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Tumor-selective hybrid system based on hydroxyapatite nanocarrier, chitosane, poly(lactic-co-glycolic acid) and androstan derivate

Nenad L. Ignjatović[1], Katarina M. Penov-Gaši[2], Victoria M. Wu[3], Jovana J. Ajduković[4], Vesna V. Kojić[4], Dana Vasiljević-Radović[5], Vuk D. Uskoković[3,6], Dragan P. Uskoković[1]
[1]Institute of Technical Sciences of SASA, Belgrade, Serbia, [2]University of Novi Sad, Faculty of Sciences, Department of Chemistry, Biochemistry and Environmental Protection, Novi Sad, Serbia, [3]Advanced Materials and Nanobiotechnology Laboratory, Department of Bioengineering, University of Illinois, Chicago, IL, USA, [4]Oncology Institute of Vojvodina, Sremska Kamenica, Serbia, [5]University of Belgrade, Institute for Chemistry, Technology and Metallurgy, Belgrade, Serbia, [6]Department of Biomedical and Pharmaceutical Sciences, School of Pharmacy, Chapman University, Irvine, CA, USA

The applicative potential of synthetic calcium phosphates, especially hydroxyapatite (HAp), has become intensely broadened in the past 10 years, from bone tissue engineering to multiple other fields of biomedicine. Previously we have shown that hydroxyapatite nanoparticles coated with chitosan-poly(D,L)-lactide-co-glycolide (HAp/Ch-PLGA) target lungs following their intravenous administration into mice. For this purpose radioactive 125-Iodine (125I), a low energy gamma emitter, was used to develop a novel in situ method for radiolabeling of particles and investigation of their biodistribution.

In this study we utilize an emulsification process and freeze drying to load the composite particles based on hydroxyapatite nanocarrier, chitosane and poly(lactic-co-glycolic acid) with 17β-hydroxy-17α-picolyl-androst-5-en-3β-acetate (A), a chemotherapeutic derivative of androstane. The picolyl androstane derivatives showed high potency in the cell inhibitors of hormone-dependent cancers (adenocarcinoma, prostate cancer, cervix carcinoma, colon cancer, etc.). 1H NMR, 13C NMR and high-resolution time-of-flight mass spectrometry (MS) techniques confirmed the intact structure of the derivative A following its entrapment within HAp/Ch-PLGA particles. The synthesized particles of A-loaded HAp/Ch-PLGA were found to be spherical in shape with a uniform size distribution of d_{50}=168 nm. The release of A from HAp/Ch-PLGA was sustained, with no burst release or plateauing after three weeks. The obtained results of the DET and MTT tests show that the particles of A-loaded HAp/Ch-PLGA exhibit almost three times higher cytotoxicity towards lung adenocarcinoma cells (A549) than towards healthy cells (MRC5), while at the same time allowing twice as fast recovery of healthy cells. We have also analyzed the period of recovery of healthy, as well as cancer cells, following the treatment with A-loaded HAp/Ch-PLGA. After treatment with A-loaded HAp/Ch-PLGA, healthy cells recover twice as fast as the malignant ones. Immunofluorescent staining of primary fibroblasts interacting with HAp/Ch-PLGA and A-HAp/Ch-PLGA particles demonstrates no negative morphological or proliferative effects on cells.