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PhD dissertation abstract

Preparation and characterization of biocomposites based on nanoapatites for theranostics

Nowadays, one of the challenges regarding nanotechnology is a search for new multifunctional biomaterials that can be simultaneously used in therapy and diagnostics – in other words "in theranostics".

In the doctoral thesis, there have been presented the possibilities of use of the designed and obtained multifunctional nanocrystalline materials based on phosphate compounds ($Ca_{10}(PO_4)_6(OH)_2$ (HAp), $Ca_{10}(PO_4)_6F_2$ (FAp) and β-$Ca_3(PO_4)_2$ (β-TCP)) doped with the lanthanide ions and lithium cations. All materials were prepared using various wet chemistry techniques e.g. the co-precipitation, hydrothermal synthesis, and sol-gel including the modified Pechini's method. The structures of the studied materials have been intentionally modified through doping with biologically active ions for so-called targeted and/or regenerative therapies. Moreover, the mesoporous ceramics based on the hydroxyapatite with a high specific surface were obtained using the dry granulation process.

The structure and morphology of the obtained materials were studied by means of X-ray powder diffraction (XRPD), scanning (SEM) and high resolution transmission (HRTEM) electron microscopy as well as selected area electron diffraction (SAED). Elemental analysis was performed using scanning electron microscopy - energy dispersive X-ray spectroscopy (SEM-EDS) and inductively coupled plasma optical emission spectrometry (ICP-OES). The spectroscopic properties were investigated using Fourier transform infrared (FT-IR) and Raman as well as emission spectroscopies (including the emission and emission excitation spectra, luminescence decays). Electrokinetic potential (ζ – Zeta potential), specific surface area (BET, Brunauer-Emmet-Teller method) and porosity (BJH, Barret-Joyner-Halenda method) analyzes as well as ion release profiles in aqueous solutions with pH similar to physiological value were carried out. Moreover, in the doctoral thesis, there has been performed a series of preliminary *in vitro* and *in vivo* biological tests (cytotoxicity and bioactivity).

The results of the research have been published in international journals belonging to the Philadelphia list (six papers). The doctoral thesis has been divided into three sections according to the scientific research criteria: (i) physicochemical studies of the nanocrystalline apatites

depending on the ionic radius and oxidation state of dopants; (ii) up-conversion emission processes in mono- and bi-phasic calcium phosphate systems (FAp and FAp/β-TCP) activated by lanthanide pairs; (iii) biocompatibility and bioactivity of obtained apatite systems for therapy and diagnostics (theranostics).

In the first stage, there were studied the effect of Li^{+} ion concentration on the charge compensation, structural and luminescent properties of the nanocrystalline FAp and HAp:Sr^{2+} activated with Eu^{3+} ions. Moreover, it was investigated the Eu^{3+} preferential site substitution into the apatite structures as a function of Li^{+} ion concentration. Furthermore, the Eu^{3+} ion was used to obtained the necessary information about the local symmetry of the occupied crystallographic positions in the studied systems. Possible charge compensation mechanisms of defects as result of the different charges and ionic sizes between the cation and the dopant, were also proposed. It was analyzed the role of Li^{+} ion as a charge compensator of trivalent lanthanide ions and its influence on their emission intensity.

In the second stage, the up-conversion emission processes in mono- and bi-phasic calcium phosphate matrices (FAp and FAp/β-TCP) doped with ion-pairs (where Yb^{3+} – sensitizer and Er^{3+} or Tb^{3+} – activator) were investigated. It was demonstrated a significant impact of particle size and degree of crystallinity on anti-Stokes emission in the studied materials Moreover, it has been shown that the lanthanide-doped materials could be a very attractive luminescent bio-markers, especially, in the spectral range of the 1st and 2nd optical windows in biological tissue (650 – 1350 nm).

In the third stage of the doctoral thesis, there was carried out a series of preliminary research of the cytotoxicity and bioactivity using adult stem cell lines and bacterial strains as *in vitro* and *in vivo* (*Galleria mellonella*) model. Additionally, it has been evaluated an influence of grain size, degree of crystallinity, type of dopants, specific surface area as well as electrokinetic potential (ζ – Zeta potential) on the biological properties of the obtained systems/compounds.