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Carbonate-containing hydroxyapatite derived from calcium tripolyphosphate gel with urea

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Carbonate containing hydroxyapatite (CO_3HAp) is one of the candidate materials as a bioresorbable bone substitute. In the present work, CO_3HAp was efficiently prepared by a hydrothermal treatment of calcium tripolyphosphate gel with urea at 140 °C for 24 h. Chemical potential plots of the CO_3HAp for estimation of its dissolution behavior suggested that the CO_3HAp is more soluble than hydroxyapatite (HAp) and is as soluble as octacalcium phosphate (OCP) and/or β-tricalcium phosphate (TCP). This material is expected to be applied to bioresorbable materials such as bone fillers.

1. Introduction

It has been well-known that each ion in the crystal lattice of hydroxyapatite (HAp; $Ca_{10}(PO_4)_6(OH)_2$), can be substituted by various ions. In particular, the apatite having carbonate ions (CO_3HAp) has advantages as a biomaterial in excellent biocompatibility and resorbability in a living body. When the CO_3HAp material is implanted into a living bone, it is dissolved by the osteclasts and the new bone is expected to form around the material [1–3]. As the result, the material may be finally replaced by the living bone [4, 5]. CO_3HAp is one of the candidate materials as a bioresorbable bone substitute.

A hydrothermal synthesis of HAp is one of the useful methods to easily prepare HAp crystals at relatively low temperature for short time [6–11]. However, few works on CO_3HAp prepared by the hydrothermal method have been reported so far.

In the present work, we investigated the hydrothermal method for preparation of CO_3HAp using calcium tripolyphosphate gel with urea. The gel has advantages in that their hydrolysis temperature is relatively low (>120 °C) and in that sizes of the obtained products is easily controlled by pH of the gel [11, 12] The reaction of the calcium tripolyphosphate gel progresses during this hydrothermal treatment, as given by (1).

$$\begin{aligned} &Ca_5(P_3O_{10})_2 + 5Ca^{2+} + 6H_2O \\ &\quad \rightarrow 10Ca^{2+} + 6PO_4^{3-} + 2OH^- + 10H^+ \\ &\quad \rightarrow Ca_{10}(PO_4)_6(OH)_2 + 10H^+ \end{aligned} \quad (1)$$

The pH value of the gel decreases during the reaction, since the protons generate with the hydrolysis of calcium tripolyphosphate gel to orthophosphate ions. While the tripolyphosphate hydrolyzes to orthophosphate ions and the orthophosphate ions react with calcium ions to form HAp, the decomposition of urea as an additive would proceed as given by (2).

$$(NH_2)_2CO + 3H_2O \rightarrow 2NH_4OH + CO_2 \uparrow \quad (2)$$

The partial pressure of the carbonate gas increases in the sealed container during this reaction and this carbonate gas dissolves in the gel. The carbonate ion is expected to be incorporated into the apatite crystal lattice.

The calcium tripolyphosphate gel was prepared by mixing 1 mol/L calcium nitrate solution and 0.1 mol/L sodium tripolyphosphate solution with Ca/P = 1.67 in mol ratio of HAp stoichiometric atomic ratio as follows.

$$\begin{aligned} &2Na_5P_3O_{10} + 10Ca(NO_3)_2 \\ &\quad \rightarrow Ca_5(P_3O_{10})_2 \downarrow + 5Ca(NO_3)_2 + 10NaNO_3 \end{aligned} \quad (3)$$

In the present work, our approach is the preparation of carbonate containing apatite (CO_3HAp) using the hydrothermal treatment of calcium tripolyphosphate gel.

2. Materials and methods

2-propanol was included in the gel as a buffer to keep pH value of >4 and to restrict formation of dicalcium phosphate anhydrous (DCPA) [12]. A 0.4 or 0.5 mol/L urea solution was added to the gel prior to starting the reaction. The gel included 125 mmol/L of calcium ion, 25 mmol/L of tripolyphosphate ion, 30 vol% of 2-propanol and 10–62.5 mmol/L urea. After the gel was stirred for 30 min to achieve the equilibrium, the pH

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value of the gel was measured as an initial pH. 40 mL of the gel was poured into a Tefron beaker (60 mL of internal volume) and put into a sealed stainless steel container. The sealed container was placed in a silicone oil bath for 1 day at 140 °C, and then cooled quickly in air. The products were collected by a suction filtration and the pH value of the filtrate was measured as a final pH value before washing the products several times with deionized water. After the resulting products were dried at 70 °C for 1 day under a reduced pressure, their crystalline phases were identified by X-ray diffractometry (XRD) and Fourier transform infrared spectroscopy (FT-IR). The weight loss of the products was measured after heating in the air at the temperature of 200–1200 °C for 15 h. The morphology of the product was observed with a scanning electron microscope (SEM). The dissolution behavior of the product was investigated in 10 mmol/L acetic acid solution adjusted to pH 5.0 at 37 °C during 2 min to 5 days. [3] Dissolved amounts of calcium and phosphate ions in the solution were measured by inductively coupled plasma-atomic emission spectroscopy (ICP-AES).

3. Results and discussion

Fig. 1 shows XRD patterns of the products derived from the gels containing urea. When the gel includes urea of ≤40 mmol/L, the resulting product consists predominantly of crystalline HAp with a trace amount of DCPA. On the other hand, the products derived from the gels including urea of 62.5 mmol/L consist of an apatite crystalline phase without by-products.

Fig. 2 shows FT-IR spectra of the products. It is known that carbonate ions exist on two distinct lattice sites of the apatite crystal, designated as site A and site B. Narasaraju and Phebe [13] CO_3HAp shows adsorption bands due to CO_3^{2-} at 884, 1465 and 1534 cm^{-1} for site A and at 864, 1430 and 1534 cm^{-1} for site B. Sites A and B are presumed that carbonate ions are substituted for hydroxyl ions and phosphate ions in the apatite crystal lattice, respectively [13]. The product derived from the gel with 62.5 mmol/L urea showed the large peaks at 877, 1418, 1458 and 1551 cm^{-1}, whereas the others with ≤40 mmol/L urea showed the small peaks at 863, 890 and 1464 cm^{-1}. It was found that CO_3HAp containing carbonate ion at both sites A and B can be derived from the gel including 62.5 mmol/L urea using the present method.

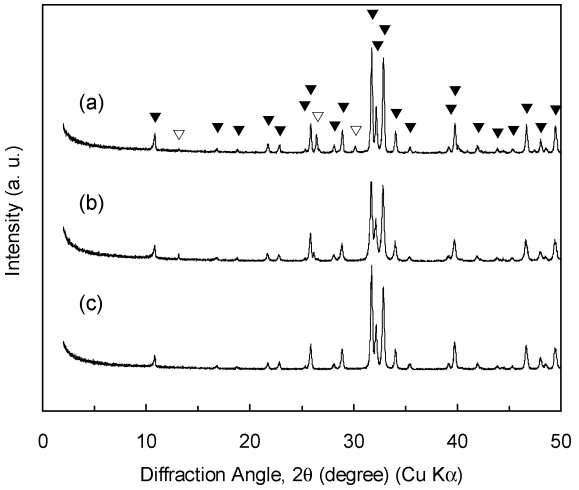

Figure 1 XRD patterns of products derived after hydrothermal treatment of the gels consisting of 125 mmol/L-calcium nitrate, 25 mmol/L-sodium tripolyphosphate and 30 vol% 2-propanol at 140 °C for 24 h (a) without urea, (b) with 40 mmol/L urea and (c) 62.5 mmol/L urea. In the figure ∇ and ▼ present DCPA and HAp, respectively.

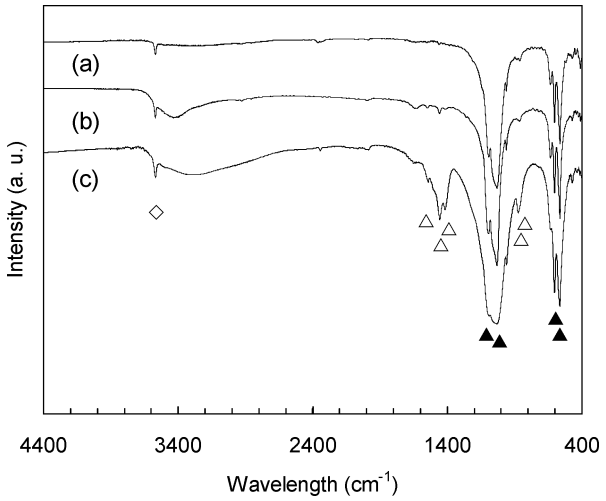

Figure 2 FT-IR spectra of products derived after hydrothermal treatment of the gels consisting of 125 mmol/L-calcium nitrate, 25 mmol/L-sodium tripolyphosphate and 30 vol% 2-propanol at 140 °C for 24 h (a) without urea, (b) with 40 mmol/L urea and (c) 62.5 mmol/L urea. △, ▲ and ◇ present CO_3^{2-}, PO_4^{3-} and OH^-, respectively.

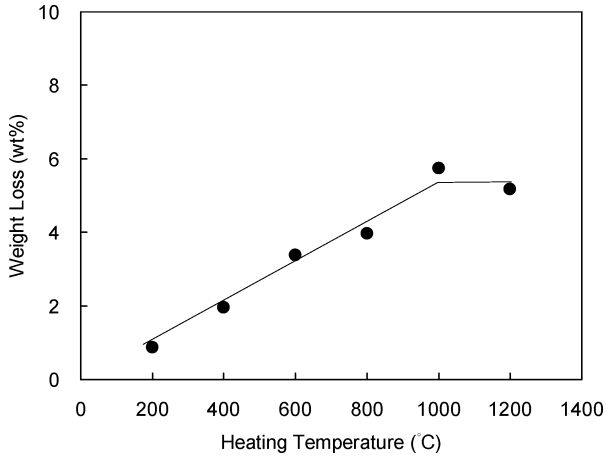

Figure 3 Changes in weight loss of the product derived after hydrothermal treatment of the gels consisting of 125 mmol/L-calcium nitrate, 25 mmol/L-sodium tripolyphosphate, 30 vol% 2-propanol and 62.5 mmol/L urea at 140 °C for 24 h as a function of heating temperature.

Fig. 3 shows weight loss of CO_3HAp prepared using the gel including 62.5 mmol/L urea at the various temperatures. The weight loss increases with increasing the heating temperature and then it shows almost constant value at above 1000 °C. Doi *et al*. reported that almost carbonate ion can be evolved at the temperature from about 400 to 1000 °C and the adsorbed H_2O can be eliminated at below 400 °C [14].

In the reactions, the initial pH values were about 5 and no initial pH was influenced by addition of the urea. The final pH value of the gel with 62.5 mmol/L urea shifted to nearly neutral, while those of the others did not change. In this reaction, protons generated with the hydrolysis of calcium tripolyphosphate can

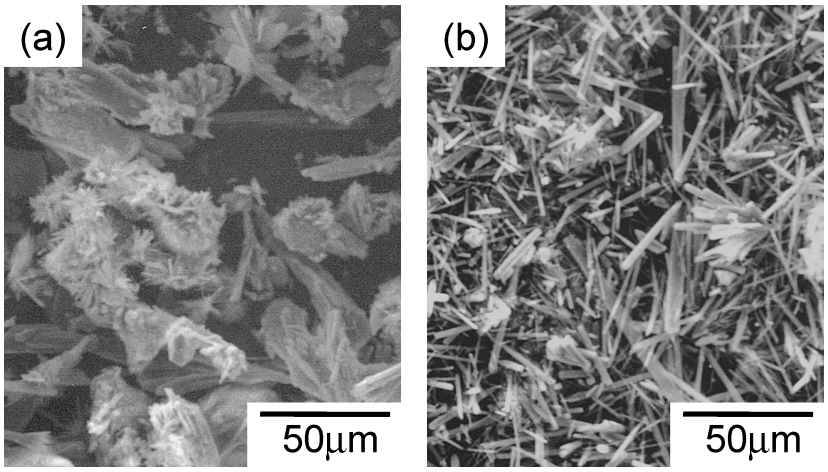

Figure 4 SEM photographs of products derived after hydrothermal treatment of the gels consisting of 125 mmol/L-calcium nitrate, 25 mmol/L-sodium tripolyphosphate and 30 vol% 2-propanol at 140 °C for 24 h (a) with 62.5 mmol/L urea, and (b) without urea.

be neutralized by ammonia decomposed from urea of 62.5 mmol/L; the final pH value of the gel including 62.5 mmol/L urea approaches to neutral. The acid dissociation constant, pKa_1 and pKa_2 of carbonate acid is 6.35 and 10.33, respectively. The carbonate ion may be easy to be incorporated to apatite crystals in the neutral region, where the carbonate acid exists as a hydrogen carbonate ion. As the result, the carbonate apatite can be obtained by including 62.5 mmol/L urea.

Fig. 4 shows SEM photographs of the CO_3HAp derived from the gel containing 62.5 mmol/L urea and HAp derived from the gel without urea. CO_3HAp has irregularly shaped morphology; large crystals are observed in the product, whereas that of HAp was relatively monodispersed. Since in case of CO_3HAp the pH range during this reaction is in the neutral which is the isoelectric point of apatite, the apatite nuclei may have a tendency to aggregate during the reaction; the irregularly shaped products would be obtained from the gel including urea.

Fig. 5 shows time profiles of pH, concentrations of phosphate and calcium ions in 10 mmol/L acetic acid solution after soaking CO_3HAp for 2 min ∼ 5 days. The pH is increasing with time. The concentrations of phosphate and calcium ions increase within 1 day and then decrease. This indicates that CO_3HAp is gradually dissolved into the solution within 1 day and then another calcium phosphate forms in the solution.

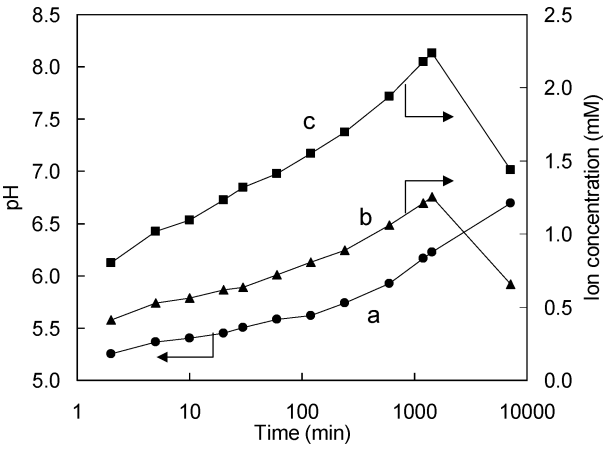

Figure 5 Time profiles of pH (a), concentrations of phosphate (b) and calcium (c) ions in 10 mmol/L acetic acid solution after soaking CO_3HAp for 2 min ∼ 5 days.

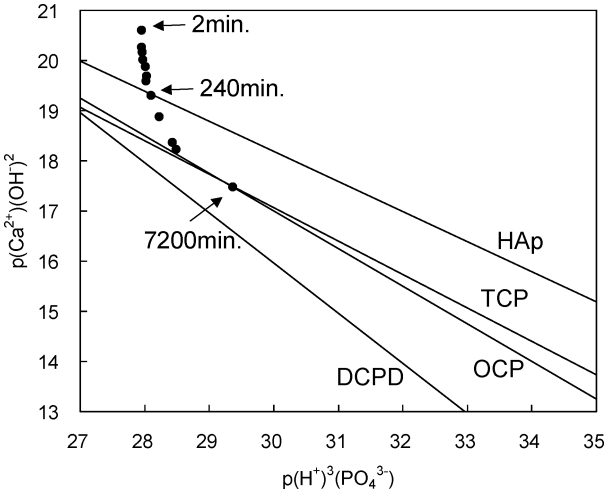

Figure 6 Chemical potential plots of the solution composition after soaking CO_3HAp in 10 mmol/L acetic acid solution pH-adjusted to 5.0 at 37 °C for 2–7200 min. The solid lines indicate the solubility lines of hydroxyapatite (HAp), β-tricalcium phosphate (TCP), octacalcium phosphate (OCP) and dicalcium phosphate dihydrate (DCPD).

Solubilities of calcium phosphates can be discussed in terms of chemical potential plots, which are evaluated with taking account of ionic strength estimated using a Davis' equation [3]. Fig. 6 shows the chemical potential plots of the solution compositions after the soaking CO_3HAp. In this figure the region below the solid line of each compound, such as HAp, TCP, OCP, and DCPD, means precipitation for the compound, whereas that above the solid line means solubility for the compound [3]. The plots of the CO_3HAp approach to the line of β-tricalcium phosphate (TCP) or octacalcium phosphate (OCP) with time. This result indicates that the solubility of the CO_3HAp is higher than that of HAp and almost same as that of TCP or OCP. Among the products, K_I, of the ionic activities for $(Ca^{2+})^5(PO_4^{3-})^3(OH^-)$ calculated at each plot, the highest value is 6.0×10^{-57}, which is higher than that of HAp (2.14×10^{-59}) and is between those of apatite containing 0.5 wt% carbonate ion (1.6×10^{-58}) and 8.7 wt% (5.4×10^{-53}) [3].

In summary, we could obtain CO_3HAp by the hydrothermal method using tripolyphosphate gel with urea; the solubility of CO_3HAp is higher than that of HAp and almost same as that of octacalcium phosphate (OCP) and/or β-tricalcium phosphate (TCP). This material is expected to be applied to bioresorbable materials such as bone fillers.

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