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Production of in-situ macropores in an injectable calcium phosphate cement by introduction of cetyltrimethyl ammonium bromide

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Abstract In the present study, cetyltrimethyl ammonium bromide (CTAB) was introduced to an injectable calcium phosphate cement (CPC) to produce macropores during the setting process to accelerate the absorbing ability in vivo. The effects of CTAB on the rheological properties, injectability, setting time, compressive strength, phase evolution, microstructure and degradation rate of CPC were studied. The results showed that the addition of CTAB increased the viscosity and yield stress, and decreased the injectability of the cement pastes. The macroporosity and total porosity increased and the compressive strength of the cement obviously decreased with the increase of CTAB. The macroporosity of the CPC prepared at 5 mM CTAB solution reached 44.2 ± 2.5% and the mass loss of the cement increased almost 50% as compared with the cement without CTAB. Considering the injectability, compressive strength and degradation rate of CPC, the preferred CTAB concentration was 5 mM. The injectable CPC with macropores is promising to be used in minimally invasive approach

1 Introduction

Since the report by Brown et al. [1] in 1986, calcium phosphate cement (CPC) received much attention in the world [2]. CPC represents an interesting alternative to traditional bone graft materials. Moreover, CPC is a highly desirable material for orthopedic applications due to its moldability, in situ self-hardening ability, excellent osteoconductivity, resorbability, and bone replacement capability [3–7]. As a result, CPC has been investigated for use in the reconstruction of frontal sinus, augmentation of craniofacial skeletal defects, endodontics and periodontal bone repair [8–10]. However, conventional CPC without the macropores absorbs slowly in vivo because the resorption of the conventional CPC only occurs layer by layer on the implant surface [11]. The absence of macropores in the conventional CPC makes the ratio of cement-bone surface area to cement volume low and the osteoclastic resorption rate slow [12].

To solve this problem, the macropores were introduced into the cement without changing its normal setting. Some water soluble additives, such as sucrose, mannitol, $NaHCO_3$, or Na_2HPO_4, were added into the cement during the setting process to increase the porosity of the cement [13–15]. This approach, however, requires dissolving these additives after setting to obtain macropores in the cement. The disadvantage of these approaches is that the macropores cannot be created during the setting process of the cement in vivo.

The aim of our research is to develop an injectable calcium phosphate cement, in which macropores developed during the setting process to allow fast bone ingrowth and to enhance the resorption of the cement.

2 Materials and methods

The CPC powder was prepared by mixing partially crystallized calcium phosphate (PCCP) and dicalcium

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phosphate dihydrate (DCPD) as described in our previous work [5–7, 16, 17]. Cetyltrimethyl ammonium bromide (CTAB, AR grade pure) was commercially obtained from Sanland-chem International Inc. The CPC powder was uniformly mixed with 0, 1, 5, 10, 15 and 20 mM CTAB aqueous solution at a liquid to powder ratio of 0.6 ml/g for 1 min, respectively. Then the pastes were ready for rheological and injectability tests as shown in our previous work [16, 17]. All preparation steps were carried out at 25 ± 2°C.

Steel cylindrical molds with an inner diameter of 6 mm and a height of 12 mm were used to prepare the samples for compressive tests [16, 17]. The compressive strength was measured using a universal material testing machine (Model 5567, Instron, USA) at a crosshead speed of 1 mm/min. Each measurement was repeated 6 times. Setting time of the cements was measured according to ASTM C191-03. The hydrated cements (milled into powders) were analyzed using XRD (X'Pert Pro, PANalytical Co., the Netherlands). Microstructure of the hydrated cements was observed with SEM (H-800, Hitachi Co., Japan). A multipoint Brunauer-Emmett-Teller (BET) nitrogen adsorption method (Tristar3000, Micrometritics Co., USA) was used to determine the gel pore size of the cement and the distribution of pore capacity. The macroporosity and total porosity of the cement was determined according to the density method [15]. The density of the cement, d_{CPC} (g/cm^3), was calculated by Eq. 1:

$$d_{CPC} = m_{CPC}/V_{CPC} = m_{CPC}/(\pi \times r_{CPC}^2 \times H_{CPC}) \quad (1)$$

where m_{CPC} is the mass of the dried cement, V_{CPC} is its volume, r_{CPC} is its radius, and H_{CPC} is its height. The total porosity was calculated from Eq. 2:

$$\text{Total porosity} = (1 - d_{CPC}/d_{HAP}) \times 100\% \quad (2)$$

where d_{HAP} is the theoretic density of synthetic hydroxyapatite (3.156 g/cm^3). The macroporosity was obtained using Eq. 3:

$$\text{Macroporosity} = (1 - d_{CPC}/d_{CPC-0}) \times 100\% \quad (3)$$

where d_{CPC-0} is the density of the dried samples without CTAB or without macropores.

The hydrated cements with a diameter of 6 mm and a height of about 6 mm were weighed and then placed in polystyrene vials containing 200 ml de-ionized water at 37°C, in a shaking bath for predetermined intervals of 6 h, 12 h, 1 day, 3 days, 7 days, 14 days, and 21 days at a cement to water ratio of 1.50 mg/ml. The water was refreshed every 24 h. After each soaking period, the soaking water was filtrated and the specimen was dried at 37°C and reweighed.

3 Results and discussion

The effects of concentration of CTAB on the rheological properties of viscosity and yield stress of the cement pastes are shown in Figs. 1 and 2, respectively. The results indicated that the addition of CTAB significantly increased the viscosity and yield stress of the cement pastes. When the concentration of CTAB was 0, 1, 5, 10, 15 and 20 mM, the yield stress of the CPC pastes was 8.2, 10.2, 17.6, 20.4, 38.7, 89.5 Pa, respectively. The dissolution of CTAB in water formed a viscous solution, which caused the increased viscosity and yield stress of the cement. Furthermore, the increase of the viscosity and yield stress of the cement partly derive from the agglomeration of the CPC particles because of the dissolved CTAB in water.

Figure 3 shows the influence of the CTAB concentration on the compressive strength and injectability of the pastes. The compressive strength of the hydrated cement significantly decreased with the increase in the concentration of CTAB. Although the injectability of the pastes diminished with the increase of the CTAB concentration, the injectability of the paste was still almost 100% even at the CTAB concentration of 10 mM.

The effect of the concentration of CTAB on the setting time of CPC is showed in Fig. 4. The initial and final setting time of the pastes were not obviously changed when the concentration of CTAB increased.

Figure 5 shows the XRD patterns of the cement with different CTAB concentration. The phase composition of the hydrated cement was hydroxyapatite. The diffraction peak intensity of HA did not obviously change with the increase in the concentration of CTAB.

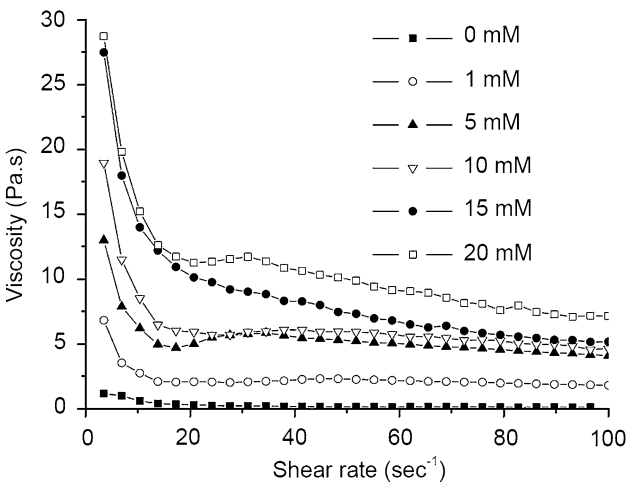

Fig. 1 Influence of the concentration of CTAB on the viscosity of the cement pastes

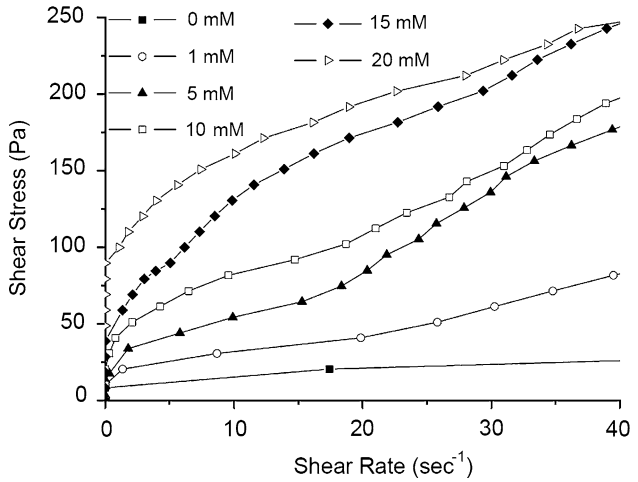

Fig. 2 Influence of the concentration of CTAB on the yield stress of the cement pastes

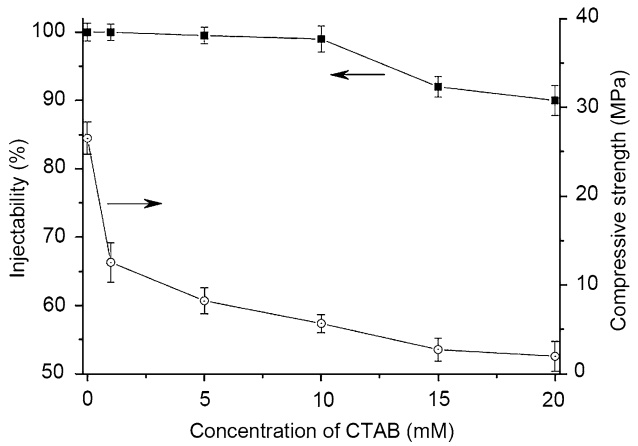

Fig.3 Influence of the concentration of CTAB on the injectability and compressive strength of the cement pastes

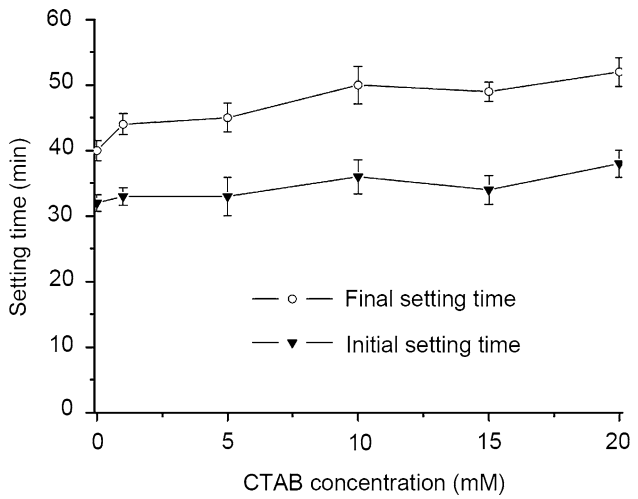

Fig. 4 Influence of the concentration of CTAB on the setting time of the cement pastes

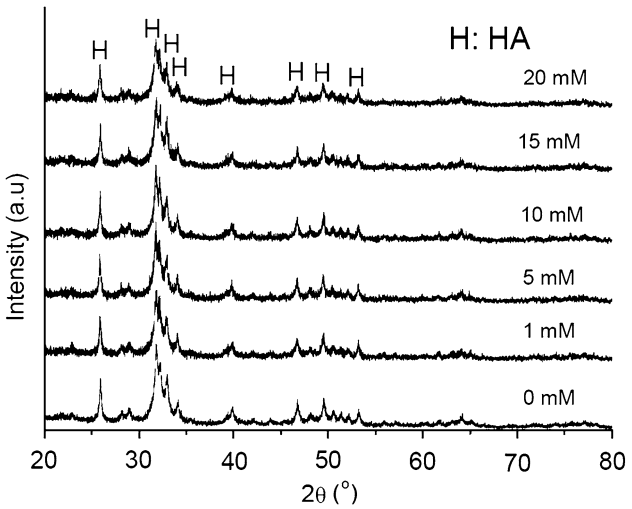

Fig. 5 Influence of the concentration of CTAB on the phase evolution of the cements

Figure 6 shows the SEM micrographs of the hydrated cements. There is no macropore (with diameters about 100 μm) in the cement without CTAB. When CTAB was introduced into the cement, almost homogeneously distributed spherical macropores appeared in the cement. Also the gelatinous micropores with diameter of 20–350 nm were presented in the cement [6]. During the mixing and injecting process of CPC, CTAB played as an air-entraining agent [11] to trap air bubbles in the cement paste, which resulted in the appearance of macropores in the cement after hydration.

The macroporosity and total porosity of the cement are shown in Fig. 7. The macroporosity and total porosity increased with the increase in the concentration of CTAB. When the concentration of CTAB was 5 mM, the macroporosity and total porosity was 44.2 ± 2.5% and 64.5 ± 2.6%, respectively. The appearance of macropores explained the decrease of the compressive strength of CPC when CTAB was introduced (Fig. 3).

As shown in Fig. 8, with the addition of CTAB, the degradation of the cement was significantly accelerated as the result of the formation of macropores. In the case of the 5 mM CTAB concentration, the mass loss of the cement increased almost 50% as compared with the cement without CTAB.

4 Conclusions

An injectable macroporous calcium phosphate cement was prepared by introducing CTAB to the cement in this study. The addition of CTAB introduced macropores in the cement. Thus the degradation of the cement was significantly accelerated. When the concentration of CTAB was

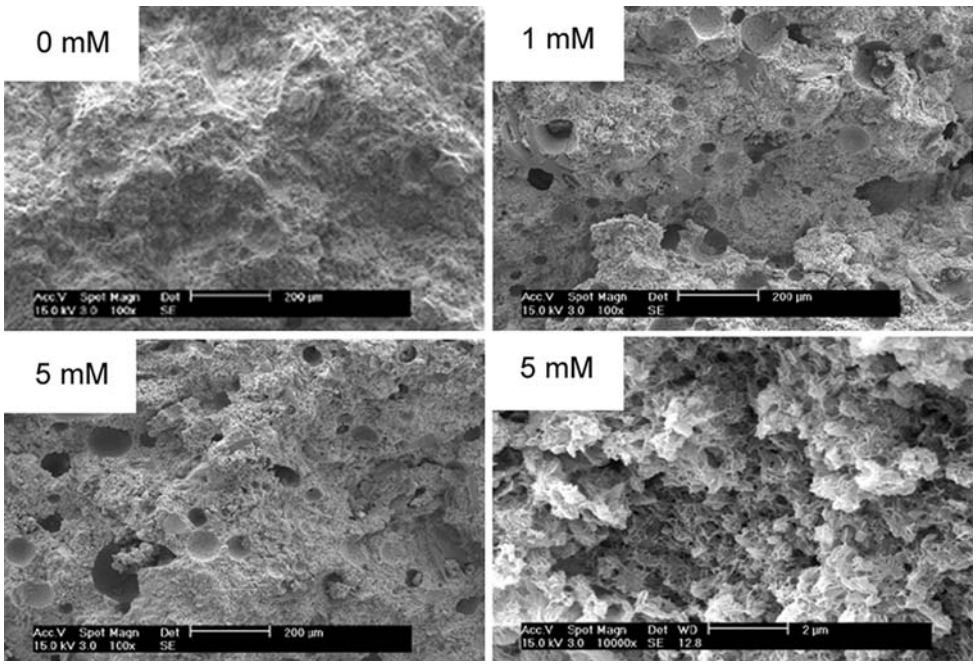

Fig. 6 SEM photographs of the cements

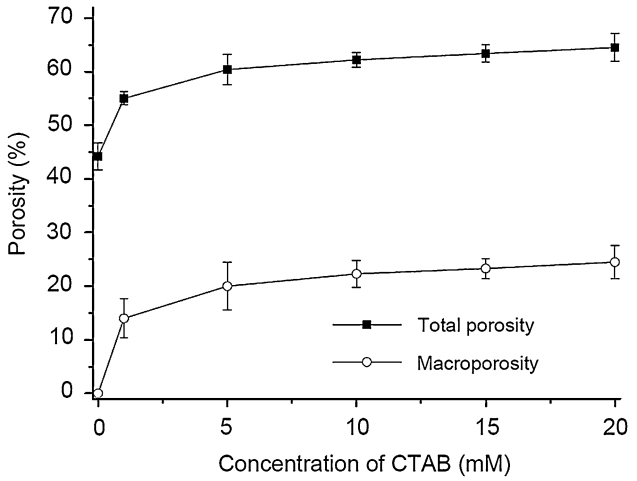

Fig. 7 Influence of the concentration of CTAB on the macroporosity and total porosity of the cements

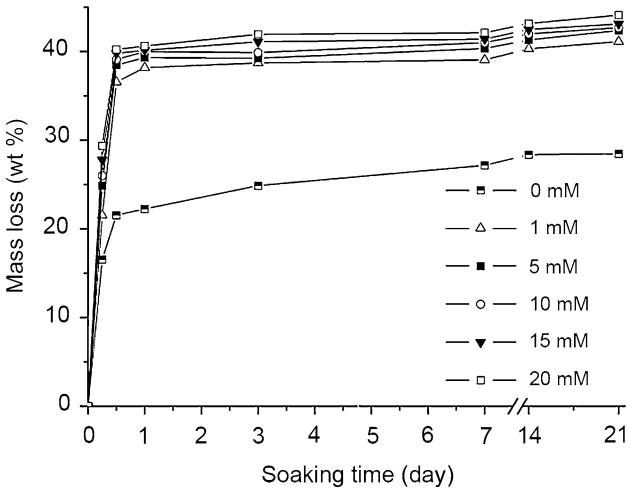

Fig. 8 Influence of the concentration of CTAB on the mass loss of the set cements

5 mM, the macroporosity of the cement was 44.2 ± 2.5% and the mass loss of the cement increased almost 50% as compared with the cement without CTAB. However, the addition of CTAB increased the viscosity and yield stress, so that decreased the injectability of the pastes. And the compressive strength of the cement obviously decreased as the result of the formation of macropores. Considering the injectability, compressive strength and degradation rate of CPC, the CTAB concentration of 5 mM was preferred.

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References

1. W.E. Brown, L.C. Chow, in *Cements Research Progress 1986*, ed. by P.W. Brown (American Ceramic Society, Ohio, 1987), p. 352
2. C. Niedhart, U. Maus, E. Redmann et al., J. Biomed. Mater. Res. **55**, 530 (2001)
3. C.D. Friedman, P.D. Costantino, S. Takagi et al., J. Biomed. Mater. Res. B **43**, 428 (1998)
4. P.D. Costantino, C.D. Friedman, K. Jones et al., Plast. Reconstr. Surg. **90**, 174 (1992)
5. X.P. Wang, J.D. Ye, Y.J Wang et al., J. Biomed. Mater Res A. **81A**, 781 (2007)
6. X.P. Wang, J.D. Ye, Y.J. Wang, Acta Biomaterialia. **3**, 757 (2007)
7. X.P. Wang, J.D. Ye, Y.J Wang, J Mater Sci: Mater Med. Published online: 1 August 2007

8. P.D. Costantino, C.D. Friedman, Otolaryng. Clin. N. Am. **27**, 1037 (1994)
9. G.D. Brown, B.L. Mealey, P.V. Nummikoski et al., J. Periodontol. **69**, 146 (1998)
10. A.M. Cherng, L.C. Chow, S. Takagi, J. Endodont. **27**, 613 (2001)
11. S. Sarda, M. Nilsson, M. Balcells et al., J. Biomed. Mater. Res. **65A**, 215 (2003)
12. E.M. Ooms, J.G. Wolke, J.P. van der Waerden et al., J. Biomed. Mater. Res. **61**, 9 (2002)
13. T. Yoshikawa, Y. Suwa, H. Ohgushi et al., Biomed. Mater. Eng. **6**, 345 (1996)
14. S. Takagi, L. Chow, J. Dent. Res. **74**, 559 (1995)
15. S. Takagi, L. Chow, J. Mater. Sci: Mater. Med. **12**, 135 (2001)
16. X.P. Wang, J.D. Ye, H. Wang, J. Biomed. Mater. Res. B **78B**, 259 (2006)
17. X.P. Wang, L. Chen, H. Xiang et al., J. Biomed. Mater. Res. B. **81B**, 410 (2006)