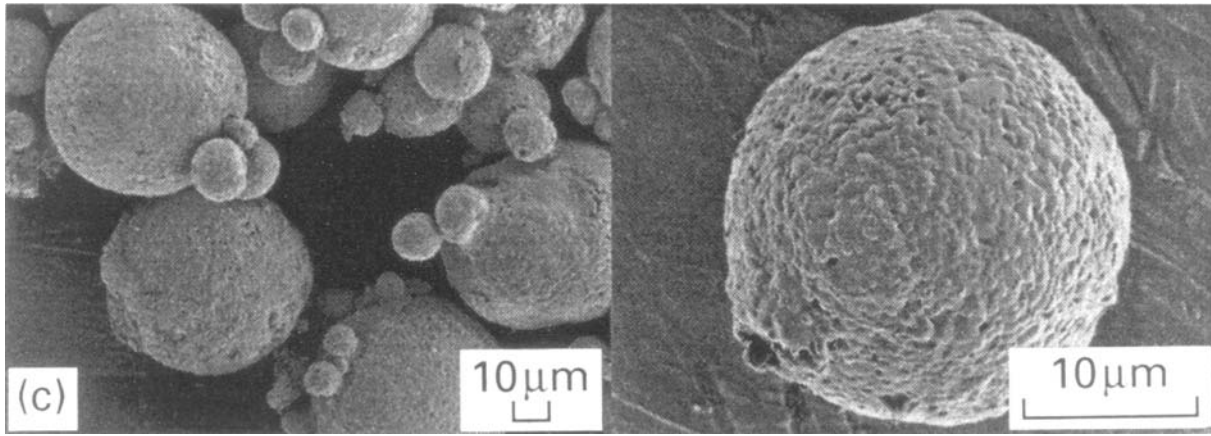


Figure 1 (Continued)

TABLE IV Experimental results

Test	Treatment	Response			
		$S_{\text{BET}}$ ( $\text{m}^2/\text{g}$ )	Liquid limit ( $\mu\text{l}/\text{g}$ )	Setting time (s)	Strength* (MPa)
1	'1'	0.51	393	225	7.10
2	a	1.08	341	160	7.68
3	b	0.38	358	300	5.82
4	ab	0.28	412	370	10.38
5	'2'	0.43	418	235	5.08
6	2a	0.79	442	125	7.34
7	2b	0.16	358	475	7.09
8	2ab	0.24	487	410	7.45
9	'3'	0.41	431	235	6.01
10	3a	0.89	954	80	9.40
11	3b	0.18	348	450	6.67
12	3ab	0.21	531	420	7.13
13	'4'	0.45	422	260	5.00
14	4a	0.93	679	100	3.52
15	4b	0.16	333	510	7.15
16	4ab	0.26	508	405	6.71

\* Average over three/four measurements. Occasionally, individual outlying results were rejected using the Cochran Q rejection test (90% confidence).

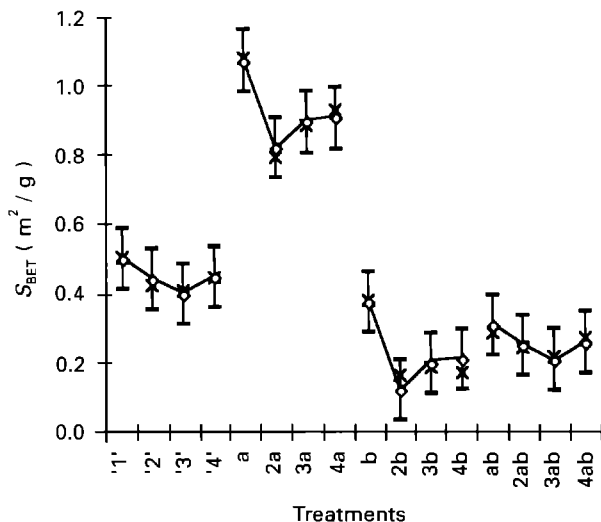


Figure 2 Specific surface areas of  $\beta$ -TCP powders. Adjusted values calculated from the statistical model ( $p < 0.05$ ). (A) Shape (spheres-agglomerates); (B) source (DAP-HAP + DCP). (1)  $d < 20 \mu\text{m}$ ; (2)  $20 < d < 50 \mu\text{m}$ ; (3)  $50 < d < 100 \mu\text{m}$ ; (4)  $d > 100 \mu\text{m}$ ;  $\times$  experimental value;  $\diamond$  adjusted value; the bars denote  $\pm 3$  S.E.

exhibit a significant internal porosity. It is not possible in the present state of knowledge to unmix these contributions.

### 3.3. Liquid limit (LL)

The experimental results are presented in Table IV, and compared in Fig. 3 with the adjusted values calculated with the statistical model ( $p < 0.05$ ). In general, the lowest LLs are obtained with spherical particles the biggest difference being observed between DAP spheres (treatments '1' to '4') and DAP agglomerates (treatments a to 4a). In the case of agglomerates, LL tend to increase with particle size, the effect being much stronger with DAP (treatments a to 4a) compared to HAP-DCP mixtures (treatments ab to 4ab); this observation indicates that DAP particles are less dense than HAP-DCP. The lowest LL values are obtained with HAP-DCP spheres ( $350 \mu\text{l}/\text{g}$ , treatments b to 4b); by using such powders injectable cements could be prepared with as little as  $0.35 \text{ ml}/\text{g}$  of mixing liquid, i.e. about half the volume used in the present experiments ( $0.67 \text{ ml}/\text{g}$ ). On the other hand, samples 3a and 4a have higher LLs than the mixing volume used in the present experiments to prepare the cements (resp.  $0.954$  and  $0.679 \text{ ml}/\text{g}$ ); these powders thus gave thick pastes, whereas the other specimens were liquid upon mixing.

### 3.4. Setting time (ST)

The setting times are reported in Table IV, and compared in Fig. 4 to the adjusted values calculated with the statistical model ( $p < 0.05$ ). In general, DAP powders give shorter STs, the shortest values being obtained with DAP agglomerates ( $ST < 160$  s, treatments a to 4a). Little difference due to particle shape is observed for HAP-DCP powders, except for a steeper increase with particle size in the case of spheres (compare treatments b to 4b, and ab to 4ab).

The main powder characteristic affecting ST is the specific surface, as shown in Fig. 5: according to the figure, a strong correlation indeed exists between  $\log(ST)$  and  $S_{\text{BET}}$ ; one point (open circle), corresponding to the highest specific surface ( $1.08 \text{ m}^2/\text{g}$ , treatment a), does not match the regression curve: this is

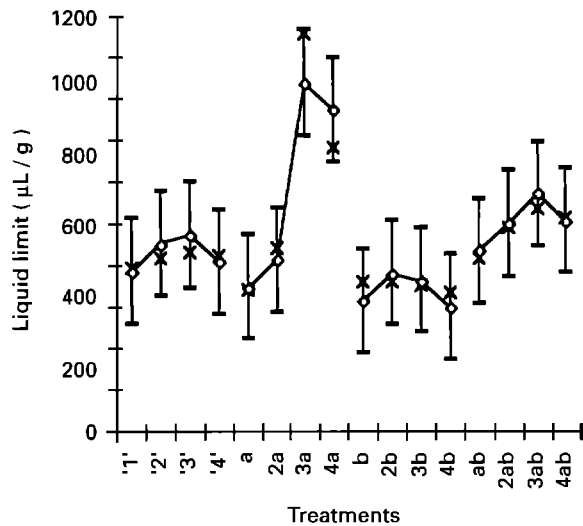


Figure 3 Liquid limits of  $\beta$ -TCP powders (in 0.5 wt % PAA-NH<sub>3</sub> aqueous solution). Adjusted values calculated from the statistical model ( $p < 0.05$ ). (A) Shape (spheres-agglomerates); (B) source (DAP-HAP + DCP). (1)  $d < 20 \mu\text{m}$ ; (2)  $20 < d < 50 \mu\text{m}$ ; (3)  $50 < d < 100 \mu\text{m}$ ; (4)  $d > 100 \mu\text{m}$ ;  $\times$  experimental value;  $\diamond$  adjusted value; the bars denote  $\pm 3$  S.E.

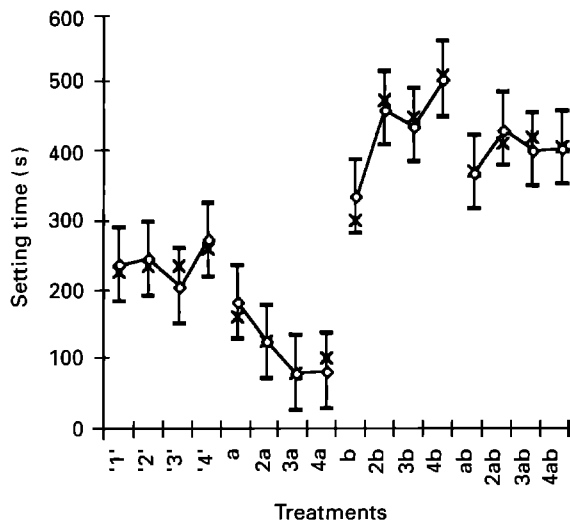


Figure 4 Setting times of CPHCs (1.5 g TCP mixed with 1.0 ml 4.0 M H<sub>3</sub>PO<sub>4</sub>, 0.25 M H<sub>2</sub>SO<sub>4</sub>, 0.20 M Na<sub>4</sub>P<sub>2</sub>O<sub>7</sub> aqueous solution). Adjusted values calculated from the statistical model ( $p < 0.05$ ). (A) Shape (spheres-agglomerates); (B) source (DAP-HAP + DCP). (1)  $d < 20 \mu\text{m}$ ; (2)  $20 < d < 50 \mu\text{m}$ ; (3)  $50 < d < 100 \mu\text{m}$ ; (4)  $d > 100 \mu\text{m}$ ;  $\times$  experimental value;  $\diamond$  adjusted value; the bars denote  $\pm 3$  S.E.

likely due to the fact that the preparation time of the specimens was too close to the short  $ST$  (about 50 s) expected for this cement, making an accurate measurement difficult.

According to the results, cements prepared with HAP-DCP powders exhibit  $ST$  values quite appropriate for clinical use ( $ST = 5 \dots 8.5$  min).

### 3.5. Diametral strength

The experimental results are presented in Table IV, and compared in Fig. 6 with the adjusted values calculated with the statistical model ( $p < 0.05$ ). The figure shows that, on the average, slightly higher

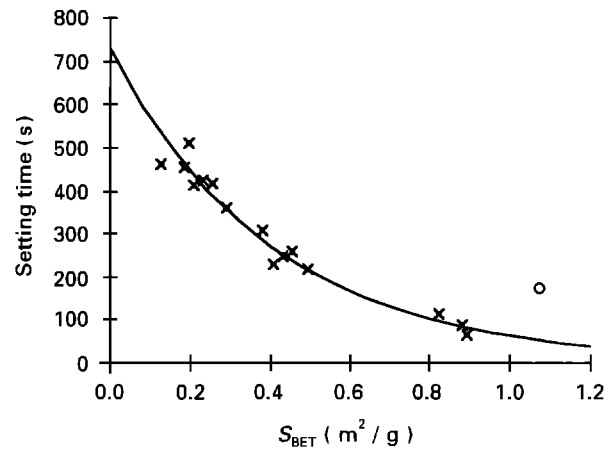


Figure 5 Correlation between setting times and specific surface areas of the  $\beta$ -TCP powders; the open circle (DAP agglomerates with  $d < 20 \mu\text{m}$ , treatment a) was rejected as an outlier.  $\text{Log}(ST/s) = aS_{\text{BET}} + b$ ;  $a = -1.07 \pm 0.052$ ,  $b = 2.86 \pm 0.025$ ;  $e = \pm 0.050$ ;  $e^2 = 97.26\%$  ( $p < 0.001$ ).

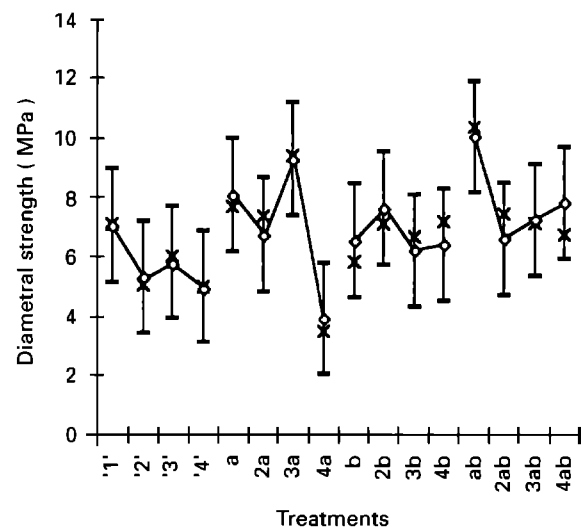


Figure 6 Diametral tensile strengths of CPHCs (1.5 g TCP mixed with 1.0 ml 4.0 M H<sub>3</sub>PO<sub>4</sub>, 0.25 M H<sub>2</sub>SO<sub>4</sub>, 0.20 M Na<sub>4</sub>P<sub>2</sub>O<sub>7</sub> aqueous solution). Adjusted values calculated from the statistical model ( $p < 0.05$ ). (A) Shape (spheres-agglomerates); (B) source (DAP-HAP + DCP). (1)  $d < 20 \mu\text{m}$ ; (2)  $20 < d < 50 \mu\text{m}$ ; (3)  $50 < d < 100 \mu\text{m}$ ; (4)  $d > 100 \mu\text{m}$ ;  $\times$  experimental value;  $\diamond$  adjusted value; the bars denote  $\pm 3$  S.E.

strengths are obtained with powder made of irregular agglomerates. The strength is less sensitive to particle size variations in the case of spherical powders, decreasing slightly with particle size for DAP powders. The lowest strength is observed for the samples made with the largest DAP agglomerates (3.5 MPa, treatment 4a), whereas the highest strength is obtained with the smallest HAP-DCP agglomerates (10.4 MPa, treatment ab). The latter result would correspond to a compressive strength of about 60 MPa, which compares favourably with the best results reported in the literature [5]. These results do not correlate clearly to any of the characteristics of the powder used. This has probably to be ascribed to the microstructural complexity of the powders used, despite the effort made to prepare materials with well-defined characteristics. It

is therefore impossible, with the present state of knowledge, to make conclusive statements as to which type of  $\beta$ -TCP powder would promote the highest mechanical properties.

#### 4. Conclusions

By using  $\beta$ -TCP powders from different origins and with variable particle sizes and shapes, it has been possible to prepare CPHCs with a large range of setting times and diametral strengths.

Shorter setting times (80 to 260 s) were usually observed with powder prepared from DAP, particularly when used in the form of irregular agglomerates; on the other hand, powders prepared by reactive sintering of HAP-DCP mixtures give longer setting times, well appropriate for clinical use (300 to 510 s). The setting rates are strongly related to the specific surfaces of the  $\beta$ -TCP powders used, higher surfaces resulting in higher rates.

Higher strengths are generally obtained with irregular agglomerates, but with a stronger sensitivity to particle size distribution. In the case of spherical powders, slightly better results were obtained with HAP-DCP powders (5.8–7.2 MPa). An unusually high strength (10.4 MPa) has been obtained with the smallest HAP-DCP agglomerates.

The results have demonstrated that the properties of a given CPHC formulation can depend strongly on the characteristics of the raw materials used. In the case of  $\beta$ -TCP based cements, the granularity of the

starting cement powder, including particle size, shape and specific surface area, is of crucial importance and should be specified when the performances of different formulations are to be compared.

#### Acknowledgements

This work was performed with the financial support of the PPM program (project 4.B.3). The company BIO-LAND is thanked for a grant.

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*Received 29 June  
and accepted 4 July 1995*