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Peculiarities of synthesis of Ag-doped hydroxyapatite ceramics

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The study is devoted to the preparation of antimicrobial Ag-containing bioactive calcium phosphate ceramics based on carbonated hydroxyapatite and to the determination of the dependence of its phase composition and microstructure on the synthesis temperature. Composite ceramics was obtained by sintering powders of carbonated hydroxyapatite (CHA), synthesized as a result of a reaction between calcium carbonate and phosphoric acid, with the addition of silver nitrate. Ceramics were sintered at 900 and 1000 °C temperatures, i.e., temperatures below and above the melting point of silver. X-ray analysis, electron microscopy, and infrared spectroscopy showed that synthesis at a 900 °C temperature (below the melting point of metallic silver) produces a two-phase composite based on CHA with inclusions of silver nanoparticles smaller than 50 nm in size. From X-ray analysis, with an increase in silver concentration, the lattice constant *a* remains practically unchanged, while the constant *c* – increases. This behavior, due to the significant difference in the ionic radii of calcium and silver (Ca^{2+} – 0.99 Å, Ag^{+} – 1.28 Å), usually leads to the preferential substitution of Ca(1) sites in the CHA and a linear increasing in the lattice parameters of the CHA with the Ag concentration. That is, even at relatively low temperatures, as a result of the solid-phase reaction in CHA, partial replacement of calcium ions by silver ions occurs and Ag-substituted ceramics are formed. At temperatures above 1000 °C, a single-phase silver-substituted product is synthesized where part of the Ca^{2+} ions is replaced by Ag^{+} ions. At the same time, the lattice constant *c* continues to increase, and in the electron microscopic images only the apatite grain structure is visible without any inclusions. Sintering of composite ceramics at a temperature when silver is in the liquid phase and more easily dissociates into ions compared to the solid phase, results in a single-phase silver-substituted ceramic.

Keywords: carbonated hydroxyapatite, silver nanoparticles, bioactive calcium phosphate ceramics, antimicrobial ceramics.

Особливості синтезу Ag-місткої гідроксиапатитної кераміки

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Робота присвячена одержанню антимікробної Ag-місткої біоактивної кальцій-фосфатної кераміки на основі карбонізованого гідроксиапатиту і з'ясування залежності її фазового складу і мікроструктури від температури синтезу. Композитна кераміка отримана шляхом спікання порошків карбонізованого гідроксиапатиту (КГА), синтезованих у результаті реакції між карбонатом кальцію і ортофосфорної кислотою, з добавками нітрату срібла. Спікання кераміки виконано при температурах 900 і 1000 °С, тобто температурах, які знаходяться нижче і вище за температуру плавлення срібла. Методами рентгенівського аналізу, електронної мікроскопії та інфрачервоної спектроскопії показано, що в результаті синтезу при температурі 900 °С (нижче температури плавлення металевого срібла) утворюється двофазний композит на основі КГА з включеннями наночастинок срібла розміром менше 50 нм. З даних рентгенівського аналізу при збільшенні концентрації срібла постійна ґратки *a* практично не змінюється а постійна *c* – збільшується. Така поведінка, через значне розходження іонних радіусів кальцію і срібла (Ca^{2+} – 0,99 Å, Ag^{+} – 1,28 Å) зазвичай призводить до переважного заміщення С (1) місць у КГА і лінійному збільшенню параметрів ґратки КГА з концентрацією Ag. Тобто, навіть при відносно низьких температурах у результаті твердофазної реакції в КГА відбувається часткове заміщення іонів кальцію іонами срібла і формується Ag-заміщена кераміка. При температурах вище 1000 ° С синтезується однофазний срібло-заміщений продукт, в якому частина іонів Ca^{2+} заміщена іонами Ag^{+}. При цьому зберігається тенденція до зростання постійної ґратки *c*, а на електронномікроскопічних знімках видно тільки зеренна структура апатиту без будь-яких включень. Спікання композитної кераміки при температурі, коли срібло знаходиться в рідкій фазі і легше дисоціює на іони в порівнянні з твердою фазою, призводить до отримання однофазної срібло-заміщеної кераміки.

Ключові слова: карбонізований гідроксиапатит, наночастинки срібла, біоактивна кальцій-фосфатна кераміка, антимікробна кераміка.

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Особенности синтеза Ag-содержащей гидроксиапатитной керамики

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Работа посвящена получению антимикробной Ag-содержащей биоактивной кальций-фосфатной керамики на основе карбонизированного гидроксиапатита и выяснению зависимости ее фазового состава и микроструктуры от температуры синтеза. Композитная керамика получена путем спекания порошков карбонизированного гидроксиапатита (КГА), синтезированных в результате реакции между карбонатом кальция и ортофосфорной кислотой, с добавками нитрата серебра. Спекание керамики выполнено при температурах 900 и 1000 °С, т. е. температурах, лежащих ниже и выше температуры плавления серебра. Методами рентгеновского анализа, электронной микроскопии и инфракрасной спектроскопии показано, что в результате синтеза при температуре 900 °С (ниже температуры плавления металлического серебра) образуется двухфазный композит на основе КГА с включениями наночастиц серебра размером меньше 50 нм. Из данных рентгеновского анализа при увеличение концентрации серебра постоянная решетки *a* практически не изменяется а постоянная *c* – увеличивается. Такое поведение, из-за значительного различия ионных радиусов кальция и серебра (Ca^{2+} – 0,99 Å, Ag – 1,28 Å) обычно приводит к преимущественному замещению Ca(1) мест в КГА и линейному увеличению параметров решетки КГА с концентрацией Ag. Т. е. даже при относительно низких температурах в результате твердофазной реакции в КГА происходит частичное замещение ионов кальция ионами серебра и формируется Ag-замещенная керамика. При температурах выше 1000 °С синтезируется однофазный серебро-замещенный продукт, в котором часть ионов Ca^{2+} замещена ионами Ag^{+}. При этом сохраняется тенденция к возрастанию постоянной решетки *c*, а на электронномикроскопических снимках видна только зеренная структура апатита без каких-либо включений. Спекание композитной керамики при температуре, когда серебро находится в жидкой фазе и легче диссоциирует на ионы по сравнению с твердой фазой, приводит к получению однофазной серебро-замещенной керамики.

Ключевые слова: карбонизованый гидроксиапатит, наночастицы серебра, биоактивная кальций-фосфатная керамика, антимикробная керамика.

1.Introduction

Synthetic hydroxyapatite (HA) and other calcium phosphates are widely used in surgical orthopedics, due to their good bioactivity, biocompatibility, and osteoconductivity [1-3]. However, in the post-surgery period, the presence of implantable material in the body is often accompanied by infections. To prevent infection, antibiotics are often used, the effect of which is short-term due to their rapid washing out by body fluid from a bone defect and weak penetration into bone tissue. In addition, to increase the duration of the action of antibiotics, their content in the implant should be quite high, while the concentration of the released antibiotic into the space surrounding the implant should not exceed the threshold above which irreversible side effects are observed [4-6]. These problems may be avoided by using metal ions or nanoparticles such as silver, copper, zinc as an antimicrobial agent [7-10]. In terms of imparting antimicrobial properties to a bone implant, the effect of silver additives in HA [5, 6, 11–21] having a strong inhibitory effect on a wide range of bacteria, was studied in more detail. Literature suggests that regardless of the form in which silver is in the implant - either in the form of ions substituting calcium isomorphically, or in the form of nanoparticles located on the surface of HA particles, or in the intergranular space of silver-containing ceramics, to a concentration about 1.5-2 wt.%, the material exhibits excellent bactericidal properties [5, 6, 11, 12]. According to some authors, the presence of Ag^{+} ions in the HA lattice instead of Ca^{2+} ions results, on the one hand, in calcium-deficient HA, which negatively affects the structural stability of HA and its osteoconductive ability, and, on the other hand, in the rapid release of silver, depending on pH, into the surrounding tissue and cytotoxic effect [6]. Therefore, the presence of silver in the composite in the form of metal nanoparticles is considered more preferable, due to the poor solubility of which, the antimicrobial effect in the body fluid will be prolonged and will not have a significant toxic effect on surrounding tissues. Therefore, the question of what type of implants exhibits the best functional properties remains open and requires detailed biological research.

To date, it is known that the maximum concentration of Ag^{+} substituting isomorphically the Ca^{2+} ions does not exceed 1.5 wt.% [11]. On the other hand, papers on silver-containing HA with a lower silver concentration are very often published, where silver does not substitute calcium, but is released as a separate phase [12, 13]. Therefore, there is a concern about the synthesis of ceramics with a predicted microstructure and phase composition.

In this paper, an attempt is made to synthesize HA ceramics with silver additives and to determine the conditions under which a single-phase synthetic silver-substituted ceramic and a two-phase composite consisting of HA and silver nanoparticles are realized.

2.Experiment

2.1. Preparation of materials

Earlier, we showed the possibility of obtaining dense carbonized ceramics in an atmosphere of carbon dioxide at temperatures much lower than the accepted sintering temperature of HA [14]. Therefore, to ensure high mechanical properties at relatively low synthesis temperatures, the initial components in the sintering of silver-containing ceramics were, on the one hand, carbonated HA (CHA) powders obtained as a result of the reaction between calcium carbonate and orthophosphoric acid, and on the other hand, water-soluble silver nitrate powder.

To obtain CHA, the required amount of fine $CaCO_3$ powder (Merck, Darmstadt, Germany, analytical purity) was mixed in distilled water. An H_3PO_4 solution (Merck, Darmstadt, Germany, analytical purity) was rapidly poured into the suspension with continuous mixing of the reaction medium at 45 °C. The precipitation was aged within 24 hours. Then it was centrifuged, dried in a drying cabinet at 90 °C, ground in an agate mortar, and sieved through a 100 μm sieve.

The obtained powder was mixed with a solution of $AgNO_3$ of a certain concentration providing silver-containing compositions with a silver concentration of 0.25 to 1.5 wt.% with a pitch of 0.25 wt.%.

Samples were prepared from powders in the form of tablets with a height of 3 mm and diameter of 8 mm by compacting the powder in a steel mold under the pressure of 120 MPa. Average porosity of the compacts was 51%. The compacts were annealed in a stream of dry CO_2 (4 ml/min) at 900 and 1000 °C for 2 hours at each temperature. Seven batches of annealed compacts were prepared (10 samples per a batch). The choice of sintering temperature is related to the melting point of metallic silver, which is 960 °C. That is, in the first case, silver additives were in solid form, in the second – in molten.

2.2. Research methods

Structural measurements were performed on a Philips APDW 40C diffractometer in copper K_α radiation ($\lambda = 0.154$ nm) with a nickel filter in the range of diffraction angles of 2θ 20÷70 , with scanning pitch of 0.01 degrees and scanning time of 0.6 s.

IR spectra were recorded using BIO-RAD FFS 175 spectrometer (Germany) with a resolution of 2 cm^{-1} according to the KBr method, operating in the transmission mode of wave numbers between 400÷4000 cm^{-1} with averaging over 200 scannings.

The morphology and microstructure of the samples were studied using an ESEM Qunta 400 scanning electron microscope (Germany).

Thermogravimetric (TG) studies were performed at up to 1200 °C in an air atmosphere (MVT Instrument, Ukraine) with a heating rate of 5 °/min; the absolute measurement error was 2%.

3. Results and discussion

The choice of temperature at which sintering of the silver-containing powder compacts was carried out is based on silver nitrate DTA, used as the silver source shown in Fig. 1. During heat treatment of $AgNO_3$, all known transformations take place: at ~ 160 °C a polymorphic transformation from rhombic to rhombohedral modification occurs, then at ~ 210 °C the last modification is melted without decomposition, decomposition of silver nitrate begins at ~ 300 °C. This process is intensified at ~ 500 °C and in the range of 500 - 960 °C the crystalline silver is the product of decomposition of $AgNO_3$. Its melting occurs at 960 °C. All observed effects are endothermic.

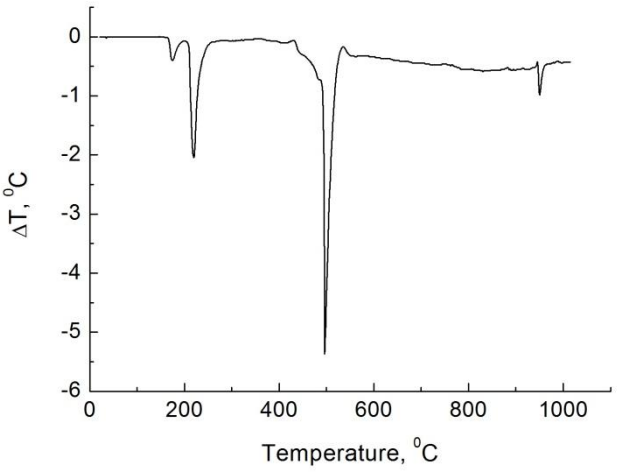

Fig. 1. DTA of silver nitrate

In this regard, when sintering compacts from a composite powder at 900 °C, the decomposition product of silver nitrate - silver particles - should be released as a separate phase. And ceramics formed during sintering will be biphase.

X-ray diffraction patterns of Ag-containing ceramics shown in Fig. 2, confirm the assumption: Starting from the concentration of 0.5 wt.% at $2\theta = 38.116°$, a line appears corresponding to the (111) reflection of metallic silver. In electron microscopy images made for ceramics with an Ag additive of 1.5 wt% (Fig. 3), silver nanoparticles with a size of less than 50 nm are visible against apatite grains.

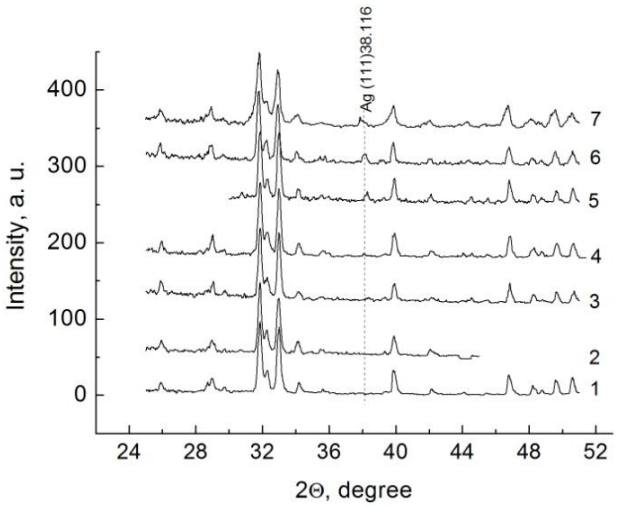

Fig. 2. X-ray diffraction patterns of Ag-containing ceramics with various silver concentrations synthesized at 900 °C: 1 – 0 wt % Ag^+ , 2 – 0.25 wt % Ag^+, 3 – 0.5 wt % Ag^+, 4 – 0.75 wt % Ag^+, 5 – 1.0 wt % Ag^+, 6 – 1.25 wt % Ag^+, 7 – 1.5 wt % Ag^+.

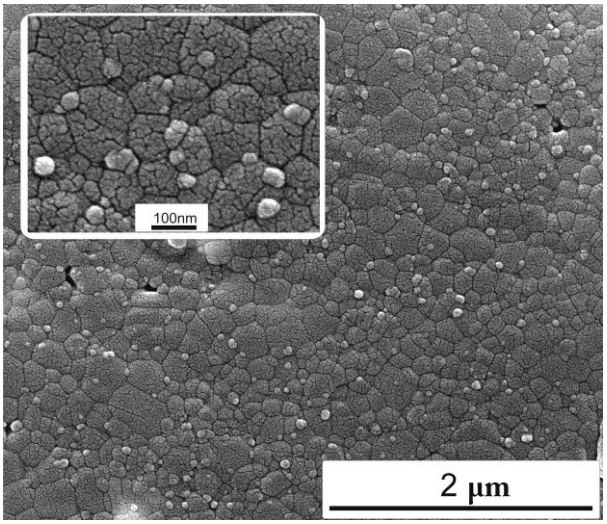

Fig. 3. SEM image of ceramic with 1.5 wt.% Ag^+ synthesized at 900 °C. The inset shows a fragment with a large magnification

However, calculation of the lattice constants (Fig. 4) showed that, at almost constant value of *a* parameter, an increase in the concentration of silver in ceramics results in increase in *c* constant. This behaviour, due to the significant difference in the ionic radii of calcium and silver (Ca^{2+} – 0.99 Å, Ag – 1.28 Å), usually results in the preferential substitution of Ca(1) places in the HA and linear increase in the HA lattice parameters with Ag concentration.

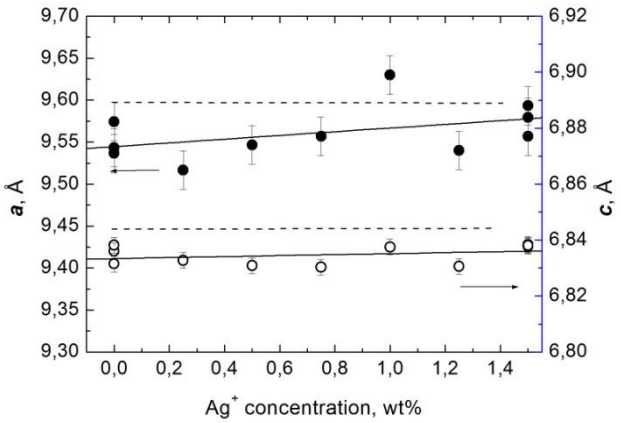

Fig. 4. Dependence of lattice constants of the composite ceramics synthesized at 900 °C vs silver concentrations

These data suggest that during composite sintering (even at relatively low temperatures) as a result of solid-phase reaction, partial substitution of calcium ions by silver ions takes place and Ag-substituted ceramics are formed. The resulting charge mismatch is compensated by the presence of carbonate ions in the apatite structure. Thus formed, the composite apatite matrix is a silver-substituted carbonized hydroxyapatite.

According to the IR spectra presented in Fig. 5, the concentration of carbonate groups in the material is almost independent of the concentration of additives. CO_3^{2} groups in the apatite lattice are predominantly in the B positions (transmission bands of 873, 1410, and 1455 cm^{-1} and lower values of *c* lattice constants compared to stoichiometric HA).

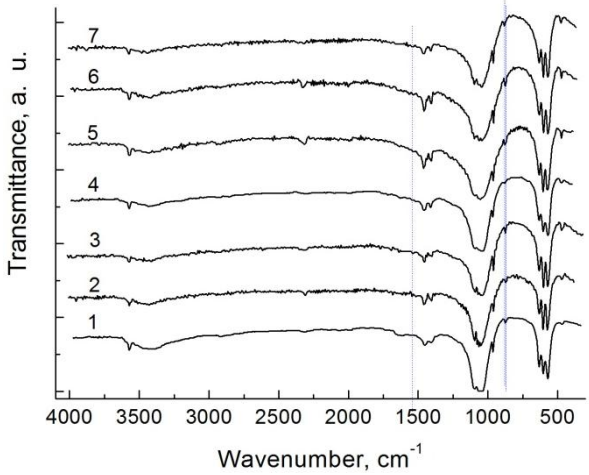

Fig. 5. IR spectra of ceramic samples synthesized at 900 °C with different silver contents: 1 – 0 wt % Ag^+ , 2 – 0.25 wt % Ag^+, 3 – 0.5 wt % Ag^+, 4 – 0.75 wt % Ag^+, 5 – 1.0 wt % Ag^+, 6 – 1.25 wt % Ag^+, 7 – 1.5 wt % Ag^+.

For ceramics synthesized at 1000 °C, the IR spectra are similar. Only diffractograms and microstructure differ. In the diffraction patterns over the entire range of

concentrations of silver additives, the synthesis at 1000 °C results in the disappearance of the most intense silver line (111). At the same time, the *c* lattice constant continues to increase, and in the electron micrographs only the apatite grain structure is visible without any inclusions (Fig. 6).

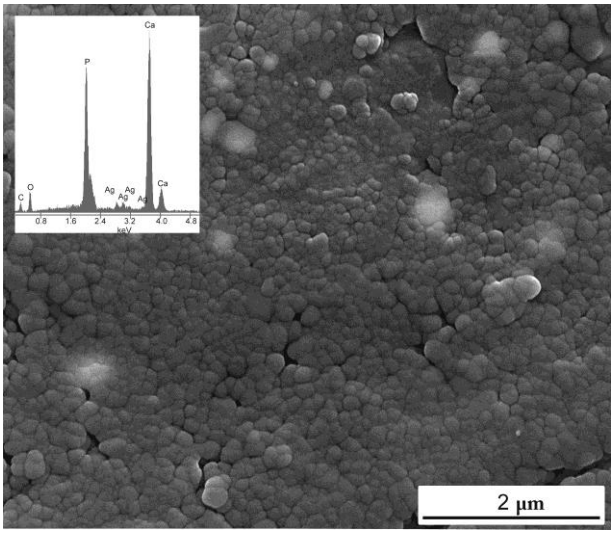

Fig. 6. SEM image of ceramics synthesized at 1000 °C with 1.5 wt.% Ag^+. The inset shows the energy-dispersive spectrum indicating the presence of silver in the sample

The performed energy dispersive studies of such ceramics (inset in Fig. 6) indicate the presence of silver in the sample.

Thus, sintering of the compacts at a temperature higher than the melting point of silver, when it is in the liquid phase and dissociates into ions more easily compared to the solid phase, resulted in the synthesis of single-phase silver-substituted ceramics.

Conclusion

For the first time, the possibility of obtaining silver-containing ceramics with silver content not exceeding 1.5 wt.%, where silver is in different structural states — in the form of nanoparticles or ions substituting calcium ions in the CHA structure, is shown in the paper. At synthesis temperatures (in the paper it is 900 °C), when the added silver additives are in solid form, the ceramic is a two-phase composite based on CHA with inclusions of silver nanoparticles. At the synthesis at above 1000 °C, a single-phase product is synthesized where some Ca^{2+} ions are substituted by Ag^+ ions.

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