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Mechanism of solid-state conversion of non-stoichiometric hydroxyapatite to diphase calcium phosphate

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Two non-stoichiometric hydroxyapatites (n-HA) with Ca/P molar ratios of 1.50 and 1.58 and one stoichiometric hydroxyapatite (s-HA) with Ca/P = 1.67 were prepared from chemically pure $CaHPO_4 \cdot 2H_2O$ and KOH. After sintering at 1050 °C for 4 h, n-HA with Ca/P = 1.50 was transformed into β-$Ca_3(PO_4)_2$, n-HA with Ca/P = 1.58 was converted to diphase calcium phosphate (DCP), while s-HA underwent no chemical transformations. The sintered and unsintered samples of hydroxyapatite were studied by IR spectroscopy, chemical analysis, and X-ray diffraction analysis. The crystallite dimensions were calculated, and a model for the DCP structure was proposed. The mechanism of the solid-state n-HA to DCP conversion was proposed on the basis of this model and published values of the volume diffusion coefficients of the OH^-, Ca^{2+}, and $PO_4{}^{3-}$ ions at 1000 °C.

Key words: hydroxyapatite, calcium phosphate, solid-state reactions, X-ray diffraction analysis, IR spectroscopy.

Diphase calcium phosphate (DCP) consisting of stoichiometric hydroxyapatite (s-HA), *viz.*, $Ca_{10}(PO_4)_6(OH)_2$, and the β-modification of calcium orthophosphate $Ca_3(PO_4)_2$ is widely used as biomaterial due to its chemical resemblance to the bone tissue.[1,2] DCP is usually obtained[3,4] by sintering of non-stoichiometric hydroxyapatite (n-HA) $Ca_{10-x}(HPO_4)_x(PO_4)_{6-x}(OH)_{2-x}$ $(0 < x < 1)$ at 1000—1200 °C for 1—4 h. The physicochemical mechanism of this process has not yet been established. It is only known[5—8] that it includes the solid-state diffusion of the OH^- and Ca^{2+} ions and results in the formation of new phases with crystallite dimensions of ~60 nm. The purpose of this work is to study of the mechanism of solid-state conversion of n-HA to DCP.

Experimental

The procedure of DCP synthesis has been described previously.[3,4,8] $CaHPO_4 \cdot 2H_2O$ and KOH (reagent grade) were used as the starting reactants. In the synthesis of n-HA, solid KOH (36 g) was added to a suspension (1 L) of $CaHPO_4 \cdot 2H_2O$ in distilled water (100 g L^{-1}). The suspension was refluxed for 4 h with continuous stirring and bubbling of pure nitrogen to avoid CO_2 absorption and cooled. A precipitate of n-HA was filtered off and washed with distilled water until the alkali reaction by phenolphthalein (pH < 8.5) was absent in the washing waters. The resulting substance was dried for 24 h at 80 °C. For DCP synthesis, the dry n-HA precipitate was sintered for 4 h at 1050 °C.

The n-HA and β-$Ca_3(PO_4)_2$ samples were prepared similarly. The only distinction was the amount of KOH added. The formation of s-HA requires alkali excess, whereas β-$Ca_3(PO_4)_2$ needs its deficient to be formed. Therefore, for the synthesis of s-HA, solid KOH (45 g) per 100 g of $CaHPO_4 \cdot 2H_2O$ is necessary, and the synthesis of β-$Ca_3(PO_4)_2$ needs 31 g of KOH per each 100 g of $CaHPO_4 \cdot 2H_2O$. The filtration, washing, drying, and sintering procedures are analogous to those presented above.

The chemical and phase compositions of all obtained calcium phosphates (both sintered and unsintered) were studied by X-ray phase analysis on a Bruker AXS, D8 Advance diffractometer (range of changing angle 2θ 10—60°; Cu-Kα radiation), IR spectroscopy on a Perkin—Elmer 1720X spectrometer (in an interval of 400—4000 cm^{-1}), and chemical analysis. In the latter case, a weighed sample (0.2 g) of calcium phosphate was dissolved in 0.5 *M* HCl (10 mL), and the concentrations of the Ca^{2+} (titration with Trilon B) and $PO_4{}^{3-}$ ions (photometric determination with the yellow molybdate complex) were measured by standard procedures.[9]

Results and Discussion

The X-ray diffraction patterns of unsintered and sintered calcium phosphates are presented in Figs. 1 and 2. The diffraction peaks for the sintered samples are always more intense and narrow compared to the analogous peaks for the unsintered samples.

A similar conclusion on the width of absorption bands can be made from the IR spectroscopic data (Figs. 3 and 4). The formation of DCP from n-HA results in the

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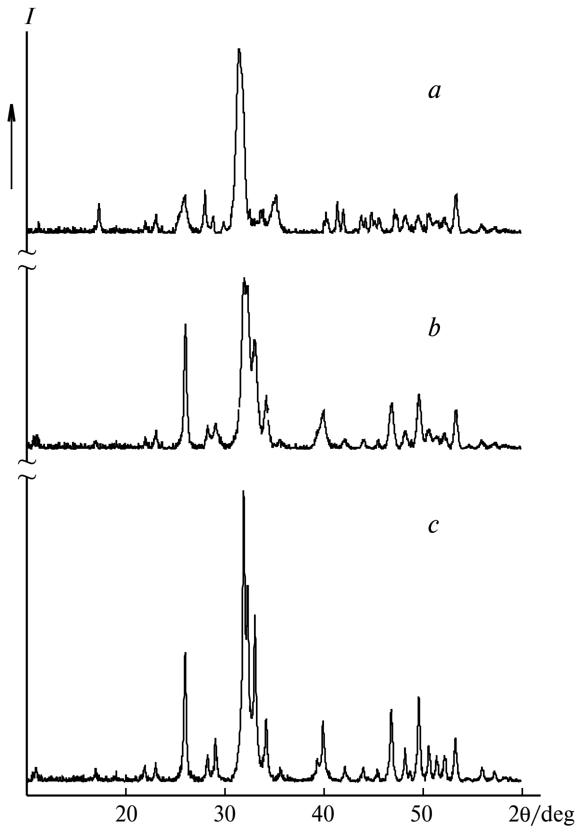


Fig. 1. X-ray diffraction patterns of unsintered calcium phosphates: *a*, $Ca_3(PO_4)_2$; *b*, n-HA; *c*, s-HA.

disappearance of the specific absorption band at 870 cm^{-1} of the HPO_4^{2-} ion and a decrease in the intensity of the absorption band at 3570 cm^{-1} of the OH^- ion.[1,2,10]

The chemical analysis results (Ca/P molar ratio) for all studied calcium phosphates are presented in Table 1.

The molecular equations of chemical reactions occurring in aqueous suspensions and affording calcium phosphates[1,2,11] are presented below.

Table 1. Results of chemical analysis (Ca/P molar ratio) and calculated average dimensions of crystallites (τ) for calcium phosphates studied

Calcium phosphate	Ca/P	β/deg*	τ/nm
Unsintered s-HA	1.66±0.03	0.35	~30
n-HA	1.58±0.03	0.5	~20
Unsintered $Ca_3(PO_4)_2$	1.49±0.03	0.9	~12
Sintered s-HA	1.68±0.02	0.12	~80
DCP (s-HA(50%) + + β-$Ca_3(PO_4)_2$ (50%))	1.59±0.02	0.15	~65
β-$Ca_3(PO_4)_2$	1.51±0.02	0.19	~50

* The width of diffraction peaks in the interval 2θ = 31—32° (the peaks with maximum intensity appear precisely in this interval, see Figs. 1 and 2).

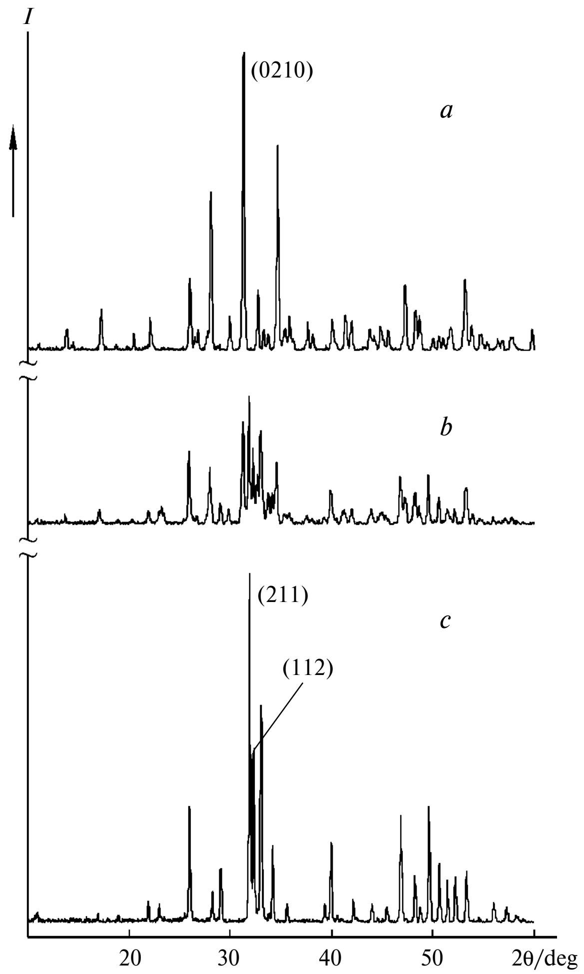


Fig. 2. X-ray diffraction patterns of sintered calcium phosphates: *a*, β-$Ca_3(PO_4)_2$; *b*, DCP consisting of s-HA (50%) + + β-$Ca_3(PO_4)_2$ (50%); *c*, s-HA. The peaks used for the calculation of the crystallite dimensions are marked.

Synthesis of s-HA

$$10\ CaHPO_4 \cdot 2H_2O + 8\ KOH = Ca_{10}(PO_4)_6(OH)_2 + 4\ K_2HPO_4 + 46\ H_2O \quad (1)$$

Synthesis of $Ca_3(PO_4)_2$

$$3\ CaHPO_4 \cdot 2H_2O + 2\ KOH = Ca_3(PO_4)_2 + K_2HPO_4 + 8\ H_2O \quad (2)$$

Synthesis of n-HA

$$CaHPO_4 \cdot 2H_2O + KOH \rightarrow Ca_{10-x}(HPO_4)_x(PO_4)_{6-x}(OH)_{2-x} + K_2HPO_4 + H_2O \quad (3)$$

$0 < x < 1$

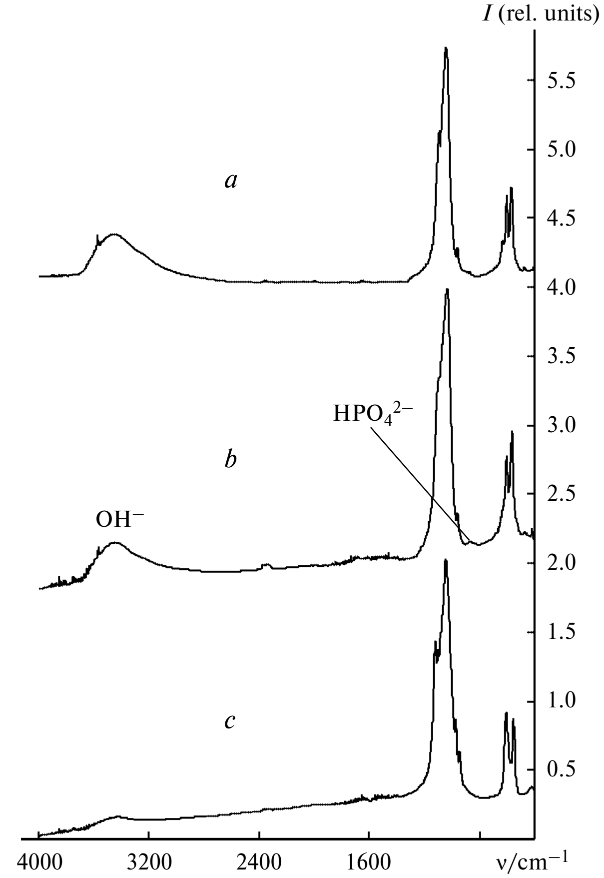


Fig. 3. IR spectra of unsintered calcium phosphates: *a*, s-HA; *b*, n-HA; *c*, $Ca_3(PO_4)_2$. The absorption bands of the OH^- (3570 cm^{-1}) and HPO_4^{2-} (875 cm^{-1}) ions are marked.

When $x = 0.5$ (after sintering, n-HA is transformed into DCP consisting of 50% s-HA and 50% β-$Ca_3(PO_4)_2$), reaction (3) can be written as

$$19\,CaHPO_4 \cdot 2H_2O + 14\,KOH = \\ = 2\,Ca_{9.5}(HPO_4)_{0.5}(PO_4)_{5.5}(OH)_{1.5} + \\ + 7\,K_2HPO_4 + 49\,H_2O. \qquad (4)$$

The stoichiometric reaction that occurs during sintering can be written only for the synthesis of n-HA, because neither s-HA, nor $Ca_3(PO_4)_2$ undergo no chemical transformations during sintering except loss of adsorbed water and recrystallization. In this case, crystallites of both calcium phosphates are enlarged (see Figs. 1 and 2), and $Ca_3(PO_4)_2$ is converted to the high-temperature β-$Ca_3(PO_4)_2$ phase. The transformation of n-HA into DCP can be described as follows:

$$Ca_{10-x}(HPO_4)_x(PO_4)_{6-x}(OH)_{2-x} \rightarrow \\ \rightarrow Ca_{10}(PO_4)_6(OH)_2 + \beta\text{-}Ca_3(PO_4)_2 + H_2O, \qquad (5)$$

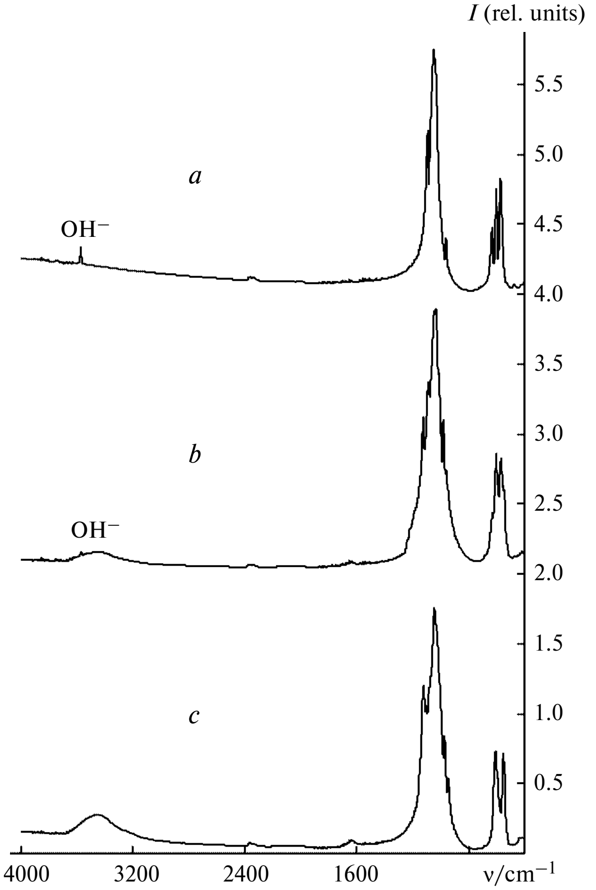


Fig. 4. IR spectra of sintered calcium phosphates: *a*, s-HA; *b*, DCP consisting of s-HA (50%) + β-$Ca_3(PO_4)_2$ (50%); *c*, β-$Ca_3(PO_4)_2$. The absorption band of the OH^- ion (3570 cm^{-1}) is marked.

where $0 < x < 1$. In the case of $x = 0.5$, reaction (5) can be written as

$$2\,Ca_{9.5}(HPO_4)_{0.5}(PO_4)_{5.5}(OH)_{1.5} = \\ = Ca_{10}(PO_4)_6(OH)_2 + 3\,\beta\text{-}Ca_3(PO_4)_2 + H_2O. \qquad (6)$$

The n-HA structure has not yet been determined, mainly because the chemical composition of n-HA is not constant.[1—4] Nevertheless, the results of chemical, spectroscopic, and X-ray diffraction studies suggest that n-HA is s-HA with ion vacancies in the sites of the Ca^{2+} and OH^- ions and with a small number of protons in the form of HPO_4^{2-} ions (see Ref. 2, p. 153). In other words, it is assumed that the n-HA structure contains some number of point defects. On sintering, the H^+ and OH^- ions in the crystalline lattice diffuse and interact to form water (see reactions (5) and (6)).[1—4] The appearance of water is indirectly confirmed by the IR spectroscopic data. Comparison of the spectrum of n-HA with that of DCP (*cf.* curves *b* in Figs. 3 and 4) shows a decrease in the

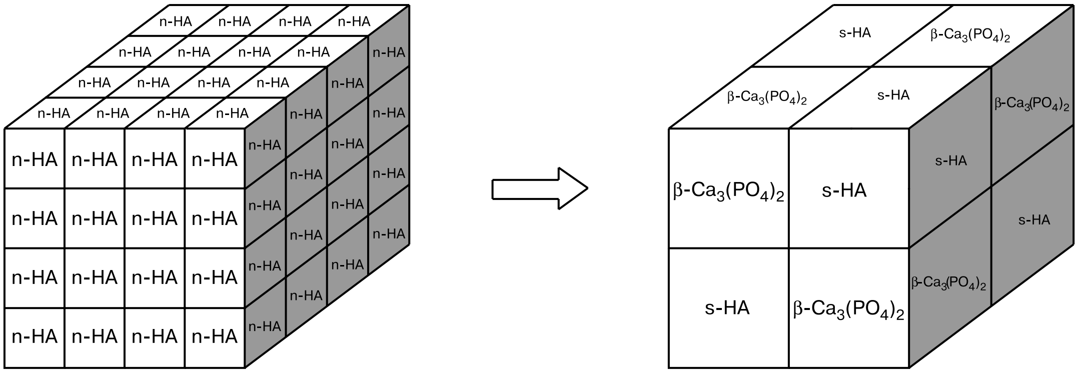


Fig. 5. Scheme of conversion of n-HA to DCP consisting of s-HA (50%) + β-$Ca_3(PO_4)_2$ (50%). The cubic structure of the crystallites is used for simplicity; the crystallite dimensions are presented in Table 1.

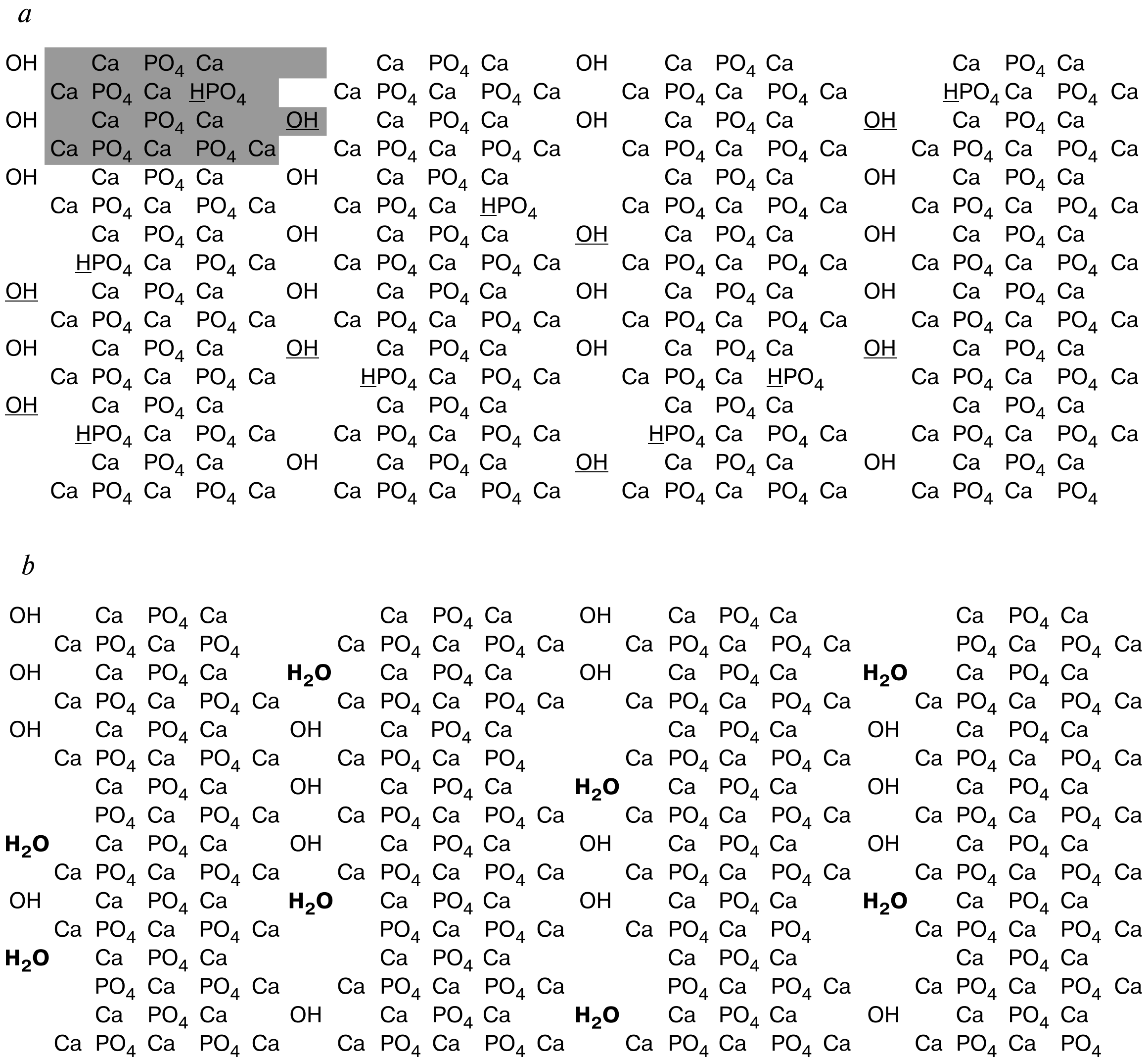


Fig. 6. Scheme of conversion of n-HA to DCP at the atomic (ionic) level: *a*, starting n-HA (the H^+ and OH^- ions reacting with each other are underlined); *b*, n-HA with water molecules (emphasized by bold) formed upon the interaction of the OH^- and HPO_4^{2-} ions; *c*, n-HA after evaporation of water (arrows indicate the main direction of diffusion of the OH^- and Ca^{2+} ions); *d*, DCP.

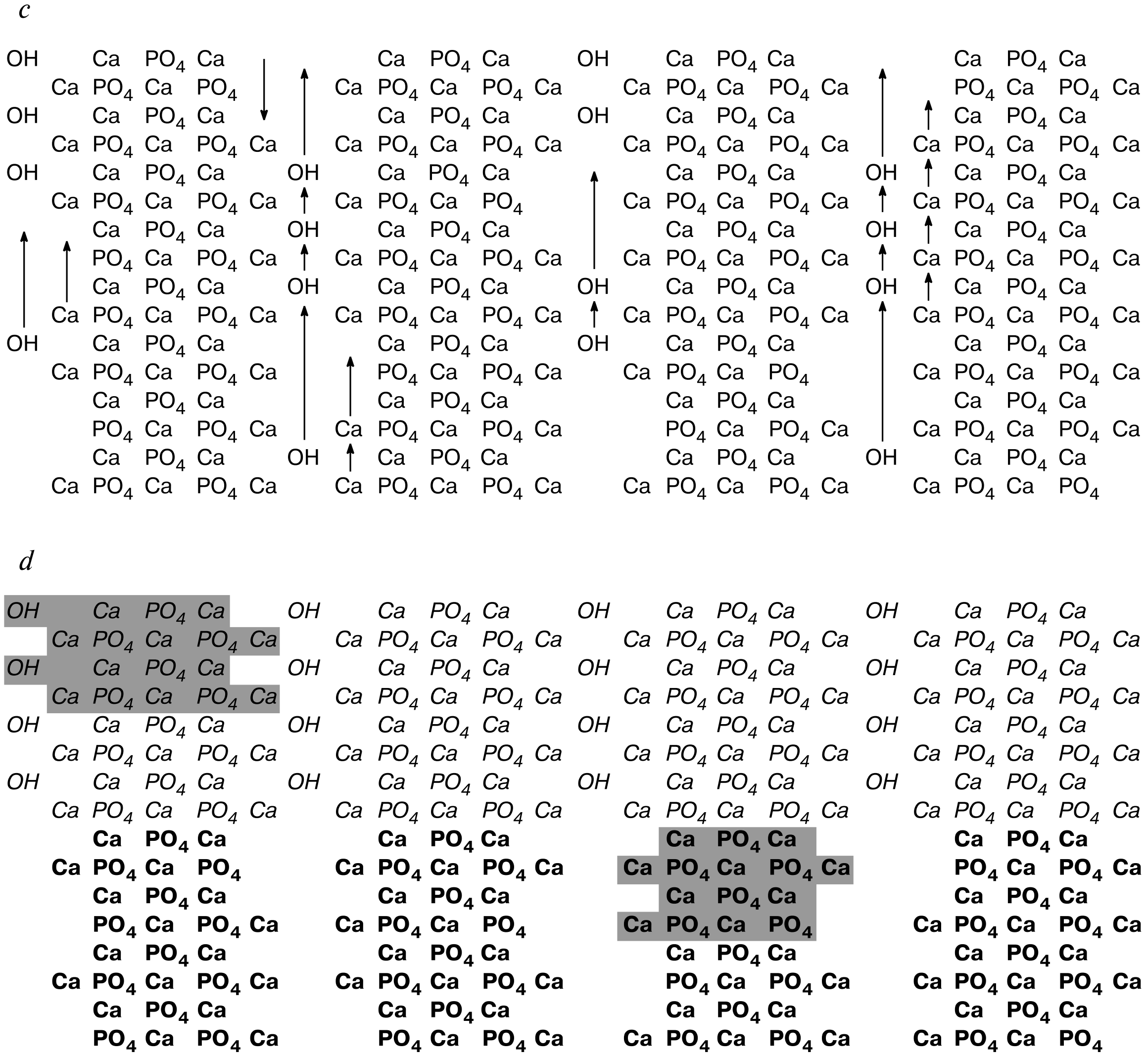
intensity of the absorption band at 3570 cm^{-1} of the OH$^-$ ion and disappearance of the absorption band at 870 cm^{-1} of the HPO_4^{2-} ion. In addition, the IR spectroscopic data indicate that the degree of ordering of calcium phosphates increases due to sintering. This follows from the contraction of the absorption bands of the phosphate groups at 500—600 and 950—1100 cm^{-1}.[1,2,10]

Based on the width of diffraction peaks and using the Scherrer equation,[12] we can estimate the average dimension of crystallites (τ) for all calcium phosphates studied

$$\tau = K\lambda/(\beta\cos\theta), \qquad (7)$$

where β (in rad) is the broadening of diffraction peaks due to a small crystallite dimension, K is the shape factor (for simplification of calculations, let us accept $K = 1$), $\lambda = 1.54056$ Å is the wavelength of the Cu-Kα radiation, and θ is the reflection angle of the diffraction peak. The results of calculations by formula (7) are presented in Table 1. Note that the broadening of the diffraction lines of unsintered calcium phosphates can also be related to point defects in their structure, and their contribution to the diffraction peak broadening cannot be estimated.

As can be seen from the data in Table 1, the width of the diffraction bands decreases and the crystallite dimensions increase with an increase in the Ca/P molar ratio in the series unsintered $Ca_3(PO_4)_2$—n-HA—unsintered s-HA and β-$Ca_3(PO_4)_2$—DCP—sintered s-HA. Probably, this is associated with a special stability of the crystal structure of s-NA.[1,2,11]



"Single molecules" (whose dimensions are equal to the crystalline lattice parameters) of n-HA and s-HA and the conglomerate of three β-$Ca_3(PO_4)_2$ molecules formed of the n-HA "single molecule" are gray-colored; n-HA is drawn by normal font; β-$Ca_3(PO_4)_2$, bold; s-HA, italic.

For all calcium phosphates, sintering simply leads to the 3—4-fold crystallite enlargement (agglomeration) (see Table 1). The dimensions of crystallites of all sintered calcium phosphates are close to the dimensions of coherent scattering blocks found[13,14] in the fluoroapatite crystals $Ca_{10}(PO_4)_6F_2$. In the case of s-HA and $Ca_3(PO_4)_2$, crystallite agglomeration occurs without changing their chemical composition (only adsorption water is lost). However, for s-HA the agglomeration is complicated by chemical transformations leading to the formation of the s-HA and β-$Ca_3(PO_4)_2$ phases (see reactions (5) and (6)). These transformations do not occur without ion diffusion, which is possible both in the bulk of crystallites and at their interfaces.

From the formal point of view, s-HA and $Ca_3(PO_4)_2$ are related by the relationship

$$3\,Ca_3(PO_4)_2 + Ca^{2+} + 2\,OH^- \rightleftharpoons Ca_{10}(PO_4)_6(OH)_2. \quad (8)$$

According to the calculated crystallite dimensions (see Table 1), several tens of small crystallites are transformed upon n-HA sintering into one large crystallite of either s-HA or β-$Ca_3(PO_4)_2$. The scheme of this process is presented in Fig. 5. In this case, the Ca^{2+} and OH^- ions should diffuse at a distance corresponding to the dimensions of one to two small crystallites (20—40 nm).

At 1000 °C, the values of volume diffusion coefficients of the hydroxide, calcium, and phosphate ions in s-HA are $2 \cdot 10^{-11}$, 10^{-15}, and $<10^{-17}$ cm^2 s^{-1}, respectively (see Ref. 2, p. 106). A relatively high value of the diffusion coefficient of the OH^- ions is explained by the specific position of these ions in channels of the crystalline lattice of s-HA.[1,2,11]

Since during diffusion the diffusant concentration in the medium approaches the equilibrium concentration according to an asymptotic law, it is difficult to determine the diffusion time. To avoid this difficulty, the characteristic duffusion time (t_{dif}) was introduced. In the simplest case, t_{dif} can be presented as

$$t_{dif} = \tau^2/D, \quad (9)$$

where τ is the average crystallite dimension, and D is the diffusion coefficient.

The time necessary for diffusion of the ions present in n-HA at distances of 20 and 40 nm was estimated by formula (9) (Table 2). As can be seen from the data in Table 2, sintering at 1050 °C for 4 h is quite sufficient for the diffusion of the OH^- and Ca^{2+} ions at specified distances and, hence, for the conversion of n-HA to DCP. The presented results of calculations show that the diffusion of the phosphate ions during the transformation of n-HA into DCP can be neglected.

The mechanism of conversion of n-HA to DCP at the atomic (ionic) level consists, likely, of two steps. At first the HPO_4^{2-} ions (more exactly, the H^+ ions because phosphate is not almost involved in diffusion) react with the nearest OH^- ions to form water (Fig. 6, *a*, *b*). Owing to a high mobility of the H^+ and OH^- ions at elevated temperatures,[2] this process is fast. Since water molecules have no electric charge, they easily leave the crystalline lattice of n-HA. The second step is the directed diffusion (both in the bulk of crystallites and at their interfaces) of the OH^- and Ca^{2+} ions (at distances of at most 40 nm), as schematically shown in Fig. 6, *c*. As a result, DCP consisting of the s-HA and β-$Ca_3(PO_4)_2$ phases is formed (Fig. 6, *d*).

Table 2. Time necessary for ion diffusion of n-HA B(t_{dif}) at a distance of 20 (I) and 40 nm (II) at 1000 °C

Ion	t_{dif}/s	
	I	II
OH^-	~0.18	~0.72
Ca^{2+}	~3610 (~1 h)	~14400 (~4 h)
PO_4^{3-}	>361000 (>4 days)	>1440000 (>16 days)

Thus, in this work we confirmed the published data,[1—4,8] according to which the sintering of s-HA and $Ca_3(PO_4)_2$ produce no chemical transformations, whereas the sintering of n-HA results in its conversion to DCP. Based on the width of the X-ray diffraction peaks, we estimated the dimensions of crystallites of all studied calcium phosphates and proposed the model for the DCP structure. The results of our study show that DCP consists of the s-HA and β-$Ca_3(PO_4)_2$ crystallites with average dimensions of ~65 nm (see Table 1). This value agrees well with available published data.[1,5—8,13,14]

Using the proposed model and published numerical values of diffusion coefficients of the ions at 1000 °C, we developed the mechanism of solid-state conversion of n-HA to DCP, according to which the transformation occurs by the directed solid-state diffusion of the OH^- and Ca^{2+} ions at distances of at most 40 nm. The ions of phosphate do not virtually diffuse.

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