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SYNTHESIS OF HYDROXYAPATITE USING VARIOUS SACCHARATE TYPES

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Abstract

The work considers the preparation of hydroxyapatite from calcium sucrate and calcium dextrates solutions by chemical precipitation. It has been shown that the use of calcium sucrate makes it possible to obtain the pure hydroxyapatite phase even without further heat treatment of the precipitate. The IR spectroscopic studies confirm the obtaining of the pure hydroxyapatite phase with carbonate-ions substitution by B-type in HAp samples. The synthesis with a low temperature dextrin leads to the production of hydroxyapatite with a small admixture of tricalcium phosphate, a further increase in temperature also leads to the production of pure hydroxyapatite. According to the X-ray analysis, all the obtained hydroxyapatite powders are characterized by the crystallite size in the nanoscale. Obtained SEM images of the powders indicate compact hydroxyapatite aggregates with the sizes of 5–30 microns when using calcium sucrate complexes and loose particles in the range of 1–20 microns when using dextrin.

Keywords: nanocrystalline hydroxyapatite; calcium sucrate; calcium dextrate; chemical precipitation; low temperature synthesis.

СИНТЕЗ ГІДРОКСИПАТИТУ З ВИКОРИСТАННЯМ РІЗНИХ ТИПІВ САХАРАТІВ

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Анотація

У роботі розглянуто одержання гідроксиапатиту з розчинів сахаратів кальцію та декстратів кальцію методом хімічного осадження. Показано, що використання сахарату кальцію дозволяє отримати фазу чистого гідроксиапатиту без використання термічної обробки осаду. ІЧ-спектроскопічні дослідження підтверджують отримання чистої гідроксиапатитової фази у зразках НАр із заміщенням карбонат-іонів за Б-типом. Низькотемпературний синтез за участю декстратів кальцію призводить до утворення гідроксиапатиту з незначною домішкою трикальцію фосфату, а подальше підвищення температури сприяє утворенню фази чистого гідроксиапатиту. Згідно рентгеноструктурного аналізу, всі отримані порошки гідроксиапатиту мають кристаліти з розміром у нанодіапазоні. Отримані СЕМ-зображення порошків вказують на наявність компактних агрегатів гідроксиапатиту із розмірами від 5 мкм до 30 мкм за умови використання сахарату кальцію та наявність пухкої структури зразків з частинками в діапазоні від 1 мкм до 20 мкм за умови використання як прекурсору декстратів кальцію.

Ключові слова: нанокристалічний гідроксиапатит; сахарат кальцію; декстрат кальцію; хімічне осадження; низькотемпературний синтез.

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СИНТЕЗ ГИДРОКСИПАТИТУ С ИСПОЛЬЗОВАНИЕМ РАЗЛИЧНЫХ ТИПОВ САХАРАТОВ

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Аннотация

В работе рассмотрено получение гидроксиапатита из растворов сахарата кальция и декстракта кальция методом химического осаждения. Показано, что использование сахарата кальция позволяет получить фазу чистого гидроксиапатита без использования термической обработки осадка. ИК-спектроскопические исследования подтверждают получение чистой гидроксиапатитовой фазы в образцах НАр с замещением карбонат-ионов по Б-типу. Низкотемпературный синтез с участием декстракта кальция приводит к образованию гидроксиапатита с незначительной примесью трикальцийфосфата, а дальнейшее повышение температуры способствует образованию фазы чистого гидроксиапатита. Согласно данным рентгеноструктурного анализа, все полученные порошки гидроксиапатита имеют кристаллиты с размером в нанодиапазоне. Полученные СЭМ-изображения порошков указывают на наличие компактных агрегатов гидроксиапатита с размерами от 5 мкм до 30 мкм при использовании сахарата кальция и наличие рыхлой структуры образцов с частицами в диапазоне от 1 мкм до 20 мкм при использовании как прекурсора декстракта кальция.

Ключевые слова: нанокристаллический гидроксиапатит; сахарат кальция; декстракт кальция; химическое осаждение; низкотемпературный синтез.

Introduction

Among the phosphate-calcium materials, hydroxyapatite (HAp) occupies a special place due to its wide use in medicine as biomaterials. Hydroxyapatite $Ca_{10}(PO_4)_6(OH)_2$ is an analogue of the mineral component of bone and dental tissue and is characterized by such properties as bioactivity and biocompatibility. For this reason, HAp-based structures are promising materials that can be used to restore damaged bones and will not be rejected by human body [1].

The HAp refers to the group of minerals called "apatite". In mineralogy, biomineralogy and biomaterials science, the name “apatite” means compounds like $Ca_5(PO_4)_3Y$ or $Ca_{10}(PO_4)_6Y_2$, where Y is fluorine, chlorine or hydroxide ions, which can be easily replaced by carbonate or sulfate anions. From the point of view of chemical composition, apatites are calcium orthophosphates [2]. Nowadays, more than a hundred chemically different natural and synthetic apatite-like compounds have been described [3]. The ability to substitute in the anionic and cationic layers of apatites and, on this basis, the variability of structural characteristics and physicochemical properties is the object of numerous studies.

Pure HAp is a stoichiometric phase of apatite with a Ca/P molar ratio of 1.67, which is stable at normal temperatures and pH from 4 to 12 [4]. However, HAp is characterized by a large variety of substitutions, therefore, the degree of symmetry and even the spatial symmetry group can change. The hexagonal crystal structure of the HAp, which has the symmetry of the $P6_3/m$ space group (see Fig.1) is encountered most frequently. With the complication of chemical composition, the symmetry class decreases and may be $P6_3$, $P2_1$, $P2_1/m$ or other [5]. In addition, diverse combinations of phosphorus and calcium oxides directly give a huge variety of phosphate-calcium compounds. Therefore, it is very important to develop reproducible methods for obtaining HAp, which would ensure 100% production of hydroxyapatite.

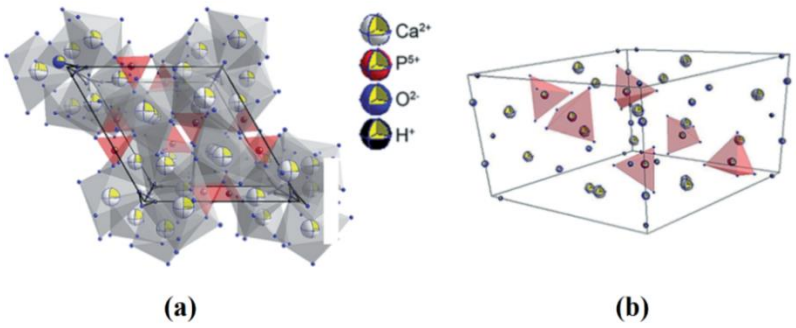

Fig. 1 The crystal structure of $Ca_{10}(PO_4)_6(OH)_2$: coordination polyhedron (a) and elementary cell (b) [6].

The HAp synthesis is carried out by various methods, such as chemical precipitation, sol-gel technique, hydrothermal synthesis, biomimetic approach and others [7].

The chemical precipitation synthesis method includes 2 «classic» ways to obtain HAp. The first method uses calcium nitrate as the source of calcium, the second uses calcium oxide. In the first case, the obtained amorphous precipitate requires high-temperature treatment for the HAp crystallization, in the second approach, the low solubility of calcium oxide does not contribute to the widespread use of this method [8; 9].

The sol-gel method is widely used as an industrial method of HAp production. The source of calcium in this case is calcium alkoxide. As a result, an amorphous precipitate is formed, which crystallizes into a well-crystallized hydroxyapatite at 500 °C [10; 11].

The hydrothermal synthesis of HAp is carried out at elevated temperatures and pressures in aqueous or alcoholic media, at which first the synthesis of amorphous calcium phosphate occurs , followed by the crystallization of HAp. The main feature of the hydrothermal HAp synthesis is the chelate calcium complexes usage [12; 13].

The solid-phase synthesis of hydroxyapatite is based on the use of solid-phase reactions, diffusion processes resulting from calcination of mixtures of pre-ground compounds containing calcium ions and phosphate ions at 1000 – 1300 °C. An atmosphere of water vapor is used as a source of OH^--groups. In mechanochemical synthesis, the starting materials are ground in a planetary mill while maintaining the stoichiometric ratio between the reactants. Usually, hydroxyapatite is obtained by these methods from the initial calcium-containing components - CaO, $Ca(OH)_2$, $CaCO_3$ - and salts containing phosphate groups [14–16].

The biomimetic method is based on the synthesis of materials that model the specific properties of natural biomineral structures, i.e. on the use of self-organization and self-assembly – the basic principles of the living systems existence. Currently, the most effective way of the HAp biomimetic synthesis is its synthesis through the self-organization with polymers [17]. To date, this promising method for obtaining bioactive HAp is still at the stage of its early development.

In addition to the methods described above for obtaining HAp, there are the so-called combined synthesis methods [18]. In order to improve the properties of the final product and the possibility of varying the phase composition of the synthesis products, two or more separate methods can be combined into one. The use of combined techniques of low and high temperature syntheses is widely used in practice.

Despite the progress made in the direction of the HAp synthesis, the development of new or modified methods for the hydroxyapatite production is still relevant. This is promoted by the development of new types of ceramics for medical purposes, which requires the creation of new methods for producing highly dispersed nanocrystalline powders based on calcium phosphate. The synthesis of nanocrystalline calcium phosphates, which do not contain aggressive byproducts and are suitable for the production of ceramic materials, can be carried out from suspensions of calcium hydroxides and phosphoric acid. In this case, water will be the byproduct of the reaction. However, this method is inconvenient in practice due to the poor solubility of calcium hydroxides. In our opinion, the alternative method is the synthesis of calcium phosphates using soluble calcium sucrates as the starting material [19; 20]. The aim of the current work was to study the physicochemical properties of hydroxyapatite obtained from various saccharates (sucrate and dextrate) solutions.

Experimental

Materials. For the synthesis by saccharate method, the following reagents were used: calcium oxide (CaO), sucrose ($C_{12}H_{22}O_{11}$), dextrin ($nC_6H_{10}O_5$) and ammonium hydro-phosphate ($(NH_4)_2HPO_4$). All reagents were of analytical grade.

Obtaining of hydroxyapatite samples. Before starting the synthesis, calcium oxide was calcined at 900 °C. Then 100 cm^3 of the sucrose (dextrin) solution with a concentration of 0.1 mol per dm^3 was prepared, 0.5 g of calcium oxide was added, and the resulting solution was left for the formation of calcium sucrate (dextrate). After that, HAp was directly synthesized: ammonium hydrogen phosphate was added to the calcium sucrate (dextrate) solution and the ammonia solution with a concentration of 20 % by weight was added dropwise with stirring up to pH 10. The obtained precipitates were filtered, dried at 80ºC during 4 hours and calcined under the conditions indicated in Table 1.

Reactions (using sucrose as an example), which took place during the synthesis process, are presented below (see Eq. 1 and Eq. 2).

$CaO + C_{12}H_{22}O_{11} \rightarrow CaC_{12}H_{20}O_{11} + H_2O,$ (1)

$10CaC_{12}H_{20}O_{11}+6(NH_4)_2HPO_4+14H_2O \rightarrow Ca_{10}(PO_4)_6(OH)_2+12NH_4OH+10C_{12}H_{22}O_{11}.$ (2)

Table 1

Conditions for the synthesis of hydroxyapatite samples

Sample	Saccharide	Calcination duration	Calcination temperature, ºC
HAp0SU	Sucrose	1 hour	-
HAp500SU	Sucrose	1 hour	500
HAp700SU	Sucrose	1 hour	700
HAp900SU	Sucrose	1 hour	900
HAp0DE	Dextrin	1 hour	-
HAp500DE	Dextrin	1 hour	500
HAp700DE	Dextrin	1 hour	700
HAp900DE	Dextrin	1 hour	900

HAp samples characterization. The thermal analysis of the HAp samples was carried out in the air atmosphere using the Derivatigraf Q-1500 analyzer (IOM, Hungary) at a heating rate of 10ºC per min. XRD (X-ray diffraction) measurements of HAp samples were conducted using X-ray diffractometer Ultima IV Rigaku with CuKa radiation. The Samples were automatically analyzed by the PDXL software package using ICDD / PDF-2 and COD databases (standard cards ICDD 01-076-0694 (HAP) and 00-029-0359 (tricalcium phosphate)) [21]. The IR spectroscopic studies of the HAp samples were performed using the Thermo Nicolet Nexus FTIR spectrometer. The morphology of the synthesized HAp samples was studied using the scanning electron microscope SEM 106M.

Results and discussion

Thermal analysis. The resulting thermograms of HAp0SU and HAp0DE samples are shown in Figure 2. According to the obtained TG curves, it can be seen that the mass loss in the HAp0SU sample is not more than 21 % when heated to 1000ºC, a larger loss is observed in the HAp0DE sample and it reaches 58 % by mass. This is due to the different amounts of adsorbed sucrose and dextrin, which, as evidenced by the exothermic effects on the DTA curves, are removed with heating. Thus, on the HAp surface sucrose is sorbed almost 3 times less than dextrin.

In the case of sucrose, the observed peaks on DTG at about 110 °C and 210 °C are associated with the removal of water, and at 360 °C – with the beginning of the sucrose removal. For DTG of the dextrin, the similar pattern is observed with the only difference that there is no peak at 210 °C.

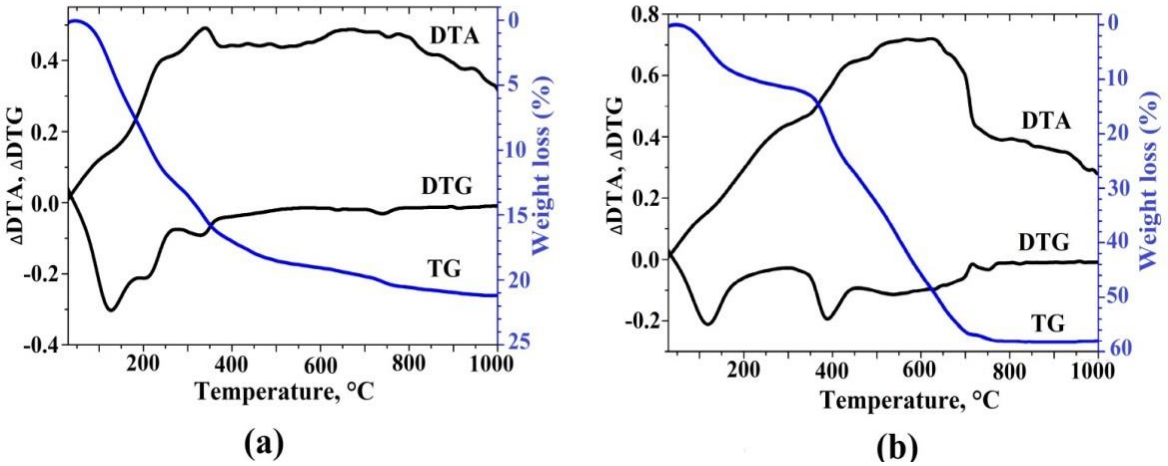

Fig. 2 Thermograms of the HAp0SU (a) and HAp0DE (b) samples

X-ray analysis. The XRD patterns and structural parameters of the hydroxyapatite samples obtained by X-ray analysis are presented in Figure 3 and Table 2.

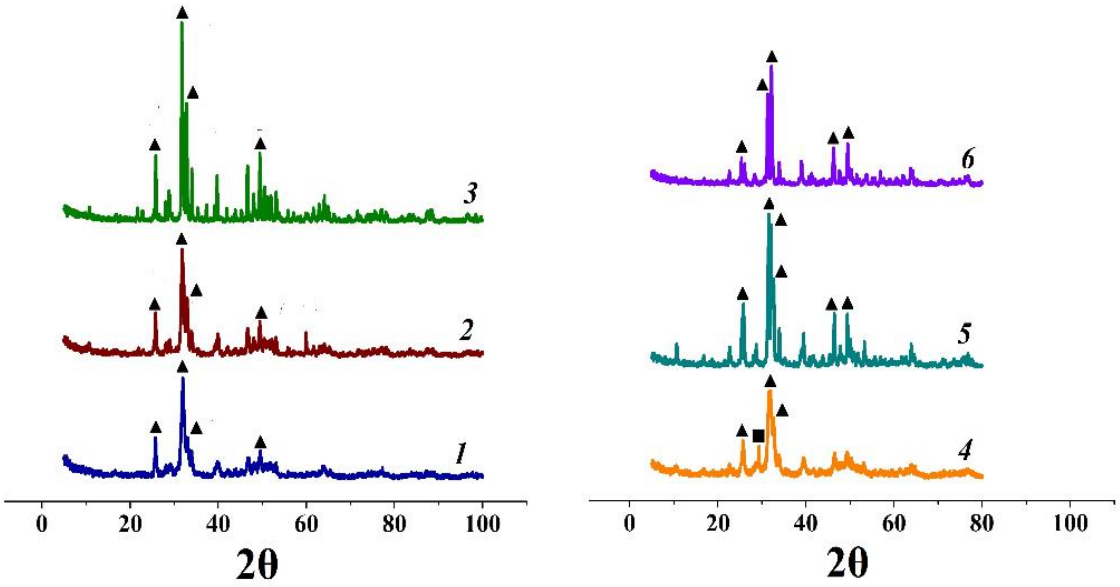

Fig. 3 The XRD patterns of the HAp samples: 1 – HAp500SU; 2 – HAp700SU; 3 – HAp900SU; 4 – HAp500DE; 5 – HAp700DE; 6 – HAp900DE (▲– hydroxyapatite,■ – tricalcium phosphate)

As can be seen from Figure 3, hydroxyapatite in all cases is formed at 500–900 °C, and only in the case of using dextrin at 500 °C the small amount of tricalcium phosphate ($Ca_3(PO_4)_2$) is present.

According to the data presented in Table 2, it can be argued that all obtained hydroxyapatite powders are nanocrystalline. As expected, the size of the crystallites in all cases increases with increasing temperature . However, in the case of dextrin, size stabilization is observed after 700 °C. It should also be noted that at lower processing temperatures (500–700 °C), the sizes of HAp crystallites, obtained with the participation of sucrose, are smaller than in the case of dextrin. This phenomenon can be explained by the smaller size of sucrose compared to dextrin, which leads to the formation of smaller crystallites. In our opinion, the larger crystallite size at higher temperature (900 °C) is connected with complete removal of sucrose from the surface of particles, resulting intensive aggregation of crystallites. The stabilization of the HAp crystallite sizes obtained with the participation of dextrin, is explained by the larger amount of the adsorbed saccharides on its surface.

Table 2

Composition and structural parameters of the obtained HAp samples

Sample	Composition	Crystallite size, nm
HAp500SU	100 % $Ca_{10}(PO_4)_6(OH)_2$	4.8
HAp700SU	100 % $Ca_{10}(PO_4)_6(OH)_2$	18.8
HAp900SU	100 % $Ca_{10}(PO_4)_6(OH)_2$	45.3
HAp500DE	92 % $Ca_{10}(PO_4)_6(OH)_2$, 8 % $Ca_3(PO_4)_2$	11.5
HAp700DE	100 % $Ca_{10}(PO_4)_6(OH)_2$	26.7
HAp900DE	100 % $Ca_{10}(PO_4)_6(OH)_2$	4.8

Microscopy. The SEM images of all the heat-treated HAp samples are shown in Fig. 4. As can be seen from the presented Figure, the HAp samples obtained with the participation of sucrose are characterized by greater compactness and have aggregates with the size of 5–30 microns. The HAp samples obtained with dextrin have a loose structure, the particle size ranges from 1 to 20 microns.

IR-spectroscopy. The HAp samples synthesized from calcium sucrate were selected for the study by IR-spectroscopy method. Infrared transmission spectra were recorded in the 4000–400 cm^{-1} region at the resolution of 8 cm^{-1}. The HAp samples were mixed with pre-annealed KBr (for spectroscopy, "Aldrich") in the ratio KBr / Sample = 1 / 30 (10 mg / 300 mg).

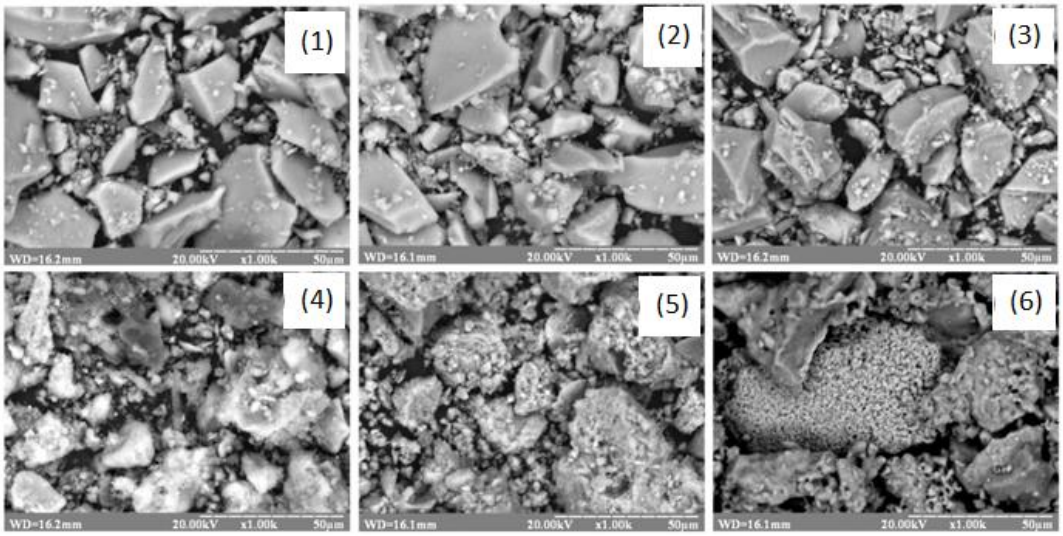

Fig. 4. SEM image of obtained HAp samples: (1) – HAp500SU; (2) – HAp700SU; (3) – HAp900SU; (4) – HAp500DE; (5) – HAp700DE; (6) – HAp900DE

The obtained IR spectra for samples HAp500SU, HAp700SU and HAp900SU are shown in Fig. 5. According to the spectra, all the samples have characteristic absorption bands for PO_4^{2-}, CO_3^{2-}, and also for the OH^- groups (Table 3). It also can be seen that when increasing the temperature of the dried phosphate-calcium precipitate, the characteristic bands both for physically adsorbed and chemically bound OH^- groups and water (2700–3800 cm^{-1}) decrease. For the HAp precipitate treated at 900 °C, they disappear altogether.

The presence of characteristic absorption CO_3^{2-} bands at 873–876 cm^{-1} and 1418-1461 cm^{-1} in all obtained spectra for the studied samples indicates the replacement of phosphate ions with CO_3^{2-} ions in the apatite, which leads to the formation of carbonate-containing B-type hydroxyapatite. In addition to the carbonate ion embedded in the apatite structure, there are also characteristic absorption bands of the adsorbed carbonate ion on the precipitate surface (bands in the range of 1992-2002 cm^{-1}). The presence of all the above-mentioned possible oscillations (ν1-ν4) should also be noted. This indicates the formation of the classical hexagonal hydroxyapatite structure without any changes.

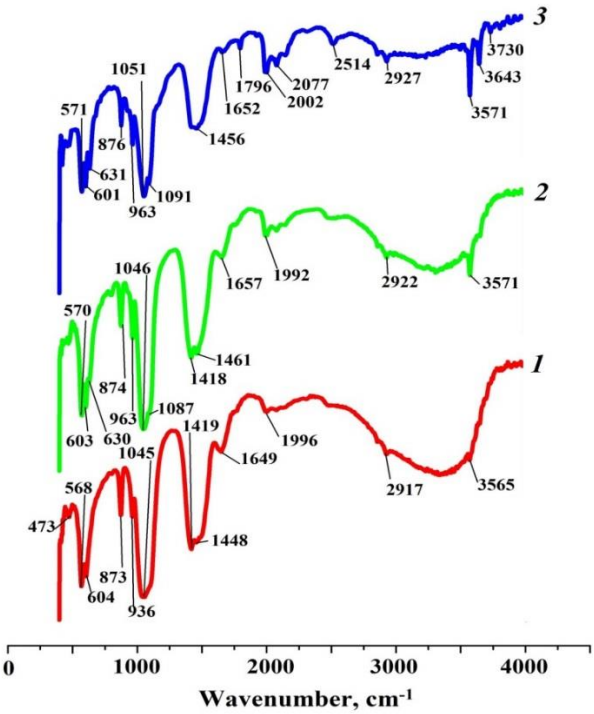

Fig. 5. IR spectra of the HAp samples: (1) – HAp500SU; (2) – HAp700SU; (3) – HAp900SU.

Table 3

Absorption bands of chemical bonds of the HAp spectrum [22–25]

Chemical groups	Absorption bands, (cm^{-1})	Description
PO_4^{2-}	460	ν2
PO_4^{2-}	560–600	ν4, bending mode
PO_4^{2-}	960	ν1
CO_3^{2-}	870–880, 1450–1460	The presence of these bands indicates the B-
OH^-	630, 1650, 3500	OH-ions in the HAp structure
Physically	2600–3600	-

The presence of the characteristic peaks of OH-ion at 630 cm^{-1}, 1650 cm^{-1} and 3570 cm^{-1} confirms the formation of hydroxyapatite. The intensity of these peaks varies ambiguously with increasing temperature: it goes up with increasing calcination temperature to 630 cm^{-1} and 3570 cm^{-1}; and at the same time goes down to 1650 cm^{-1}.

Phase analysis of HAp treated at low temperatures. Obtaining the pure phase in almost all the cases when using sucrose urged the study of the phases in the HAp samples synthesized at lower temperatures, namely at 80ºC (sample HAp0SU), 150 °C (sample HAp150SU) and 300 °C (sample HAp300SU). Received XRD patterns of the above listed samples are presented in Figure 6. As can be seen from XRD data, the pure hydroxyapatite phase (without other phosphates) is formed in all cases, and the sizes of crystallites practically do not change in this temperature region and range from 3 nm to 4 nm.

Thus, based on the X-ray diffraction patterns, it can be argued that using the calcium sucrate complex as the initial reagent allows to obtain the hydroxyapatite phase without additional heat treatment, which greatly simplifies the process of HAp synthesis, as well as reducing its cost. It also should be noted that this method (using sucrose) is a reproducible method for obtaining HAp, which, as shown by our numerous studies, ensures 100 % production of hydroxyapatite.

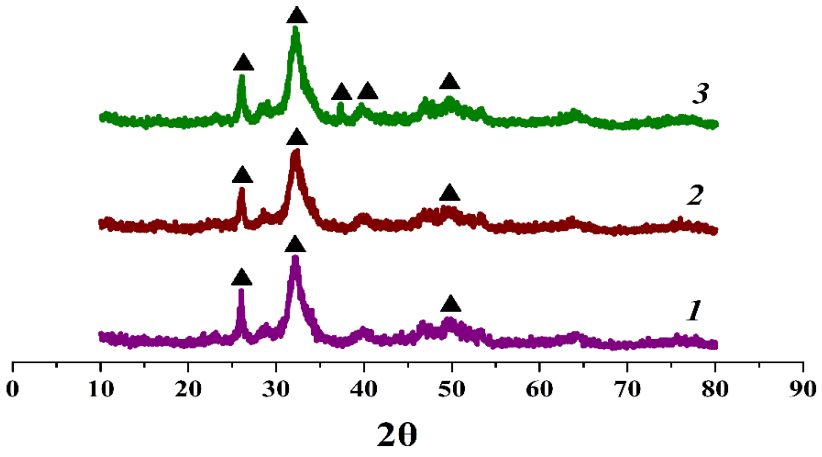

Fig. 6 XRD patterns of the HAp samples: (1) – HAp0SU; (2) – HAp150SU;(3) – HAp300SU (▲– hydroxyapatite).

Conclusions

The article describes the simple method of HAp synthesis by chemical precipitation using sucrose and dextrin, the role of which is reduced to the transfer of calcium to the water-soluble state. The thermal analysis of the obtained HAp precipitates showed that the dextrin content in them was about 3 times higher than in sucrose. It was established that the subsequent heat treatment of HAp precipitates led to the increase in the crystallites size, which had the size in the nano-region (3-45 nm). Scanning electron microscopy established the size of the aggregates: for HAp, obtained with sucrose, at the level of 5-30 microns; for, HAp, synthesized with the participation of dextrin, about 1-20 microns. Obtaining the pure HAp phase was additionally proved by IR spectroscopy, and the presence of carbonate ions replacing phosphate ions in the apatite structure was discovered, that indicated

the formation of carbonate-containing B-type hydroxyapatite. Obtaining the pure HAp-phase was further proved by infrared spectroscopy, and the presence of carbonate ions replacing phosphate ions in the apatite structure was detected, indicating the formation of a carbonate-containing B-type hydroxyapatite. It was shown the use of sucrose solution allows to obtain hydroxyapatite phase without additional heat treatment (low temperature synthesis) of the obtained precipitate. The method of obtaining HAp studied in the article is a reproducible technique that ensures 100% production of pure hydroxyapatite (without other phosphates).

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