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# Synthesis of amorphous calcium phosphates for hard tissue repair using conventional melting technique

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The technical use of phosphate glasses has been restricted because of their strong hygroscopic nature. Traditionally phosphate glasses have been used as an opaline in silicate glasses since the solubility of phosphate in silicate glasses at lower temperature is very poor. Their poor chemical durability can be improved by the introduction of higher valency elements such as Ba, Al, or Be. The most important property of the phosphate glass is its ability to dissolve some elements and oxides that are insoluble or poorly soluble in glasses of other materials and crystalline compounds. Another important use of phosphate glasses is their application as biomaterials based on the calcium phosphate system. Their similarities in composition to bone and teeth make them ideal candidates. The first proposed application of the calcium phosphate glass to the biomaterials was proposed as dental restorative materials such as the crown because of their excellent castability as well as sufficient mechanical strength [1, 2].

The purpose of this study was to explore calcium phosphate glasses having an amorphous structure as potential biomaterials in hard tissue repair. We synthesized amorphous calcium phosphate glasses by melting and subsequent quenching process. Batches in the system $CaO–CaF_2–P_2O_5–MgO–ZnO$ were prepared with six kinds of Ca/P ratios from 0.2 to 1.2 using $CaCO_3$, $CaF_2$, $H_3PO_4$, MgO, and ZnO as raw materials. The molar ratio of $CaO/CaF_2$ was fixed to 9. MgO and ZnO were added at 1 wt%, respectively. Mixed batches were dried at 80 °C and melted at temperatures ranging from 800 to 1550 °C depending on the Ca/P ratios. They were subsequently quenched onto the graphite plate at room temperature after melting.

In order to determine the crystallinity and crystalline phases of the as-quenched samples, X-ray diffraction analysis was performed using Philips APD 3720 X-ray diffraction apparatus with a fine focus copper target X-ray tube. As shown in Fig. 1, there was no crystalline peak up to Ca/P of 0.6. When Ca/P ratio was 0.8, the sample exhibited the $Zn_3(PO_4)_2$ as well as $Ca_2P_2O_7$; the former had disappeared but the latter still remained. $Ca_2P_2O_7$ phase partially transformed to $Ca_4P_2O_7$ with increasing Ca/P to 1.2. Crystallinity obtained from the XRD peak intensity decreased with increasing Ca/P ratio.

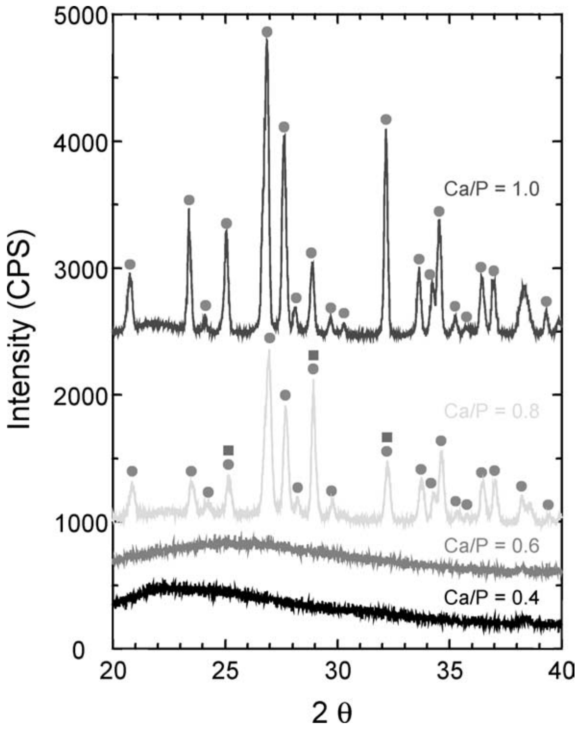


*Figure 1* XRD patterns of the as-quenched samples. ● and ■ denote $Ca_2P_2O_7$ and $Zn_3(PO_4)_2$, respectively.

As-quenched samples were also examined by IR analysis. Absorption spectra were collected using a Perkin-Elmer 983G quadruple grating spectrophotometer with scanning range from 4000 to 400 $cm^{-1}$ after mixing the samples with KBr powder and pressing at 10 000 psi in a vacuum. As exhibited in Fig. 2, absorption spectrum with Ca/P of 0.4 showed broad peaks, which is a typical pattern in amorphous glass materials [3–5]. There were five peaks including four fundamental vibration peaks for the phosphate structure. The first vibration peak of phosphate is the asymmetric stretching mode ($\nu_3$) observed in the range of 1230–1390 $cm^{-1}$, the second vibration peak of phosphate is the symmetric bending mode ($\nu_4$) observed in the frequency range of 780–940 $cm^{-1}$, the third vibration

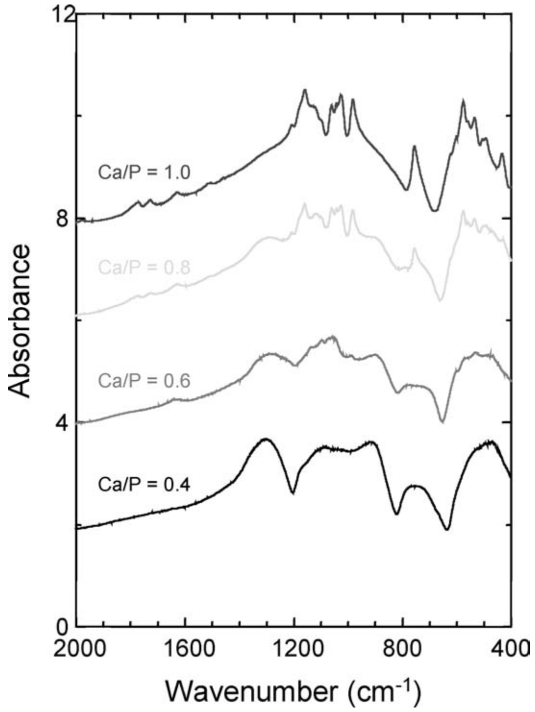


*Figure 2* IR absorption spectra of the as-quenched samples.

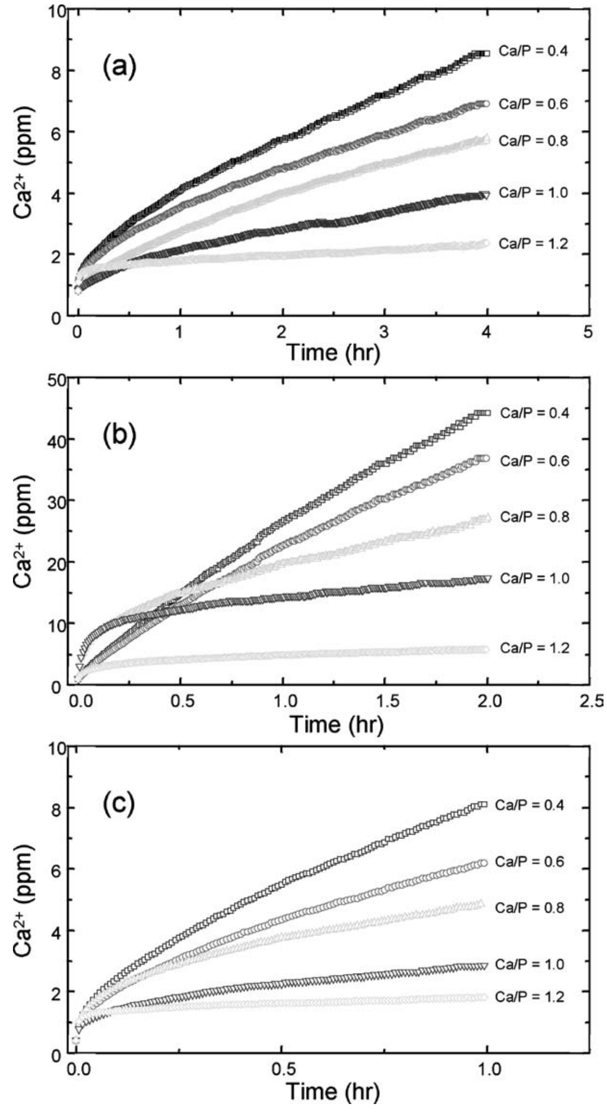
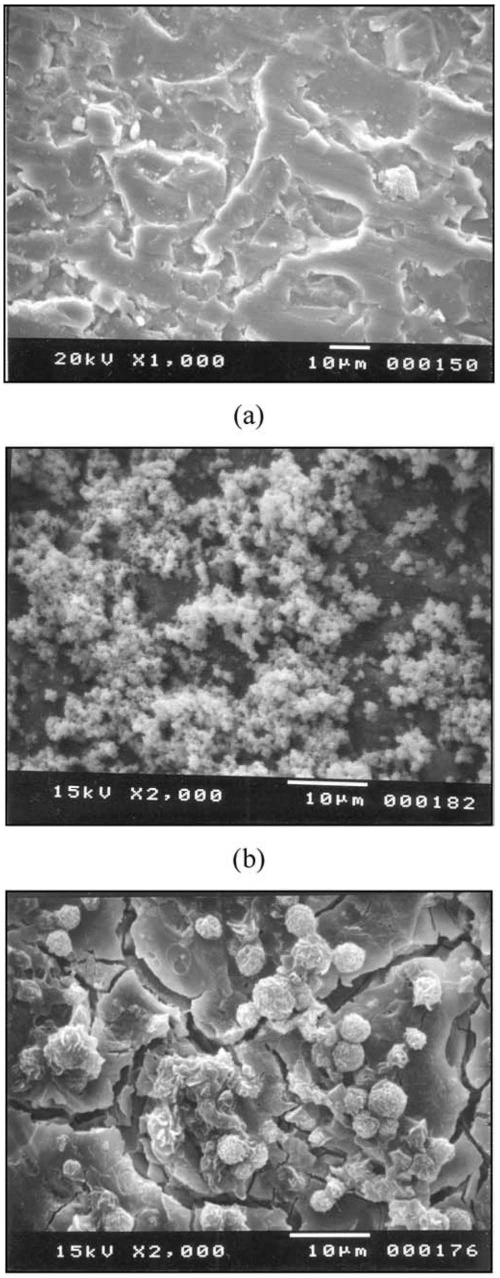


*Figure 3* Dissolution of Ca$^{2+}$ ion at 37 °C with (a) pH 7.3 and (b) pH 3 in 0.1 M tris-aminomethane solution for 2 and 4 hr, respectively, and (c) pH 6 in 0.1 M potassium acetate solution for 1 hr.

peak of phosphate is the symmetric stretching ($\nu_1$) observed in the frequency range of 530–780 cm$^{-1}$, and the last vibration peak of phosphate is the harmonics of symmetric bending and asymmetric stretching modes ($\nu_2$) observed in the range of 470–800 cm$^{-1}$ [13–15]. Another peak around 1100 cm$^{-1}$ is due to F-O in phosphate [3] originating from CaF$_2$ as a precursor. The IR peak which changed from broad to sharp shape with increasing Ca/P ratio indicates increasing crystallinity in accordance with the XRD results shown in Fig. 1.

As-quenched samples were reduced either powder less than 40 $\mu$m or pellets sized 10 × 10 × 1 mm using ball milling or low speed saw, respectively. Powders were employed in a dissolution test in buffer solutions and pellets were exposed to the simulated body fluid (SBF) as well as fetal bovine serum (FBS). Dissolution properties were investigated in acidic buffer solutions



(a)

(b)

(c)

*Figure 4* SEM photographs of the samples with the Ca/P ratio of 0.6 (a) before and after exposure to (b) SBF and (c) FBS for one week at 37 °C.

such as 0.1 M tris-aminomethane with pH 3 and 7.3 and 0.1 M potassium acetate with pH 6 at 37 °C by immersing 25 mg of powder into 50 ml of each acidic buffer solution. The dissolved quantity of $Ca^{2+}$ ions was measured with Metrohm selective calcium ion electrode and automatically transferred to a computer in every 30 s while continuously stirring at 500 rpm with a Caframo RZR 2000 precision digital stirrer. They were recorded during 2, 1, and 4 hr when the pH of the buffer solutions was 3, 6, and 7.3, respectively. The extent of dissolved $Ca^{2+}$ ions is shown Fig. 3. Fig. 3a and b present the dissolved amounts with pH 3 and 7.3 in 0.1 M tris-aminomethane solution, respectively, while that after exposure to 0.1 M potassium acetate solution with pH 6 is shown in Fig. 3c. We observed that the lower extent of dissolution decreased with increasing Ca/P ratio in every measurement, possibly due to the decrease of crystallinity. It has already been reported that the amorphous calcium phosphate formed in the plasma-sprayed coatings on dental and orthopedic implants as well as metal substrates had a significant effect on the properties of the coatings; especially it increased the extent of dissolution [6].

Each pellet was kept in both 15 ml of SBF and FBS at 37 °C. SBF was prepared according to previously described methods [7]. After one week, the surface morphology of the pellets was examined by JEOL 5400 SEM after a thin layer of metal of a few angstrom was coated in a sputter coater. SEM photographs are illustrated in Fig. 4. There was no crystallite on the surface of pellets prior to exposure to SBF or FBS as shown in Fig. 4a. Tiny crystallites were formed on the surface of pellets after exposure to SBF as shown in Fig. 4b, while the agglomerated larger crystals were precipitated after suspension in FBS as exhibited in Fig. 4c. Both crystals were characterized as hydroxyapatite phase by the transmission Laue method using H700 Hitachi TEM.

To summarize, the opacity, crystallinity, and extent of dissolution decreased with increasing Ca/P ratio of the synthesized amorphous calcium phosphate glasses: the higher the Ca/P ratio, the less transparent, the higher the crystalline/non-crystalline ratio, and the lower the extent of dissolution in all buffer solutions of tris-aminomethane and potassium acetate with pH of 3, 7.3, and 6. Exposure to either SBF or FBS caused precipitation, thereby potential bioreactivity of calcium phosphate glasses.

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