Synthesis of nano-sized hydroxyapatite by ultrasound irradiation

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Abstract. Ultrasound irradiation is an effective means of synthesizing fine particles by promoting contact between ions in a solution. We previously reported the synthesis of nano-sized amorphous calcium carbonate particles (specific surface area: 70 m²/g) using this method. The present study focused on the production of nano-sized hydroxyapatite (HAp) particles with a high specific surface area using ultrasound irradiation. The initial Ca/P atomic ratio was adjusted from 1.00 to 2.00 and the effects on the resulting HAp particles was investigated. HAp particles were found to be easily formed within 5 min of the start of the reaction, and were confirmed to have a single phase using X-ray diffraction analysis. The maximum specific surface area of the particles was approximately 130 m²/g.

1. Introduction
Ultrasound corresponds to elastic waves with frequencies at and above 20 kHz. When ultrasound irradiation is applied to liquid phase chemical reactions, it has the same effect as high-speed stirring. For example, a frequency of 20 kHz corresponds to 20000 vibrations (oscillations)/s. This results in an increase in the number of contacts between ions in the liquid, which can facilitate the synthesis of extremely fine particles 1-3). We previously reported the synthesis of a fine calcium carbonate compound by ultrasound irradiation during an aqueous reaction 4,5). Precipitation of calcium carbonate particles was achieved by bubbling CO₂ through a quicklime suspension. The particles had a specific surface area of 100 m²/g. However, in the case of calcium sulfate dihydrate (gypsum dihydrate), for which the precipitation process had a non-zero induction period, it was found to be extremely difficult to form fine particles in the presence of ultrasound irradiation. However, the technique was successful in producing fine particles of dicalcium phosphate dihydrate (CaHPO₄·2H₂O; DCPD) from a solution of Ca(H₂PO₄)₂, which is the only water-soluble phosphate. Upon continued irradiation of the DCPD suspension, a transformation was found to occur from DCPD to hydroxyapatite (HAp). This implies that ultrasound irradiation is capable of promoting dissolution-precipitation in addition to merely increasing the ion contact frequency. This study investigated the synthesis of hydroxyapatite with high specific surface area by ultrasound irradiation.

2. Experimental
A 0.1 – 0.2 mol/dm$^3$ CaCl$_2$ solution was first irradiated with ultrasound (Branson, Sonifier 250D (200W) or 2000bdc 40 (400 W)) at a frequency of 20 or 40 kHz, and an amplitude of 123 or 39 µm, respectively. A 0.1 mol/dm$^3$ Na$_3$PO$_4$ solution was rapidly added and ultrasound irradiation was continued. Ca/P atomic ratios of 1.00, 1.50, 1.67 and 2.00 were used and the reaction time was in the range 3 – 20 min. The final sample was obtained by filtering the suspension and heating at 70 °C.

The samples were characterized using X-ray diffraction (XRD; Rigaku, MultiFlex), infrared (IR) absorption spectroscopy (Shimazu, FTIR-8400s), thermal analysis (TG-DTA; Rigaku, Thermo Plus), inductively coupled plasma (ICP; SII, SPS1200A) and field emission scanning electron microscopy (FE-SEM; Hitachi, s-4500).

3. Results and discussion

The temperature of the solutions was found to increase as a result of ultrasound irradiation. The 70% amplitude of 20 kHz and 40 kHz is 86 µm and 27 µm, respectively. Figure 1 shows the temperature of a suspension as a function of irradiation time at 20 and 40 kHz. In the case of 20 kHz, it increased to 80 °C during the first 10 min and reached 90 °C after 20 min. Moreover, in the case of 40 kHz, higher temperatures were achieved compared with 20 kHz, because the number of oscillations per second of the ultrasonic horn was larger. HAp is synthesized at temperature more than 80 °C.

3.1 Synthesis of HAp by ultrasound irradiation at 20 kHz

Precipitation occurred rapidly when the Na$_3$PO$_4$ solution was added to the CaCl$_2$ solution. The formation of precipitates was also confirmed by changes in the electric conductivity of the solution. The pH of the solution was monitored during the reaction. For a Ca/P atomic ratio of 1.00, the pH following the reaction was found to be 12, which was the same as that of the initial Na$_3$PO$_4$ solution. For other Ca/P atomic ratios, the pH was observed to decrease immediately after the reaction. Following formation of the deposit, the pH of the suspension declined rapidly and then remained constant in the range 3 - 5.

Figure 2 shows XRD patterns of powder specimens produced at a Ca/P atomic ratio of 1.67 for different reaction times. After 3 min, a halo can be observed at 20=30 – 35°, suggesting the formation of amorphous calcium phosphate (ACP) 6),7). After 5 min, the characteristic diffraction pattern associated with crystalline HAp was observed. For reaction times above 10 min, the crystallinity of the HAp continued to increase, although little further improvement occurred after 15 min. This sample was subjected to differential thermal analysis, and an exothermic peak due to crystallization of ACP was only weakly observed at about 700 °C.8) However, an endothermic peak due to dehydration of ACP was observed at approximately 100 – 200 °C. The above results seem to suggest that ACP is produced in the initial stage of the reaction.

In addition, the HAp was evaluated using IR absorption spectroscopy. In the case of commercial HAp, three absorptions appear at positions close to 600 cm$^{-1}$. The HAp obtained in the present study for different synthesis times was found to exhibit two additional absorptions at about 1100 cm$^{-1}$, which are associated with PO$_4^{3-}$, thus indicating that the HAp is Ca$^{2+}$ deficient.
Figure 3 shows the chemical compositions of the samples products obtained in the present study. Figure 3(a) shows the Ca/P atomic ratio and Fig. 3(b) shows the Na/Ca atomic ratio. These compositions were the average value of the sample which were dissolved with nitric acid, and were measured with ICP. It can be seen that for all initial Ca/P atomic ratios, the Ca/P atomic ratio of the final HAp product was always in the range 1.3 – 1.5, again indicating that it is Ca\(^{2+}\) deficient. On the other hand, the Na/Ca atomic ratio for the HAp synthesized with an initial Ca/P atomic ratio of 1.00 decreased with increasing reaction time from 0.4 to 0.2. This value is very high and suggests the formation of a NaCaPO\(_4\) precursor.

Figure 4 shows the effect of the initial Ca/P atomic ratio and the reaction time on the specific surface area of the HAp product. The specific surface area was highest for initial Ca/P atomic ratio of 1.00. However, since it is believed that this HAp was mixed together with the NaCaPO\(_4\) precursor, this result was excluded from the analysis. For initial Ca/P atomic ratio of 2.00, the specific surface area of the HAp increased during the first 10 min, reaching a value of approximately 130 m\(^2\)/g, because fine HAp particles were being formed by crystallization of ACP. It then decreased as a result of HAp crystal growth by a thermally driven dissolution-precipitation mechanism (see Fig. 1).

![Figure 3](image_url)

**Figure 3** Chemical compositions of HAp products obtained by ultrasound irradiation.

![Figure 4](image_url)

**Figure 4** Effect of initial Ca/P atomic ratio on specific surface area of HAp obtained by ultrasound irradiation.

![Figure 5](image_url)

**Figure 5** FE-SEM micrographs of HAp products obtained by ultrasound irradiation.

![Figure 6](image_url)

**Figure 6** XRD patterns of HAp synthesized by ultrasound (40 kHz) irradiation.

3.2 Synthesis of HAp by ultrasound irradiation at 40 kHz

Next, the ultrasound frequency was changed to 40 kHz. At this frequency, the horn oscillates more rapidly but the oscillation amplitude decreases.

Figure 6 shows XRD patterns of products synthesized
ratio of 1.67. As discussed in Section 3.1, for a frequency of 20 kHz, a halo-like pattern was observed after 3 min (Fig. 2). However, at a frequency of 40 kHz, the characteristic pattern of HAp was already observed for a reaction time of 3 min, and the crystallinity increased with increasing reaction time.

Figure 7 shows the dependence of the specific surface area of the products on the ultrasound frequency and reaction time. As a reference, the specific surface area of HAp which was synthesized by stirring at 80 °C was approximately 100 m²/g. It can be seen that higher specific surface areas were obtained at 40 kHz than at 20 kHz. This is due to the increased oscillation frequency of the horn, which accelerates the transformation from ACP to HAp. The maximum specific surface area for HAp particles synthesized at 40 kHz was 115 m²/g for a reaction time of 5 min.

Figure 8 shows FE-SEM micrographs of HAp particles synthesized at 40 kHz. The particles have sizes of about 30 nm and a spindle shape. In the case of the reference HAp specimen synthesized by stirring, the particles were also spindle shaped but their average size was about 50 nm.

4. Summary

This study investigated the synthesis of fine HAp particles in a liquid-phase reaction under ultrasound irradiation. At an ultrasound frequency of 20 kHz, ACP was formed in the initial stage of the reaction, and Ca²⁺-deficient HAp was then formed by crystallization of ACP. The specific surface area of HAp synthesized at a Ca/P atomic ratio of 2.00 for 10 minutes was 130 m²/g and the average particle size was determined to be 30 – 50 nm. At 40 kHz, HAp particles formed more rapidly than at 20 kHz, and their sizes were smaller. Thus, ultrasound irradiation is capable of producing fine HAp particles with specific surface areas of over 100 m²/g and is therefore a very promising method for biomaterials and ion-exchange material

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