ABSTRACT

of the doctoral dissertation (PhD) with majors in 8D07113 - “Nanomaterials and Nanotechnologies” of

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“Synthesis of hydroxyapatite nanofibers for targeted drug delivery”

General description of the paper

The work involves obtaining hydroxyapatite (HA) - based biodegradable scaffolds and their application for bone regeneration. HA and calcium pyrophosphate (CPP) nanopowders were obtained from eggshell waste, and metallic nano-silicates as resin reinforcement precursors were synthesized using the sonochemical method. In addition, a biodegradable resin was prepared in which Polylactic acid-polyurethane was used as the main matrix. Printed scaffolds' physicochemical, mechanical, in vitro, and in vivo properties were studied.

Relevance of the research

Bone fractures are a global public health issue; however, no comprehensive study of their incidence and burden has been done. The biggest problem of bone disease, especially osteoporosis, is fractures, which may be patients' first visible sign of disease. Each year an estimated 2 million individuals suffer a fracture only in the US (including fractures in patients with osteoporosis).

According to the data provided by the Institute for Health Metrics and Evaluation (IHME), Globally, in 2019, there were 178 million new fractures (an increase of 33·4%), 455 million prevalent cases of acute or long-term symptoms of a fracture (an increase of 70·1%), and 25·8 million YLDs (an increase of 65·3%) across the 21 GBD regions and 204 countries and territories from 1990 to 2019. Males also had higher rates of fractures than females throughout the study period for all ages combined.

In cases where conventional methods cannot repair bone fractures, bone scaffolds promise effective therapies. In conventional techniques, there is a change in structure and function by biological substitutes when used for repairing the damaged bone. In addition to other problems such as a long period of convalescence, the need to remove some of the implanted material after the treatment period, the impossibility of blood flow and nutrients at the fracture site, infections due to the indestructible implanted material, etc.

3D printing of biodegradable scaffolds can solve such problems with scaffolds' porous structure and interconnected pore networks with proper pore size for efficient mass-transport activities, including nourishment of cells, oxygen, exchange of nutrients, and cell migration. They can be designed according to each patient's specific and individual defects in a short time with the lowest cost and side effects.

In this regard, **justification of this scientific and research thesis is** achieving an optimal infill model of TPMS and FGLS structures, the resin composition of 3D printed scaffolds, and the study of their physicochemical and mechanical properties is undoubtedly relevant.

Scope of the research. Obtaining a biodegradable bone scaffold by 3D printing technology to use in tissue engineering.

The subject of research is obtaining an optimal model of TPMS and FGLS structures as the primary scaffold model and a biodegradable resin composition for bone regeneration in orthopedic surgery.

Purpose of the thesis research. This work aims to obtain optimal TPMS and FGLS structures as the primary scaffold model and a biodegradable resin composition for bone regeneration in orthopedic surgery.

The following **tasks** were resolved to achieve the assigned purpose:

1. Obtaining HA and CPP from eggshells, developing optimal conditions for synthesis, selecting the optimum composition with bioactivity properties, and studying their physicochemical properties.
2. Obtaining Nanofibrous biologically soluble scaffolds as an effective drug delivery system by electrospinning.
3. Synthesizing biodegradable resin from PLA/PUA as the oligomer, TEGDMA as the diluent, and Irgacure 819 as an initiator.
4. Synthesizing of nano-metallic silicates as precursor and reinforcement agent by sonochemical method.
5. Achieving and developing an optimal model of TPMS and FGLS structures as the primary scaffold model.
6. Study of the scaffolds' mechanical properties for various medical uses.
7. Implanting scaffolds in dog femur bone and study of the in-vivo properties and their effect on the healing process.

Methodological framework of the research is the synthesis of hydroxyapatite/ calcium pyrophosphate and nano resin reinforcement precursors and obtaining an optimal TPMS/FGLS structure to use as the bone scaffold.

Scientific novelty of this research. For the first time, the following results were obtained:

- Developing several algorithms for the parametric design of TPMS and FGLS structures from a unit cell.
- Using a simple and Eco-friendly sonochemical method to synthesize nano reinforce additives.
- Synthesizing a UV-cured/Reinforced biodegradable resin that can be used in standard SLA 3D printers.

- Physico-chemical, mechanical, in-Vitro, and in-Vivo studies of printed scaffolds showed the possibility of using them as functional scaffolds for bone surgery.

Defended provisions:

1. Mechanical tests showed that the TPMS and FGLS structures have good resistance against crushing and tension forces besides improving efficient mass-transport activities and can be used as potential medical scaffolds.
2. Results of different analyses confirmed that nanomagnetic resin precursors enhanced Osteogenesis.
3. Printed scaffolds coated with HA could decrease the period of convalescence compared to filing the fracture with HA powder.

Scientific and practical significance of the research. The main regularities of synthesis/design/3D printing of HA-based scaffolds by sonochemical and precipitation method were established.

- For the First time, coated TPMS-based bone scaffolds were designed and implanted in the republic of Kazakhstan.
- The optimal condition for manufacturing hydroxyapatite and calcium pyrophosphate from eggshells was determined, and the obtained powders were used to obtain nanofibers.
- Several algorithms were developed to create TPMS structures by parametric design.
- Different resin precursors were synthesized as resin additives to improve the scaffold's osteogenesis and mechanical properties.
- In-Vivo and In-Vitro tests were done to measure the bioactivity properties of scaffolds.

The author's personal contribution is carrying out experiments, summarizing and interpreting the obtained results, and writing articles and reports. The research of structural properties, surface morphology, elemental analysis of the obtained samples was performed with the assistance of KazNU named after al-Farabi experts. The obtained results were discussed and analyzed in cooperation with the research supervisor, Professor Z.A Mansurov and foreign consultant, Professor Salavati Niasar M. during the foreign internship at the Kashan University.

Approval of the conducted researches. The results of the thesis research were presented at the following scientific international and foreign conferences:

- International Kazakh-Russian symposium “Chemical physics and nanomaterials” dedicated to the 125th anniversary of N.N.Semenov (Almaty, Kazakhstan, April 09, 2021).
- VI Conference of students and young scientists “Chemical physics and nanomaterials” (Almaty, Kazakhstan, 18 March 2021).

- VII Conference of students and young scientists “Chemical physics and nanomaterials” (Almaty, Kazakhstan, 18 March 2022).

Publications. The results of the thesis are reflected in 7 scientific papers, including:

Three scientific articles published in journals having an impact factor according to the **Scopus database**;

- M. Shams, Z. Mansurov, C. Daulbayev, and B. Bakbolat, “Effect of Lattice Structure and Composite Precursor on Mechanical Properties of 3D-Printed Bone Scaffolds”, Eurasian Chem.-Technol. J., vol. 23, no. 4, p. 257–266, Dec. 2021.
- Chingis Daulbayev; Fail Sultanov; Maiya Aldasheva; Aliya Abdybekova; Baglan Bakbolat; Mohammad Shams; Aruzhan Chekiyeva; Zulkhair Mansurov. Nanofibrous biologically soluble scaffolds as an effective drug delivery system. Comptes Rendus. Chimie, Volume 24 (2021) no. 1, pp. 1-9. doi : 10.5802/crchim.58
- M. Shams, Z. Mansurov, C. Daulbayev, and B. Bakbolat, “Effect of Lattice Structure and Composite Precursor on Mechanical Properties of 3D-Printed Bone Scaffolds”, Eurasian Chem.-Technol. J., vol. 23, no. 4, p. 257–266, Dec. 2021.

Four oral abstract presentations at international conferences and symposia;

Scope and structure of the dissertation.

The thesis is presented in 77 pages and includes 42 Figures, 15 Tables, and 12 formulas. The work includes an introduction, literature review, description of objects and research methods, results and discussion, conclusion, and list of references, including 115 names.