Effect of Phase Transformations during Synthesis on the Chemical Composition and Structure of Calcium-Deficient Hydroxyapatite

N. V. Kitikova, I. L. Shashkova, Yu. G. Zonov, O. A. Sycheva, and A. I. Rat'ko

Institute of General and Inorganic Chemistry, Belarussian Academy of Sciences, ul. Surganova 9, Minsk, 220072 Belarus e-mail: kitikova@igic.bas-net.by Received October 3, 2006; in final form, March 14, 2007

Abstract—The chemical and phase changes during the precipitation of calcium-deficient hydroxyapatite from a solution of natural chalk in a mixture of phosphoric and nitric acids, with the use of aqueous ammonia as the precipitant, have been studied by potentiometric titration and physicochemical analysis. The initial solution concentration and precipitation time are shown to have a significant effect on the composition and structure of the precipitate. The processes in the solution and precipitate are interpreted in terms of the degree of protonation of phosphate ions under various conditions.

DOI: 10.1134/S0020168507100160

INTRODUCTION

The crystallization of hydroxyapatite (HA), $Ca_{10}(PO_4)_6(OH)_2$, is of considerable scientific and technological interest because HA is widely used in biomedical and other technological applications both as an individual compound and in composites. Special attention has been given to nonstoichiometric HA, whose composition can be represented by the general formula $Ca_{10-x}(HPO_4)_x(PO_4)_{6-x}(OH)_{2-x}$ with $0 \le x \le 2$. Calcium-deficient HA is an analog of biological HA, has a higher solubility [1], bioactivity, and biocompatibility [2] in comparison with stoichiometric HA, and offers good sorptive properties in chromatographic separations of bioorganic polymers [3] and considerable catalytic activity [4, 5].

The best approach for the synthesis of nonstoichiometric HA is chemical precipitation from solution [5, 6]. The mechanism of HA formation under various experimental conditions has been the subject of extensive studies because the processes involved are rather complex: HA formation in supersaturated solutions is always preceded by the precipitation of one or more intermediates [7, 8]. These include crystalline anhydrous calcium hydrogen phosphate (CHP), CaHPO₄; calcium hydrogen phosphate dihydrate (CHPD), CaHPO₄ · 2H₂O; and Ca₄H(PO₄)₃ · 2.5H₂O; also possible is the formation of amorphous tricalcium phosphate (TCP), $Ca_3(PO_4)_2 \cdot nH_2O$ [8, 9]. The precipitation sequence of these phases as a function of pH and solution composition depends not only on the solubility product of the corresponding phosphate but also on kinetic factors [7, 8]. The transformation sequence of metastable intermediates determines the composition and properties of the final reaction product. Therefore, the key to understanding the process of HA formation under various experimental conditions, in particular for the targeted synthesis of HA with controlled properties, lies in studying phase formation and its effect on the stoichiometry of the material [10].

HA is commonly precipitated by pouring together calcium nitrate and ammonium hydrogen phosphate solutions having the same pH, from 6 to 12 [5, 7], or by neutralizing a calcium hydroxide suspension with a phosphoric acid solution [6, 11]. Calcium carbonate is often used as the calcium precursor, especially in the synthesis of carbonated HA [12]. Use can also be made of Ca(OH)₂ suspensions prepared from CaO after firing calcium carbonate at 1000°C for 24 h [13]. In contrast to conventional processes, we prepared calcium-deficient HA by precipitation from a pH 1 reaction mixture based on natural chalk, using aqueous ammonia as the precipitant. The chalk was dissolved in a mixture of phosphoric and nitric acids. Nitric acid was added in order to maintain the pH value at 1, thereby preventing early formation of calcium hydrogen phosphates, which otherwise would have impeded further chalk dissolution and HA crystallization [14]. Phase formation in different stages of the reaction was studied by analyzing the products formed at the equivalence points in the pH curves obtained in the course of precipitation. As shown in many studies, the factors determining the crystallization behavior of HA include the pH and concentration of the starting solutions and the reaction time [7]. The purpose of this work was to study the effect of

KITIKOVA et al.

Final sample no.	Synthesis conditions			Intermediate	Solution parameters at the equivalence points		Characteristics of phases at the equivalence point	
	[Ca], mol/l	[H ₃ PO ₄], mol/l	$NH_3 \cdot H_2O$ introduction rate, ml/min	sample no.	рН	OH ⁻ /Ca ²⁺ molar ratio	Ca/P molar ratio	<i>S</i> , m ² /g
1	0.11	0.06	2.7*	1-1	4.2	1.95	1.74	47
				1-2	7.4	2.84	1.56	76
				1-3	9.5	5.29	1.45	88
2	0.42	0.25		2-1	3.6	0.77	1.11	16
			2.7	2-2	7.1	1.42	1.19	58
				2-3	9.5	2.84	1.40	85
3	0.70	0.42		3-1	3.2	0.57	1.22	17
			2.7	3-2	6.7	1.20	1.06	33
				3-3	9.5	2.46	1.36	87
4	0.42	0.25	4.0**	_	3.8	0.97	_	_
					6.6	1.57	—	—
					9.5	2.76	-	-
5	0.42	0.25	2.7**	-	3.8	0.86	_	_
					6.9	1.54	—	—
					9.5	2.76	-	-
6	0.42	0.25	1.3**	-	3.4	0.72	-	_
					7.1	1.36	-	-
					9.5	2.53	—	—

Table 1. Synthesis conditions and characteristics of intermediate phases in calcium-deficient HA precipitation

*10.5 M aqueous ammonia.

**5.3 M aqueous ammonia.

the initial solution concentrations and precipitation rate of the conversion of metastable intermediates to calcium-deficient HA.

EXPERIMENTAL

The calcium source used was natural chalk (96%)-pure calcite, CaCO₃).¹ In our preparations, we used the size fraction 0.09-0.25 mm.

The chalk was dissolved in a reaction vessel containing a stirrer and the electrodes of a pH meter. Calcium carbonate (10 g) was gradually added (≈ 0.1 g/min) to an appropriate amount of phosphoric acid, while maintaining the pH at 1 by adding 30% nitric acid. The initial Ca/P molar ratio in the solutions corresponded to the HA stoichiometry, 1.67. To the resultant solution was added aqueous ammonia at a constant rate (deviation within ± 0.1 ml/min), using a micropump, until the solution pH reached 9.5. During precipitation, the solution pH was visualized in the form of a potentiometric titration curve using an XY recorder. Dissolution and precipitation were conducted at a temperature of 20°C, which was maintained by a water thermostat. The synthesized samples were stored in the mother solution for 24 h, followed by washing with hot distilled water, filtration, and drying, first in air and then at 150°C for 3 h (the reaction intermediates were dried at 65° C).

We carried out several series of experiments, of which two were selected to illustrate the effects of the initial solution concentrations (series 1) and precipitation rate (series 2). The initial calcium and phosphateion concentrations in the reaction mixtures and the precipitant (aqueous ammonia) concentration and introduction rate are given in Table 1. To study the phase formation process, the reaction intermediates in series 1 were taken at pH values corresponding to equivalence points.

The structure and composition of the synthesized materials were determined by x-ray diffraction (XRD), IR spectroscopy, thermal analysis (DTA + TG), and chemical analysis. XRD patterns were collected on a DRON-3 powder diffractometer (Cu K_{α} radiation). Lattice parameters were refined using the 002, 211, 222, 213, 321, 410, and 004 reflections. IR spectra were

¹ Vitebsk oblast, Belarus.



Fig. 1. Variation in pH and derivative curves (primed numbers) for the synthesis of calcium-deficient HA (a) from solutions of different concentrations and (b) at different precipitation rates; the numbers at the curves identify the samples as referenced in Table 1; $[NH_3 - H_2O] = (a) 10.5$ and (b) 5.3 mol/l; $[H_3PO_4] = (1) 0.06$, (2, 4-6) 0.25, and (3) 0.42 mol/l; precipitation rate of (4) 4.0, (1-3, 5) 2.7, and (6) 1.3 ml/min.

measured from 400 to 4000 cm⁻¹ on a Midac Fourier transform IR spectrometer, using 2-g samples prepared as KBr pellets.

Thermal analysis was performed in a Paulik–Paulik–Erdey thermoanalytical system during heating in air from 20 to 1000°C at a rate of 10°C/min. The specific surface area S (m²/g) was determined by low-temperature nitrogen adsorption measurements. The chemical composition of solid products was determined by elemental analysis after dissolving a sample in nitric acid. Calcium was determined by back titration with Trilon B and ZnSO₄ solutions [15], and phosphorus, by the phosphovanadomolybdate spectrophotometric method [16]. The uncertainty in our determinations was estimated at ±0.02 mmol/g.

RESULTS AND DISCUSSION

Figure 1 shows potentiometric titration curves illustrating the variation in the pH of the mother solution in pseudoequilibrium with the precipitate during the introduction of the precipitant for a varied initial solution concentration and a constant rate of precipitation from solutions of various concentrations (Fig. 1a) and for a varied precipitant introduction rate at a constant solution concentration (Fig. 1b). The parameters of the solutions at the equivalence points in their titration curves and the chemical compositions of the corresponding intermediates are listed in Table 1.

The presence of a family of curves representing the precipitation process as a function of reaction time (Fig. 1b) is characteristic of systems in which the formation of primary products is followed by secondary chemical processes at the interface between the forming phase and the mother solution. The resulting precipitate has a variable composition [17]. The formation of reaction intermediates depends on the reaction conditions, as evidenced by chemical analysis, XRD, IR spectroscopy, and DTA data.

HA crystallization in dilute solutions (Table 1, sample *I*; Fig. 1a, curve *I*) is preceded by the formation of poorly crystallized TCP (Fig. 2) with a large Ca/P molar ratio (Table 1). In the IR spectra of the reaction intermediates (Fig. 3), the bands at 3580 and 630 cm⁻¹, due to constitutional OH⁻ groups, are missing, but the band around 875 cm⁻¹ attests to the presence of trace levels of the hydrogen phosphate ion. This impurity accounts for the weight loss at 330 and 720°C, due to the polymerization of the hydrogen phosphate ion [18] (Fig. 4). Raising the solution pH to 9.5 leads to the topochemical transformation of TCP to HA, as evidenced by the XRD pattern of the as-precipitated final product (Fig. 2).

Increasing the initial solution concentration causes precipitation to begin at pH 2–3 (Fig. 1a, sample 2, curve 2). The resultant well-crystallized phase had a reduced Ca/P molar ratio (Table 1) and was identified by a combination of physicochemical characterization techniques (Figs. 2–4) as CHP [19–21]. In the pH range 3.7-4.5, the plateau is broader than that in curve 1. Starting above pH 9, HA begins to form, as evidenced by extra lines in the XRD pattern (Fig. 2) and the increase in Ca/P molar ratio (Table 1). This behavior is associated with the fact that, in alkaline solutions, the hydrogen phosphate solubility is higher [22], and the dissolution of the intermediate is followed by HA crystallization.



Fig. 2. XRD patterns of reaction intermediates in samples I-3 at the (I-1, 2-1, 3-1) first and (I-2, 2-2, 3-2) second equivalence points and (I-3, 2-3, 3-3) those of the as-precipitated final product; the numbers at the curves identify the samples as referenced in Table 1; (*I*) HA, (*II*) CaHPO₄ · 2H₂O, (*III*) CaHPO₄.

Curve 3 in Fig. 1, representing the variation in pH during HA synthesis at the highest solution concentration, $[H_3PO_4] = 0.42 \text{ mol/l}$, has a different shape. In the first step, we observe the formation of an amorphous phase (Fig. 2) with a trace amount of the dihydrogen phosphate ion, $H_2PO_4^-$. The presence of this ion is evidenced by the IR spectrum, which shows, in addition to the band at 875 cm⁻¹, several features in the range 3000–3500 cm⁻¹. These latter arise from the stretching mode v(OH) and are characteristic of the spectrum of $Ca(H_2PO_4)_2 \cdot H_2O$ [20]. The presence of the dihydrogen phosphate ion is also evidenced by the endotherms at 150, $\simeq 270^{\circ}$ C, and 335°C in the DTA curve, which correspond to three-step water removal [23]. The first jump in pH is followed by a decrease, rather than by a plateau, and then by a second jump in pH, due to the formation of CHP (Fig. 2), which has a less perfect crystal structure in comparison with sample 2. Like in solutions of medium concentrations, the final step of HA formation occurs at pH above 9.0, where the intermediate, less thermodynamically stable phases dissolve, and the most stable phase, HA, is formed.

A noteworthy feature of the primary phases that form in the first step at phosphoric acid concentrations from 0.25 to 0.42 mol/l is the high concentration of NO_3^- ions, which seem to be adsorbed by the precipitate surface [10] and can be identified from the IR band at 1380 cm⁻¹, which becomes stronger with increasing initial solution concentration. Increasing the amount of the precipitant leads to washing out of the nitrate ion, which is then missing in the final product. The presence of the nitrate ion and quantitative changes in its content are also demonstrated by the TG curves, which attest to NO₂ removal at temperatures from 500 to 600° C.

In addition, the precipitation process is influenced significantly by the synthesis duration, which is determined by the precipitant introduction rate. The variation in pH has then some features in common with the curves obtained at different solution concentrations. Curve 4 in Fig. 1b represents the variation in the pH of the reaction mixture at the highest precipitation rate and is similar in shape to curve 1 in Fig. 1a, which was obtained in dilute solutions. Accordingly, the OH⁻/Ca²⁺ molar ratio at the equivalence points in curve 4 is larger compared to curves 5 and 6, which were obtained at slower precipitation rates (Table 1). Moreover, with decreasing precipitation rate, curves 5 and 6 show a characteristic drop in pH after the first step of precipitation, like at high solution concentrations (Fig. 1a, curve 3).

Reducing the precipitant concentration and increasing the reaction time have nearly the same effect, as follows from comparison of samples 2 and 5 (Fig. 1a, curve 2; Fig. 1b, curve 5).

This difference between the effects of initial solution concentration and pH on the phase formation process can be accounted for by the presence of a diversity of phosphate ions with different degrees of dissociation

INORGANIC MATERIALS Vol. 43 No. 10 2007



Fig. 3. IR spectra of reaction intermediates in samples 1-3 at the (1-1, 2-1, 3-1) first and (1-2, 2-2, 3-2) second equivalence points; the numbers at the curves identify the samples as referenced in Table 1.

and protonation, which were studied in detail earlier [24, 25].

In the first step of H_3PO_4 dissociation, at pH 1–4, the solution contains, in addition to the dihydrogen phosphate ion $(H_2PO_4^-)$, undissociated H_3PO_4 molecules and $H(H_2PO_4)_2^-$ and $(H_2PO_4)_2^{2-}$ dimers. In the second step of dissociation, the solution contains both monomers, HPO_4^{2-} , and $H_2PO_4^-$, and dimers, $H_2(HPO_4)_2^{2-}$ and $H(HPO_4)_2^{3-}$. As follows from earlier data, at the lowest initial H_3PO_4 concentration in this study, 0.06 mol/l, the protonated form H_3PO_4 prevails up to pH 2.5, whereas at the highest concentration, 0.42 mol/l, the concentrations of the dihydrogen phosphate ion and protonated molecules differ very little. At pH > 2.5, the degree of protonation decreases markedly with decreasing initial solution concentration.

INORGANIC MATERIALS Vol. 43 No. 10 2007

As pointed out by Abbona et al. [9], HA formation in uncontrolled-pH processes is due to the reaction between the dihydrogen phosphate and calcium ions, accompanied by a decrease in pH and the predominant formation of CHPD, CHP, $Ca_4H(PO_4)_3 \cdot 2.5H_2O$, and TCP, which crystallize more rapidly:

$$Ca^{2+} + H_2PO_4^- \longrightarrow CaHPO_4 + H^+,$$
 (1)

$$3Ca^{2+} + 2H_2PO_4^- \longrightarrow Ca_3(PO_4)_2 + 4H^+.$$
 (2)

That reaction (1) prevails in the first step of precipitation was pointed out in many reports (see, e.g., [7, 8]). Moreover, according to Heughebaert et al. [10], the forming solid phase maintains electroneutrality owing to Ca^{2+} and OH^{-} removal, whereas the hydrogen phosphate ion is incorporated into the crystalline phase, forming an apatite structure. For this reason, the relationship between the calcium and dihydrogen phosphate ion concentrations plays a central role in determining the reaction path.



Fig. 4. TG and DTA curves of reaction intermediates; the numbers at the curves identify the samples as referenced in Table 1.

Given the degree of protonation of phosphate ions, an important feature of the reaction medium in HA synthesis in the dilute solutions (Fig. 1a, curve 1) is the higher content of the acid in predominantly low-reactivity, molecular form, which results in a significant excess of calcium ions compared to high-reactivity phosphate ions. Under such conditions, the reaction only begins after a significant OH⁻ excess is introduced and the pH reaches a level needed for reaction (2) to take place. The unreacted Ca2+ ions are actively sorbed by the surface of the forming precipitate, which features a high adsorption capacity because of the small size of the primary particles and, accordingly, the relatively large specific surface [10]. This accounts for the high calcium content of the solid product in the first step (Table 1). Moreover, the HA formation through amorphous TCP by reaction (2) is favored by the more rapid rise in OH⁻/Ca²⁺ molar ratio, which ensures neutralization of the released protons. At a solution pH near 7, the acid dissociation in the first step is followed by a second jump in pH (Fig. 1a), accompanied by reaction (1), which reduces the Ca/P molar ratio in the forming material (Table 1).

The same reaction underlies the formation of calcium hydrogen phosphates in the second step in more concentrated solutions, containing a larger fraction of $H_2PO_4^-$ ions (Fig. 1a, curve 2). At the highest solution

concentration in this study, the presence of the $H_2PO_4^$ ion in the reaction intermediate, evidenced by its IR spectrum, indicates that the dimeric phosphate ions react with calcium:

$$Ca^{2+} + H(H_2PO_4)_2^{-} \longrightarrow Ca(H_2PO_4)_2 + H^+.$$
 (3)

The minimum in the potentiometric titration curve (Fig. 1a, curve 3) after the first jump in pH is then, most likely, due to the insufficient precipitant introduction rate, so that the amount of released protons increases more rapidly than that in the dilute solutions. The increase in the degree of protonation of phosphate ions after dissociation in more concentrated solutions in the second step also contributes to the considerable rise in the concentration of dihydrogen phosphate ions, which react with calcium by reaction (2). This accelerates the reaction compared to the precipitation from the dilute solutions, as evidenced by the relative heights of the peaks in the derivative curves (Fig. 1a). If the precipitation and neutralization processes cancel one another, as at the medium solution concentrations (Fig. 1a, curve 2), the curve has a plateau. The minimum in the potentiometric titration curves at reduced precipitant concentrations (Fig. 1b, curve 5) or precipitant introduction rates (Fig. 1b, curves 5, 6) lends support to this assumption.

Thus, the formation of reaction intermediates under controlled pH conditions is governed by the relationship between the initial calcium concentration and the hydroxyl concentration in the precipitant solution and also by the nature and amount of phosphate ions resulting from dissociation. Because of the dissimilarity between the processes involved in crystallization, the final reaction products differ markedly not only in chemical and phase compositions but also in crystal structure and morphology (Table 2, Figs. 5, 6).

According to XRD and chemical analysis data, the synthesized HA is a compound of variable composition, with a Ca/P molar ratio from 1.34 to 1.60, and has the same hexagonal structure as pure HA, even at the largest deviation from stoichiometry and in the presence of calcium hydrogen phosphate impurity (Fig. 5).

INORGANIC MATERIALS Vol. 43 No. 10 2007

Final sample no	Ca/P molar ratio		$S m^2/a$			
i mai sample no.		<i>a</i> , nm	c, nm	<i>V</i> , nm ³	5, m /g	
1	1.60	0.939 ± 0.002	0.690 ± 0.001	0.528 ± 0.002	143	
2	1.51	0.947 ± 0.003	0.693 ± 0.001	0.539 ± 0.003	93	
3	1.40	0.948 ± 0.002	0.695 ± 0.001	0.541 ± 0.002	80	
4	1.55	0.947 ± 0.002	0.693 ± 0.001	0.538 ± 0.002	99	
5	1.50	0.950 ± 0.003	0.693 ± 0.001	0.542 ± 0.003	90	
6	1.34	0.951 ± 0.003	0.693 ± 0.001	0.543 ± 0.003	84	

Table 2. Characteristics of final products in the synthesis of calcium-deficient HA

The present XRD and IR spectroscopy data lead us to assume that Ca-deficient HA may form by different processes, which can be represented, according to Rodriguez-Lorenzo [26], by three models:

surface adsorption of hydrogen phosphate groups,

substitutions in the crystal lattice, and

the formation of an intercrystalline mixture of HA and $Ca_4H(PO_4)_3 \cdot 2.5H_2O$.

Heughebaert et al. [10] identified adsorbed hydrogen phosphate groups on the surface of samples which were not washed thoroughly enough to remove the residual mother solution. According to their results, such groups are characterized, in addition to the well known IR absorption bands at 875 and 1640 cm⁻¹, by a band at 1215 cm⁻¹, which was missing in our spectra (Fig. 6).

The present IR spectroscopy data attest to partial substitution of hydrogen phosphate ions, HPO_4^{2-} , by PO_4^{3-} groups, as evidenced by the band at 875 cm⁻¹, due to stretches of the hydrogen phosphate group, and the band at 1640 cm⁻¹, corresponding to the bending mode of water [27]. These bands were present in all of the spectra. At the same time, only in sample *I* was this substitution not accompanied by changes in the bands near 3500 cm⁻¹, due to vibrations of water molecules.



Fig. 5. XRD patterns of the final products; the numbers at the curves identify the samples as referenced in Table 1; the phases are designated as in Fig. 2.

INORGANIC MATERIALS Vol. 43 No. 10 2007



Fig. 6. IR spectra of the final products; the numbers at the curves identify the samples as referenced in Table 1.

This sample has the largest Ca/P ratio, 1.60, and the smallest lattice parameters, which leads us to conclude that the Ca deficiency in this sample is indeed due to substitutions in the crystal lattice. In contrast, in all of the other samples, both the *a* parameter and unit-cell volume increase markedly as the Ca/P molar ratio decreases to 1.34, and their IR spectra undergo significant changes in the range 3165–3536 cm⁻¹. In addition, the XRD patterns from some of the samples, e.g., 2 and 4, show only peaks from HA, whereas the samples with a = 0.948 nm and greater contain an impurity phase, as evidenced by XRD data and the band at 896 cm⁻¹, characteristic of CHP [20]. These results suggest that, during HA crystallization in more concentrated solutions, through the formation of calcium hydrogen phosphates as reaction intermediates, the intermediate is dissolved only partially in the final step, at pH > 9, because of the small OH⁻/Ca²⁺ molar ratio, ≤ 1.5 . As a result, the new phase grows on residual primary particles as on crystallization centers, forming either an intercrystalline mixture (samples 2, 4) or a two-phase system (samples 3, 5, 6), depending on the HPO_4^{2-} content. In contrast to what was reported by Rodriguez-Lorenzo [26], the impurity phases in our samples are CHP and CHPD, instead of $Ca_4H(PO_4)_3 \cdot 2.5H_2O_2$

Analysis of the potentiometric titration curves, chemical analysis data, and phase compositions of the final products leads us to conclude that there is a general tendency for similar potentiometric titration curves and, accordingly, that the processes involved are identical. During precipitation from dilute solutions, which contain an excess of Ca²⁺ ions relative to the high-reactivity phosphate ions, $H_2PO_4^-$, because of the dissociation in the first step and the high degree of protonation of phosphate ions, or precipitation at high rates, which produce an excess of hydroxyls, the primary phase is poorly crystallized TCP. As a result of topochemical reactions, this phase then converts to Ca-deficient HA, containing hydrogen phosphate groups instead of PO_4^{3-} . The samples synthesized under such conditions have a small particle size and, accordingly, large specific surface.

Increasing the initial solution concentration or reaction time increases the $H_2PO_4^-$ concentration in the solution and leads to the formation of $H(H_2PO_4)_2^$ dimers, which is favorable for the formation of hydrogen and dihydrogen phosphates as primary phases. Subsequent HA formation in the final step, at pH > 9, involves, in contrast to the processes in dilute solutions, dissolution of reaction intermediates and formation of either an intercrystalline mixture of HA and calcium hydrogen phosphate or a mechanical mixture of these phases. A distinguishing feature of the final product is the substantially increased calcium deficiency and small specific surface, which may be due to aggregation of primary particles.

CONCLUSIONS

We prepared calcium-deficient HA with a Ca/P molar ratio in the range 1.34 to 1.60 via precipitation from an acid calcium phosphate solution by aqueous ammonia under controlled pH conditions.

The formation of Ca-deficient HA in dilute solutions (below 0.1 M H_3PO_4) at high precipitation rates (short reaction times) is preceded by the formation of amorphous TCP, which then converts to Ca-deficient HA containing HPO_4^{2-} groups through topochemical reactions.

Raising the initial solution concentration to above 0.25 mol/l or reducing the precipitation rate leads to the formation of calcium hydrogen phosphate as a primary phase, which then dissolves and recrystallizes into Cadeficient HA. As the calcium deficiency increases, incomplete dissolution of the primary phase leads to the formation of either an intercrystalline mixture or a two-phase system of HA and calcium hydrogen phosphate crystals.

In contrast to conventional processes in pH \geq 7 solutions, the precipitation of Ca-deficient HA from pH 1–2 solutions of a calcium salt in phosphoric acid enables an effective process control owing to the variable

degree of protonation of the phosphoric acid and the presence of different phosphate ions in the solution.

REFERENCES

- Mavropoulos, E., Rossi, A.M., Rocha, N.C.C., et al., Dissolution of Calcium-Deficient Hydroxyapatite Synthesized at Different Conditions, *Mater. Charact.*, 2003, vol. 50, nos. 2–3, pp. 203–207.
- Raynaud, S., Champion, E., Lafon, J.P., and Bernache-Assollant, D., Calcium Phosphate Apatites with Variable Ca/P Atomic Ratio: III. Mechanical Properties and Degradation in Solution of Hot Pressed Ceramics, *Biomaterials*, 2002, vol. 23, no. 4, pp. 1081–1089.
- Tanaka, H., Watanabe, T., and Chikazawa, M., FTIR and TPD Studies on the Adsorption of Pyridine, *n*-Butylamine, and Acetic Acid on Calcium Hydroxyapatite, *J. Chem. Soc., Faraday Trans.*, 1997, vol. 93, no. 24, pp. 4377–4381.
- Dykman, A.S., Origin of the Catalytic Activity of Imperfect Hydroxyapatite, *Zh. Prikl. Khim.* (S.-Peterburg), 2003, vol. 76, no. 2, pp. 234–236.
- Matsumura, Y., Kanai, H., and Moffat, J.B., Catalytic Oxidation of Carbon Monoxide over Stoichiometric and Non-stoichiometric Hydroxyapatites, *J. Chem. Soc.*, *Faraday Trans.*, 1997, vol. 93, no. 24, pp. 4383–4387.
- Gibson, I.R., Rehman, I., Best, S.M., and Bonfield, W., Characterization of the Transformation from Calcium-Deficient Apatite to β-Tricalciumphosphate, *J. Mater. Sci.: Mater. Med.*, 2000, vol. 11, no. 12, pp. 799–804.
- Van Kemenade, M.J.J.M. and De Bruyn, P.L., A Kinetic Study of Precipitation from Supersaturated Calcium Phosphate Solutions, *J. Colloid Interface Sci.*, 1987, vol. 118, no. 2, pp. 564–585.
- 8. Boistelle, R. and Lopez-Valero, I., Growth Units and Nucleation: The Case of Calcium Phosphates, *J. Cryst. Growth*, 1990, vol. 102, no. 3, pp. 609–617.
- Abbona, F., Lundager Madsen, H.E., and Boistelle, R., The Final Phases of Calcium and Magnesium Phosphates Precipitated from Solution of High to Medium Concentration, *J. Cryst. Growth*, 1988, vol. 89, no. 4, pp. 592–602.
- Heughebaert, J.C., Zawacki, S.J., and Nancollas, G.H., The Growth of Nonstoichiometric Apatite from Aqueous Solution at 37°C: I. Methodology and Growth at pH 7.4, *J. Colloid Interface Sci.*, 1990, vol. 135, no. 1, pp. 20– 32.
- Altunina, L.I., Pechkovskii, V.V., Eshchenko, L.S., and Gafarova, A.F., Formation Conditions and Properties of Hydroxyapatite, *Zh. Neorg. Khim.*, 1986, vol. 31, no. 5, pp. 1107–1112.
- 12. Sampath Kumar, T.S., Manjubala, I., and Gunasekaran, J., Synthesis of Carbonated Calcium Phosphate Ceramics Using Microwave Irradiation, *Biomaterials*, 2000, vol. 21, no. 16, pp. 1623–1629.

- Lazic, S., Zec, S., Miljevic, N.D., and Milonjic, S., The Effect of Temperature on the Properties of Hydroxyapatite Precipitated from Calcium Hydroxide and Phosphoric Acid, *Thermochim. Acta*, 2001, vol. 374, no. 1, pp. 13–22.
- Shashkova, I.L., Kitikova, N.V., Rat'ko, A.I., and D'yachenko, A.G., Preparation of Calcium and Magnesium Hydrogen Phosphates from Natural Dolomite and Their Sorptive Properties, *Neorg. Mater.*, 2000, vol. 36, no. 8, pp. 990–994 [*Inorg. Mater.* (Engl. Transl.), vol. 36, no. 8, pp. 826–829].
- 15. Schwarzenbach, G. and Flaschka, H., *Die komplexometrische Titration*, Stuttgart: Ferdinand Enke, 1965.
- Charlot, G., Les méthodes de la chimie analytique: Analyse quantitative minérale, Paris: Masson, 1961, 4th ed, part 2.
- 17. Vasserman, I.M., *Khimicheskoe osazhdenie iz rastvorov* (Chemical Precipitation from Solutions), Moscow: Khimiya, 1980.
- Perdok, W.G., Christoffersen, J., and Arends, J., The Thermal Lattice Expansion of Calcium Hydroxyapatite, *J. Cryst. Growth*, 1987, vol. 80, no. 1, pp. 149–154.
- 19. ASTM Standard X-ray Diffraction Powder Patterns, Inorganic, Philadelphia: ASTM, 1967.
- 20. Atlas infrakrasnykh spektrov fosfatov: Ortofosfaty (Atlas of Infrared Spectra of Phosphates: Orthophosphates), Pechkovskii, V.V. et al., Eds., Moscow: Nauka, 1981.
- 21. Lepilina, R.G. and Smirnova, N.M., *Termogrammy neorganicheskikh fosfatnykh soedinenii* (Thermal Analysis of Inorganic Phosphates), Leningrad: Nauka, 1984.
- Shashkova, I.L., Rat'ko, A.I., and Kitikova, N.V., Removal of Heavy Metal Ions from Aqueous Solutions by Alkaline-Earth Metal Phosphates, *Colloids Surf.*, A, 1999, vol. 160, pp. 207–215.
- Pechkovskii, V.V., Salonets, G.I., Dzyuba, E.D., and Chubarov, A.V., Electrical Conductivity of Calcium and Barium Monophosphates during Dehydration, *Zh. Neorg. Khim.*, 1980, vol. 25, no. 2, pp. 387–390.
- Ivanenko, V.I., Udalova, I.A., Lokshin, E.P., and Kalinnikov, V.T., State of Phosphate Ions in Aqueous Solutions in the Presence of NaCl, KCl, NaNO₃, and KNO₃, *Zh. Neorg. Khim.*, 2002, vol. 47, no. 6, pp. 1026–1032.
- 25. Prodan, I.E., Eshchenko, L.S., and Pechkovskii, V.V., Role of Complexation in the Crystallization of Iron Phosphates, *Zh. Neorg. Khim.*, 1990, vol. 35, no. 4, pp. 843–848.
- Rodriguez-Lorenzo, L.M., Studies on Calcium Deficient Apatites Structure by Means of MAS-NMR Spectroscopy, *J. Mater. Sci.: Mater. Med.*, 2005, vol. 16, no. 5, pp. 393–398.
- Cheng, Z.H., Yasukawa, A., Kandori, K., and Ishikawa, T., FTIR Study on Incorporation of CO₂ into Calcium Hydroxyapatite, *J. Chem. Soc., Faraday Trans.*, 1998, vol. 94, no. 10, pp. 1501–1505.