ANNOTATION

dissertations for the degree of Doctor of Philosophy (PhD) in the specialty **6D072300 - Applied Physics** on the topic **"Study of nanostructured apatite-biocomposite materials and coatings",** performed by

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General description of work. The thesis is devoted to experimental studies of the structural-phase state of materials based on hydroxyapatite (HA) and sodium alginate (Alg) with zinc doping, the study of their antibacterial properties and biocompatibility, as well as the development of technological modes of deposition of biocomposite materials on biomimetic metal structures obtained by reverse-engineering. We used advanced experimental experimental research methods carried out in the laboratories of research centers in Kazakhstan and the near and far abroad.

Relevance of the work. Bone tissue (BT) is a composite natural material that includes an organic component (collagen, type I) in which nanocrystals of non-stoichiometric hydroxyapatite (biological apatite) are embedded. This structure is durable both in tension (due to the organic component) and in compression (due to the inorganic component). Biological apatite includes a number of inorganic ions. It has been established that the inclusion of a small amount of such ions, in particular zinc, magnesium, copper and silver ions, into the structure of bioapatite has a significant effect on its properties. Zinc ions contribute to an increase in BT density, prevent bone loss, improve protein adhesion and increase antibacterial activity. However, this aspect (the inclusion of inorganic ions of various metals) is poorly studied from the point of view of the morphology and symmetry of the HA molecule in the replacement of calcium atoms with zinc.

The widespread use of drugs with antimicrobial action led to the formation of resistance of microorganisms to a wide range of antibiotics. One of the approaches to solving this problem all over the world is the active search for inorganic antimicrobial components or modification of biomaterials with inorganic bioactive ions to initiate a controlled reaction in tissues and to ensure antimicrobial activity. In the works, the antibacterial properties of hydroxyapatite (HA), as well as other materials and coatings with doping with Zn, Cu, Au, etc. ions were studied. Recently, the high antibacterial properties of a composite material based on zinc sulfide with sodium alginate (ZnS + alginate) were demonstrated against a number of gram-positive and gram-negative bacteria. Sodium alginate is a biocompatible, non-toxic natural polysaccharide consisting of β-D-manuronic and α-L-guluronic acid monomers, it binds and removes radionuclides from the body, lowers blood cholesterol and does not cause allergies. It is also known that materials based on ZnO are characterized by pronounced biological activity, high tensile strength, ability to withstand extreme operating conditions. The interaction of zinc with alginate and HA is discussed in the papers. ZnO studies are conducted mainly as an independent compound, and as a result, the results of the analysis of the phase state of zinc oxide, the processes of calcium substitution by zinc in

calcium apatite and sodium alginate, the effect of the phase state of zinc on antibacterial properties and biocompatibility of materials are almost completely absent. Therefore, the study of the interaction of zinc with the remaining components of the composite, as well as the structural phase state of zinc in the Alg matrix is an urgent task at present. when replacing calcium atoms with zinc.

One of the important properties of the implant is the ability to osseointegration. Also required properties are biocompatibility and corrosion resistance. Modern trends in medical technology, aimed at the development of new materials with osteoconductive and antibacterial properties.

The deposition process is non-equilibrium. The consequence of this, between the substrate and the applied coating, are differences in the elemental, phase composition, degree of crystallinity and / or degree of amorphization, microstructure, and surface morphology. These parameters depend both on the deposition process and on the use or non-use of the treatment before and after application.

This paper is devoted to a comprehensive study of the properties of biomimetic composites close to bone tissue and consisting of hydroxyapatite, nanostructured ZnO particles and sodium alginate. The effect of the polymer on the uniformity of the distribution of ZnO particles in the composite, as well as the effect of ZnO on the porosity and the degree of absorption (swelling) of the liquid, was investigated. Samples are presented in the form of granules and hydrogel, ensuring the filling of defects of complex geometry with a minimum gap between the bone and the implant. The technical problem of obtaining metal implants with a biomimetic architecture with a bioactive zinc-doped hydroxyapatite coating has been solved. doped with zinc.

Object of study. Obtaining nanostructured biocomposite materials based on hydroxyapatite, sodium alginate and zinc oxide, as well as the process of coating based on hydroxyapatite on porous metal structures, the development of biomimetic architecture of the substrate.

Subject of study. The effect of the inclusion of zinc oxide and sodium alginate on the phase and functional composition, antibacterial properties, cytotoxicity and biocompatibility of the apatite-composite material and coatings based on it on metallic biomimetic substrates.

Research methods. In carrying out this dissertation, experimental methods were used to study morphology (raster electron microscopy), functional composition (IR spectrometry), structural phase state (X-ray diffraction analysis and transmission electron microscopy). The development of biomimetic architecture was carried out by optical 3D scanning with subsequent reverse engineering. The optical 3D scanner Smarttech3D Universe (Poland) was used, the obtained point clouds were processed using Geomagic Design X software. The printing of substrates was carried out using the method of selective laser melting of the powder on a Mlab cusing R (Concept Laser, Germany). The coating was carried out by the methods of hydrothermal deposition and microplasma spraying. The antibacterial properties of the synthesized materials were studied on colonies of gram-positive and gram-negative bacteria using agar diffusion and co-

incubation methods. The cytotoxicity of the materials was investigated on cell cultures of mouse osteoblasts and NIH-3T3 fibroblasts by the method of co-cultivation (Aachen University of Applied Sciences, Germany).

Objective. The aim of the thesis is to conduct a comprehensive study of the structure, phase composition of the composite based on hydroxyapatite and sodium alginate doped with zinc oxide. Development of techniques and technologies for the creation of a composite biomimetic implant.

In accordance with the goal, the main objectives of the research were formulated:

1. To modify the process of synthesizing composite materials based on hydroxyapatite and sodium alginate, by chemical precipitation with the purpose of their nanostructuring. Determination of the effect of zinc oxide on the elemental, phase, functional composition of pure hydroxyapatite in powder form (HAp), in the form of a hydrogel (HAg) and composites GA-Alg, GA-Alg-ZnO.

2. Obtaining prototypes of medical implants with trabecular biomimetic architecture using reverse engineering from steel 316L and medical alloy Ti6Al4V.

3. To develop a modified method of applying calcium phosphate coatings, in order to obtain a coating of crystalline hydroxyapatite doped with zinc. Determine the modes and features of the application of the composite nanostructured coating HA - ZnO on porous metal printed structures obtained by the method of selective laser melting.

4. Investigate in vitro cytotoxicity and biocompatibility of the HA-Alg-ZnO, HA-ZnO composite material and HA, HA-ZnO coatings using the example of connective tissue cell culture (mouse NIH-3T3 fibroblasts), antibacterial properties of HA-Alg-ZnO composite materials and HA-ZnO;

Scientific novelty

• For the first time, a composite material based on hydroxyapatite and sodium alginate doped with zinc oxide nanocrystals in a two-phase state was obtained and studied.

• Calcium phosphate coatings deposited on porous biomimetic metal structures obtained by the method of selective laser melting (SLP) were investigated for the first time; A new type of orthopedic implant with an artificial trabecular structure for use in medicine was obtained.

• A mechanism for the antimicrobial activity of ZnO nanocrystals in its two-phase state was proposed, so ZnO nanoparticles with a cubic structure have greater solubility and, as a consequence, a greater contribution to antibacterial activity than hexagonal nanoparticles.

The scientific and practical significance of the work

The results of experimental research methods provide a deeper understanding of the morphology, physics of the interaction of sodium alginate and hydroxyapatite with the addition of zinc oxide, the processes and mechanisms of the antimicrobial activity of composite materials with the addition of zinc oxide. Proved two-phase state of zinc oxide, which has a significant impact on the

mechanism of antibacterial activity. This work is of practical importance, which is confirmed by experimental studies on the evaluation of antimicrobial properties, cytotoxicity and biocompatibility. The introduction of this material in medical practice will have a positive effect on the speed of healing of defects and healing of the bone.

Conducted research creates the prerequisites for creating new materials that can be used in various areas of medicine.

Connection of work with research projects

The work was carried out in accordance with thematic plans of the University R & D according to the following subprogram: 0005 / PCF-17 “Development of the technology for manufacturing medical products from tantalum and niobium” state number. registration number 0117RK00047 within the framework of the PTsF Targeted Scientific and Technical Program of the East Kazakhstan State Technical University. A. Serikbayeva, focused on the development of new types of products for production at the leading industrial enterprises of the East Kazakhstan region "for 2017-2019.

Personal contribution of the author

The author has analyzed the literature data on the research topic, conducted the bulk of the experiments, processed and analyzed the experimental data, participated in writing publications, discussing the results at conferences and exhibitions. Discussion and interpretation of the results of the analysis, as well as the formulation of the main conclusions were held under the guidance of the foreign scientific consultant Professor A.D. Pogrebnyak, and domestic scientific consultant Professor S.V. Plotnikov. Assistance was provided in conducting and interpreting studies on the determination of cytotoxicity and antimicrobial activity by the staff of the Al-Farabi Kazakh National University. Savitskaya I.S. and Ph.D. Kistaubaeva A.S., as well as employees of SSU, A.Sci. Suhodub L.B. and member.kor. National Academy of Sciences of Ukraine A. f. Suhodub lf ..

The main provisions for the defense

• Modification of the method of chemical deposition, ultrasonic and microwave radiation leads to a change in the symmetry of the HA molecule, replacing calcium atoms with zinc, when ZnO is added to HA and the HA-Alg composite, as evidenced by the shift of the O — P — O group line, as well as the results of the FEM study and SEM.

• ZnO nanocrystals in the composite material based on hydroxyapatite and sodium alginate have a two-phase state, with a cubic and hexagonal structure, when ultrasound radiation is assisted during synthesis.

• Hydroxyapatite-based coatings obtained by hydrothermal deposition with additional assistance of the electric field, applied to metal implants with biomimetic architecture, developed and obtained by reverse engineering, have better crystallinity than coatings obtained by microplasma methods.

The reliability of the results obtained is ensured by the use of independent complementary and well-tested experimental research methods. The results of research were obtained using modern instruments and equipment of physical materials science, such as: JSM-6390LV scanning electron microscope (JEOL)

(Japan), JEOL JEM-2100 (Japan) electronic transmission microscope with electron energy up to 200 keV, PanAnalytical Xpret X-ray diffractometer , energy dispersive X-ray spectroscopy (EDX) using a JEM-2100 scanning electron microscope (Japan), FTIR-801 Simex IR spectrometer, as well as instruments for determining cytotoxicity and antibacterial activity.

The results obtained in general, are consistent with the results of other researchers in the CIS and foreign countries. The main aspects of the work done are presented in international conferences and published in peer-reviewed scientific journals abroad and within Kazakhstan.

Approbation of research results. The main experimental results of the thesis were reported and discussed:

- at the XIII International Scientific and Technical Conference “By the Hot Woman in Bilim -2018”, April 12, ENU. L.N. Gumilyov, Astana, 2018, Kazakhstan;

- at the IV International Scientific and Technical Conference of Students, Undergraduates and Young Scientists, April 13, EKSTU named after A. Serikbayev, Ust-Kamenogorsk, 2018, Kazakhstan;

- At the 8th International Conference NAP-2018, “Nanomaterials: Applications & Properties”, September 9-14, Zatoka, Ukraine.

- at the 27th International Conference of Metallurgy and Materials "Metal 2018", May 23-25, 2018, Brno, Czech Republic and also were reflected in international scientific publications, including articles recommended by WAC.

Publications. Materials of the thesis are presented in 12 publications, including 4 scientific journals recommended by the Committee on the Control of Education and Science MES RK, indexed in the database "Web of Science", in 6 materials of international conferences, including in 2 materials indexed by the SCOPUS database and Web of Science ”, in a journal indexed by the SCOPUS database, with an impact factor of 3,057 (2017).

The structure and scope of the thesis. The thesis consists of an introduction, 5 chapters, conclusions, bibliography containing 198 titles. The main text is set out on 115 pages, contains 45 figures, 7 tables, 2 annexes.

The introduction shows the relevance, presents a review and formulation of the problem studied in this work, formulates goals and objectives, describes the novelty of the results obtained, substantiates their scientific and practical value. The main provisions for the defense, the personal contribution of the author, publications, approbation and a summary of the thesis are given.

The first section is devoted to the literature review: the main materials used in modern orthopedics, the description of calcium phosphates, biological apatite and bone tissue, the description of zinc oxide nanoparticles.

The second section discusses the objects of research, as well as describes in detail the principles, methods of preparation, means of testing and determining the antibacterial properties, biocompatibility and cytotoxicity of nanostructured apatite-biocomposite materials and coatings.

The third section describes the results of a study of a composite material with a nanoscale architecture based on bioapatite, sodium alginate and ZnO

microparticles. The effects of electromagnetic and ultrasonic radiation during the synthesis on the properties of the final material are discussed.

The fourth section presents the results of deposition of calcium-apatite coatings on porous structures of 316L and Ti6Al4V by methods of modified hydrothermal deposition and microplasma spraying.

The fifth section presents the results of the study of the antibacterial properties, cytotoxicity and biocompatibility of composite materials with a nanoscale architecture based on bioapatite, sodium alginate and ZnO microparticles and their coatings

In the conclusion summarizes and formulates the main results of the thesis.