Fe AND Zn CO-SUBSTITUTED BETA-TRICALCIUM PHOSPHATE: SYNTHESIS, STRUCTURAL, MAGNETIC, MECHANICAL AND BIOLOGICAL PROPERTIES

Agne Kizalaite[1], Lauryna Sinusaite[1], Diana Griesiute[1], Anton Popov[1], Andris Antuzevics[2], Kestutis Mazeika[3], Dalis Baltrunas[3], Jen-Chang Yang[4], Aivaras Kareiva[1], Aleksej Zarkov[1]

[1] Institute of Chemistry, Vilnius University, Naugarduko 24, LT-03225 Vilnius, Lithuania
[2] Institute of Solid State Physics, University of Latvia, Kengaraga 8, LV-1063 Riga, Latvia
[3] Center for Physical Sciences and Technology, Vilnius LT-02300, Lithuania
[4]College of Biomedical Engineering, Taipei Medical University, 250 Wu-Hsing St, Taipei 11052, Taiwan
agne.kizalaite@chgf.vu.lt

Calcium phosphates (CPs) are the main inorganic part of biological hard tissues such as bones or teeth and play an essential role in human life. This reason makes synthetic CPs widely used in medicine for repair and reconstruction of diseased or damaged parts of bone. For these purposes CPs can be used in different forms varying from thin coatings on metallic implants to sintered bioceramics [1-3]. One of the CPs most frequently used for the fabrication of bioceramics is beta-tricalcium phosphate (β-TCP, $Ca_3(PO_4)_2$), which attracts practical interest due to several reasons such as excellent biocompatibility, osteoconductivity and chemical composition similar to natural bone [4].

Partial substitution of Ca by other biologically active ions has been proposed as a promising tool to the superior biological performance of CP based materials [5]. Chemical modification can drastically affect physicochemical, mechanical and anti-bacterial properties of materials, to cause changes in morphology, density, solubility and ion release kinetics [6]. Substitution-induced properties allow to combine biocompatibility of CPs with newly obtained properties resulting in application of these materials in new areas such as various imaging modalities including fluorescence, magnetic resonance or multimodal imaging, as well as for various therapeutic approaches including chemotherapy, gene therapy, hyperthermia or combination therapy [7].

Despite the fact that different CPs have been reported to be substituted with a huge variety of ions, co-doping of CPs still remains relatively new approach. Since substitution with single ions opens so many horizons for new applications, it makes sense to use multielement substitution for the synergistic effect or multifunctioning of CP-based materials [8]. The main goal of the present work was to develop synthetic approach and comprehensively characterize β-TCP bioceramics with magnetic and biological properties. Due to these reasons β-TCP partially substituted with Fe^{3+} and Zn^{2+} ions was chosen and series of products with different substitution level was investigated in detail.

Fe^{3+} and Zn^{2+} co-substituted β-tricalcium phosphate (β-TCP) has been synthesized by wet co-precipitation method. Co-substitution level in the range from 1 to 5 mol% has been studied. The thermal decomposition of the as-prepared precipitates was analysed through thermogravimetric (TG) analysis. The phase purity and structure of the synthesized compounds were evaluated using X-ray diffraction (XRD) analysis, electron paramagnetic resonance (EPR) and Fourier-transform infrared spectroscopy (FTIR). Scanning electron microscopy (SEM) was used for the characterization of morphological features of the synthesized products. Chemical composition of the compounds was confirmed by inductively coupled plasma optical emission spectrometry (ICP-OES). Cytotoxicity of the synthesized species was estimated by in vivo assay using zebrafish (*Danio rerio*).

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[1] W. Habraken, P. Habibovic, M. Epple et al., Calcium phosphates in biomedical applications: materials for the future?, Mater. Today **19**, 69-87 (2016).
[2] E.A. Chudinova, M.A. Surmeneva, A.S. Timin et al., Adhesion, proliferation, and osteogenic differentiation of human mesenchymal stem cells on additively manufactured Ti6Al4V alloy scaffolds modified with calcium phosphate nanoparticles, Colloids Surf. B **176**, 130-139 (2019).
[3] S.V. Dorozhkin, Calcium orthophosphate-based bioceramics, Materials, **6**, 3840-3942 (2013).
[4] R.G. Carrodeguas, S. De Aza, α-Tricalcium phosphate: Synthesis, properties and biomedical applications, Acta Biomater. **7**, 3536-3546 (2011).
[5] E. Boanini, M. Gazzano, A. Bigi, Ionic substitutions in calcium phosphates synthesized at low temperature, Acta Biomater. **6**, 1882-1894 (2010).
[6] B. Yilmaz, A.Z. Alshemary, Z. Evis, Co-doped hydroxyapatites as potential materials for biomedical applications, Microchem. J. **144**, 443-453 (2019).
[7] C. Qi, J. Lin, L.H. Fu, P. Huang, Calcium-based biomaterials for diagnosis, treatment, and theranostics, Chem. Soc. Rev. **47**, 357-403 (2018).
[8] S. Sprio, L. Preti, M. Montesi et al. Surface phenomena enhancing the antibacterial and osteogenic ability of nanocrystalline hydroxyapatite, activated by multiple-ion doping, ACS Biomater. Sci. Eng. **5**, 5947-5959 (2019).