Synthesis of Sulfate-ion-substituted Hydroxyapatite from Amorphous Calcium Phosphate

Takeshi Toyama*, Shunichi Kameda and Nobuyuki Nishimiya

Department of Materials and Applied Chemistry, College of Science and Technology, Nihon University, 1-8, Kanda-Surugadai, Chiyoda-ku, Tokyo 101-8308, Japan

**Abstract**

The composition of Hydroxyapatite (HAp) is expressed by the formula Ca$_{10}$(PO$_4$)$_6$(OH)$_2$. Many reports have been published on the synthesis of HAp in which Ca ions are substituted by various cations (e.g., Sr, Ba). On the other hand, studies on the synthesis of sulfate-ion-substituted hydroxyapatite (SAp) have rarely been conducted. The present study investigated the conditions for the synthesis of SAp from amorphous calcium phosphate (ACP, Ca$_{10}$(PO$_4$)$_6$.nH$_2$O) as the starting material, which can readily incorporate various ions into its structure. Sodium sulfate (Na$_2$SO$_4$) was added to ACP, and then, the mixture was hydrothermally processed at 220°C for 3 h. SAp obtained under these conditions had a Ca-deficient-type HAp structure. The SO$_4$/PO$_4$ molar ratio in SAp increased with increasing amounts of added Na$_2$SO$_4$, reaching a maximum value of 0.5, meaning that 1/3 of the PO$_4^{3–}$ ions contained in HAp were substituted by SO$_4^{2–}$ ions.

**Keywords:** Substituted apatite; Sulfate; Amorphous calcium phosphate; Composition control; Hydrothermal process

**Introduction**

Apatite is a general term to indicate hexagonal minerals that are represented by the chemical formula M$_n$(ZO$_4$)$_6$X$_2$. Apatite of different properties can be synthesized by replacing M, Z, and X with various elements. Among others, the apatite in which M, Z, and X are Ca, P, and OH, respectively, is called Hydroxyapatite (HAp, Ca$_{10}$(PO$_4$)$_6$(OH)$_2$). HAp has good biocompatibility and protein adsorption properties and is an important compound used to produce biomaterials. Moreover, HAp has high ion-exchange capacity, and research concerning the synthesis and functionalization of HAp in which various cations are substituted by virtue of its ion-exchange capacity is underway [1]. Particularly, there are many reports on the synthesis of HAp where Ca is substituted with various cations (e.g., Sr, Ba, Pb, Cd) [2–4]. However, studies on the synthesis of HAp in which PO$_4$ is substituted with SiO$_4$, and CO$_3$ have been reported only occasionally [5–7], while the synthesis of sulfate-ion-substituted hydroxyapatite (SAp), in which SO$_4$ has been introduced, has been rarely studied.

We conducted a series of studies on the synthesis and properties of amorphous calcium phosphate (ACP, Ca$_{10}$(PO$_4$)$_6$.nH$_2$O) [8–12]. ACP is a precursor that appears in the initial stage of the formation of various calcium phosphate compounds and is easily crystallized into HAp. If HAp is crystallized in the presence of various ions, various substituted HAp species incorporating different ions can be obtained. Therefore, we investigated the conditions for the synthesis of SAp from ACP as the starting material that are effective for controlling the composition of HAp.

**Materials and Methods**

**Experimental method**

ACP was obtained by the hydrolysis of Ca(H$_2$PO$_4$)$_2$;H$_2$O. The synthesis of SAp was as follows. Sodium sulfate was added to ACP or HAp so that the weight ratio of Na$_2$SO$_4$/(ACP or HAp) was 0–6. The mixture was hydrothermally processed at 220°C for 3 h, and then, SAp was obtained after filtering, washing, and drying the processed sample. The same procedure was carried out with stoichiometric HAp as the starting material, for comparison.

*Corresponding author: Takeshi Toyama, Department of Materials and Applied Chemistry, College of Science and Technology, Nihon University, 1-8, Kanda-Surugadai, Chiyoda-ku, Tokyo 101-8308, Japan, E-mail: toyama.takeshi@nihon-u.ac.jp

Received June 27, 2013; Accepted July 17, 2013; Published September 09, 2013


Copyright: © 2013 Toyama T, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.
could be observed in the products, not even when the amount of added Na$_2$SO$_4$ was increased. However, in the cases where ACP was used as the starting material, the SO$_4$/PO$_4$ molar ratio in the products tended to increase with the amount of added Na$_2$SO$_4$. The maximum SO$_4$/PO$_4$ molar ratio was about 0.5, implying that about 1/3 of the PO$_4^{3-}$ ions in the structure of HAp were substituted with SO$_4^{2-}$ ions. The chemical formula of the product can be represented by Ca$_9$(PO$_4$)$_4$(SO$_4$)$_2$(OH)$_2$.

The X-ray diffraction patterns of the obtained products are shown in Figure 2. None of the patterns coincided with the Joint Committee on Powder Diffraction Standards (JCPDS) data for HAp (pdf#09-432), and there was no evidence for the existence of sulfate species such as gypsum. Moreover, since the crystallinity of HAp decreased with increasing SO$_4$/PO$_4$ molar ratio, it could be suggested that SO$_4^{2-}$ ions were incorporated in the structure of HAp.

**Structure of sulfate-ion-substituted hydroxyapatite**

The relation between SO$_4$ content and lattice constant, used to study the substitution of SO$_4^{2-}$ ions, is shown in Figure 3. If it is simply assumed that PO$_4^{3-}$ ions (ionic radius: 0.16 nm) and SO$_4^{2-}$ ions (ionic radius: 0.230 nm) in HAp were exchanged, there should have been a change in the lattice constant due to the difference in the ionic radii. However, the results of this experiment showed no change in the lattice constant, not even when the SO$_4$/PO$_4$ molar ratio was increased. Therefore, this result suggested that PO$_4^{3-}$ and SO$_4^{2-}$ ions were not exchanged. The lattice strain calculated by Hall's equation [13] is shown in Figure 4. The calculated lattice strain of SAp indicated that the lattice strain proportionally increased with increasing SO$_4$/PO$_4$ molar ratio. These results suggested that ions that have the same radii were substituted in the crystal lattice, although no changes in the lattice constant were detected.

The IR absorption spectra of SAp are shown in Figure 5. The HAp obtained by crystallization of ACP in deionized water (SO$_4$/PO$_4$ molar ratio: 0) showed a small, sharp absorption peak at around 3600 cm$^{-1}$ attributable to OH$^-$ ions, in addition to a strong absorption peak attributable to PO$_4^{3-}$ ions around 1000 cm$^{-1}$. Moreover, a small absorption peak at around 880 cm$^{-1}$ attributable to HPO$_4^{2-}$ ions was observed. Thus, the obtained HAp was identified as having a calcium-deficient-type HAp structure because the ACP starting material had a Ca/P atomic ratio of approximately 1.5. Furthermore, similar to HAp, an absorption peak attributable to PO$_4^{3-}$ ions was also observed in the obtained SAp, in addition to a slightly weak absorption peak at around 3600 cm$^{-1}$ attributable to OH$^-$ ions; hence, it can be inferred that SAp has an apatite structure. Moreover, the absorption at 1180 cm$^{-1}$ attributable to SO$_4^{2-}$ ions, which was absent from the spectrum of HAp, was not observed in SAp. Therefore, we considered that HPO$_4^{2-}$ ions may play an important role in the substitution of SO$_4^{2-}$ ions within the HAp structure. The ionic radius and valence of PO$_4^{3-}$ and HPO$_4^{2-}$ are different from those of SO$_4^{2-}$, whereas the ionic radius of HPO$_4^{2-}$ closely matches that of SO$_4^{2-}$ (HPO$_4^{2-}$: 0.236 nm; SO$_4^{2-}$: 0.230 nm); both anions have the same valence. Therefore, it could be suggested that SAp was formed by the substitution of SO$_4^{2-}$ and HPO$_4^{2-}$ ions, which have similar radii, in the HAp structure.

Based on the results mentioned above, the reaction for the formation of SAp using ACP as the starting material is as follows:

\[
3\text{Ca}_3(\text{PO}_4)_2\cdot n\text{H}_2\text{O} \rightarrow \text{C}_{a_9}(\text{HPO}_4)_2(\text{PO}_4)_4(\text{OH})_2 \quad \text{[Ca-deficient-type HAp]} \quad \text{(1)}
\]

\[
\text{C}_{a_9}(\text{HPO}_4)_2(\text{PO}_4)_4(\text{OH})_2 + 2\text{Na}_2\text{SO}_4 \rightarrow \text{C}_{a_9}(\text{PO}_4)_4(\text{SO}_4)_2(\text{OH})_2 + 2\text{Na}_2\text{HPO}_4 \quad \text{(2)}
\]
When using ACP, for which the Ca/P molar ratio is low, as the starting material, the first step of the reaction involves the formation of the Ca-deficient-type HAp precursor (equation 1). As the Ca-deficient-type HAp incorporates $\text{HPO}_4^{2-}$ in its structure, $\text{HPO}_4^{2-}$ and $\text{SO}_4^{2-}$ ions are exchanged, and SAp is formed (equation 2).

**Conclusion**

SAp could be synthesized using ACP, which is a precursor of HAp, as the starting material. Moreover, the amount of $\text{SO}_4^{2-}$ ions incorporated in SAp could be controlled by changing the amount of added $\text{Na}_2\text{SO}_4$, and the maximum $\text{SO}_4$/PO$_4$ molar ratio was 0.5. The chemical formula of the obtained SAp corresponded to $\text{Ca}_9(\text{PO}_4)_4(\text{SO}_4)_2(\text{OH})_2$. Moreover, SAp was considered to be produced by the substitution of $\text{HPO}_4^{2-}$ ions with $\text{SO}_4^{2-}$ ions, which have similar radii and valences.

**References**