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LETTERS
TO THE EDITOR

Glycine, Biocompatible Growth Regulator for Preparation of Inorganic Nanomaterials for Medicine

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Recently, a fast growing area of science is nanomedicine, whose mission is to create new and modify existing methods of treatment and diagnosis of various diseases using nanomaterials. These latter should meet certain requirements, like biocompatibility, and also a particular set of physicochemical characteristics depending on a planned range of their application. These characteristics are defined by a size of nanoparticles, which form the basis for a final biomedical material. Therefore regulating nanoparticle sizes is an extremely important and actual problem, and thus much attention is given to the methods of the synthesis of nanoscale objects possessing desired characteristics.

The distinctive feature of nanomaterials consists in their large specific surface area and high surface energy, therefore the main attention is given to the limitation of particle sizes and the variation of their morphology. The basic most demanded nanomedicine fields are tumours diagnostic bone tissue engineering. Biocompatible magnetic nanoparticles of iron oxides, which can be applied as contrasting agents for MRT and hyperthermia destructtion of tumours, are considered as promising material for the first field. Polymeric inorganic composites, which perform a supporting function and provide three-dimensional growth of cells, are used in the second field. The inorganic component is hydroxyapatite, which is a part of natural bones and produces osteoinduction and bone formation.

The regulation of particle sizes is carried out using growth inhibitors, which represent either surfactants or chelating agents. At the critical concentration surfactants form micelles serving as "nanoreactors," a micella size limiting a particle size. Chelating agents interact with energy excessive surface areas of growing particles, thus governing their growth. Undoubtedly, this is the second type of growth inhibitors which is most promising for the variation of morphological parameters of nanoscale objects, like the size and the shape of particles. A number of such compounds are known, however, further application of the obtained nanomaterials in medicine causes the necessity to use the biocompatible growth inhibitors. Glycine, which is the simplest and inexpensive aminoacid, can act as one of them. This work is devoted to the examination of its influence on morphological parameters of nanoparticles of various chemical nature obtained by various methods.

Iron oxides and hydroxyapatite nanoparticles, which are the most promising nanomaterials for medicine, have been selected as the subject of this investigation. Earlier we have shown that it is possible to put a peroxide group on the hydroxyapatite surface [1] and also to regulate nanoparticle sizes of iron oxides using various growth inhibitors [2]. The most spread methods of the hydroxyapatite synthesis are the hydrothermal synthesis and precipitation, therefore they were the methods which we used for the study of the possibility of glycine application as a growth inhibitor for $Ca_{10}(PO_4)_6(OH)_2$ nanoparticles. We obtained nanoparticles of iron oxides by the hydrothermal method, advantages of which consist in a good crystal structure of the product and a possibility of scaling the synthesis process. The phase composition and morphology of

samples were studied by a complex of independent methods, namely by the X-ray analysis, transmission electron microscopy, and determination of a specific surface area by the Brunauer-Emmett-Teller method.

According to the X-ray data, hydroxyapatite samples obtained in hydrothermal conditions are three-phase and contain calcium hydroorthophosphate, hydroxyapatite, and calcium hydroxide, which can be due to the insufficient dissolution of calcium hydroxide and a corresponding low pH value, whereas, to obtain hydroxyapatite, it is necessary to create pH > 10 in a reaction medium. Addition of glycine results in the essential increase in the hydroxyapatite fraction in samples and, therefore, in the appearance of polydispersity, which was detected by the appearance of an additional fraction in TEM microphotographs and by the variation of specific surface area values. Apparently, glycine is adsorbed on the surface of originally formed hydroxyapatite and prevents its disintegration on the pH decrease during the chemical reaction.

Hydroxyapatite samples obtained by a precipitation method are monodisperse and represent pure stoichiometric hydroxyapatite with particle length and width less than 50 nm. As the amino acid concentration increases, the specific surface area increases, and the shape of particles in microphotographs changes from spindles to spheres. Thus, the application of glycine results in obtaining "individual" nanoparticles and also changes their spindle shape to the spherical shape.

When glycine is used as a growth inhibitor in the hydrothermal synthesis of iron oxides, its effect on the shape and, therefore, on the phase composition of the reaction product was detected. The iron oxide obtained in the absence of glycine represents FeOOH and consists of needle-shaped particles. The synthesis in the presence of the amino acid provides α-Fe_2O_3 spheres with a diameter less than 100 nm. It is known that, depending on the shape and size of particles, iron oxides crystallize to form various phases, which was also proved by our results.

The effect observed of more significant influence of glycine on morphology of hydroxyapatite nanoparticles, as compared with nanoparticles of iron oxides, is most likely caused by different stability constants of chelate complexes of the amino acid with calcium and iron ions.

Thus, it has been shown that the biocompatible growth regulator, glycine, can be applied in syntheses under various conditions for the limitation of sizes of nanoparticles various in chemical nature.

Nanoparticles of iron oxides were obtained by the hydrothermal method at 170°C from iron(III) hydroxide preliminary prepared by the iron chloride hydrolysis. Nanoparticles of hydroxyapatite were synthesized by the precipitation method at pH 10 and temperature 40°C and by the hydrothermal method at 240°C using calcium nitrate and phosphoric acid. We applied glycine as the growth inhibitors in both methods. The TEM measurements were carried out on a JEOLS JEM-107 microscope. The X-ray analysis of samples was carried out at the Saint Petersburg State University Research Centre for X-ray Diffraction Studies on a Bruker D2 PHASER diffractometer with CuK_α radiation. The determination of phase composition of synthesized products was carried out using a PDF card-file.

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