PREPARATION OF LARGE-SIZED HYDROXYAPATITE WHISKERS USING CALCIUM TRIPOLYPHOSPHATE

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Abstract: Hydrothermal methods are useful for preparation of hydroxyapatite (HAp) whiskers. In particular, the method utilizing tripolyphosphate compound as a starting material has an advantage in that the whiskers can be prepared with high production efficiency at relatively low hydrothermal temperature. In the present work, large-sized HAp whiskers of 50 – 85 µm in length were prepared by a hydrothermal treatment of calcium tripolyphosphate using a nitric acid to adjust the pH value before the reaction at 140°C for 24 h. The whisker length was controlled by content of the nitric acid. Formation of by-products could be inhibited by addition of a trace amount of titanium dioxide.

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INTRODUCTION

Recently, calcium phosphate porous materials with an excellent continuous pore structure have received attention as a bone filler or a scaffold for regenerative medicine using tissue engineering. The pore structure plays an important role in integration ability with living bone; the tissues, the blood vessels or the cells surrounding the materials can be easily invaded and the new bone may form in them when they are implanted in a defect of living bone.\(^{[1-3]}\)

Hydroxyapatite (HAp) whisker is expected to be applied to the porous materials by utilizing its morphology; the materials may be prepared by interlocking HAp whiskers one another. HAp is an inorganic component of the hard tissue and has excellent biocompatibility.

HAp whiskers can be easily prepared using hydrothermal methods.\(^{[4-11]}\) Their sizes have been reported to be in the range of 90 nm – 50 µm. In particular, large-sized HAp whiskers of more than 30 µm are derived from low concentration of starting materials at relatively high temperature (\(\geq 200°C\)).

A tripolyphosphate compound is useful for the hydrothermal synthesis of HAp whiskers\(^{[11]}\); it plays an important role in supply of orthophosphate ions for formation of HAp at low temperature; the hydrolysis temperature of the tripolyphosphate ion to orthophosphate ion is relatively low (\(>120°C\)). The tripolyphosphate ion can be utilized for the high production efficiency of monodispersed HAp whiskers; the ion can be easily reacted with calcium ion of another source for HAp formation to form calcium tripolyphosphate gel. Both of the starting materials and the products are solid, and coexisting ionic concentration is maintained low in the reactant liquid during the hydrothermal treatment and the monodispersed crystals may be obtained even when the loading of starting materials is high to prepare a large amount of product.

The reaction during this hydrothermal treatment using the calcium tripolyphosphate gel progresses as follows: the pH value of the gel decreases during the reaction, since protons generate with the hydrolysis of the tripolyphosphate ions to orthophosphate ions. For formation of HAp, a buffer should be added to the gel to neutralize the protons and to prevent formation of the dicalcium phosphate anhydrous (DCPA), which shows the lowest solubility among calcium phosphate compounds in the range of pH \(\leq 4\) as reported by Brown \textit{et al.}\(^{[12,13]}\) The effective buffer for this method was reported to be 2-propanol.\(^{[14]}\) Using 2-propanol as a buffer, the pH value during the reaction could be controlled in the range of 4 to 5, and HAp whiskers of 30 – 50µm in length could be obtained.

\[
\text{Ca}_3(\text{P}_2\text{O}_7)\text{O}_2\ + 5\text{Ca}^{2+} + 6\text{H}_2\text{O} \\
\rightarrow 10\text{Ca}^{2+} + 6\text{PO}_4^{3-} + 2\text{OH}^- + 10\text{H}^+ \\
\rightarrow \text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2 + 10\text{H}^+ \quad (1)
\]

In the present work, our purpose is to control the size of HAp whiskers and to obtain the large-sized HAp whiskers of more than 50 µm in length to be applied to preparation of the porous materials. Our approach is to control the pH of the liquid during the hydrothermal reaction using tripolyphosphate ion; the pH before the hydrothermal reaction is in the acid range controlled by a nitric acid. In the controlled pH range, the solubility of HAp is high and HAp...
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whiskers grow easily.

MATERIALS AND METHODS

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

\[
2\text{Na}_5\text{P}_3\text{O}_{10} + 10\text{Ca(NO}_3\text{)2} \rightarrow \text{Ca}_3(\text{P}_3\text{O}_{10})_2 \downarrow + 5\text{Ca(NO}_3\text{)2} + 10\text{NaNO}_3
\]  

(2)

2-propanol was included in the gel liquid as a buffer to keep pH > 4 after hydrothermal treatment and to restrict formation of DCPA. [14] A 0.1 or 1.0 mol/L HNO₃ solution was added to the gel liquid prior to starting the reaction for adjustment of pH. The gel liquid included 125 mmol/L of calcium nitrate, 25 mmol/L of sodium tripolyphosphate, 30 vol% of 2-propanol and 5 ~ 200 mmol/L HNO₃. When the liquid included HNO₃ of 100 ~ 200 mmol/L, the liquid became homogeneous solution due to the gel dissolution.

In order to examine effect of TiO₂ addition on enhancement of HAp formation, TiO₂ sol consisting of 10.5 wt% TiO₂ and 0.2 wt% NH₃ was included in the water before formation of the calcium tripolyphosphate gel.

After the gel or solution was stirred for 30 minutes to achieve the equilibrium, the pH value of the liquid was measured as an initial pH. Forty mL of the liquid were 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 24 h at 140 °C, and then cooled quickly in air. The products were collected by a suction filtration and washed several times with deionized water. The pH value of the liquid was measured as a final pH. After the resulting products were dried at 70 °C for 24 h under a reduced pressure, their crystalline phases were identified by X-ray diffractometry (XRD). The morphology of the product was observed with a scanning electron microscope (SEM). Average length of the whiskers obtained were determined by 20–30 products sampled randomly in the SEM photograph.

RESULTS AND DISCUSSION

Fig. 1 shows the initial and the final pH values, which are the pH values of the liquid before and after the hydrothermal treatment, respectively. The initial pH values have a tendency to decrease with increasing the nitric acid concentration. On the other hand, the final pH values are independent on the nitric acid concentration and they are in a range from 4.2 to 4.6. The result shows that the buffer of 2-propanol is not broken even when 200 mmol/L nitric acid are involved in the liquid prior to the hydrothermal treatment. The final pH value is an important guideline to obtain HAp, since it has been reported that calcium phosphate compound having the lowest solubility depends on pH value of reactant liquid. [12,13] The most stable compound in pH > 4 is HAp, whereas that in a pH < 4 is DCPA.

Fig. 2 shows the XRD patterns of products after hydrothermal treatment of the liquids containing nitric acid. Crystalline phases in the obtained products are suggested to be influenced by the concentration of nitric acid. HAp can be obtained with a trace amount of DCPA using the liquid with the low concentration of nitric acid (≤50 mmol/L), as shown in Fig. 2 (a) ~ (d).

Fig. 3 shows the relationship between the nitric acid concentration and the XRD peak intensity ratio of (300)/(002) for the products which are identified as HAp. The intensity ratio increases with increasing nitric acid concentration. Fig. 4 shows SEM photographs of these products. Figs. 3 and 4 suggest that the products are HAp whiskers elongated along c-axis. Large-sized HAp whiskers are found to be derived from calcium tripolyphosphate liquid including 50 mmol/L nitric acid and their average length is about 65 μm, as shown in Fig. 4 (d).

Fig. 5 shows average length and aspect ratio of the HAp whiskers derived from the liquid containing nitric acid. The average length increases with increasing of the nitric acid concentration, while the aspect ratio is independent on the concentration. This result indicates that HAp whiskers grow largely in the liquid with low initial pH. It has been reported that solubility of HAp depends on pH of aqueous solution.
and HAp has high solubility in the acid range. [12,13] Since supersaturation concerning HAp is low in the liquid where the solubility of HAp is high, HAp nucleation does not actively occur.

By addition of the excess amount of nitric acid, DCPA forms in the products. It has been reported that HAp nucleation is enhanced on a hydroxyl group of TiO$_2$. [15,16] TiO$_2$ addition into the liquid was examined for enhancement of HA whisker formation. Fig. 6 shows XRD patterns of the products derived from calcium triplyphosphate liquids containing 200 mmol/L nitric acid and various amounts of TiO$_2$. The XRD patterns show that the by-product decreases with increasing the content of TiO$_2$; HAp without by-products can be obtained using 1.79 mmol/L TiO$_2$. As mentioned above, the pH value during the hydrothermal reaction influences the crystalline phase of the obtained products. When 0, 1.07 and 1.79 mmol/L titanium dioxide were included in the liquid, the initial pH values of all samples are the same value of 1.0 and the final pH values are 4.3–4.4. The initial and final pH values are independent on TiO$_2$ content. The effect of TiO$_2$ addition is suggested to be due to the enhancement of HAp nucleation; since the activation energy for HAp formation is larger than that for DCPA formation [17]. DCPA is easier to form in the liquid at the initial pH of 1.0. When TiO$_2$ is included to the reactant liquid, the HAp nucleation would be enhanced to form on TiO$_2$ particle surface.

Fig. 7 shows the SEM photographs of these products. The morphologies of the products are almost same and their average sizes are about 85 μm in length.

CONCLUSION

In the present work, we could successfully obtain the large-sized HAp whiskers using the hydrothermal treatment of calcium triplyphosphate liquid containing nitric acid.

1) The size of the HAp whiskers was controlled by the content of nitric acid.

2) HAp whisker formation was enhanced by TiO$_2$ addition in the liquid. Large-sized HAp whiskers of 85 μm in length could be prepared without by-products from calcium triplyphosphate liquid containing a trace of TiO$_2$.

These HAp whiskers are believed to be significant for fabrication of a porous material with an excellent continuous pore structure suitable for the biomaterials, such as a bone filler or a bone tissue engineering scaffold.

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Fig. 4 SEM photographs of products derived from the liquid 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 nitric acid and (b-d) with nitric acid. The nitric acid concentrations are (b) 5mmol/L, (c) 10mmol/L and (d) 50mmol/L.

Fig. 5 Changes in average of whisker length and aspect ratio of products derived from the liquid consisting of 125 mmol/L-calcium nitrate, 25 mmol/L-sodium tripolyphosphate and 30 vol% 2-propanol at 140 °C for 24 h as a function of the nitric acid concentration. ● and △ present averages of the length and the aspect ratio, respectively.
Fig. 6 XRD patterns of products derived from the liquids consisting of 125 mmol/L-calcium nitrate, 25 mmol/L-sodium tripolyphosphate and 30 vol% 2-propanol and 200 mmol/L-nitric acid at 140 °C for 24 h (a) without TiO$_2$ and (b, c) with TiO$_2$. TiO$_2$ contents are (b) 1.07 mmol/L and (c) 1.79 mmol/L. △ and ▽ present DCPA and HAp, respectively.

Fig. 7 SEM photographs of products derived from the liquids consisting of 125 mmol/L-calcium nitrate, 25 mmol/L-sodium tripolyphosphate and 30 vol% 2-propanol and 200 mmol/L nitric acid at 140 °C for 24 h (a) without TiO$_2$ and (b, c) with TiO$_2$. TiO$_2$ contents are (b) 1.07 mmol/L and (c) 1.79 mmol/L.
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