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Radiolabeled Surface-modified Single-core $(Mg,Fe)_3O_4$ Colloidal Nanoparticles as Vectors in RadionuclideTherapy of Cancer

M. Ognjanović,[a,*] T. Stanojković,[b] B. Dojčinović,[c] M. Radović,[a] M. Mirković,[a] D. Janković,[a] S. Vranješ-Đurić,[a] and B. Antić[a]

[a]*University of Belgrade, VINČA Institute of Nuclear Sciences, Belgrade, Serbia*
[b]*Institute for Oncology and Radiology of Serbia, Pasterova 14, 11000 Belgrade, Serbia*
[c]*University of Belgrade, Institute of Chemistry, Technology and Metallurgy, Belgrade, Serbia*
*miloso@vin.bg.ac.rs

A series of $Mg_xFe_{3-x}O_4$ (x=0, 0.1, 0.2, 0.4, 0.6, 0.8, and 1) magnetic nanoparticles (MNP) were synthesized by a two-step procedure, a co-precipitation method followed by hydrothermal treatment in a microwave field. The MNP are single-core, with crystallite size gradually decreasing from 15.5(3) up to 2.5(3) nm with an increase of$x$. TEM images show pseudospherical log-normally distributed particles with an average particle diameter of 19.8 nm and a polydispersity index of 26.1% for magnetite. The particle diameter decreases with the increase of magnesium (x) in the formula unit. The colloidal stability of MNP was achieved by their surface modification with citric acid (CA), oleic acid (OA) and polyethylene glycol (PEG). The cytotoxic activity of uncoated and coated $Mg_{0.6}Fe_{2.4}O_4$ was tested against target malignant cells (HeLa, LC174, A549) and normal MRC5 cells. The investigated MNP show moderate cytotoxic activity against the tested malignant cells *in vitro*. In contrast, MNP didn't show any significant cytotoxic effect against normal cells. HeLa cells exhibited the highest susceptibility among the malignant cells. $Mg_{0.6}Fe_{2.4}O_4$@OA show good cytotoxic activity against all examined malignant cells, significantly higher than other tested MNP. It can be seen that $Mg_{0.6}Fe_{2.4}O_4$@PEG show a lower cytotoxic activity compared to all analyzed MNP. A direct method was used for labeling with radionuclide ^{90}Y, which involves incubation of MNP with ^{90}Y at a certain temperature and time. The labeling yield of the ^{90}Y-coated MNP was determined by analyzing the radiochemical purity after labeling. ^{90}Y-$Mg_{0.2}Fe_{2.8}O_4$@PEG were labeled in high yield (100%), while the yield for ^{90}Y-$Mg_{0.2}Fe_{2.8}O_4$@CA was 83%.*In vitro* stability of ^{90}Y-coated MNP at room temperature in physiological solution and human serum was monitored within 72 h from the moment of labeling by determining the radiochemical purity of ITLC-SG by radio chromatographic method. The stability of ^{90}Y-$Mg_{0.2}Fe_{2.8}O_4$@PEG was about 97%, while ^{90}Y-$Mg_{0.2}Fe_{2.8}O_4$@CA stability was 73%. The results of this study indicate that radiolabeled surface-modified $(Mg,Fe)_3O_4$ can be used as vectors in radionuclide therapy of malignant diseases.

Keywords: iron oxide, surface modification, cytotoxicity, radiolabeling, cancer nanotechnology.