

# Synthesis of Calcium Phosphate Powder from Calcium Lactate and Ammonium Hydrogen Phosphate for the Fabrication of Bioceramics

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**Abstract**—A calcium phosphate powder has been synthesized from aqueous 0.25, 0.5, and 1.0 M calcium lactate and ammonium hydrogen phosphate solutions at a Ca/P = 1, without pH adjusting. According to X-ray diffraction data, the as-synthesized powder consisted of brushite ( $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$ ) and octacalcium phosphate ( $\text{Ca}_8(\text{HPO}_4)_2(\text{PO}_4)_4 \cdot 5\text{H}_2\text{O}$ ). After heat treatment in the range 500–700°C, the powders were gray in color because of the destruction of the reaction by-product. The powders heat-treated in the range 500–700°C consisted largely of  $\gamma\text{-Ca}_2\text{P}_2\text{O}_7$ . The ceramics prepared from the synthesized powders by firing at 1100°C consisted of  $\beta\text{-Ca}_2\text{P}_2\text{O}_7$  and  $\beta\text{-Ca}_3(\text{PO}_4)_2$ .

**Keywords:** synthesis, calcium lactate, brushite, octacalcium phosphate, reaction by-product, calcium pyrophosphate, tricalcium phosphate, bioceramics

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## INTRODUCTION

Ceramic materials for the fabrication of bone implants are produced predominantly from synthetic calcium phosphate (CP) powders [1, 2]. CP powders of target phase composition are typically prepared through precipitation from solutions [3, 4]. Synthesis of CP from soluble salts of calcium (nitrate, chloride, and acetate) is used widely [5]. The use of ammonium hydrogen phosphate and phosphoric acids allows one to prepare CP powders containing reaction by-products removable by heat treatment, which is important for the preparation of calcium phosphate ceramics of target composition [6]. The phase composition and other properties of synthetic CP powders depend on the pH in the reaction zone, temperature, synthesis time, and the pair of precursors chosen [7–9]. To obtain CP-based resorbable ceramics, powders are needed that ensure that, after firing, the Ca/P molar ratio lies in the range  $0.5 \leq \text{Ca/P} \leq 1.5$  [10, 11]. This composition range includes calcium polyphosphate,  $\text{Ca}(\text{PO}_3)_2$  (CPolyP), Ca/P = 0.5); tromelite,  $\text{Ca}_4\text{P}_6\text{O}_{19}$  (Ca/P = 0.66); calcium pyrophosphate,  $\text{Ca}_2\text{P}_2\text{O}_7$  (CPP, Ca/P = 1.0); tricalcium phosphate,  $\text{Ca}_3(\text{PO}_4)_2$  (TCP, Ca/P = 1.5); and ceramic composites containing the above CPs. These CPs form due to the high-temperature treatment of synthetic hydrated acid or basic CPs or due to solid-state reactions. For example, CPP forms

from brushite,  $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$ ; monetite,  $\text{CaHPO}_4$ ; or hydrated CPP,  $\text{Ca}_2\text{P}_2\text{O}_7 \cdot x\text{H}_2\text{O}$  [12, 13]. TCP forms from amorphous  $\text{Ca}_3(\text{PO}_4)_2 \cdot x\text{H}_2\text{O}$ ; from calcium-deficient hydroxyapatite,  $\text{Ca}_{10-x}(\text{PO}_4)_6-x(\text{OH})_{2-2x}$  [14]; or as a result of reaction between two calcium phosphates with Ca/P molar ratios above and below 1.5 [15].

There is particular interest in production of ceramic composites from amorphous or single-phase powders. In a previous study [16], a ceramic composite containing TCP and hydroxyapatite (HA),  $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$ , was prepared from HA synthesized by reacting calcium acetate,  $\text{Ca}(\text{CH}_3\text{COO})_2$ , with ammonium hydrogen phosphate,  $(\text{NH}_4)_2\text{HPO}_4$ . CPP/TCP ceramic composites were prepared from octacalcium phosphate (OCP),  $\text{Ca}_8(\text{HPO}_4)_2(\text{PO}_4)_4 \cdot 5\text{H}_2\text{O}$ , which has an intermediate Ca/P molar ratio of 1.33 [17]. A CPP/TCP ceramic composite was prepared from powder consisting of a mixture of brushite ( $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$ ) and a reaction by-product:  $\text{NH}_4\text{Cl}$  synthesized by reacting calcium chloride,  $\text{CaCl}_2$ , with ammonium hydrogen phosphate,  $(\text{NH}_4)_2\text{HPO}_4$  [18]. A CPP/tromelite/CPolyP ceramic composite was prepared from amorphous hydrated CPolyP,  $\text{Ca}(\text{PO}_3)_2 \cdot x\text{H}_2\text{O}$ , synthesized from calcium acetate,  $\text{Ca}(\text{CH}_3\text{COO})_2$ , and polyphosphoric acid,  $\text{HPO}_3$ , in the presence of aqueous ammonia [19]. In a number of

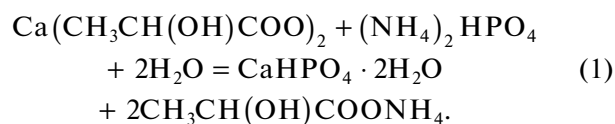
cases, HA/TCP [20, 21] or TCP/CP [22] ceramic composites were prepared from powders synthesized at an intentionally varied pH level [23, 24]. CP powders prepared previously [16, 18] were synthesized without controlling pH in the reaction zone. The result of CP synthesis in solution is known to be determined to a significant degree by the pH of the solution. It was emphasized in Refs. [16, 18] that a buffer solution was formed in the reaction zone, favoring the synthesis of powder that converted into a two-phase composite at high temperatures. In such cases, the reaction zone in solution contains substances capable of acting as components of buffer solutions. Ammonium acetate,  $\text{CH}_3\text{COONH}_4$  [25, 26], and ammonium chloride,  $\text{NH}_4\text{Cl}$  [27], are known in the food industry as the acidity regulators E510 and E264, respectively [28]. To the best of our knowledge, the synthesis of CPs from calcium salts of carboxylic acids other than acetates has not been described in the scientific or patent literature.

In this study, a CP powder suitable for the fabrication of bioceramics was prepared from calcium lactate and ammonium hydrogen phosphate at a Ca/P = 1 in the starting solutions. This ratio corresponds to the Ca/P molar ratio in brushite and CPP. Reaction between the precursors chosen was expected to give the desired product (CP) and ammonium lactate,  $\text{CH}_3\text{CHOHCOONH}_4$ , as a reaction by-product. Both calcium lactate and ammonium lactate are used as food additives (E327 and E328, respectively), namely, as acidity regulators. In addition, it is known that calcium lactate ensures pH 5–6 in a 5% aqueous solution [27], ammonium lactate has neutral pH [29], and an aqueous ammonium hydrogen phosphate solution has pH 8 [30]. If the pH in the reaction zone is varied in the range from 8 to 4, a product can probably be synthesized that will ensure the formation of a CPP phase with a Ca/P molar ratio of 1 and a TCP phase with a Ca/P molar ratio of 1.5 in the ceramic composite. Ammonium lactate was used previously as a chelating agent in the synthesis of titanium oxide [29] or barium titanate [31]. Ammonium and calcium lactates are known to be used in the food industry [32]. At the same time, to the best of our knowledge, calcium lactate has not been used in the synthesis of CPs. The choice of this pair of precursors ensures that the synthesized powder contains a reaction by-product capable of being carbonized on heating and completely removable by firing. The ability of one component to be carbonized allows one to impart a dark (brown, black, or gray) color to the synthetic powder, without influencing the formation of the phase composition of the ceramic. Imparting a dark color to a powder, analogous to the addition of a dye, is necessary if ceramic bodies are planned to be produced by stereolithogra-

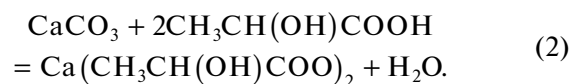
phy, in order to improve printing resolution by reducing lateral scattering [33].

## EXPERIMENTAL

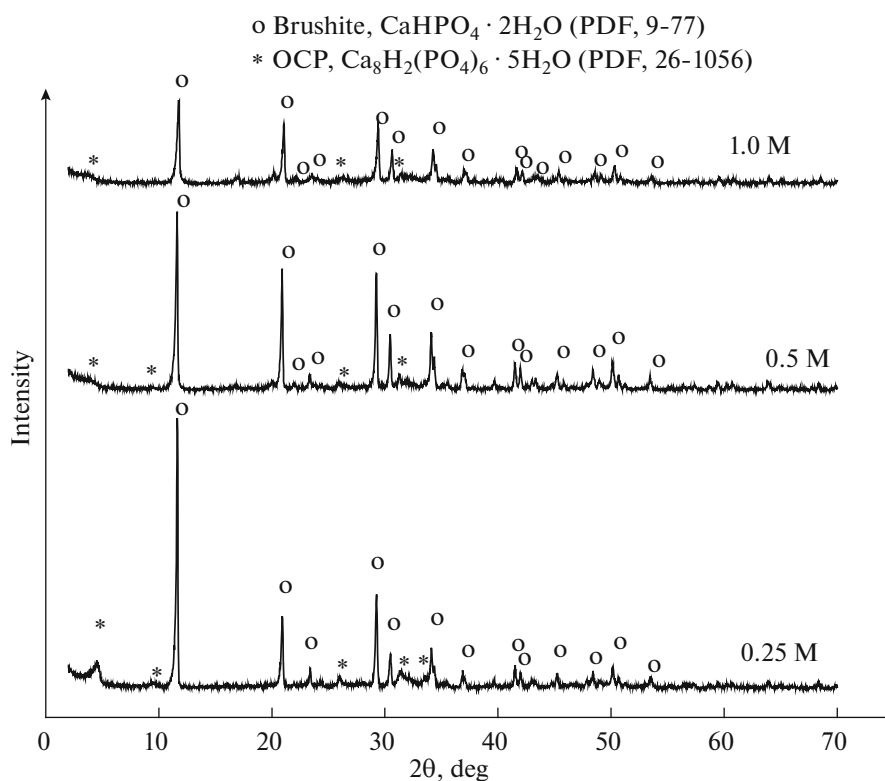
CP powders were synthesized from aqueous calcium lactate ( $\text{Ca}(\text{CH}_3\text{CH}(\text{OH})\text{COO})_2$ ) and ammonium hydrogen phosphate ( $(\text{NH}_4)_2\text{HPO}_4$ , Sigma-Aldrich, Germany) solutions of various concentrations (0.25, 0.5, and 1.0 M) at a Ca/P molar ratio of unity. The amounts of the starting chemicals were calculated for the reaction



Calcium lactate was synthesized using a 80% lactic acid (RusKhim, Russia) solution, which was brought to a necessary concentration (0.25, 0.5, and 1.0 M) by adding water. To the resultant lactic acid solution was added calcium carbonate (Sigma-Aldrich, Germany) in an amount corresponding to the reaction



An aqueous ammonium hydrogen phosphate solution of controlled concentration was added dropwise to the calcium lactate solution over a period of 1 h. The resultant suspension was stirred at room temperature for 24 h on a magnetic stirrer. The synthesis product was then separated from the mother liquor in a Buchner funnel. After synthesis, the calcium phosphate precipitates were placed in plastic containers and dried in air for a week. The powders were disaggregated by grinding in a planetary mill in zirconia vials for 10 min at a rotation rate of 7000 rpm, using zirconia grinding media and acetone as a disaggregation medium. The powder-to-ball weight ratio was 1 : 5. After disaggregation, the powders were dried in a drying oven at 40°C for 1 h. Next, the powders were passed through a sieve with a nominal aperture size of 200  $\mu\text{m}$ . The synthesized powders were placed in porcelain boats and heat-treated at 500, 600, and 700°C (heating rate of 5°C/min, holding at the required temperature for 30 min). The resultant powders were pressed at 100 MPa into disk-shaped compacts 12 mm in diameter and 2–3 mm in thickness on a Carver Laboratory Model c manual press (USA). The by-product (presumably, ammonium lactate) or its destruction products formed during heat treatment in the range 500–



**Fig. 1.** X-ray diffraction patterns of the powders synthesized from aqueous calcium lactate and ammonium hydrogen phosphate solutions of various concentrations.

700°C acted as a temporary process binder. The green powder compacts were fired in a furnace at a temperature of 1100°C (heating rate of 5°C/min, holding at the required temperature for 2 h, furnace-cooling).

The linear shrinkage and geometric density of the samples were determined by measuring their mass and dimensions before and after firing.

The phase composition of the as-prepared powder and heat-treated samples was determined by X-ray diffraction on a Rigaku D/Max-2500 rotating-anode diffractometer (Japan). The phases present were qualitatively identified using ICDD PDF2 data. Intensity data were collected in reflection geometry with  $\text{CuK}\alpha$  radiation ( $2\theta = 2^\circ\text{--}70^\circ$ , scan step of  $0.02^\circ$ , continuous scan rate of  $5^\circ/\text{min}$ ).

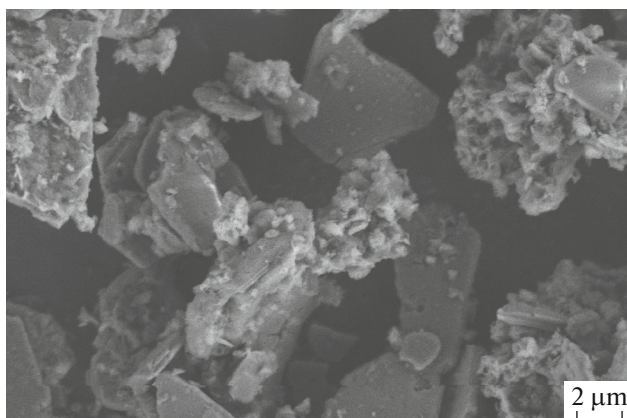
The samples were characterized by thermal analysis using a Netzsch STA 409 PC Luxx thermoanalytical system (Netzsch, Germany). The composition of the vapor phase resulting from the decomposition of the samples was determined using a QMS 403C Aëolos quadrupole mass spectrometer (Netzsch, Germany), combined with the Netzsch STA 409 PC Luxx thermoanalytical system. Mass spectra were taken for the mass numbers 18, 17 (corresponding to  $\text{H}_2\text{O}$  and  $\text{OH}/\text{NH}_3$ ), 15 (NH), 30 (NO), and 44 ( $\text{CO}_2$ ). The heating rate was  $10^\circ\text{C}/\text{min}$  and the temperature range

was 40–1000°C. The sample weight was at least 10 mg. Particle size distributions were obtained using an Analysette-22 MicroTec plus analyzer (Fritsch, Germany). The microstructures of the as-prepared and heat-treated powders and ceramics after firing were examined by scanning electron microscopy (SEM) on a LEO SUPRA 50 VP scanning electron microscope (Carl Zeiss, Germany; field emission source) under low vacuum at an accelerating voltage of 20 kV (VPSE secondary electron detector) or at voltages in the range 3–20 kV (SE2 detector). Secondary electron images were obtained at magnifications of up to 20 000 $\times$ .

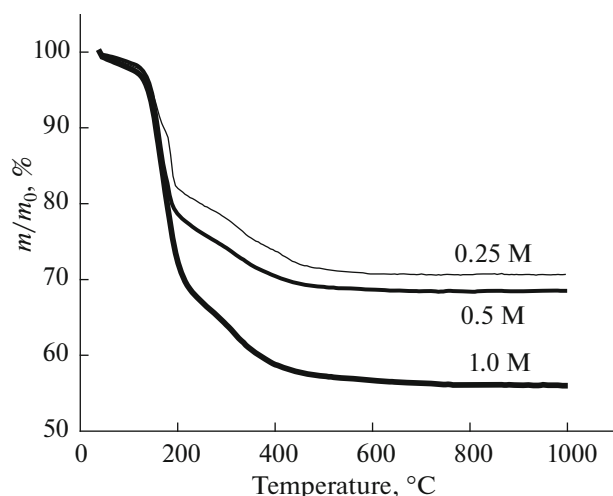
## RESULTS AND DISCUSSION

According to X-ray diffraction data (Fig. 1), the phase composition of the powders synthesized from aqueous calcium lactate and ammonium hydrogen phosphate solutions was presented predominantly by brushite and OCP. The intensity of the strongest reflection from OCP decreases with increasing solution concentration. One possible reason for this is that dilute solutions provide conditions for the growth of larger crystals.

Micrographs of the powder synthesized from the aqueous 0.5 M calcium lactate and ammonium hydrogen phosphate solutions at a Ca/P molar ratio of 1



**Fig. 2.** Micrograph of the CP powder synthesized from the aqueous 0.5 M solutions.

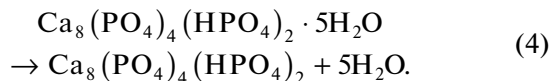


**Fig. 3.** Thermal analysis data for the synthesized CP powders.

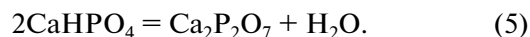
(Fig. 2) demonstrate that the powder consists predominantly of platelike particles. The micrograph in Fig. 2 shows large platelike particles 2 to 6  $\mu\text{m}$  in size, consisting of thinner platelets fused to each other, and small, irregularly shaped particles 0.5 to 1  $\mu\text{m}$  in size, which form large agglomerates ranging in size from 4 to 7  $\mu\text{m}$ . A platelike shape is characteristic of synthetic brushite particles. It is reasonable to assume that the aggregates of irregularly shaped particles consist of OCP.

Figure 3 presents thermal analysis data. The total mass loss of the powders at 1000°C increases with increasing initial solution concentration and is 30, 32, and 44% for the powders synthesized from the 0.25, 0.5, and 1.0 M solutions. In all of the powders, the adsorbed water loss does not exceed 2%. The major weight loss occurs in the range 100–250°C and is due to the decomposition of brushite [reaction (3)] into monetite, OCP decomposition [reaction (4)], and

reaction by-product decomposition, as illustrated in Fig. 4 by the example of the powder synthesized from the 1 M solutions:



It is known that monetite typically converts into CPP at 400°C:



However, the temperature dependences of the mass for the powders synthesized from calcium phosphate and ammonium hydrogen phosphate do not have any characteristic step at this temperature. Most likely, the presence of dehydrated OCP,  $\text{Ca}_8(\text{PO}_4)_4(\text{HPO}_4)_2$ , which decomposes to form CPP and TCP during further heating [17], determines the monotonic behavior of the curve during heating in the range 250–600°C.

The observed peak in the mass spectrometric curve for mass 18 particles ( $\text{H}_2\text{O}$ ) corresponds to 160°C, and a water release was detected in the range 110–550°C. An ammonia release, evidenced by the curve for mass 15 particles ( $\text{NH}$ ), was observed in the range 125–580°C, with the highest release rate at 250 and 310°C. The  $\text{CO}_2$  release (mass 44 particles), characterizing the decomposition of the reaction by-product, presumably ammonium lactate or lactic acid, occurs in three steps, with peaks at 205, 325, and 615°C.

The powders heat-treated at various temperatures and the compacts produced from them were gray in color, with various hues. With increasing initial solution concentration, the color intensity increases, reaching a maximum depth after heat treatment at 600°C. The as-prepared and disaggregated powders, as well as the compacts produced from them, were white in color. All of the powders prepared from aqueous calcium lactate and ammonium hydrogen phosphate solutions of various concentrations and then heat-treated for 30 min in the range 500–700°C were found to contain  $\gamma\text{-Ca}_2\text{P}_2\text{O}_7$  (Fig. 5). The powders heat-treated at 500°C were found to contain monetite. Synthetic OCP consists of alternating HA and brushite layers, and it is the brushite which converts into monetite. Each brushite layer is sandwiched between HA layers, so the water of crystallization is difficult to remove from the brushite. It is for this reason that monetite persists to a relatively high temperature. The transformation of  $\gamma\text{-Ca}_2\text{P}_2\text{O}_7$  into  $\beta\text{-Ca}_2\text{P}_2\text{O}_7$  is known to occur at 700°C. The powders heat-treated at 700°C were found to contain both  $\gamma\text{-Ca}_2\text{P}_2\text{O}_7$  and  $\beta\text{-Ca}_2\text{P}_2\text{O}_7$ , which was most likely due to the relatively slow process kinetics and the insufficient heat treatment time (30 min).

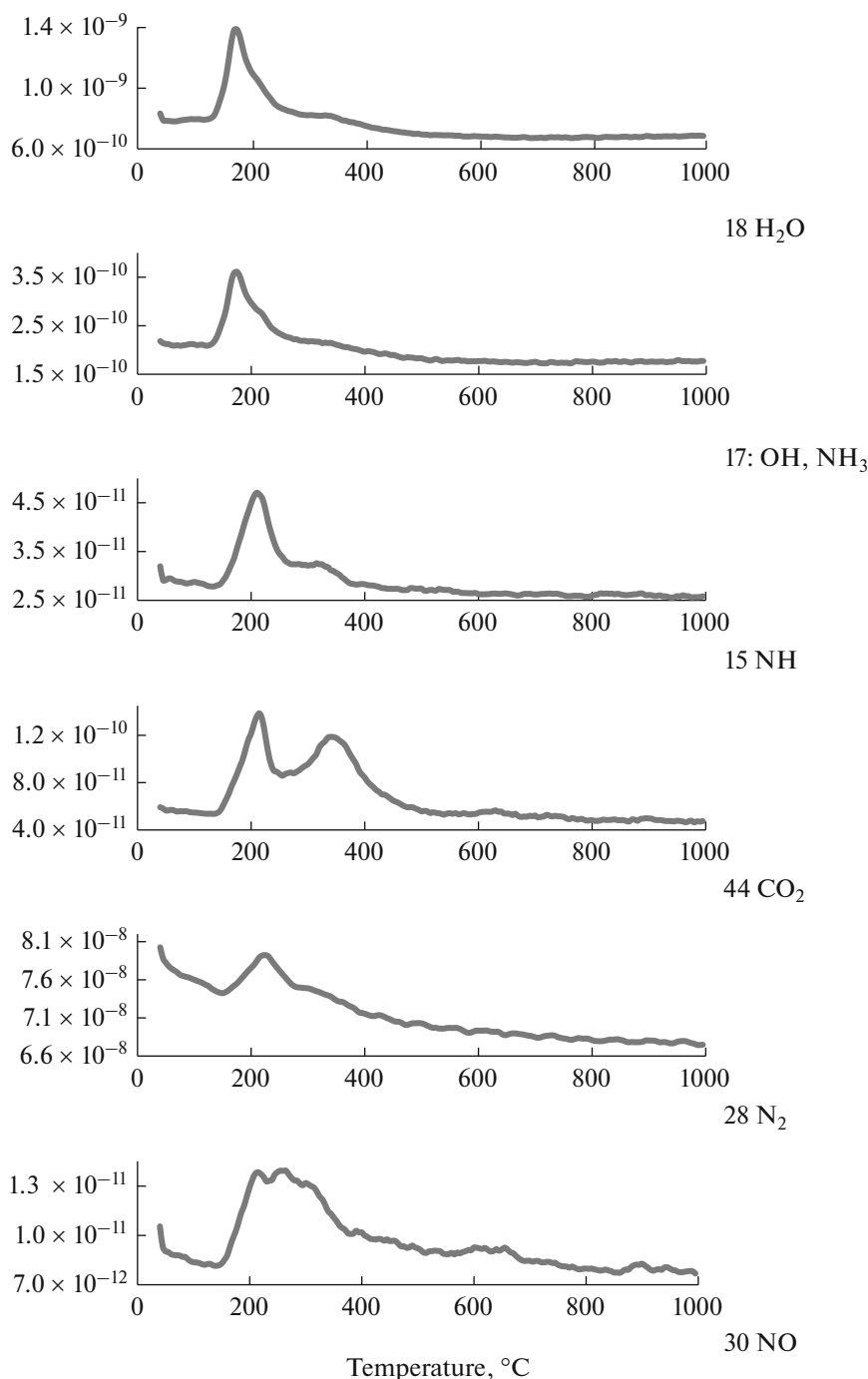
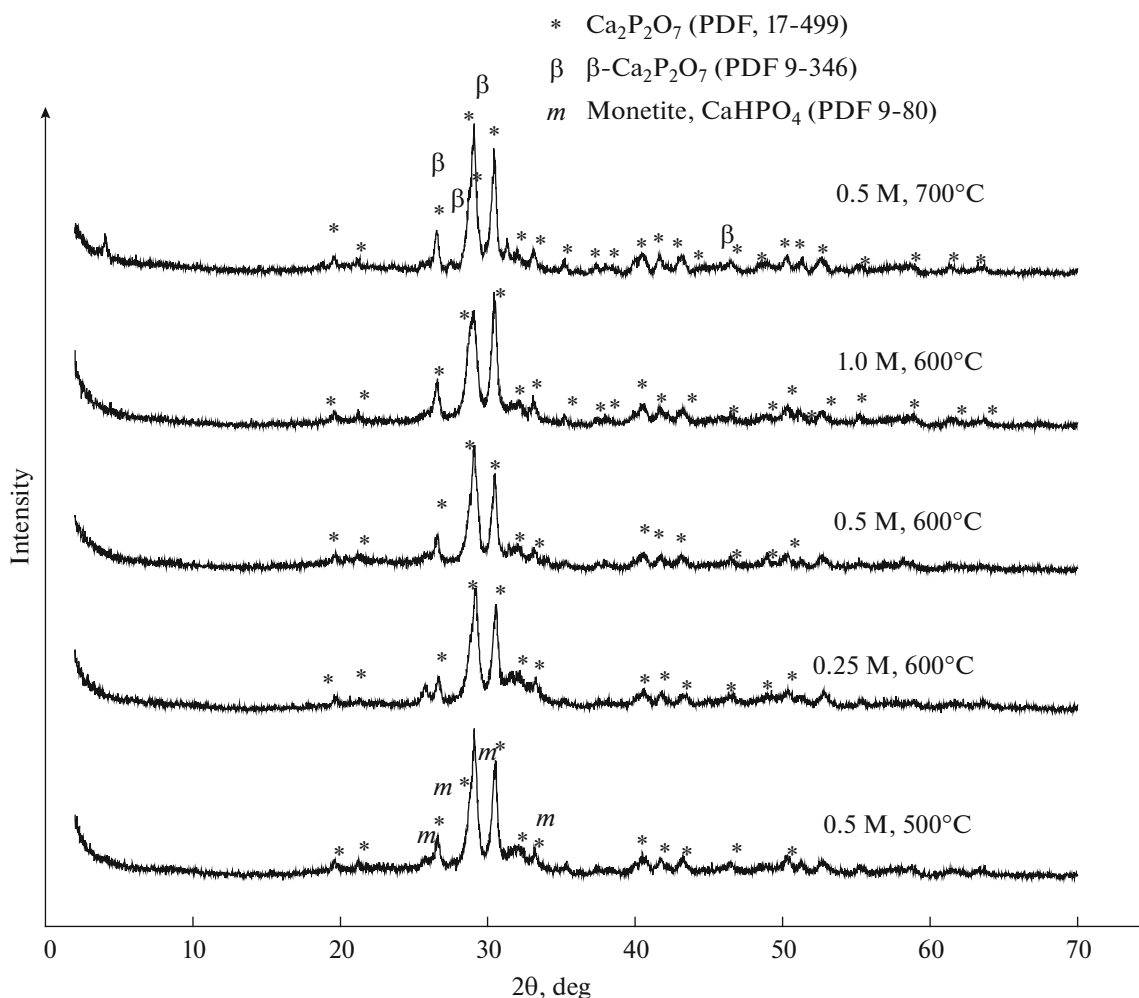


Fig. 4. Mass spectrometry data for the powder synthesized from the aqueous 1.0 M solutions.

According to SEM data, the powders heat-treated in the range 500–700°C (Fig. 6) are essentially identical to the as-synthesized powders. There are also platelike particles and aggregates of smaller, irregularly shaped particles. At a larger magnification (20 000 $\times$ ), the platelike particles are seen to have characteristic, aligned disruptions (pores), which result from the removal of the water of crystallization during heating: first from brushite and then from monetite. The parti-

cles in the aggregates have a ribbonlike or flaky structure (no more than 100 nm in thickness) and there are also isometric particles (no more than 100 nm in size).

Figure 7 shows the particle size distributions of the as-synthesized powder and the samples heat-treated at 500, 600, and 700°C for 30 min. The most probable aggregate size in the as-synthesized powder and the powder heat-treated at 500°C is about 7  $\mu\text{m}$ . After heat treatments at 600 and 700°C, the most probable aggre-



**Fig. 5.** X-ray diffraction patterns of the powders synthesized from aqueous solutions with various concentrations and then heat-treated for 30 min at 500, 600, and 700°C.

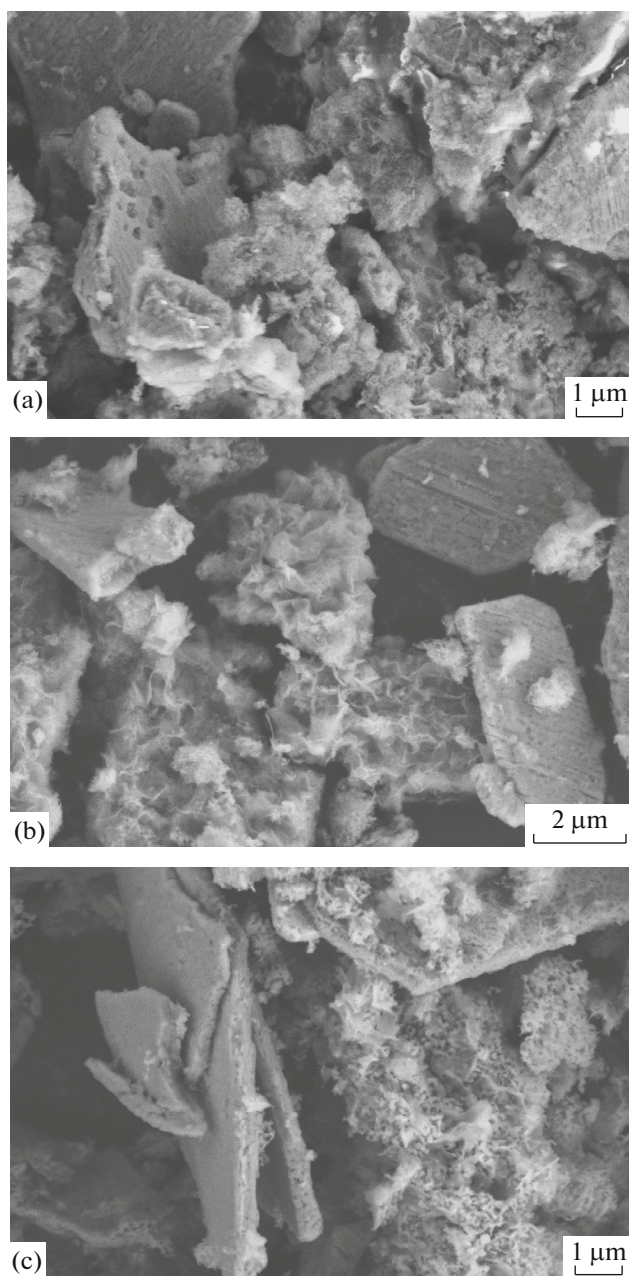
gate size is 6.1 and 5.7  $\mu\text{m}$ , respectively. The as-synthesized powder contains aggregates ranging in size from 1 to 24  $\mu\text{m}$ , and the aggregates in the powder heat-treated at 700°C range in size from 0.7 to 24  $\mu\text{m}$ . With increasing heat treatment temperature, the most probable aggregate size increases only slightly, and the distribution extends toward smaller aggregate sizes.

Green powder compacts were produced from the as-synthesized powders containing reaction by-products and the powders heat-treated in the range 500–700°C, which contained reaction by-product carbonization products. Figure 8 shows the density of the green powder compacts as a function of initial solution concentration. The highest density (1.42  $\text{g}/\text{cm}^3$ ) was offered by the samples from the powder synthesized from the 0.5 M solutions and then heat-treated at 600°C. The green compacts prepared from the powders synthesized from the 1.0 M solutions had a relatively low density (0.96–1.10  $\text{g}/\text{cm}^3$ ), which was prob-

ably caused by the considerable content of the reaction by-products or their thermal destruction products, which impeded densification. The density of the green compacts from the powders synthesized from the 0.25 M solutions slightly exceeded that of the green compacts from the powders synthesized from the 1.0 M solutions: 1.10–1.22  $\text{g}/\text{cm}^3$ . A low density of the green powder compacts (1.10–1.17  $\text{g}/\text{cm}^3$ ) was also observed for the samples from the powder containing the reaction by-product, which impeded densification. The green compacts from the powder heat-treated at 700°C also had a relatively low density because, unlike the powder synthesized from the 0.5 M solution and then heat-treated at 500 and 600°C, it contained no carbonized residues of the reaction by-product, whose amount should be optimized to ensure better densification.

According to the X-ray diffraction data in Fig. 9, the ceramics after firing consisted of  $\beta\text{-Ca}_2\text{P}_2\text{O}_7$  and

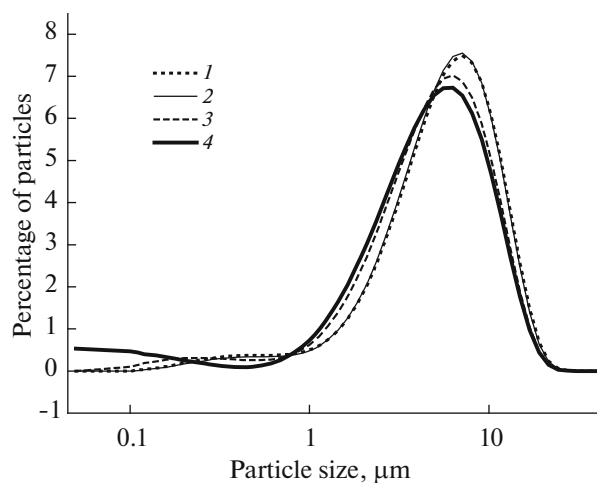




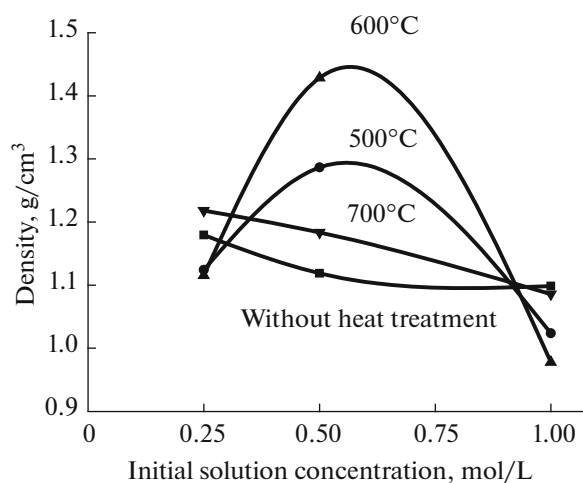
**Fig. 6.** Micrographs of the CP powders synthesized from the 0.5 M solutions and then heat-treated at (a) 500, (b) 600, and (c) 700°C.

$\beta$ - $\text{Ca}_3(\text{PO}_4)_2$ , independent of the initial solution concentration and heat treatment temperature. The precursors of the  $\beta$ - $\text{Ca}_2\text{P}_2\text{O}_7$  phase were brushite and OCP, and the formation of  $\beta$ - $\text{Ca}_3(\text{PO}_4)_2$  was due to the presence of OCP in the starting powder.

The density of the green powder compacts was not inherited by the ceramic samples prepared by firing at 1100°C for 2 h (Fig. 10). By contrast, the ceramic samples produced from the powder heat-treated at 700°C had the highest density, which however did not exceed



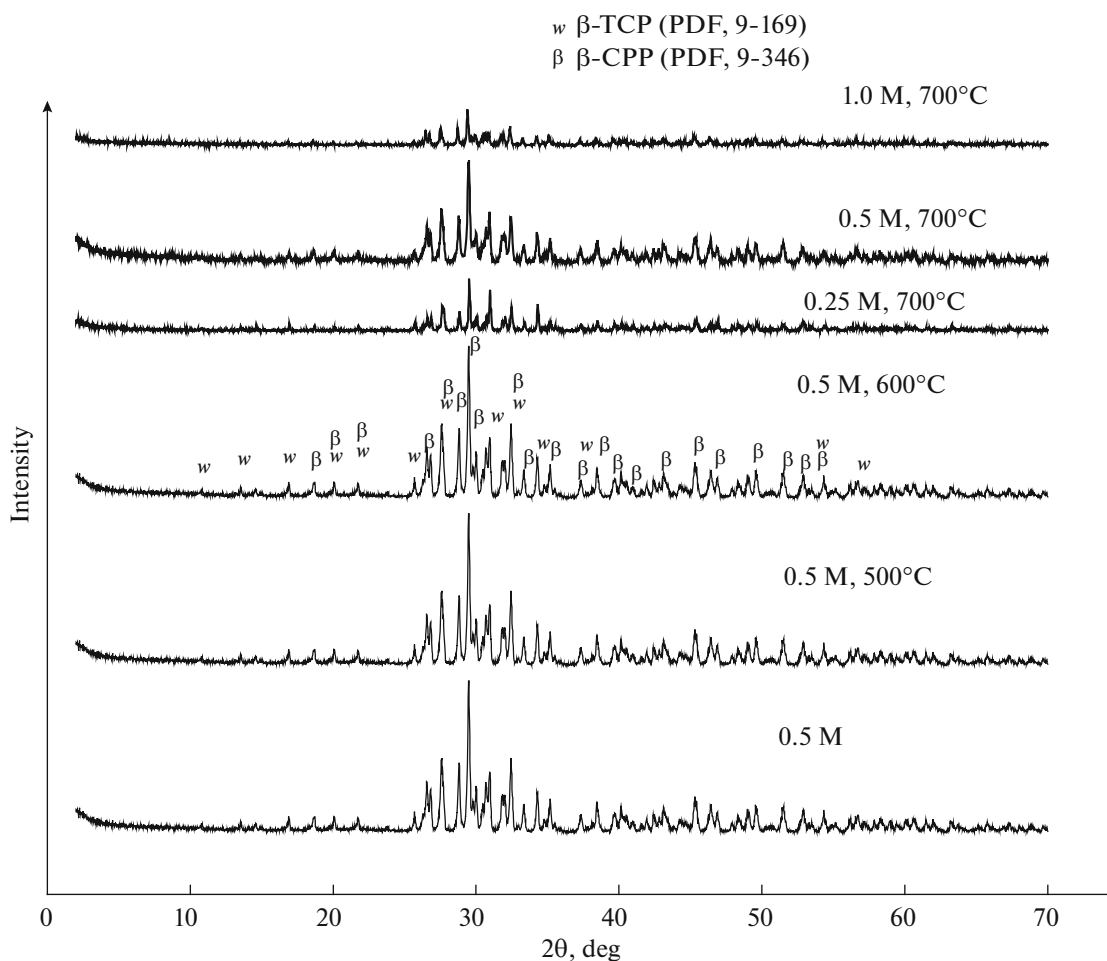
**Fig. 7.** Particle size distributions of the powder synthesized from the 0.5 M solutions (1) and then heat-treated for 30 min at 500 (2), 600 (3), and 700°C (4).



**Fig. 8.** Effect of powder preparation conditions on the density of the green powder compacts.

54% of theoretical density (3.09 g/cm<sup>3</sup> for CPP and 3.07 g/cm<sup>3</sup> for TCP). Here we observe not only the effect of the low density of the green powder compacts but also that of the presence of powder components that decompose releasing gaseous products.

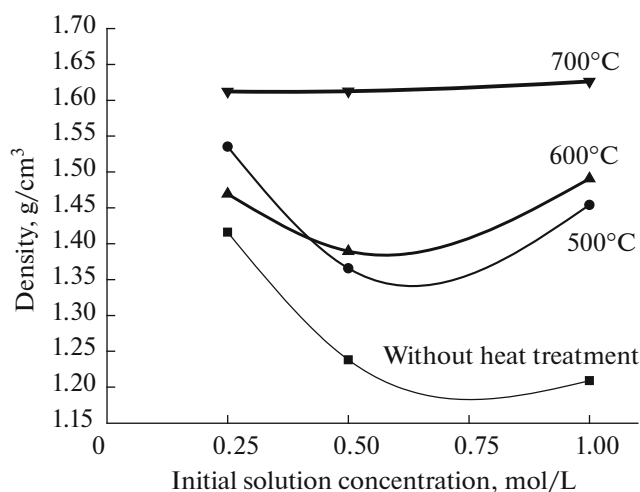
Figure 11 shows micrographs of the ceramic samples produced by firing at 1100°C for 2 h from the powders synthesized from the 0.5 M calcium lactate and ammonium hydrogen phosphate solutions and heat-treated in the range 500–700°C. The ceramic sample from the powder containing the reaction by-product appears the least sintered, with a considerable pore volume. The ceramic sample with the smallest pore volume was obtained from the powder heat-treated at 700°C for 30 min. In all of the samples, the grain size



**Fig. 9.** X-ray diffraction patterns of the ceramics produced by firing at 1100°C for 2 h from powders synthesized under various conditions.

was about 1  $\mu\text{m}$ . Note that some of the grains were sintered to each other to form plates which ranged in size up to 10  $\mu\text{m}$ . The size of visible pores was 2 to 4  $\mu\text{m}$ .

Micrographs of fracture surfaces of the ceramics let us to assume that the pores were connected and permeable.

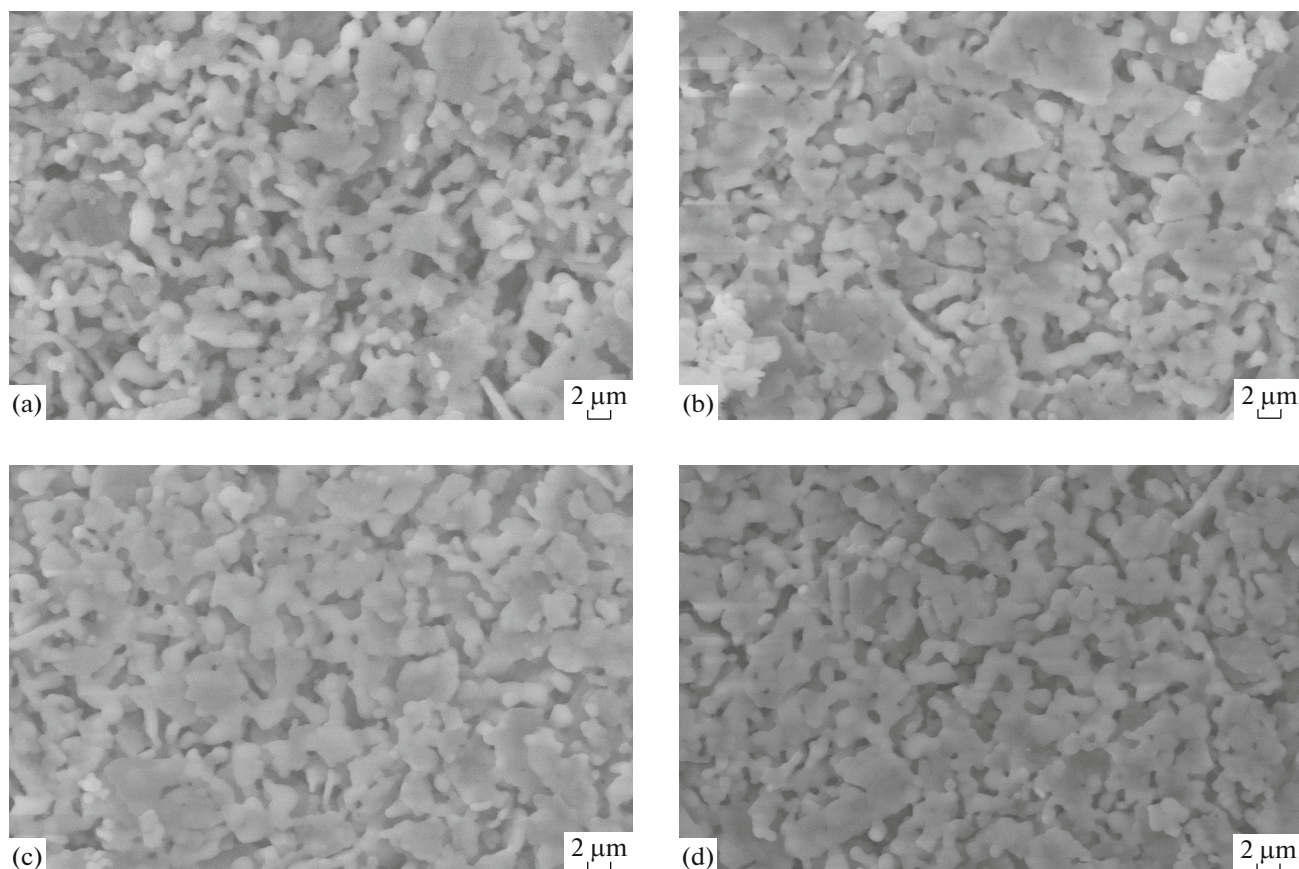


**Fig. 10.** Effect of powder preparation conditions on the density of the ceramics produced by firing at 1100°C for 2 h.

## CONCLUSIONS

The use of aqueous 0.25–1.0 M calcium lactate and ammonium hydrogen phosphate solutions allows one to obtain calcium phosphate powders at room temperature without adjusting pH. Their phase composition includes brushite ( $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$ ) and OCP ( $\text{Ca}_8(\text{HPO}_4)_2(\text{PO}_4)_4 \cdot 5\text{H}_2\text{O}$ ). After heat treatment in the range 500–700°C, the powders were gray in color because of the presence of the reaction by-product destruction products. The presence of destruction products in the powder prepared from the 0.5 M solutions and then heat-treated at 600°C facilitates the densification process during pressing, reducing the friction of the powders against the steel mold. The CP powders colored by the destruction products can be used to produce slurries based on light-curable monomers intended for stereolithographic printing of





**Fig. 11.** Micrographs of ceramic samples prepared by firing at 1100°C for 2 h from the powders synthesized from the 0.5 M solutions: without heat treatment (a) and after heat treatment for 30 min at 500 (b), 600 (c), and 700°C (d).

porous, openwork green ceramic structures. The presence of reaction by-products and their destruction products in the powders makes it impossible to produce high-density ceramics. In the case of CP-containing ceramics intended for use as implants, micro-porosity can be regarded as an advantageous property. It ensures a surface roughness necessary for a comfortable existence of the bone cells responsible for bone tissue regeneration.

After heat treatment in the range 500–700°C, the phase composition of the powders is dominated by  $\gamma$ - $\text{Ca}_2\text{P}_2\text{O}_7$ . The phase composition of the ceramics prepared from the synthesized powders heat-treated at 1100°C included the biocompatible and bioresorbable phases of CPP ( $\beta$ - $\text{Ca}_2\text{P}_2\text{O}_7$ ) and TCP ( $\beta$ - $\text{Ca}_3(\text{PO}_4)_2$ ). The CP-based ceramic materials produced in this study from synthetic powders can be recommended for the fabrication of bone implants.

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