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Ultrasonic synthesis of hydroxyapatite in non-cavitation and cavitation modes

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ABSTRACT

The size control of materials is of great importance in research and technology because materials of different size and shape have different properties and applications.

This paper focuses on the synthesis of hydroxyapatite in ultrasound fields of different frequencies and intensities with the aim to find the conditions which allow control of the particles size. The results are evaluated by X-ray diffraction, Transmission Electron Microscopy, morphological and sedimentation analyses. It is shown that the hydroxyapatite particles synthesized at low intensity non-cavitation regime of ultrasound have smaller size than those prepared at high intensity cavitation regime. The explanation of observed results is based on the idea of formation of vortices at the interface between phosphoric acid and calcium hydroxide solution where the nucleation of hydroxyapatite particles is taken place. Smaller vortices formed at high frequency non-cavitation ultrasound regime provide smaller nucleation sites and smaller resulting particles, compared to vortices and particles obtained without ultrasound. Discovered method has a potential of industrial application of ultrasound for the controlled synthesis of nanoparticles.

1. Introduction

Hydroxyapatite $Ca_{10}(PO_4)_6(OH)_2$ (HAP) is the material closest to the bone tissue in its chemical and crystallographic composition [1]. It is widely used as a substituting material in dentistry and for repair of bone injuries, and as an important component in various composite materials for medical applications. Hydroxyapatite has significant advantages such as biocompatibility, osteoconductivity and bioactivity [2,3]. Another important HAP feature is its high specific adsorption capacity, making it useful for the development of the targeted drug delivery methods [4–6]. Different materials based on HAP are used in chromatography for the separation of macromolecules of natural origin [7,8].

A successful application of HAP as a sonosensitizer and the carrier of radionuclides in sonodynamic and radionuclide therapy of oncological diseases had been recently reported [9–11]. The size and the shape of HAP crystals play very important role in these applications. A wide spectrum of HAP applications determines the variety of requirements for the size of its crystals, their morphology, adsorption properties, ability to aggregate, speed of their dissolution, etc.

Various methods were used for the synthesis of HAP including hydrothermal synthesis, sol–gel method, high power ultrasound and many others [12–15]. The obtained HAP materials differ in terms of morphology and size depending on the method of synthesis, initial precursors and the stoichiometry of the reactants mixture [16]. One of the most effective and technologically appealing methods of the hydroxyapatite synthesis is the precipitation of HAP by phosphoric acid from solutions of $Ca(OH)_2$ or suspensions of CaO [17–19]. It is well-known that the small clusters of complex composition are formed at the beginning of HAP formation, which then aggregate and crystallize at the next stage [19,20]. Variations of the experimental conditions, such as the speed of the reagents intake, the intensity of mixing and the temperature of the synthesis, provide the control of the morphology and the size of the final product. The use of external mechanical agitation, such as ultrasound, at different stages of the synthesis allows a more extended parameter control of the synthesized HAP crystals.

Ultrasound is widely used in many industrial processes. Among its advantages are the intensification of technological processes and the increase of the products dispersion. Ultrasound decreases the induction period of crystallization, the width of the metastable zone, and decreases the supersaturation when used in crystallization processes [21].

Technological effects of ultrasound are mainly associated with its

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various nonlinear effects, namely: radiation forces, acoustic flows of different scales, pulsation of gas bubbles, surface effects and cavitation. Each of these effects is characterized by its energy spectrum and is associated with the phenomena, affecting the processes of mass crystallization (microflows, flotation, shock waves, microjets of fluid, acoustic turbulence, etc.). It is worth noting, that from the standpoint of the final results (the size, the shape of crystals, the defect structure) these effects can work in opposite direction. Due to this reason, the crystallization process can be quite realistically controlled by controlling the parameters of ultrasound process.

In many papers on the experimental studies of the crystallization processes and hydroxyapatite synthesis under ultrasound irradiation, some of the key parameters, essential both for understanding the mechanisms of the ultrasound effect and for successfully reproducing the results, were missing. Usually the authors indicate the value of electrical power, the frequency of ultrasound and the temperature [22–24] during experiments. In addition to these parameters, the hydrodynamic conditions in the reactor are sometimes taken into account [25]. It is also important to calibrate the equipment during experiments on the effect of ultrasound on mass crystallization processes [26], using, for example, the oxidation of potassium iodide [27] as a probe of acoustic cavitation.

Taking into account the factor of multistep nature of the crystallization process (nucleation, crystal growth, aggregation, disintegration), and the multifactorial character of ultrasonic cavitation, and the absence of the general theory explaining the origin of the ultrasound impact on the crystallization, there is a strong demand for a detailed description of the experimental conditions. We believe that it should include the values of acoustic power and ultrasonic intensity, the geometry and volume of the reactor, the position of the irradiating surfaces in relation to the points of reagent inlet, the stage at which ultrasound is acting (nucleation, crystal growth, final stage or all of the processes), cavitation conditions, and hydrodynamic characteristics of the reagent mixing. It is obvious that the objective of the experiment determines to a great extent how much or little comprehensive the process description will be. If it is limited to the grinding of the product, then the sonication time in a standard ultrasonic bath would be enough. If the purposes of work includes finding general regularities in the course of some specific synthesis, then the task becomes more complicated, and the number of the parameters to be monitored increases.

This article is dedicated to the ultrasonic modification of HAP synthesis when it is precipitated with phosphoric acid from CaO suspensions. The aim of this work is to study the effect of ultrasound parameters on the structure, size and morphology of hydroxyapatite particles. The effects of the intensity and frequency of ultrasound, the relative position of the ultrasonic transducer and the phosphoric acid inlet point into the reaction medium, and the hydrodynamic conditions in the reactor are studied in details. The fine-grained hydroxyapatite particles obtained as a result of this work can be used in sonodynamic therapy of oncological diseases as a sonosensitizer [10].

2. Experimental

2.1. Materials

High purity phosphoric acid and calcium carbonate were purchased from Reachim (Russia). Calcium oxide was obtained by thermal decomposition of calcium carbonate at 1100 °C.

Phosphoric acid of the required concentration was prepared by addition of distilled water to the chemically pure phosphoric acid (87% concentration). The concentration of the solution was monitored by its relative density by densimeter. Acid solution with 3.28 M concentration was used in experiments. The ratio of reagents for the synthesis was set in such a way that the Ca/P ratio in the final product was 1.67 ± 0.03. The pH of the solution was monitored during the synthesis.

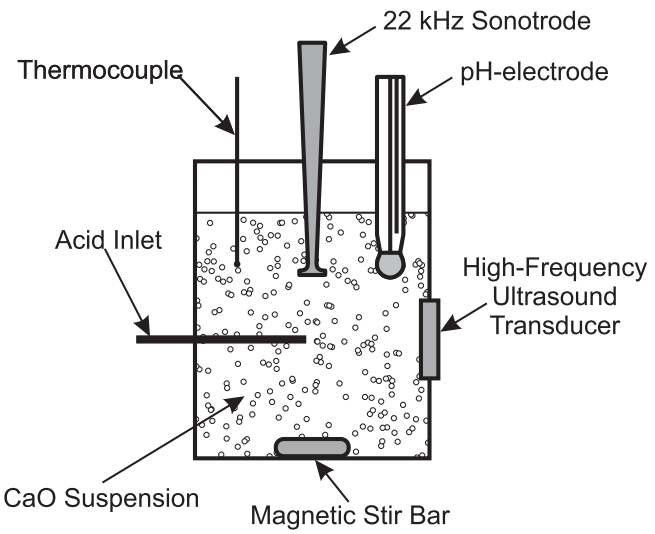

Fig. 1. Schematic diagram of the reaction chamber for the hydroxyapatite synthesis.

2.2. Experimental setup

The reaction container used for the hydroxyapatite synthesis was a cylindrical Teflon vessel, 50 mm in diameter and 100 mm in height (Fig. 1). 0.88 MHz and 2.64 MHz replaceable piezoceramic transducers were mounted on the sidewall of the vessel. The 22 kHz sonotrode radiator was brought into the vessel through the central opening in the reactor head. The horn had a capacity of moving vertically to change the distance between the horn tip and the capillary tube delivering phosphoric acid. The pH and temperature sensors were mounted on the reactor's lid as well. Phosphoric acid inserted into the reactor through a ceramic tube with 1 mm in diameter, which was inserted through the reactor sidewall and oriented perpendicularly to the surface of high-frequency ultrasound transducer. The tube could be moved forth and back horizontally. The acid flow rate in each experiment was kept 0.01 ml/s. Parameters of ultrasound irradiation are given in Table 1.

The acoustic power was measured using the calorimetric method [28]. The ultrasound intensity was calculated using the dimensions of the irradiating surfaces. Relative cavitation activity at various ultrasonic conditions was estimated based on the rate of potassium iodide oxidation [27]. A 0.2 M aqueous solution of potassium iodide saturated with carbon tetrachloride was used as a test solution for the measurements the cavitation activity. The test solution was placed in the reactor and sonicated for 10 min in the hydrodynamic conditions of the experiments. When ultrasound is irradiated into an aqueous KI solution, I^- ions are oxidized to give I_2. When excess I^- ions are present in solutions, I_2 reacts with the excess I^- ion to form I_3^- ion. The absorbance of I_3^- at 355 nm was measured using Shimadzu UV-1280 spectrophotometer. The activity of cavitation was estimated by the yield of the formed I_3^-. The results are used for relative measurements of cavitation activity and presented in Table 1. The absence of I_3^- after sonication of KI solutions indicates the absence of cavitation, as in the case of

Table 1
Experimental conditions of hydroxyapatite synthesis.

Ultrasound frequency	Total acoustic power (W)	Average acoustic intensity (W/cm^2)	KI oxidation rate (a.u.)
22 kHz	60	25	35
22 kHz*	60	25	35
0.88 MHz	8	2.7	10
1.76 MHz	0.6	0.2	0
2.64 MHz	5	1.7	1

* The tip of the horn was placed 5 mm away from the acid inlet from the capillary tube.