ANNOTATION

on the thesis for the degree of Doctor of Philosophy (PhD)
on specialty 6D074000 - "Nanomaterials and nanotechnology"

of

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PREPARATION OF NANOSTRUCTURED COMPOSITES BASED ON CALCIUM HYDROXYAPATITE AND THEIR APPLICATION IN BIOPRINTING

The general description of work. The dissertation is devoted to the study of the production of calcium hydroxyapatite, which is a mineral component of the bone structures of the human skeleton, and its physicochemical properties, as well as the experimental study of the application of the obtained product in such areas as 3D printing and the process of electroforming of nanosized polymer fibers.

The relevance of the research topic. Today, modern advances in nanotechnology are widely used in various fields of human activity. Materials on a nanometer scale have unique physicochemical properties, namely electrical, mechanical, optical, catalytic, and magnetic. They are of great interest in their potential applications in biomedicine, particularly in regenerative medicine and targeted drug delivery. Tissue engineering or regenerative medicine is an interdisciplinary field that combines the achievements of various fields of science, including nanotechnology, to develop and create biological systems used to restore or maintain the function of human tissue. The application of nanotechnology in tissue engineering can be divided into several directions:

- transplantation of cells/tissues into damaged areas of the body
- the introduction of substances that have a positive effect on the growth and restoration of cellular structures
- the creation of biological scaffolds containing cellular structures (e.g., stem cells, osteoblasts)

However, at the present stage of development, the use of nanotechnology and nanomaterials in biomedicine requires detailed studies of the materials used and methods for their preparation; it should be noted that the complexity of the synthesis of nanomaterials and their high cost also significantly limit their widespread use in medicine.

To solve these problems, the dissertation shows the promise of using calcium hydroxyapatite (HAP), which was synthesized by chemical deposition, in such areas as 3D printing technology and the process of electroforming nanoscale fibers by obtaining biological scaffolds based on HAP. Biological scaffolds based on polymers and crystalline HAP powder have great potential due to an excellent combination of properties: biocompatibility of HAP and polymers' mechanical strength. The successful combination of various properties of polymers with the

biological properties of HAP will lead to tissue engineering development, which will allow the use of HAP-based composites in medicine. Polycaprolactone was chosen as the polymer since this polymer is biodegradable, non-immunogenic, non-carcinogenic, and non-toxic with excellent biocompatibility, making it possible to use it to obtain composite films that are widely used in the field of tissue engineering. Its chemical and biological properties, such as biological compatibility and mechanical strength, make it possible to implant hard tissues in the body, where healing also takes a long period.

Among the existing methods, the electroforming method and 3D printing technology are promising directions for the manufacture and study of biological scaffolds used in tissue engineering, due to the ability to obtain them with unique characteristics such as a high surface area to volume ratio, high porosity with small pore sizes, and improved mechanical properties. Moreover, the ability to quickly resorb in a biological environment. All other manufacturing methods have limitations in terms of the materials used, and they are laborious and complex processes. With the help of 3D printing technology, it has now become possible to create replacements of individual elements of the human body based on nanostructured materials, and, possibly, shortly, using 3D printing, it will be possible to obtain individual organs such as the heart, kidneys, lungs, etc.

This technology for obtaining nanostructured materials is actively used in modern medicine. It is carried out in several stages: first of all, the selection and synthesis of materials that will satisfy all the conditions of biocompatibility, and secondly, the development of technology for the use of the obtained materials in 3D printing and the method of electroforming of nanoscale fibers, allowing to obtain materials with certain physical and chemical characteristics.

All this indicates the need to conduct a study of HAP's physicochemical properties with its subsequent use in various fields of medicine. The use of the obtained HAP in additive technology in Kazakhstan will lead to the development of priority areas of science and technology in nanomaterials, nanotechnology, and medical equipment.

The purpose of the work. The purpose of this thesis is to obtain calcium hydroxyapatite, with specified physicochemical and biological properties, and composites based on it, for their use in electroforming technologies and three-dimensional printing / 3D printing.

The tasks of work. In order to achieve the assigned aim, the following tasks were solved:

- to synthesize nanostructured HAP according to a modified technology, which has physicochemical properties close to the inorganic component of solid human bone tissue; to study the physicochemical properties and surface morphology of the synthesized nanostructured HAP;
- to form and investigate biologically soluble film-frames based on polymer fibers with the addition of nanostructured HAP, obtained by the method of electroforming;

- to simulate the process of movement of nutrients in the porous structure of a three-dimensional framework with the addition of nanostructured HAP.

The main provisions for the defense:

- The heat treatment temperature can effectively control the phase composition and physicochemical properties of the synthesized HAP;biologically soluble films and scaffolds based on polymer nanoscale fibers with the addition of HAP for tissue engineering, obtained by electroforming method;
- The spatial orientation of polymer fibers modified with nanostructured HAP can effectively control the direction of the electric field strength;glucose- based nutrient diffusion rate in the porous structure of HAP;
- The speed of propagation of motion through a 3D printing with different porosities, consisting of a composite polymer, is determined by the speed of rotation of the framework in a plane perpendicular to the direction of fluid movement, which is essential both when creating a framework using 3D printing / 3D printing and for the growth of cell structures.

The object of study is HAP powder containing nanoparticles with different phase composition and composites based on it.

The subject of study Physicochemical properties of HAP and composites based on it.

The Research Methods. During solving the tasks, which is necessary to achieve the assigned aim, the following research methods were used: X-ray phase analysis (XRD), scanning electron microscopy (SEM), a method for determining the specific surface area, and determining the physical and mechanical characteristics of the materials obtained.

The scientific novelty of the research. In the work the following results were obtained for the first time:

- It has been established that the phase composition (ratio of the amorphous and crystalline phases) of the HAP powder and its physicochemical properties are determined by the heat treatment temperature of the synthesized crystalline HAP;
- For the first time, it was found that the orientation of polymer fibers modified with nanostructured HAP when produced by the method of electroforming is determined by the direction of the electric field strength;
- Using computer simulation methods, it has been shown that the speed of fluid movement in a 3D printing, consisting of a composite polymer, is determined by the rotation speed of the 3D printing.

The theoretical significance. The theoretical significance of the work lies in the fact that it developed a model of the movement of nutrient fluid in the porous structure of 3D frameworks, which considers the parameters of both polymer and HAP powder, which allow predicting the properties of the grown tissue. The theoretical significance is confirmed by the fact that the results obtained within the

framework of the proposed model can be applied not only for frames with the addition of HAP but also for composite frames based on various materials.

The practical significance. The paper proposes a method for obtaining HAP powder with different phase compositions. The revealed in this work the possibility of controlling the orientation of composite polymer fibers obtained by the method of electroforming is an essential parameter for cell structures' growth. The revealed in this work the ability to control the speed of movement of the nutrient fluid in 3D scaffolds with different porosities is important when creating tissues with desired properties.

Relationship with research and government programs. The work was carried out in the framework of the scientific project "Creation and Organization of the 3D Printing Scientific Center", funded under the program-targeted funding of grants, No. 0268/PTF by the Committee of Science of the Ministry of Education and Science of the Republic of Kazakhstan (2015 - 2017).

The approbation of work. Materials of the thesis were reported and discussed at various international, republican conferences and symposia:

- PJISCP 2015. VIII Proceedings of the Joint International Symposium Combustion and Plasmochemistry (Almaty, Kazakhstan, September 16-18, 2015);
- IX International Symposium "Physics and Chemistry of Carbon Materials / Nanoengineering" and "Nanoenergy Materials and Nanoenergy" (Almaty, Kazakhstan, 2016);
- The world conference on Carbon: Common fundamentals, remarkably versatile applications (Pennsylvania, USA, 10-15 July 2016).

The personal contribution of the author lies in the setting of research objectives, performing theoretical and experimental research, discussion and generalization of the results.

The publications. The results of the performed work are reflected in 14 scientific papers, including:

1 Temirbayev M.A., Mansurov Z.A., Daulbayev Ch.B., Dosmatova K.R. Nanocrystallic hydroxyapatite from biological material for practical health care // Quarterly Scientific and Practical Journal. – 2017. – Vol. 4. – P. 46-49.

2 Досматова К.Р., Темирбаев М.А., Мансуров З.А., Даулбаев Ч.Б. Сравнительный анализ нанокристаллического гидроксиапатита и его аналогов различного производства // Вестник АГИУВ. – 2018. – № 3. – С. 51-55.

3 Бакболат Б., Даулбаев Ч.Б., Мансуров З.А., Султанов Ф.Р. Получение биологически растворимых пленок на основе полимерных нановолокон и гидроксиапатита кальция // Горение и плазмохимия. – 2018. – Vol. 16. – P. 213-216.

4 Sultanov F.R., Daulbayev Ch., Bakbolat B., Mansurov Z.A. Development of electroforming method for coating of polymer membranes by graphene oxide // Eurasian Journal of Physics and Functional Materials. – 2018. – Vol. 2, №2. – P. 104-109.

5 Даулбаев Ч.Б., Серовайский С.Я., Мансуров З.А. Моделирование движения питательных веществ в пористой структуре биокаркаса на основе гидроксиапатита кальция // Горение и плазмохимия. – 2019. – Т.17, №4. – С. 203-208.

6 Даулбаев Ч.Б., Родин М.И., Елемесова Ж.К., Алиев Е.Т., Мансуров З.А. Определение добавки, ускоряющей время схватывания бетонной массы для 3D принтинга // Механизация строительства. – 2017. – Т.78. – С. 135-143.

7 Sultanov F.R., Daulbayev Ch., Bakbolat B., Mansurov Z.A. Development of electroforming method for coating of polymer membranes by graphene oxide // Eurasian Journal of Physics and Functional Materials. – 2018. – Vol. 2, №2. – P. 104-109.

8 Dmitriyev T., Daulbayev Ch., Abish S., Topanov B., Aliyev E., Mansurov Z. 3D printing as an alternative method of alloys obtaining // Химический Журнал Казахстана. – 2017. – Т.57. – С. 143-153.

9 Даулбаев Ч.Б., Дмитриев Т.П., Алиев Е.Т. Аддитивные технологии в Казахстане: актуальные задачи, достижения и перспективы на будущее // Горение и плазмохимия. – 2017. – Т.15. – С. 268-276.

6 Papers in **Scopus**:

1 Daulbaev Ch.B., Dmitriev T.P. Sultanov F.R., Mansurov Z.A., Aliev E.T. Obtaining Three-Dimensional Nanosize Objects on a "3D Printer + Electrospinning" Machine // Journal of Engineering Physics and Thermophysics. – 2017. – Vol. 90(5). – P. 1115-1118.

2 Daulbaev Ch.B., Bodykov D.U., Aliev E.T. Influence of the electric field on the ultrasonic capillary effect // Journal of Engineering Physics and Thermophysics. – Vol. 89. – P. 1156-1164.

3 Daulbayev Ch., Mansurov Z., Mitchell G., Zakhidov A., Sultanov F. Obtaining of biologically soluble membranes based on polymeric nanofibres and hydroxyapatite of calcium // Eurasian Chemico-Technological Journal. – 2018. – Vol. 20. – P. 119-124.

4 Sultanov F., Daulbayev C., Bakbolat B., Daulbayev O., Bigaj M., Mansurov Z., Kuterbekov K., Bekmyrza K. Aligned composite $SrTiO_3$/PAN fibers as 1D photocatalyst obtained by electrospinning method // Chemical Physics Letters. – 2019. – Vol. 737. – P. 287-294.

5 Sultanov F., Daulbayev Ch., Azat S., Kuterbekov K., Bekmyrza K., Bakbolat B., Bigaj M., Mansurov Z. Influence of metal oxide particles on bandgap of 1D photocatalysts based on $SrTiO_3$/PAN fibers // Nanomaterials. – 2020. – Vol. 10. – P. 1734.

6 Daulbayev Ch., Mansurov Z., Sultanov F., Shams M., Umirzakov A., Serovajsky S. A Numerical Study of Fluid Flow in the Porous Structure of Biological Scaffolds // Eurasian Chemico-Technological Journal. – 2020. – Vol. 22. – P. 149-156.

The patent for utility model No.3650 of the Republic of Kazakhstan “A method for producing fine hydroxyapatite” was obtained (published on February 15, 2019, Bull. No. 7).

The volume and structure of the work. The thesis is presented on 88 pages of printed text, includes 25 figures and 13 tables. The work consists of introduction, 3 sections, conclusion, list of references including 117 sources and 3 annexes.

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