JOURNAL OF MATERIALS SCIENCE: MATERIALS IN MEDICINE 9 (1998) 425–428

Some factors controlling the injectability of calcium phosphate bone cements

I. KHAIROUN, M. G. BOLTONG, F. C. M. DRIESSENS, J. A. PLANELL
Department of Materials Science and Metallurgy, Universitat Politècnica de Catalunya, Avda, Diagonal 647, E-08028 Barcelona, Spain

The injectability of four calcium phosphate bone cements (CPBCs) was measured using a commercial disposable syringe. It varied considerably with the cement powder composition, with the liquid/powder ratio, with the time after starting the mixing of liquid and powder, with the accelerator concentration (% Na_2HPO_4), and with the ageing time of the cement powder which was prepared by milling. The injectability test could be used to determine accurately the dough time of CPBCs. Relations between the setting time and the cohesion time are discussed.

1. Introduction

In previous papers [1, 2] it was established that there are about 15 different binary combinations of calcium phosphates which give pastes upon mixing with water or aqueous solutions, so that the pastes set at room or body temperature into a solid cement. From these basic systems, secondary formulations can be derived containing additional or even non-reactive compounds, but still setting like cements. Such materials are known as calcium phosphate cements, and, because they are suitable for the repair, augmentation and regeneration of bone, they are also called calcium phosphate bone cements (CPBCs) [3]. They are not only biocompatible, but also osteotransductive, i.e. after implantation in bone defects they show rapid osteointegration after which they are slowly resorbed and simultaneously transformed into new bone tissue. Recently, the suggestion has been made that they might also compete with the PMMA bone cements and the apatite coatings for fixation of metal endoprostheses in orthopaedics and oral implantology [4].

For implantation of CPBCs, a relatively thick and putty paste [5] can be used but, in principle, one can also use a relatively thin and injectable paste [1]. For certain applications, injectability is even a prerequisite [6, 7]. Some CPBCs show demixing into a thin paste which is extruded, and a solid mass which stays behind in the syringe, when put under pressure. This phenomenon is called filter pressing [6]. Therefore, a good cohesion of the paste is necessary in order to avoid this phenomenon.

One of the objectives of the present study was to operationalize the injectability as a quantity which can be measured. The other objective was to determine the main factors on which the injectability of CPBCs depend.

2. Materials and methods

Disposable syringes of several brands were used for obtaining an impression about their suitability. Finally, 20 ml syringes of Millipore (Bedford, Massachusetts) Catalogue Number XX 1102012, were selected. They have an opening of 2 mm. Amounts of 2.0–4.0 g cement paste were used, and "injectability" was taken to mean the percentage by weight of that part of this amount of CPBC paste which could be extruded from such a syringe, either by hand or by a force of 100 N maximum.

Four CPBCs were prepared. The composition of their powders is given in Table I. α-TCP is alpha-tertiary calcium phosphate, PHA is precipitated hydroxyapatite and DCP is dicalcium phosphate. As cement liquid, a 1% aqueous solution of Na_2HPO_4 was used. The injectability was determined for liquid/powder ratios, L/P, of 0.35 and 0.40 ml g^{-1}, 1.5 min after the beginning of mixing powder and liquid.

Biocement H was selected to determine the injectability over a wider range of L/P ratios from 0.32–0.42. Measurements were done in triplicate for both injection by hand and injection with an Instron Universal Testing machine type 4507 using a compression rate of 15 mm min^{-1} and a maximum force of 100 N, so that absolute values and standard deviations of both methods could be compared.

Biocement D was selected to study the injectability by hand (at L/P = 0.40 ml g^{-1}) as a function of the time, measured from the beginning of mixing of powder and liquid, until setting of the paste. First, injection by hand and by machine were compared for concentrations of 2%, 3% and 4% Na_2HPO_4 as accelerator in the cement liquid. Further, the effect of a time lapse of either 1 or 4 d from the milling of the cement powder until injectability measurement on the value of the injectability, was measured for 2%, 3% and 4% Na_2HPO_4 in the cement liquid. Finally, time lapses of 1/2, 1, 4, 7 and 12 d were studied for 3% Na_2HPO_4 in the cement liquid. From these data the times after mixing at which the injectability reaches 0% were derived for different concentrations of

0957–4530

TABLE I Composition of the powder of four CPBCs

CPBC	Composition (%)			
	α-TCP	PHA	DCP	$CaCO_3$
Biocement H	98	2		
Biocement F	64	9	27	
Biocement B	90	5		5
Biocement D	58	8.5	25	8.5

TABLE II Percentage injectability by hand of four CPBCs at two different L/P ratios 1.5 min after starting mixing of powder and liquid

CPBC	Injectability (%)	
	L/P = 0.35	L/P = 0.40
Biocement H	53	75
Biocement F	89	93
Biocement B	76	90
Biocement D	91	94

Na_2HPO_4. These times were compared with the initial setting time which is measured with the light and thick Gilmore needle [8].

3. Results

The % injectability of Biocements H, F, B and D is given in Table II. It is observed that the injectability increases with increasing L/P ratio, thus with decreasing viscosity of the paste. Neither of these CPBCs gave any demixing or filter pressing during extrusion from the syringe. It is also observed that the phase composition of the CPBC powders has a big influence on the injectability. Further, there appears to be a practical upper limit to the injectability as measured by this method because the minimum amount of cement paste remaining in the syringe was 190 ± 10 mg. This means that Biocement D reaches that practical limit and thus has the ideal injectability. When a triple amount of cement paste of Biocement D was tried, the apparent value of the injectability rose to 98%, for that reason and the same amount of 190 ± 10 mg remained in the syringe.

Fig. 1, shows the dependence of the injectability of Biocement H on the L/P ratio in the range from 0.32–0.42, both by hand and by machine 1.5 min after starting mixing the powder and the liquid. The values were higher for injection by hand, but the standard deviations were slightly higher for injection by machine.

Fig. 2 is a plot of the injectability of Biocement D at L/P = 0.40 versus time after starting the mixing of powder and liquid for accelerator concentrations of 2%, 3% and 4% Na_2HPO_4 both by hand and by machine. Again the values for injection by machine are lower, whereas 0% injectability is reached earlier than with injection by hand. The time, at which the injectability reaches 0% may be called the dough time, t_d, of the cement. In Table III the dough time for injection by hand is compared with the initial setting time, t_I, and the final setting time, t_F, for Biocement D. It is observed that the initial setting time, t_I, is about twice as large as the dough time, t_d, whereas the final setting time, t_F, is about five times as large. The ageing time of the cement powder after preparation by milling up to injectability measurement was 4 d in Fig. 1.

In Fig. 3 the injectability of Biocement D by hand at L/P = 0.40 is plotted as a function of the time after starting the mixing for accelerator concentrations of 2%, 3% and 4% Na_2HPO_4, but now the ageing time of the cement powder after preparation by milling up to the injectability measurement was either 1 or 4 d. Accordingly, the dough time, t_d, increased with ageing. The ageing effect was inspected more extensively for

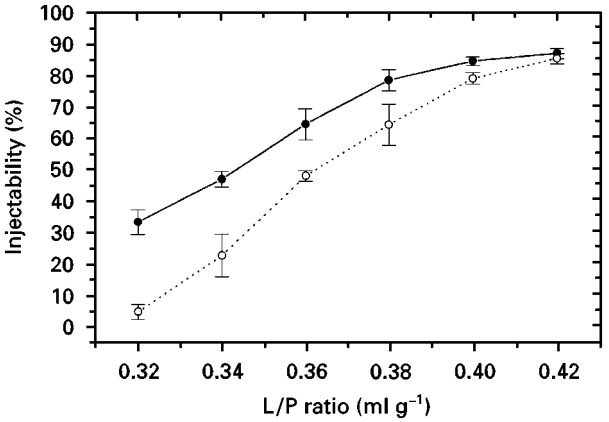

Figure 1 Injectability of Biocement H at 1% Na_2HPO_4 and 1.5 min as a function of the L/P ratio of the cement paste: (●) hand, (○) instron.

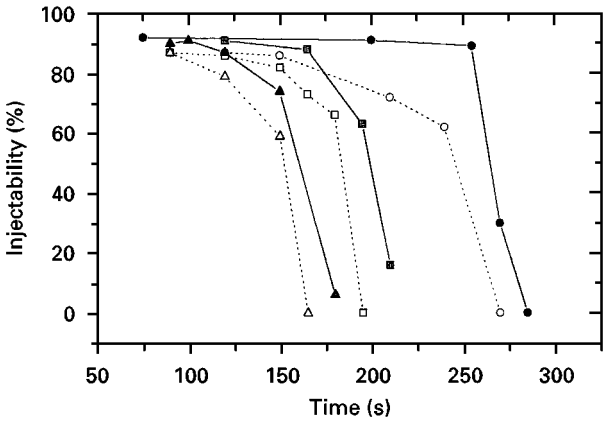

Figure 2 Injectability of Biocement D at L/P = 0.40 as a function of time after start of mixing, by (●, ■, ▲) hand, or (○, □, △) machine. (●, ○) 2% Na_2HPO_4, (■, □) 3% Na_2HPO_4, (▲, △) 4% Na_2HPO_4.

TABLE III Dough time, t_d, initial setting time, t_I, and final setting time, t_F, of Biocement D at L/P = 0.40 ml g^{-1}

Na_2HPO_4 (%)	t_d (min)	t_I (min)	t_I/t_d (min)	t_F (min)	t_F/t_d
2	4.66	9.5	2.0	22.5	5.0
3	3.5	7	2.0	18	5.1
4	2.75	4.5	1.6	13	4.7

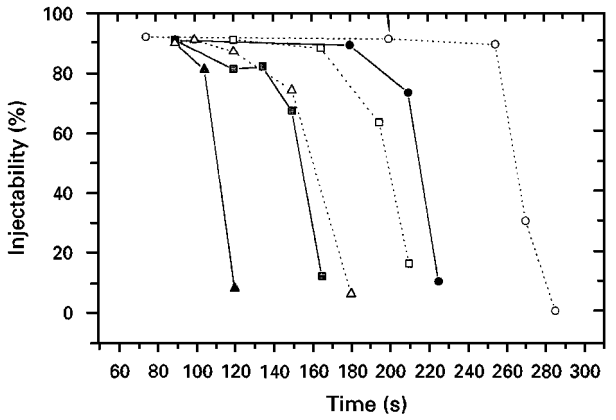

Figure 3 Injectability of Biocement D by hand at L/P = 0.40 as a function of the time after start of mixing for two ageing times: (○, ■, ▲) 1d, (○, □, △) 4d. (●, ○) 2% Na_2HPO_4, (■, □) 3% Na_2HPO_4, (▲, △) 4% Na_2HPO_4.

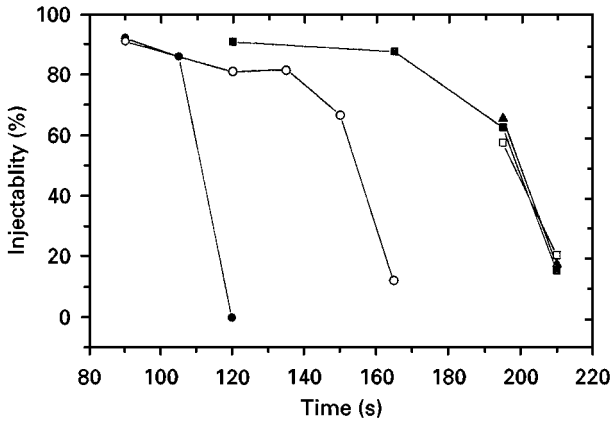

Figure 4 Injectability of Biocement D by hand at L/P = 0.40 and 3% Na_2HPO_4 as a function of the time after start of mixing for various ageing times: (●) 0.5 d, (-○-) 1 d, (■) 4 d, (□) 7 d, (▲) 12 d.

3% Na_2HPO_4. The data are given in Fig. 4. They show that the powder has become stable after 4 d ageing following preparation by milling.

4. Discussion

The results in Table II suggest that finding a good powder formulation is one of the most suitable ways to control the injectability of a CPBC. That the injectability of the cement paste varies inversely with its viscosity as shown in Fig. 1, was expected, but it is not always possible to stay in the desired range of strength and setting times by varying the L/P ratio, even when in addition the accelerator concentration can be adjusted [9].

A side-effect of this study on the injectability was that it yielded a rapid and accurate way to determine the dough time of CPBCs as derived from Fig. 2. Up to now, dough times could be approached only by determining the time of deformation just not leading to decreased strength after complete hardening, but this method is very crude [10]. So the dough time can be defined as the period during which the cement paste can be moulded without damaging the structure which is forming during the setting of the paste. After the dough time, the mechanical behaviour of the cement paste becomes more and more brittle. Obviously, implantation of cement pastes of CPBCs should occur before the dough time for mechanical reasons.

Another important property of CPBCs is their cohesion time. The reason is that the pastes of CPBCs disintegrate upon early contact with aqueous solutions like body fluids [5, 11, 12]. The cohesion time can be measured by immersion of setting cement pastes into Ringer's solution and observation of disintegration during 24 h immersion [13]. It can be defined as the time necessary to develop enough cohesion within the setting cement paste in order to prevent the disintegration upon early contact with aqueous solutions. It is obvious for that reason that a cement paste should be implanted after reaching the cohesion time.

Accurate measurements of the dough time of Biocement D were given in Table III. The cohesion time of Biocement D has been reported elsewhere [9]. In the range of 2%–4% accelerator and at a P/L between 0.35 and 0.40 ml g^{-1}, which is the most suitable range, the cohesion time and the dough time coincide precisely for this cement. This poses a problem because, as mentioned above, application should be done before the dough time and after the cohesion time. The only way to overcome this problem is by lowering the cohesion time without affecting the other properties. How this can be done, will be mentioned in a follow-up study.

The effect of ageing of the freshly milled cement powder is as expected. High-energy fracture surfaces will be subject to surface diffusion of particles to the active sites, thereby decreasing the rate of reaction for the cement setting with time. Similar surface diffusion phenomena occur during dissolution and precipitation reactions of ionic compounds [14] from aqueous solutions.

Acknowledgements

This study was supported by grants from the Direccion Cientifica y Tecnica of Spain and from Merck GmbH in Darmstadt, Germany. The authors also thank the CICYT for funding this work through project MAT 94-0911.

References

1. F. C. M. DRIESSENS, M. G. BOLTONG, O. BERMUDEZ, J. A. PLANELL, M. P. GINEBRA and E. FERNANDEZ, *J. Mater. Sci. Mater. Med.* **5** (1994) 164.
2. F. C. M. DRIESSENS, *Fourth Euro Ceram.* Vol. **8**, edited by A. Ravaglioli, Faenza, Italy, (1995) 77.
3. F. C. M. DRIESSENS, J. A. PLANELL and F. J. GIL, in Encyclopedic Handbook of Biomaterials and Bioengineering, Part B, Applications, Vol. 2, edited by D. L. Wise, D. J. Trantolo, D. E. Altobelli, M. J. Yaszemski, J. D. Gresser, and E. R. Schwarz (Marcel Dekker, New York, 1995) pp. 855–77.
4. F. C. M. DRIESSENS, E. FERNANDEZ, M. P. GINEBRA, M. G. BOLTONG and J. A. PLANELL, *Anal. Quimica Int. Ed.* **93** (1997) S38.
5. K. KURASHINA, H. KURITA, M. HIRANO, A. KOTANI, C. P. A. T. KLEIN and K. de GROOT, *Biomaterials* **18** (1997) 539.

6. J. LEMAITRE, H. ANDRIANJATOVO, C. BIOURGE, K. OHURA and P. HARODOUIN, *Oberflachen Werkstoffe* **9** (1994) 13.
7. L. C. CHOW, M. MARKOVIC, S. TAKAGI and M. CHERNG, *Innov. Techn. Biol. Med.* **18** (1997) 11.
8. F. C. M. DRIESSENS, M. G. BOLTONG, O. BERMUDEZ and J. A. PLANELL, *J. Mater. Sci. Mater. Med.* **4** (1993) 503.
9. I. KHAIROUN, M. G. BOLTONG, F. C. M. DRIESSENS and J. A. PLANELL, *Biomaterials*, **18** (1997) 000.
10. M. P. GINEBRA, E. FERNANDEZ, M. G. BOLTONG, O. BERMUDEZ, J. A. PLANELL and F. C. M. DRIESSENS, *Clin. Mater.* **17** (1994) 99.
11. J. A. JANSEN, J. E. de RUIJTER, H. G. SCHAEKEN, J. P. C. M. van der WAERDEN, J. A. PLANELL and F. C. M. DRIESSENS, *J. Mater. Sci. Mater. Med.* **6** (1995) 653.
12. K. ISHIKAWA, S. TAKAGI, L. C. CHOW and Y. ISHIKAWA, *ibid.* **6** (1995) 528.
13. E. FERNANDEZ, M. G. BOLTONG, M. P. GINEBRA, F. C. M. DRIESSENS, O. BERMUDEZ and J. A. PLANELL, *J. Mater. Sci. Lett.* **15** (1996) 1004.
14. F. C. M. DRIESSENS and R. M. H. VERBEECK, "Biominerals", (CRC Press, Boca Raton, FL, 1990).

Received 29 July
and accepted 16 September 1997