Effect of temperature and immersion on the setting of some calcium phosphate cements

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Calcium phosphate cements based on powders containing α-$Ca_3(PO_4)_2$ and aqueous solutions containing Na_2HPO_4 as accelerator were used to determine the effects of accelerator concentration, temperature and immersion on the setting time. Increases in accelerator concentration and temperature increased the rate of setting, but immersion had a retarding effect. These results were used to design a method whereby a syringe filled with cement paste can be kept ready for injection of the paste into the implantation site for a long time, whereas setting of the cement paste in the body takes place in a short time.

1. Introduction

In a previous study [1] it was found that combinations of several solid calcium phosphates could be made which resulted in cementitious pastes upon mixing with aqueous solutions so that setting occurred at room and body temperature. Biocement H was made in this way by reaction of water with a mixture of α-$Ca_3(PO_4)_2$ (α–TCP) and some precipitated hydroxyapatite (PHA) [2]. By dissolution of Na_2HPO_4 or $NaH_2PO_4 \cdot 2H_2O$ into the cement liquid the setting time of this cement could be reduced considerably [3]. In this way it was possible to obtain values for the initial setting time t_I in the range $4 \leq t_I(\text{min}) \leq 8$ and for the final setting time t_F in the range $10 \leq t_F(\text{min}) \leq 15$ which seemed to be appropriate for clinical handling of this material [4]. However, with these measurements the adjustment of this material to the requirements for clinical applications was far from complete.

In the operating theater ''room temperature'' may mean something from about 18 °C to about 27 °C in areas of moderate climates, whereas upon implantation the material is adjusted to body temperature. As a matter of fact at 22 °C t_I and t_F of a Biocement H sample were 9 and 19 min, respectively. However, at 37 °C the same sample in air had t_I and t_F values of 6 and 15 min [5, 6]. Therefore, before a material like Biocement H is distributed for animal and clinical experiments the dependence of its setting characteristics on the temperature should be investigated more extensively. This was the first purpose of this study.

Further, early observations on the behavior of Biocement H upon implantation [7] showed that early contact of the material with body fluids led to mechanical instability and marginal disintegration of the implant. Therefore, an *in vitro* method for accurate measurement of the so-called cohesion time t_c at room temperature was developed [8]. The rationale was that the material should be applied before t_I but after t_c. It appeared that Biocement H did not meet this last requirement because t_c and t_I coincided. Hence, it was not suitable for implantation [9]. However, by addition of dicalcium phosphate, calcium carbonate or combinations of these compounds to the cement powder it was possible to obtain Biocements which had a cohesion time which was considerably shorter than the initial setting time [9, 10] so that compliance with this requirement was obtained. As early immersion of Biocement H into an aqueous solution had a considerable effect on the integrity of its structure, it is expected that immersion also has an effect on the setting times t_I and t_F. Determination of this effect was another purpose of the present study.

Finally, the combined effect of temperature and immersion on the setting characteristics should be investigated. Room temperature conditions include variations of the temperature from about 18 to 27 °C whereas implantation brings the temperature to 37 °C and immersion into body fluids.

2. Materials and methods

The initial setting time t_I was determined with the thick and light Gilmore needle, as described previously [11]. In the first series of experiments Biocement H (see Table I) was made with an aqueous solution containing 2.5% Na_2HPO_4 as accelerator as a function of the liquid/powder ratio L/P. After mixing powder and liquid, the samples were immersed into the same solution at either 20, 27 or 37 °C and t_I determined.

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TABLE I Composition of the powder of three calcium phosphate bone cements

Cement	α-TCP (%)	PHA (%)	DCP* (%)	$CaCO_3$ (%)
Biocement H	98	2	–	–
Biocement F	64	9	27	–
Biocement D	58	8.5	25	8.5

*DCP = dicalcium phosphate $CaHPO_4$.

In a second series of experiments the same Biocement H was either immersed in the same liquid or kept in air at 20 °C while t_I was determined.

In a third series of experiments Biocement F and Biocement D were made with 2.5% Na_2HPO_4 and t_I was measured either in air at 20 or 27 °C or immersed in 2.5% Na_2HPO_4 solution at 37 °C.

In the last series of experiments Biocement D was made either with water or with 1% Na_2HPO_4 solution and then t_I was determined for samples held in air at 20 or 27 °C or immersed in 2.5% Na_2HPO_4 at 37 °C.

In order to demonstrate the usefulness of especially these last data, the injectability of Biocement D was also determined at certain times after mixing with water or 1% Na_2HPO_4 solutions at liquid to powder ratios of 0.35 and 0.40 ml/g. Amounts of 2 to 4 g of cement paste were used and ''injectability'' was taken to mean the percentage by weight of that part of this amount of Biocement D paste which could be extruded from the selected syringe [12] by hand.

3. Results and discussion

Fig. 1 shows the initial setting time t_I for Biocement H with 2.5% accelerator under immersion for different temperatures as a function of the L/P ratio. It appears that at 37 °C setting is 3 to 4 times as fast as at 20 °C.

Fig. 2 shows the initial setting time t_I of Biocement H with 2.5% accelerator in air and under immersion at 20 °C as a function of the L/P ratio. Immersion retards the setting considerably, especially at higher L/P ratios.

Fig. 3 contains the data for t_I of Biocement F with 2.5% accelerator as a function of the L/P ratio. Higher temperatures accelerate the setting in air, but setting in air at 27 °C is about as fast as under immersion at 37 °C.

Fig. 4 shows similar data to Fig. 3 but now for Biocement D except for the fact that now setting in air at 27 °C is considerably slower than under immersion at 37 °C. Comparison of Figs 1, 3 and 4 for 37 °C shows that Biocement H sets relatively slowly, Biocement F is considerably faster but even slightly faster is the setting of Biocement D, all with 2.5% accelerator.

Setting of Biocement D at lower contents of accelerator in the liquid (see Figs 4 and 5) is only slightly slower at 37 °C under immersion, but considerably slower at room temperature at 20 as well as at 27 °C in air.

From these results it can be concluded that increasing temperature increased the setting rate of calcium phosphate cements, whereas immersion retards setting. The combined effect of both variables strongly depends on the type of cement formulation. In this respect it

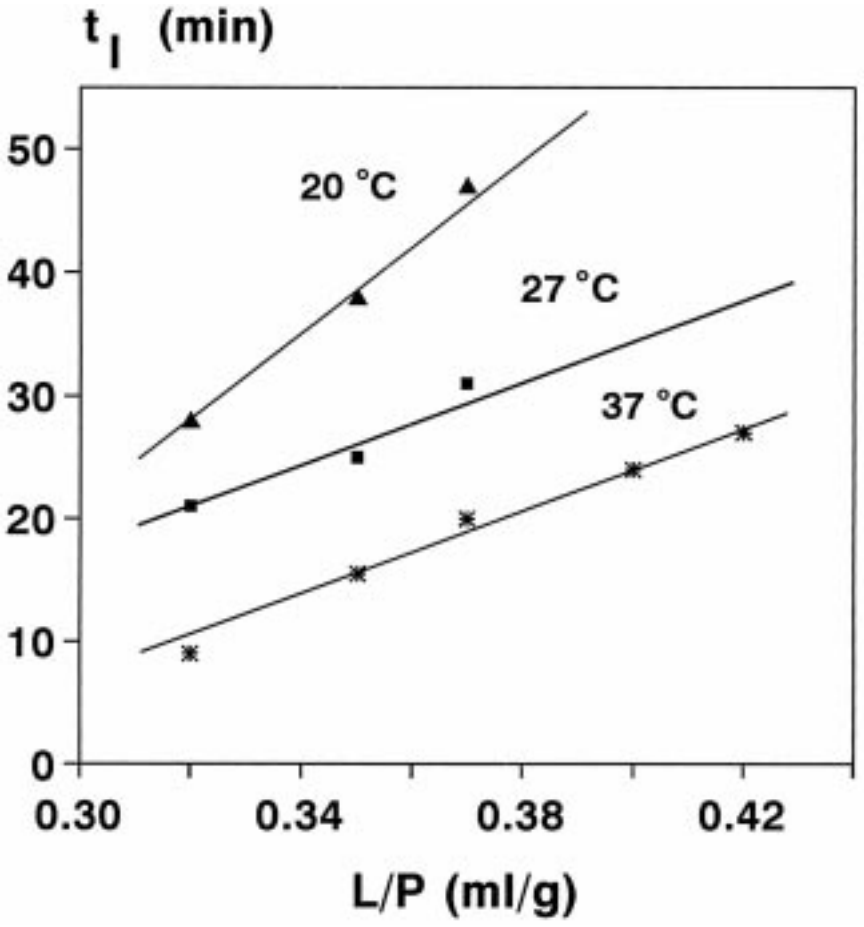

Figure 1 Initial setting time t_I of Biocement H, made with 2.5% Na_2HPO_4, during immersion into 2.5% Na_2HPO_4 at 20, 27 and 37 °C as a function of the liquid/powder ratio L/P.

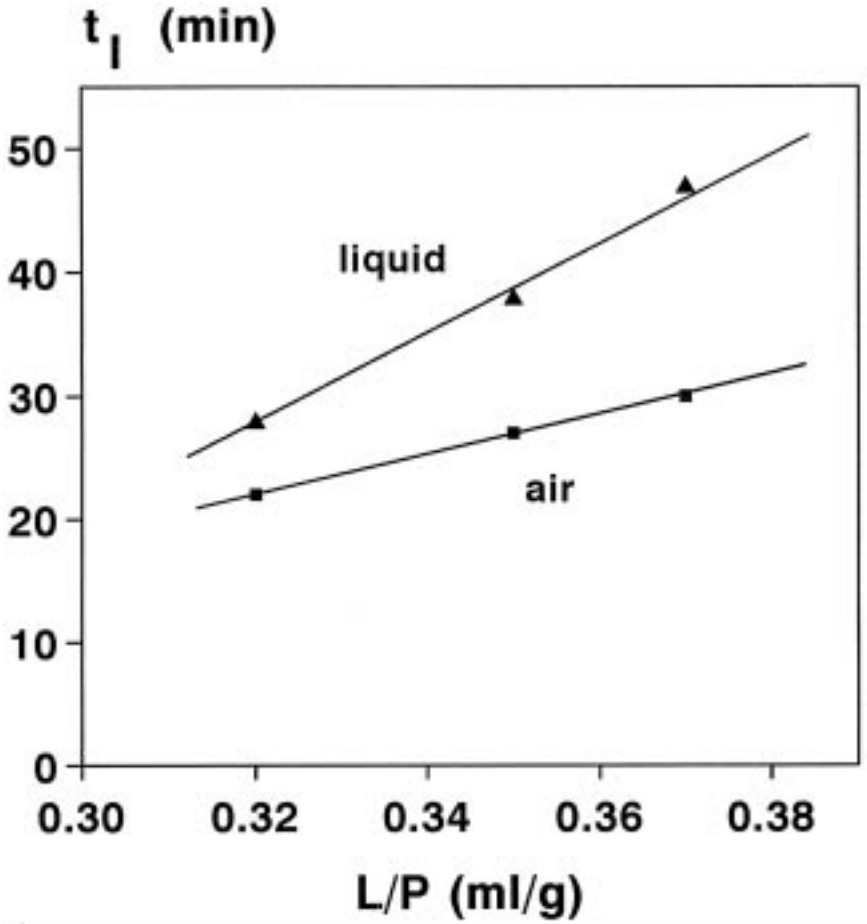

Figure 2 Initial setting time t_I of Biocement H, made with 2.5% Na_2HPO_4, at 20 °C either in air or during immersion in 2.5% Na_2HPO_4 as a function of the liquid/powder ratio L/P.

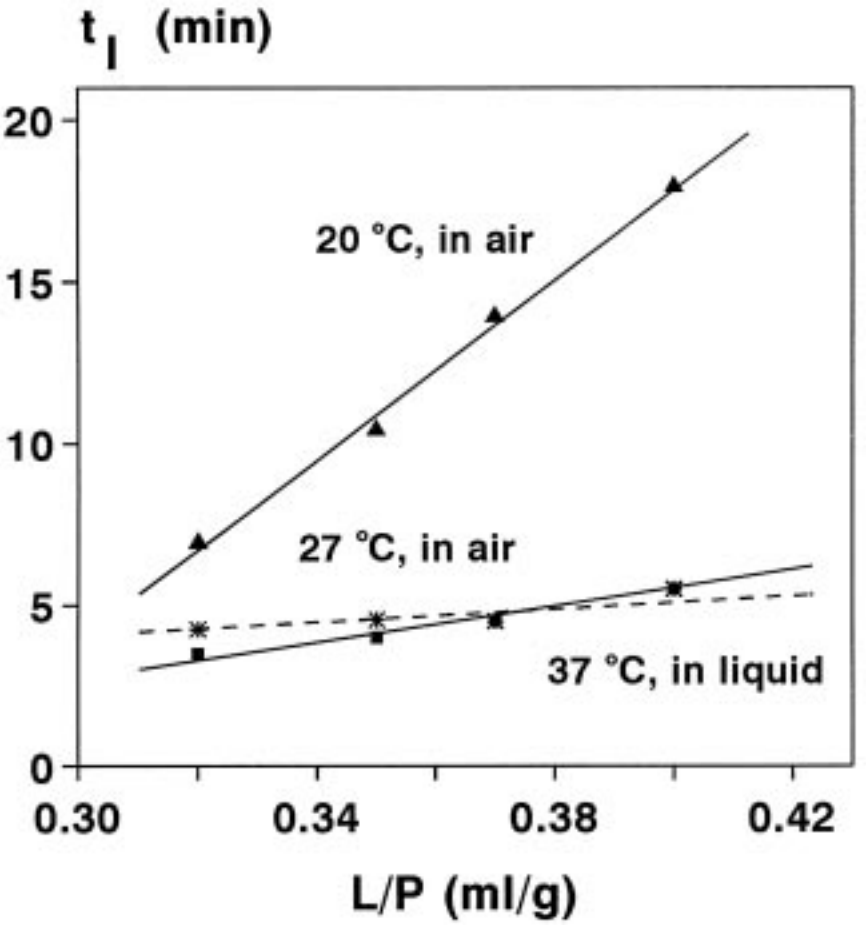

Figure 3 Initial setting time t_I of Biocement F, made with 2.5% Na_2HPO_4, in air at 20 and 27 °C or immersed at 37 °C in 2.5% Na_2HPO_4 as a function of the liquid/powder ratio L/P.

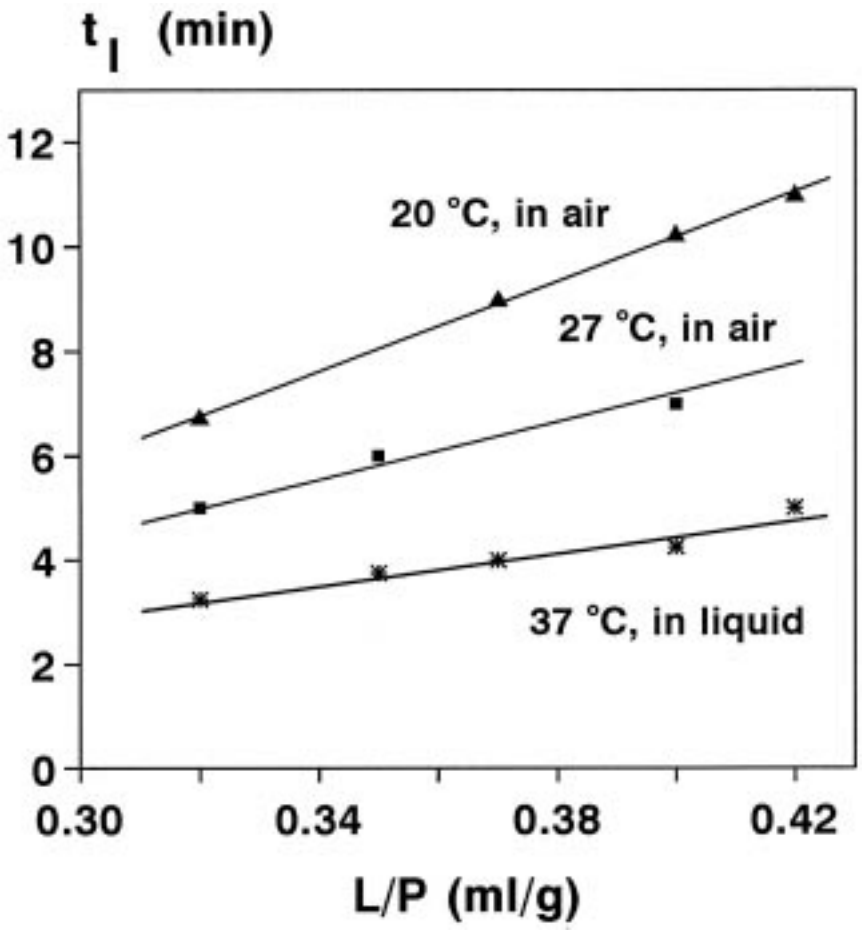

Figure 4 Initial setting time t_I of Biocement D, made with 2.5% Na_2HPO_4, in air at 20 and 27 °C or immersed at 37 °C in 2.5% Na_2HPO_4 as a function of the liquid/powder ratio L/P.

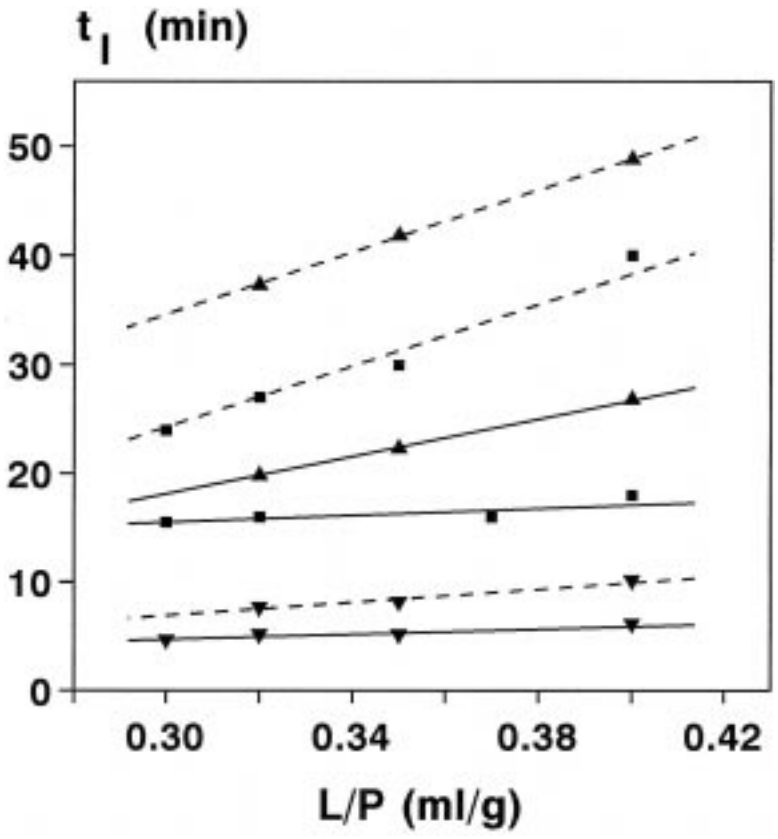

Figure 5 Initial setting time t_I of Biocement D, made with water (- - -) or 1% Na_2HPO_4 (—), in air at 20 °C (▲), and 27 °C (■) or immersed at 37 °C (▼) in 2.5% Na_2HPO_4 as a function of the liquid/powder ratio L/P.

TABLE II Percentage injectability of Biocement D with or without accelerator at different times after the start of mixing

L/P	% Na_2HPO_4	Time (min)	% injectability
0.35	1	9	93
0.40	1	12	88
0.35	0	18	94
0.40	0	22	94

seemed that Biocement D sets at room temperature under air much slower than under immersion at 37 °C. An appropriate choice of accelerator concentration and L/P ratio then allows to further adjust the setting characteristics. This effect can be used in the clinic, because when a syringe is filled with cement paste it can be held for a long period of time ready for injection of the cement paste, whereas after injection in the implantation site setting will proceed rapidly. In order to demonstrate this, some data about the % injectability of Biocement D at 20 °C are given in Table II. The times at which the injectability was determined in this experiment were chosen at 45 to 50% of t_1 as this appeared to be the ultimate time of high injectability with 4% Na_2HPO_4 in the cement liquid in a previous study [12]. It appears that for Biocement D made with water at $L/P = 0.4$ and 20 °C the surgeon can work with one syringe for at least 22 min, while satisfactory short setting at 37 °C is obtained and the material becomes sufficiently strong for application in trabecular bone [9].

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