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Fluoride ion-promoted reaction of β-tricalcium phosphate to fluoridated hydroxyapatite

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Abstract

Solvothermal reaction of β-tricalcium phosphate (β-TCP) [$Ca_3(PO_4)_2$] with ammonium fluoride in water-1-octanol biphase proceeds to afford fluoridated hydroxyapatite (FHAp) [$Ca_{10}(PO_4)_6(OH)_{2(1-x)}F_{2x}$] quantitatively. It was found that FHAps with various fluoride contents were more easily prepared under mild reaction conditions and that higher crystallinity of FHAp was obtained, compared with the reaction of α-TCP with fluoride ions. The solvolysis reaction of β-TCP did not proceed without fluoride ions, whereas the reaction of α-TCP proceeded with or without fluroide ions. This indicates that the former reaction is promoted by fluoride ions. © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Fluoridated apatite; β-Tricalcium phosphate; Solvothermal reaction; Fluoride ion; Biphasic system

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1. Introduction

It is known that fluorine is one of the elements contained in biological apatites in trace amounts and that it is closely related to the crystallinity and solubility of the apatites [1,2]. Thus, along with hydroxyapatite (HAp) fluoridated hydroxyapatite (FHAp) is a biologically interesting material. FHAp has a hydroxyapatite structure in which the OH groups are partially replaced with F^- [$Ca_{10}(PO_4)_6(OH)_{2(1-x)}F_{2x}$], but it is not easily prepared by the fluoride replacement reaction of HAp [2]. In general, FHAp is synthesized by a sol–gel method from a mixture containing Ca^{2+}, PO_4^{3-}, and F^- components [3,4]. FHAp is also prepared by thermal reaction of tricalcium phosphate (TCP) [$Ca_3(PO_4)_2$] and CaF_2 over 900°C [5,6]. On the other hand, for conversion of tricalcium phosphate to hydroxyapatite under mild reaction conditions below 100°C it is known that solvothermal reaction of α-tricalcium phosphate (α-TCP) occurs in basic water but that of β-tricalcium phosphate (β-TCP) does not [7]. According to this line, it has been reported that the solvothermal reaction of α-TCP with ammonium fluoride in water proceeds to form FHAp, but a similar reaction of β-TCP has not been reported as far as we know [8].

We have previously reported that the solvothremal reaction in a water-1-octanol biphasic system is an efficient method for controlling the crystal sizes and forms of apatites by the crystal size of the used α-TCP [9,10]. And we have recently found that not only α-TCP but also β-TCP were solvolyzed to the apatite form in the presence of fluoride ions in the biphasic system [11,12]. We now report a synthesis of fluoridated hydroxyapatite by the solvothermal reaction of β-TCP with ammonium fluoride in water-1-octanol biphase.

$$NH_4F + \underset{\beta\text{-TCP}}{Ca_3(PO_4)_2} \xrightarrow[H_2O\text{-1-octanol}]{} \underset{\text{FHAp}}{Ca_{10}(PO_4)_6(OH)_{2(1-x)}F_{2x}}$$

2. Results and discussion

There are α- and β-forms of the crystal structure in tricalcium phosphate (TCP). The β-TCP crystal structure (rhombohedral space group *R*3*C*) is not looser than the high temperature-stable structure of α-TCP (monoclinic space group $P2_1/a$) and has lower internal energy and, therefore, lower reactivity in water [2]. Solvothermal reaction of

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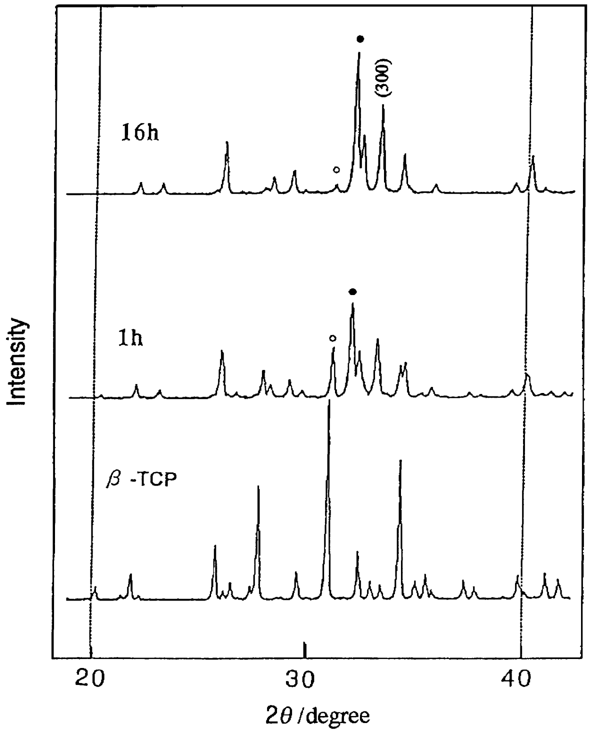

Fig. 1. Variation of powder X-ray diffraction patterns in the conversion process of β-TCP to FHAp (with 0.18 molar ratio of NH_4F/TCP at 70°C).

β-TCP powder to hydroxyapatite (HAp) in aqueous ammonia solution (pH = 11) did not proceed at 90°C for 1 day, whereas the reaction of α-TCP to HAp proceeded under similar conditions, as reported by Monma [7]. On the contrary, a heterogeneous reaction of β-TCP powder with aqueous ammonium fluoride solution (NH_4F/TCP molar ratio = 0.18) in 1-octanol proceeded at 70°C for 24 h to afford the apatite form quantitatively. The reaction was followed by variation of powder X-ray diffraction patterns of the solid reaction mixtures as shown in Fig. 1. This indicates that the solvothermal reaction of β-TCP is induced by the fluoride ion.

With various amounts of ammonium fluoride, reactions of β-TCP to the apatite form completely proceeded in water-1-octanol biphase at 40–70°C. Fig. 2 shows the reaction profiles in the cases of 0.18 and 0.70 molar ratio of NH_4F/TCP at various reaction temperatures. The relative conversion of TCP to apatite was estimated by the height ratio of each maximum peak of β-TCP and apatite in X-ray diffraction patterns of the solid reaction mixtures (the marked peaks of '○' β-TCP and '•' apatite as shown in Fig. 1). The reaction rate of β-TCP increased with increasing reaction temperature. The rates also depended on the fluoride amount; the rates at 0.70 molar ratio of NH_4F/TCP were faster than those at 0.18 of NH_4F/TCP. At 70°C with NH_4F/TCP = 0.70 the conversion of β-TCP was over 95% yield after 4 h, which had maximal reactivity.

We summarized the reaction conditions and the chemical composition of the obtained apatite in Table 1. Apatite crystals are hexagonal with space group $P6_3/m$ [2]. From the shifts of (300) reflection peak in powder X-ray diffraction patterns and thus the shortening of a axis lattice constant calculated from these peaks, it was confirmed that the fluoride incorporation occurred at the OH site of apatite and that the obtained products were fluoridated hydroxyapatite (FHAp) represented by $Ca_{10}(PO_4)_6(OH)_{2(1-x)}F_{2x}$ [13,14]. The fluoride amount incorporated to FHAp depended on the used amount of NH_4F. By controlling the amount of NH_4F, FHAps with various fluoride contents can be obtained.

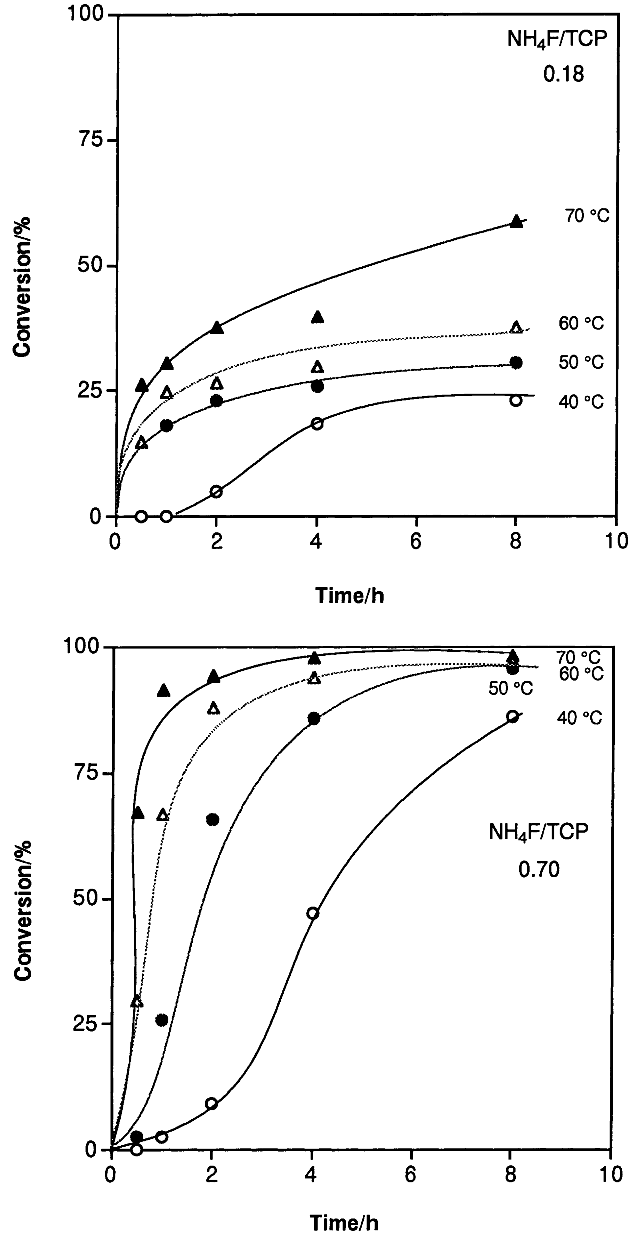

Fig. 2. Reaction profiles of β-TCP to FHAp with 0.18 and 0.70 molar ratios of NH_4F/TCP.

When a larger amount of fluoride (NH_4F/TCP = 0.70) than the stoichiometric amount (NH_4F/TCP = 0.60) to

Table 1
Analyses of FHAps obtained from the reaction of β-TCP and NH_4F

Reaction conditions				Analysis of the obtained FHAp					
Starting materials NH_4F/TCP, molar ratio	Reaction temperature (°C)	Reaction time (h)	Final pH	F content (mmol/g)	Ca content (mmol/g)	P content (mmol/g)	Ca/P molar ratio	Lattice constant *a*-axis[b] (nm)	F content: x estimated as $Ca_{10}(PO_4)_6(OH)_{2(1-x)}F_{2x}$[d]
0	70	24		–	–	–	–	–	–
0.18	70	24	7.0	0.443	9.760	6.062	1.61	0.9439	(0.22)[e]
0.35	40	72	8.4	0.820	9.773	6.033	1.62	0.9434	(0.41)[e]
0.35	70	24	7.9	0.900	9.900	6.074	1.63	0.9435	(0.45)[e]
0.70	40	72	9.1	1.690	9.842	5.893	1.67	0.9383	0.85
0.70	70	17	8.8	1.823	9.939	5.916	1.68	0.9386	0.92
0[a]	70	24		0	10.113	6.401	1.58	0.9440	0
TCP calcd. for $Ca_3(PO_4)_2$				0	9.671	6.447	1.50		–
HAp calcd. for $Ca_{10}(PO_4)_6(OH)_2$				0	9.995	5.973	1.67	0.9417[c]	0
FAp calcd. for $Ca_{10}(PO_4)_6F_2$				1.984	9.915	5.950	1.67	0.9367[c]	1.0

[a] α-TCP was used.

[b] See Section 3.

[c] See [2]. FAp is hexagonal with space group $P6_3/m$.

[d] A slight amount of CO_3^{2-} was observed by FT-IR (ν 1460, 1410 cm^{-1}).

[e] A small amount of $(HPO_4)^{2+}$ was observed by FT-IR (ν 870 cm^{-1}). It is Ca-deficient FHAp represented by $Ca_{10-y}(HPO_4)_y(PO_4)_{6-y}(OH)_{2(1-x)-y}F_{2x}$.

forming fluoroapatite (subscript $x = 1$ in the formula) was used, the obtained FHAp showed 1.67–1.68 molar ratio of Ca/P, which corresponded to the calculated value of the apatite form. In the case, the incorporated fluoride amount attained to about 90% based on that of fluoroapatite. From FT-IR analysis, the HPO_4^{2-} group of Ca-deficient FHAp ($Ca/P = 1.61-1.63$) was detected, especially, in the cases of low molar ratios of NH_4F/TCP. A slight amount of carbonate apatite (CO_3Ap) formation was observed in all syntheses by FT-IR. No formation of CaF_2 was detected in all cases. In our preparation the formation of CO_3Ap can be suppressed by using a degassed solvent in a closed reaction system. The Ca-deficiency of FHAp can be improved by controlling pH of the reaction solution.

For preparing FHAp by the solvothermal reaction β-TCP was preferable to α-TCP. In the case of β-TCP it was found that FHAps with various fluoride contents were more easily prepared and that higher crystallinity of FHAp was obtained, compared with the case of α-TCP. For example, the reaction of β-TCP with NH_4F ($NH_4F/TCP = 0.70$) at 70°C was complete after 17 h, whereas the reaction of α-TCP was complete after 10 days. Fig. 3 shows powder X-ray diffraction patterns of FHAps obtained in these reactions. In the case of β-TCP (b) reflection peaks were sharper, indicating higher crystallinity. However, the purity of the products described above was similar to that in α-TCP. Similar results was observed in a water phase as well as in the water-1-octanol biphasic system. The detailed investigations for solvothermal reactions of both TCPs to FHAps with ammonium fluoride in a water phase will be reported in another paper [15].

Fig. 4 shows SEM pictures of the starting β-TCP powder and the obtained FHAps. It was observed that the shapes of FHAps varied with the incorporated fluoride amount. Such shape dependence on the fluoride content is observed in the case of the sol–gel method using Na_2SiF_6 instead of HF [4]. For our heterogeneous reaction, at least, it is considered that the fluoride ion participates in the formation process and the crystal growth process. In all cases the crystal sizes were controlled in 3 to 5 μm, which were larger than the starting β-TCP powder (0.5–2 μm). The crystal sizes were larger in a water-1-octanol biphasic system than that in water (1–2 μm), although there was no difference in the reaction rates and the fluoride contents of FHAps for both solvent

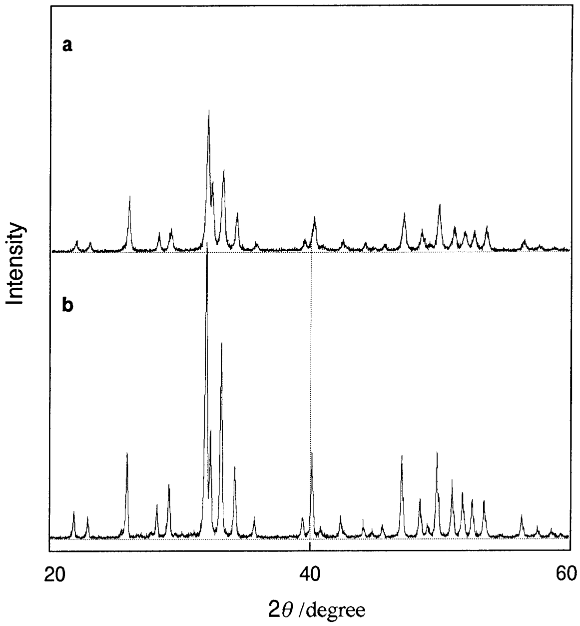

Fig. 3. Powder X-ray diffraction patterns of FHAps obtained from α-TCP (a) and β-TCP (b).

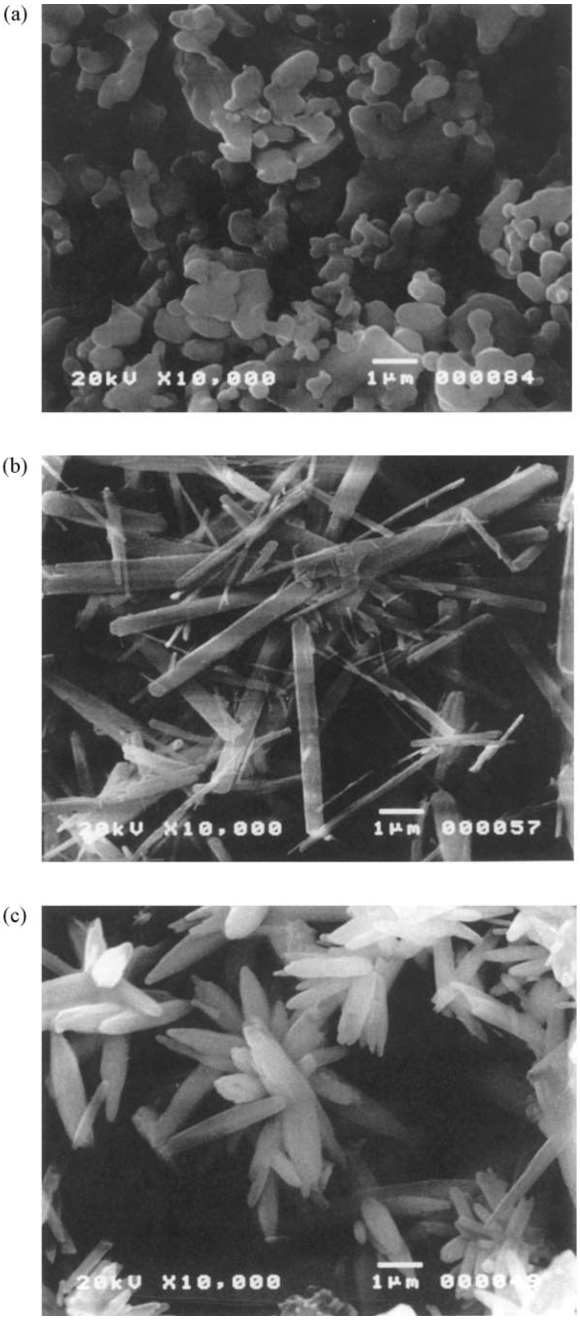

Fig. 4. SEM photograms of FHAps obtained by hydrolysis of β-TCP (a) in the presence of NH_4F; molar ratios of $NH_4F/TCP = 0.18$ (b) and 0.70 (c).

systems [15]. It is apparent that a water-1-octanol biphasic system assists the process of crystal growth.

In conclusion, it was found that solvothermal reactions of β-TCP with various amounts of ammonium fluoride in water-1-octanol biphase proceeded to afford fluoridated hydroxyapatite quantitatively. Remarkably, the obtained apatites showed high crystallinity without sintering. The solvolysis reaction of β-TCP did not proceed without fluoride ion differing from that of α-TCP, and the reaction rate increased on increasing the amount of the fluoride ion. The results indicate that it is a fluoride ion-promoted reaction. β-TCP is generally used as bone-forming components in vivo, although hydrolysis of β-TCP to apatite does not occur easily in vitro. On the other hand, it is known that a fluoride ion is absolutely necessary for forming bones together with Mg^{2+}, Fe^{2+}, Zn^{2+}, etc. [1,2,16–18]. The fluoride ion-promoted reaction process of β-TCP to apatite can be of importance in connection with the conversion process from β-TCP to apatite in vivo bone formation.

3. Experimental procedure

β-TCP was provided by Taihei Chemical Industrial Co. Ltd. β-TCP powder was passed through a 200-mesh sieve after grinding, heated at 800°C for 3 h prior to use. Heterogeneous reactions of β-TCP powder (0.620 g, 2.00 mmol) with various amounts of ammonium fluoride (0.35, 0.70, or 1.40 mmol of NH_4F) were carried out in a water-1-octanol (18 and 25 ml) biphasic system under mild heating. The fluoride amounts were used at 0.18, 0.35, or 0.70 molar ratio of NH_4F/TCP, respectively, based on 0.60 molar ratio required to form fluoroapatite $[Ca_{10}(PO_4)_6F_2]$. The relative conversion of TCP to apatite (Fig. 2) was estimated with the height ratio of each maximum peak of β-TCP and apatite in X-ray diffraction patterns of the solid reaction mixtures (the marked peaks of '○' β-TCP and '●' apatite as shown in Fig. 1). This method was confirmed by calibration with β-TCP-apatite mixtures of known composition. After stirring the reaction mixture for 4–120 h at 40–70°C, the solid products were collected by filtration, washed with ethanol and distilled water, and dried in air for 5 h at 40°C. The obtained products were identified by powder X-ray diffractometry using Rigaku Rint 2500 V with a graphite monochrometer (Cu $K\alpha_1$), and by FT-IR spectrometry using Burker IFS-113 V. The lattice parameters of the apatite structure were determined by the least-squares method using several diffraction peaks. Chemical composition analyses were carried out by the fluoride selective ion electrode method (Orion Research Inc.) and by X-ray fluorescence analysis method using Philips PW1480. The crystals were observed by scanning electron microscope (SEM) using JEOL JSM-5400S.

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