Setting time and formability of calcium phosphate cements prepared using modified dicalcium phosphate anhydrous powders

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ABSTRACT:

Calcium phosphate cements (CPCs) were prepared using $Ca_4(PO_4)_2O$ (TeCP) and modified $CaHPO_4$ (DCPA) to evaluate the effects of the powder properties for DCPA particles on the setting time and formability of the resulting CPCs. Two types of modified DCPA were prepared by milling commercially available DCPA with ethanol (to produce E-DCPA) or distilled water (to produce W-DCPA). The E-DCPA samples consisted of well-dispersed, fine primary particles, while the W-DCPA samples contained agglomerated particles, and had a smaller specific surface area. The mean particle size decreased with increased milling time in both cases. The raw CPC powders prepared using W-DCPA had a higher packing density than those prepared using E-DCPA, regardless of the mean particle size. The setting time of the CPC paste after mixing with distilled water decreased with decreases in the mean particle size and specific surface area, for both types of DCPA. The CPCs prepared using W-DCPA showed larger plasticity values compared with those prepared using E-DCPA, which contributed to the superior formability of the W-DCPA samples. The CPCs prepared using W-DCPA showed a short setting time and large plasticity values, despite the fact that only a small amount of liquid was used for the mixing of the raw CPC powders (a liquid-to-powder ratio of $0.25 \ g \cdot g^{-1}$ was used). It is likely that the higher packing density of the raw CPC powders prepared using W-DCPA was responsible for the higher performance of the resulting CPCs.

INTRODUCTION

In orthopedic, plastic, and dental surgeries, ceramic bone graft substitutes have been applied to repair bone defects caused by disease and trauma [1-5]. Because hydroxyapatite (HA:$Ca_{10}(PO_4)_6(OH)_2$) is biocompatible and osteoconductive [6-9], it is one of the most widely used and effective materials for devices used in clinical applications [10-14]. It is often necessary to prepare custom-shaped devices before medical operations, or to shape them during surgery, to adjust to bone defects with various shapes and sizes on each bone site [15-16]. Calcium phosphate cement (CPC) has attracted considerable interest as a bone graft substitute [17-22], because CPC pastes obtained by mixing calcium phosphate powders with liquid (typically water) show formability, injectability, and setting behavior with conversion to HA through hydration reactions [23].

Many kinds of CPC consisting of various calcium phosphate compounds have been reported [24-29]. The setting behavior of CPC is fundamentally the result of the precipitation of HA crystals from calcium ions—which are supplied from calcium-rich compounds (e.g., $CaCO_3$, $Ca_4(PO_4)_2O$)—and phosphate ions, which are supplied from phosphate-rich compounds (e.g., $CaHPO_4$、 α-$Ca_3(PO_4)_2$). CPC derived from tetracalcium phosphate (TeCP:$Ca_4(PO_4)_2O$) and dicalcium phosphate anhydrous (DCPA:$CaHPO_4$) was reported by Brown and Chow; this material showed good properties for bone substitution, including a setting reaction at neutral pH, and a sufficient mechanical strength that was attained in a shorter period compared with CPCs consisting of other calcium phosphates [30-32]. Ishikawa et al. reported the setting reaction of CPC prepared from TeCP and DCPA; the dissolution of DCPA was the rate-controlling step,

and the phosphate for the formation of HA was predominantly supplied by the DCPA. In addition, the setting time of CPC was shortened by the addition of a neutral phosphate solution into the mixing liquid [33-35]. The supply of phosphate ions provided by the dissolution of DCPA depends on the crystal structure and grain size of the DCPA. Fine particles of DCPA show high solubility, and supply a large amount of phosphate ions. Raw CPC consisting of fine particles needs a large amount of liquid, because of the low packing density of the CPC powders [23]. The resulting high porosity in the setting body can reduce the mechanical strength of the final material.

In the present work, two types of modified DCPA were prepared as starting materials for raw CPC powders. The setting time and formability of the resulting CPCs were examined, to evaluate the effects of the powder properties changes in the DCPA particles on these performances. The objective of this work was to prepare high-performance CPC exhibiting a shorter setting time, without the need for large amounts of liquid.

MATERIALS AND METHODS

Two types of DCPA were prepared by treating raw DCPA with ethanol (E-DCPA) or distilled water (W-DCPA). One hundred and fifty grams of commercially available DCPA powders (Taihei Chemical Industrial, Nara, Japan, mean particle size: 8.0 μm, specific surface area (SSA) : 1.0 $m^2 \cdot g^{-1}$) were milled with 300 mL of ethanol or distilled water (DW) for 6–48 h using an alumina ball mill (500 g of alumina balls with 5 mm diameter and 2000ml of alumina pot) at 74 rpm of rolling rate, and then dried at 120°C for 20 h. TeCP was prepared from dihydrous dicalcium phosphate (DCPD: $CaHPO_4 \cdot 2H_2O$; Kanto Kagaku, Tokyo, Japan) and calcium carbonate ($CaCO_3$; Kanto Kagaku). One hundred and thirty grams of DCPD and 74.1 g of $CaCO_3$ was mixed with 750 mL of DW for 24 h, using an alumina ball mill. The mixture was dried in an oven at 120°C for 24 h, fired at 1550°C for 10 h in an electrical furnace, and quenched at room temperature. The resulting matter was crushed using an alumina mortar to give a mean particle size of 200 μm.

The morphology of each DCPA particle sample was observed using a scanning electron microscope (S-2500; Hitachi, Japan). Five lines were drawn randomly on scanning electron micrographs that magnifies 10000 diameters and the mean particle size was calculated from length of intersected line at each DCPA particles using the intercept method, referring to the international standard ISO 13383-2012 for fine ceramics (Microstructural characterization -- Part 1: Determination of grain size and size distribution) The SSA was measured using the BET method for N_2 gas adsorption (Multisorb-12; Yuasaionics, Japan) and the particle size distributions were measured using laser diffraction particle

distribution analyzer (LA-500; Horiba, Japan) after DCPA particles were homogenized by using an ultrasonic homogenizer in ethanol. The significance of the differences between the values for the different samples was determined using the Student's t-test.

The raw CPC powders were prepared from 67.5 g of TeCP and 32.5 g of DCPA by mechanical mixing using an automatic mortar and 2 g of raw CPC powders were mixed manually with 0.5 g of DW at a liquid-to-powder ratio (L/P; $g \cdot g^{-1}$) of 0.25 for 1 min using a spatula and a glass dish, resulting in the preparation of a CPC paste. To measure the setting time of the resulting CPC paste, the CPC paste was used to fill the void in a stainless steel ring (10 mm in inner diameter, 5 mm in height) and flattened on its top surface. A vicker needle (300 g in weight, 1 mm^2 in cross-sectional area) was set on the top surface of the filled CPC paste at 37°C and 95% relative humidity. The setting time was determined as the time at which no dent was formed by the needle (n = 5). The packing density of the CPC powders was calculated from the volume and weight of the CPC powders in a graduated cylinder, after sufficient tapping. To measure the plasticity value, the molded CPC paste (9 mm in diameter, 10 mm in height) was compressed under a load of 0.14 MPa for 2 min after the onset of the mixing with DW. The plasticity value was calculated from the diameter of the CPC paste, using the following equation (n = 5):

Plasticity value (%) = (b-a) / $a \times 100$,

where a and b are the diameter of the CPC paste before and after compression, respectively.

RESULTS

Powder properties of DCPA

Figure 1 shows the mean particle size and SSA for E-DCPA and W-DCPA. In both samples, the

mean particle size decreased and the SSA increased with increasing milling time. W-DCPA showed a

smaller mean particle size than E-DCPA at milling times of 12, 18, and 24 h; the mean particle sizes in the

samples showed very similar values after milling times of 36 and 48 h, as shown in Fig. 1(a). In contrast,

the SSA values for E-DCPA were larger than those for W-DCPA at every milling time, as shown in Fig.

1(b). The SSA values for W-DCPA were always smaller than those for E-DCPA, when compared at a

similar particle size, as shown in Fig. 1(c).

Figure 2 shows scanning electron micrographs of the DCPA particles. Both of the DCPA samples

consisted of fine particles. However, the primary particles in W-DCPA agglomerated and formed

secondary particles that were several tens of micrometers in size, while the particles in E-DCPA were

dispersed well.

Figure 3 shows the particle size distributions of the DCPA particles. In the case of E-DCPA, most of

particle size was several micrometer. However, particle size of W-DCPA ranged from 0.1µm to several

ten micrometer and the frequency of particle size was largest at approximately 20 µm.

Setting time of CPC

The effects of the mean particle size and SSA of DCPA on the setting time are demonstrated in Fig. 3.

The setting time decreased with decreasing DCPA particle size, regardless of the process used to treat the

DCPA, as shown in Fig. 3(a). The CPCs prepared using E-DCPA showed a longer setting time than those prepared using W-DCPA in the SSA range of 2.0–6.0 $m^2 \cdot g^{-1}$, while there was no difference between the setting times for SSA values > 6.0 $m^2 \cdot g^{-1}$, as shown in Fig. 3(b).

Packing density and plasticity of CPC

Figure 4 shows the packing density of the raw CPC powders as a function of the mean particle size and SSA of the DCPAs. In the case of E-DCPA, the packing density decreased with decreasing mean particle size, and decreased with increasing SSA. In contrast, in the case of W-DCPA, high packing densities were obtained, and an almost constant packing density was maintained, independent of the mean primary particle size and SSA (1.4 $kg \cdot m^{-3}$).

Figure 5 shows the relationship between the plasticity value of the CPC pastes and the packing density of the raw CPC powders. The plasticity value depended on the packing density; larger plasticity values were obtained for the CPC powders with higher packing densities. The CPC pastes made from W-DCPA showed larger plasticity values compared with those made from E-DCPA. It was visually confirmed that the CPCs prepared using pastes with a plasticity value of > 50% showed good formability, while the CPCs prepared using pastes with a plasticity value of < 50% showed brittle behavior; some cracks were included in both DCPA cases.

DISCUSSION

W-DCPA showed smaller SSA values and smaller mean particle sizes compared with E-DCPA. The primary particles in W-DCPA agglomerated, while E-DCPA consisted of well-dispersed fine particles. This was because of the differences in the solubility of DCPA in DW and ethanol, and the differences in surface tension between DW and ethanol. The surface tension of pure water is 71.99 mN·m^{-1}, and that of ethanol is 21.97 mN·m^{-1}, at 25°C [36]. The raw DCPA powders partially dissolved and simultaneously precipitated during the milling in DW, and then agglomerated during the drying; this did not occur during the processing in ethanol.

The differences in the powder properties of DCPA influenced the characteristics of the resulting CPCs. Finer primary particles of DCPA resulted in the shortening of the setting time, likely because they dissolved easily and supplied phosphate ions effectively, thus accelerating the hydration reaction with TeCP.

As shown in Fig. 6, the CPCs prepared using W-DCPA showed high packing densities and good formability, even though they contained a relatively small amount of liquid (with L/P = 0.25). In general, the packing density of particles through tapping is influenced by their kinetic energy and interaction force, which depend on the particle size [37]: when large-sized particles are tapped, they are more closely-packed then small-sized ones. The superior formability of the CPC pastes prepared using W-DCPA was most likely because of the high packing density.

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CONCLUSION

CPCs were prepared using two types of DCPAs (W-DCPA and E-DCPA), to evaluate the effects of the powder properties changes in the DCPAs on the properties of the resulting cements; these properties were assessed by measuring the setting times and plasticity values. The setting time depended on the mean particle size in the DCPA, and was shortened when smaller particles of DCPA were present. In addition, the plasticity value of the CPC pastes, which corresponded to the formability, depended on the packing density of the CPC powders. The CPCs prepared using W-DCPA showed high packing densities and large plasticity values, even though only a small amount of liquid was added to the CPC powders. This might have been due to the small SSA of W-DCPA, which was caused by the agglomeration of the fine primary particles.

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Figure captions

Figure 1. (a) Mean particle size, and (b) specific surface area of DCPA milled with ethanol (E-DCPA) and distilled water (W-DCPA) as a function of milling time, and (c) mean particle size as a function of the specific surface area of DCPA. The average values with standard deviations were shown (n=3). Significant differences by Student's t-test was established as follows: *$p<0.05$,**$p<0.01$

Figure 2. Scanning electron micrographs of DCPA particles (a, b) untreated, (b, c) E-DCPA, and (d, e) W-DCPA. The milling time was 24 h.

Figure 3. Particle size distributions of DCPA particles. The milling time was 24 h.

Figure 4. Setting time of CPC pastes as a function of (a) the mean particle size, and (b) the specific surface area of DCPA. The average values with standard deviations were shown (n=5).

Figure 5. Packing density of raw CPC powders as a function of (a) the mean particle size, and (b) the specific surface area of DCPA. The average values with standard deviations were shown (n=5).

Figure 6. Plasticity value of CPC pastes as a function of the packing density of raw CPC powders. The average values with standard deviations were shown (n=5).