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Rozprawa doktorska pt. **„Polimerowo - ceramiczne biomateriały do regeneracji tkanki kostnej"**

Streszczenie w języku angielskim

The number of bone injuries among the society is growing and concerns traumatic fractures, fractures resulting from progressive osteoporosis and bone defects after tumors resection. Therefore, the development of new, synthetic, biocompatible and bioresorbable implant materials establishes interest in the field of bone tissue engineering. Researchers are looking for new biomaterials and methods of forming them into bone scaffolds that will stimulate the process of osseointegration after implantation. It is required that such materials should simultaneously resorption in favor of the regrowing native bone tissue.

This PhD thesis demonstrates new methods of chemical surface modification of hydroxyapatite and bioactive glass particles, which are commonly used in polymer-ceramic composites, as well as biphasic bone scaffolds consisting of calcium phosphates and poly(L-lactide) (PLLA) microspheres. L-lysine, which promotes the adhesion and proliferation of osteoblasts, and polydopamine, which, apart from adhesive and bioactive properties, is also a material with high affinity for bone-forming cells, were used to functionalization the surface of hydroxyapatite particles. The L-lysine and polydopamine were used as a linker in the covalent attachment of poly(ethylene glycol) with different molar masses to ceramic surfaces. The bioactive glass particles were modified with L-lysine using a silane precursor and a carbodiimide coupling agent. The functionalized ceramic particles were then used to form PLLA-based composites by solvent casting. Influence of surface functionalization of ceramic particles on the physicochemical and biological properties of PLLA was determined and the *in vitro* degradation profiles of the composites were evaluated.

The paper also presents the formation of biphasic, macroporous scaffolds consisted of calcium phosphate cements (CPC) and PLLA microspheres using extrusion-based 3D printing. The method of manufactured PLLA microspheres with a diameter of less than 50 μm, the rheological properties of pastes for 3D printing and the physicochemical and biological properties of biphasic CPC/PLLA scaffolds are described. *In vitro* degradation profiles of PLLA microspheres and CPC/PLLA composites were also determined.

Based on experimental studies, the effectiveness of functionalization of hydroxyapatite particles with L-lysine and poly(ethylene glycol) with a carboxyl end group as well as polydopamine and poly(ethylene glycol) with an amine/thiol end group was confirmed. The proposed method of functionalization of bioactive glass particles using 3-aminopropyltriethoxysilane and L-lysine was characterized by the highest efficiency of the coupling reaction. As a result of surface modification of ceramic particles, multifunctional fillers for polymer matrices were created, which can act as nucleating agents, plasticizers and bioactive groups. It was found that the modification of ceramic particles improves the thermal stability of PLLA and composites of PLLA and ceramic fillers, which is important from the perspective of thermal processing of composites to obtain personalized bone constructs. In addition, it was found that the immobilization of L-lysine, polydopamine and poly(ethylene glycols) on ceramic particles supports the process of mineralization of polymer-ceramic composites. The presented new composites are cytocompatible towards L929 mouse fibroblasts and hFOB 1.19 human osteoblasts.

Based on the physicochemical studies for the CPC/PLLA systems, it was found that the increase in the content of PLLA microspheres in composite pastes for extrusion of scaffolds causes an increase in the viscosity of the systems, as well as obtaining stable scaffolds after extrusion with the assumed macroporosity of the constructs. Due to poor adhesion on the interface between CPC and PLLA microspheres, the mechanical strength of the composites is lower than the CPC control scaffolds. These biphasic scaffolds and the PLLA microspheres induce the mineralization process in the simulated body fluid during the 28 weeks of experiment. It was found that the PLLA microspheres did not affect the rate of degradation of the CPC/PLLA scaffolds and did not cause the formation of new pores in the crosslinked strands of the CPC during the degradation tests. The manufactured CPC/PLLA composites are not cytotoxic and support the adhesion, proliferation and migration of hTERT-MSC mesenchymal stem cells on the entire surface of the scaffolds and inwards the macropores.

The presented new polymer-ceramic composites exhibit the potential for applications in the regeneration of bone tissue.