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Large-sized hydroxyapatite whiskers derived from calcium tripolyphosphate gel

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Abstract

Hydrothermal methods using calcium phosphate gels as precursor have an advantage in high production efficiency of hydroxyapatite (HAp), but almost no large-sized HAp has been obtained so far. In the present work, large-sized HAp whiskers were prepared by a hydrothermal treatment of calcium tripolyphosphate gel controlled at pH 4–6 using various alcohols at 140 °C for 24 h. Long HAp whiskers of 30–50 μm in length were successfully prepared using 2-propanol; their sizes were several ten times larger than those prepared via conventional gel processes. The whisker length and aspect ratio were controlled by content of additive solvents with high specific dielectric constant.
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Keywords: Hydrothermal method; Hydroxyapatite; Whisker; Alcohol; Calcium tripolyphosphate gel

1. Introduction

Recently, a great deal of attention is being paid to regenerative medicine using tissue engineering. It has a great advantage in that the materials combined with cells restore the internal organs positively and regenerate the injured site finally. Tissue engineering is also expected to be applied to hard tissues of living body. Scaffolds play an important role in the tissue engineering; they should have excellent biocompatibility and the pore structure where cells and/or blood vessels can be easily proliferated and/or made in the materials.[1–3]

Hydroxyapatite (HAp) whiskers are expected to be applied to the scaffold for the tissue engineering, since HAp is the inorganic component of the hard tissue and the porous materials having large porosity may be prepared using the whiskers. HAp whiskers can be easily prepared using hydrothermal methods. Two important routes have been reported; one is a homogeneous precipitation method using an agent such as EDTA–Ca complex solution,[4–8] and the other is a method using calcium phosphate gels as the starting materials utilizing reactions such as dissolution–reprecipitation and hydrolysis in the gels.[9–12]

In general monodispersed whiskers need to be prepared by control of the coexisting ionic concentration. When the ionic concentration increases in the electrolytic solution, a repulsive force between the crystal nuclei decreases. If the repulsive force is smaller than a van der Waals force between the crystal nuclei, the aggregation of the crystal nuclei may proceed and the obtained whiskers have no tendency to be monodispersed. On the other hand, if the repulsive force is larger than a van der Waals force between the crystal nuclei, the obtained whiskers tend to be monodispersed.

In the case of the hydrothermal method using gels as starting materials, both of the starting materials and the products are solids. Ionic concentrations are maintained low in the reactant gel during the hydrothermal treatment and the monodispersed crystals may be obtained even when the loading of starting materials is high to prepare the large amount of products. As a result, the method is advantage in the high

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production-efficiency for the preparation of the monodispersed whiskers. However, it is not easy to prepare the large-sized HAp whiskers using the conventional methods using gels.[9–12]

In the hydrolysis method using calcium tripolyphosphate gel, the length of the obtained HAp whiskers was less than 5 μm.[12] The reaction during this hydrothermal treatment progresses as follows.

The pH value of the gel decreases during the reaction, because the protons generate with the hydrolysis of calcium tripolyphosphate gel to orthophosphate ions. For formation of HAp, an alkali agent should be added to the gel to neutralize the proton and to prevent the formation of the dicalcium phosphate anhydrous (DCPA), which show the lowest solubility among calcium phosphate compounds in the range of pH <4 as reported by Brown and co-workers[13,14] Since the pH during the reaction was in the basic range of pH 8–10 due to the addition of ammonia as an alkali agent, the solubility of HAp is relatively small and the crystal growth rate is not high.

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

In the present work, our approach for preparation of large-sized HAp whiskers is to maintain the pH value of the reactant gel from 4 to 6 during the hydrothermal treatment using calcium tripolyphosphate gel. In order to buffer the pH of the reactant gel, the different amphiprotic solvents were examined as the buffer additives. The widely used buffers (e.g. acetate acid) having carboxyl groups, easily adsorb on the surface of HAp crystals, and it may inhibit the crystal growth of HAp. The objective of the study is to prepare the large-sized HAp whiskers of more than 10 μm in length by utilizing the hydrothermal method of the gel, which has an advantage in the high production efficiency.

2. Experimental procedure

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 of HAp stoichiometric atomic ratio as follows:

$$2Na_5P_3O_{10} + 10Ca(NO_3)_2$$
$$\rightarrow Ca_5(P_3O_{10})_2 \downarrow + 5Ca(NO_3)_2 + 10NaNO_3$$

The desired amount (10–50 vol.%) of water-soluble non-aqueous solvents, such as methanol, ethanol, 1-propanol and 2-propanol was added to the gel prior to starting of the reaction. The gel included 0.125 mol/L of calcium ion, 0.025 mol/L of tripolyphosphate ion and the desired amount of the additive solvents. After the gel was stirred for 30 min to achieve the equilibrium, the pH 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 in 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 1day under a reduced air pressure using an air-removal pump, their crystalline phases were identified by X-ray diffractometry (XRD) (RU-200, Rigaku, Japan). The morphology of the products was observed with a scanning electron microscope (SEM) (S-2500, Hitachi, Japan). The average length and aspect ratio of whiskers were determined by randomly sampling 20–30 HAp whiskers in the SEM photograph of the product.

3. Results and discussion

Table 1 shows the initial and the final pH values, which are the values of the gel before and after the hydrothermal treat-

Table 1
Initial and final pH values of the gels consisting of 0.125 mol/L of calcium nitrate and 0.025 mol/L of sodium tripolyphosphate including methanol, ethanol, 1-propanol, 2-propanol, 2-methyl-1-propanol, 2-methyl-2-propanol and 1,4-dioxane

Additive	Content (vol.%)	Initial pH	Final pH
None	–	5.4	3.2
Methanol	10	5.2	2.9
	20	5.0	2.7
	30	4.9	3.5
	40	4.9	3.5
	50	4.8	3.7
Ethanol	10	5.1	3.6
	20	4.9	3.6
	40	4.7	3.9
	50	4.7	4.3
1-Propanol	10	5.0	3.0
	20	4.9	3.7
	30	4.9	3.9
	40	4.8	4.1
	50	4.7	4.5
2-Propanol	10	5.1	3.9
	20	4.9	4.2
	30	5.0	4.6
	40	4.7	4.9
	50	4.6	6.2
2-Methyl-1-propanol	10	5.0	2.9
	20	5.1	3.8
	30	5.0	3.7
	40	5.0	3.8
	50	4.8	3.9
2-Methyl-2-propanol	20	4.9	3.7
	30	4.8	3.6
	40	4.7	3.7
	50	4.6	3.6
1,4-Dioxane	10	5.1	3.3
	20	5.0	3.3
	30	4.9	3.3
	40	4.8	3.4
	50	4.7	3.6

ment, resepectively. These initial pH values are in a range from 4.6 to 5.4. On the other hand, there are the relatively large changes in the final pH values, which are the values of the gels after the hydrothermal treatment. They are in the range from 2.7 to 6.2. The pH value of the gel changes during the hydrothermal reaction, because protons generate with the hydrolysis of calcium tripolyphosphate gel to orthophosphate ions. Using some alchols as an additive, they buffer the generated protons and prevent the decrease of pH value during the reaction. The final pH values have a tendency to increase with increasing the additive content.

Fig. 1 shows the XRD patterns of products after hydrothermal treatment of the various gels. The crystalline phases in the obtained products are suggested to be influenced by the final pH values. The amount of DCPA in the products decreased with increase in the final pH values. This figure shows that a large amount of HAp can be obtained when the final pH values are above 3.9. It has been reported that the compound having the lowest solubility among calcium phosphate in the pH range above around 4 is HAp, whereas that in the pH range below around 4 is DCPA.[13,14]

Fig. 2 shows the typical morphologies of the products, which are prepared using 2-propanol as an example. The product derived from the gel without additives consists of plate-like particles, which are identified as DCPA by XRD analysis (Fig. 1a), as shown in Fig. 2a. The needle-like

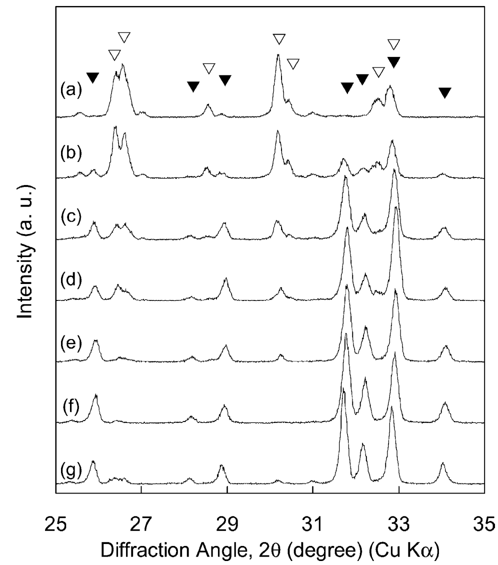

Fig. 1. XRD patterns of products by hydrothermal treatment of the gels consisting of 0.125 mol/L of calcium nitrate and 0.025 mol/L of sodium tripolyphosphate at 140 °C for 24 h at various final pH. The final pH values are (a) 3.2 [without additive], (b) 3.5 [40 vol.% methanol], (c) 3.9 [10 vol.% 2-propanol], (d) 4.2 [20 vol.% 2-propanol], (e) 4.6 [30 vol.% 2-propanol], (f) 4.9 [40 vol.% 2-propanol] and (g) 6.2 [50 vol.% 2-poropanol], where amount and kind of additives are presented in the square bracket. In the figure ▽ and ▼ present DCPA and HAp, respectively.

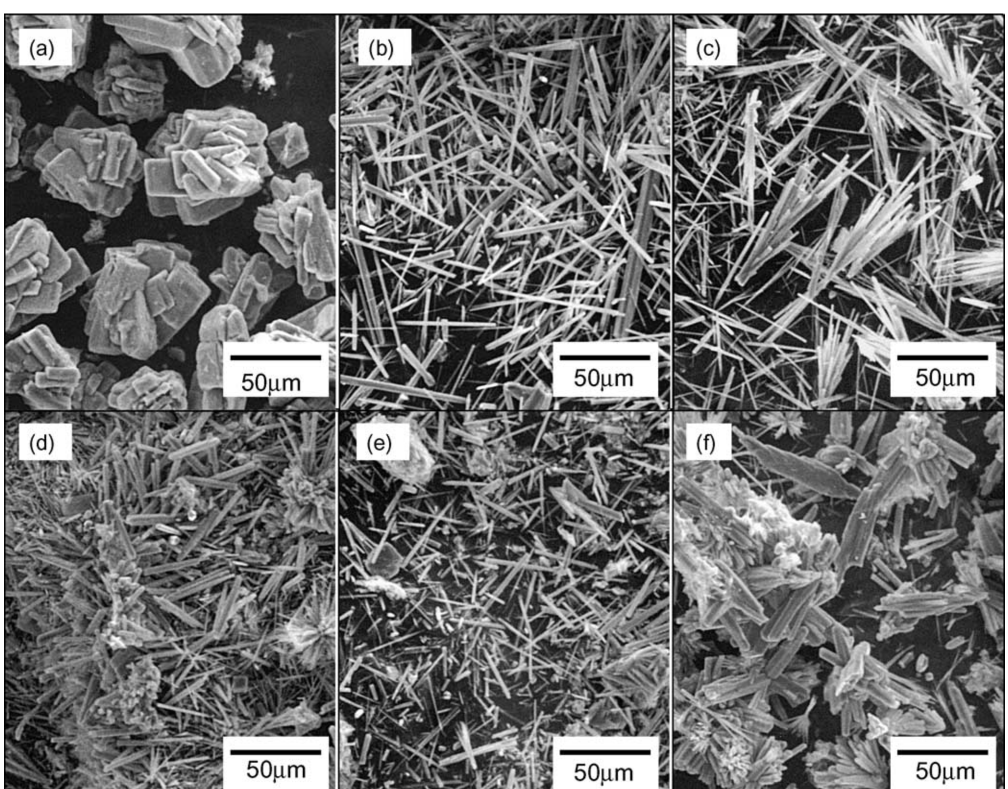

Fig. 2. SEM photographs of products by hydrothermal treatment of the gels consisting of 0.125 mol/L calcium nitrate and 0.025 mol/L sodium tripolyphosphate at 140 °C for 24 h (a) without an additive and including 2-propanol of (b) 10 vol.%, (c) 20 vol.%, (d) 30 vol.%, (e) 40 vol.% and (f) 50 vol.%.

Table 2
Averages of whisker length and aspect ratio of products by hydrothermal treatment of the gels consisting of 0.125 mol/L of calcium nitrate and 0.025 mol/L of sodium tripolyphosphate at 140 °C for 24 h including ethanol, 1-proapnol and 2-propanol, and products prepared via a conventional gel process

Additive	Content (vol.%)	Whisker length (μm)	Aspect ratio
Ethanol	40	47	16
	50	50	18
1-Propanol	40	46	16
	50	53	17
2-Propanol	10	46	16
	20	48	18
	30	32	13
	40	30	11
	50	33	6
2-Methyl-1-propanol	50	30	13
Prepared using a conventional gel process	–	2	8

whiskers of 30–50 μm in length in Fig. 2b–f are identified as HAp by XRD measurement (Fig. 1c–g).

Table 2 shows the average lengths and average aspect ratios of HAp whiskers derived from the gel including various additives. In the present work, the sizes of all products derived from the gels of which the final pH value is between 4 and 6 are several tens times larger than those prepared via some conventional gel processes. The sizes of the products prepared via the conventional gel process using an alkali agent was reported to be less than 5 μm.[12] The pH value during the hydrothermal treatment can be maintained between 4 and 6 by utilizing the buffer ability of the additives and the pH range is lower than that in the conventional method. When the degree of supersaturation concerning a crystalline phase is low in the solution, the small numbers of nuclei have a tendency to form and grow. On the other hand, when the degree of supersaturation is high, the large numbers of nuclei form and they may be not easy to grow largely. The sizes of HAp whiskers may be controlled by the solubility of HAp in the reactant pH range. The large-sized HAp whiskers can be obtained in the pH range from 4 to 6, where the solubility of HAp is relatively high.

Averages of the length and aspect ratio of the HAp whiskers are shown in Fig. 3 as a function of specific dielectric constant of the additive. The whisker length and the aspect ratio have a tendency to increase with increasing the specific dielectric constant. The solubility of HAp whisker is relatively high in the presence of the additive with high specific dielectric constant.[15] The specific dielectric constant of the gels including the additives is also controlled by the content of the additive. Fig. 4 shows the changes in the whisker length and aspect ratio of the products as a function of 2-propanol amount in the gel. The length and the aspect ratio decrease with increasing the 2-propanol amount.

In the case of 2-propanol addition, the relatively monodispersed whiskers could be obtained when the content was low,

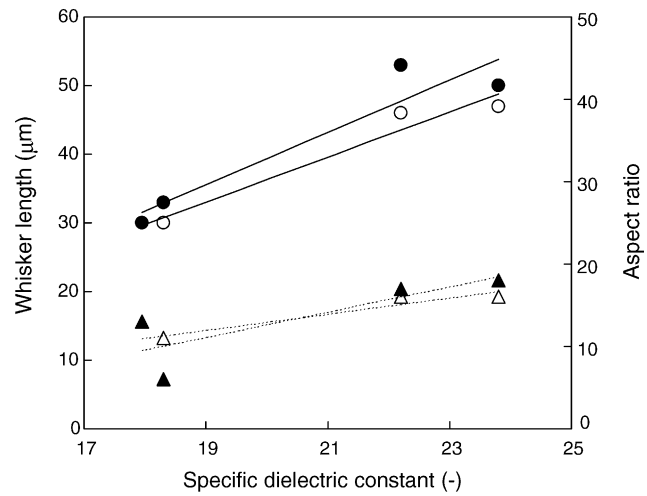

Fig. 3. Whisker lengths and aspect ratios of products by hydrothermal treatment of the gels consisting of 0.125 mol/L of calcium nitrate and 0.025 mol/L of sodium tripolyphosphate at 140 °C for 24 h as function of specific dielectric constant of additives. In the figure, (○, △) and (●, ▲) present 40 and 50 vol.% addition of the additives, and (○, ●) and (△, ▲) present whisker length and aspect ratio, respectively.

as shown in Fig. 2b–f. However, the morphology of HAp was irregular when the gel included 50 vol.% 2-propanol. The final pH value is closely related with the 2-propanol amount and the pH value decreases with decreasing the 2-propanol content. By the addition of the low content in the range from 10 to 30 vol.%, where the pH value of the reactant gel is relatively acidic and also in the range of HAp precipitation, the small number of monodispersed HAp nuclei may form and grow homogeneously, since the pH range of the reactant gel is not close to neutral and it is far from the isoelectric point of HAp. On the other hand, in the case of 50 vol.% 2-propanol,

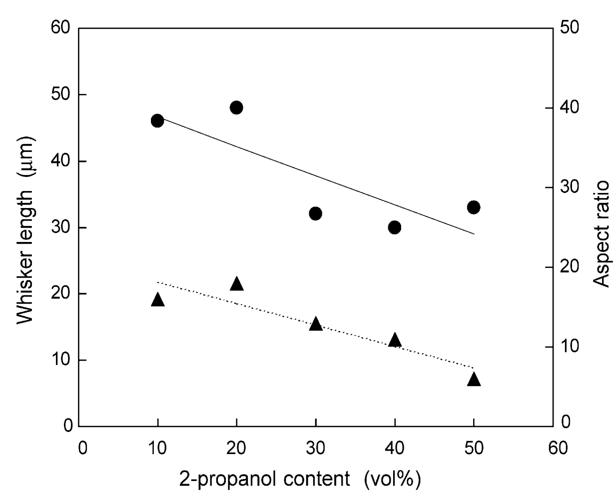

Fig. 4. Whisker lengths and aspect ratios of products by hydrothermal treatment of the gels consisting of 0.125 mol/L of calcium nitrate and 0.025 mol/L of sodium tripolyphosphate at 140 °C for 24 h as function of different content of 2-propanol. In the figure, ● and ▲ present whisker length and aspect ratio, respectively.

the final pH value is close to neutral and HAp nuclei are suggested to be aggregated; the HAp may have a tendency to grow irregularly, resulting in formation of various shaped crystals.

4. Conclusion

The large-sized HAp whiskers could be successfully derived from calcium tripolyphosphate gel using ethanol, 1-propanol, 2-propanol and 2-methyl-1-propanol under the hydrothermal condition. These solvents could buffer the pH value of the reactant gel during the hydrothermal treatment and the pH values were held in the range from about 4 to 6. The sizes of HAp whiskers were 30–50 μm in length and these are several times larger than those of the whiskers prepared via a conventional gel process using an alkali agent as the pH adjustment. These HAp whiskers are believed to be applied for the fabrication of a porous material with high porosity suitable for the biomaterials.

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