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# Barium ferrite magnetic nanoparticles labeled with 223Ra: a new potential radiobioconjugate for targeted alpha therapy and magnetic hyperthermia

Among all alpha particle emitters, only a few nuclides are in considerable interest for targeted radionuclide therapy because of their properties, such as half-live, high cytotoxicity and short path length. One of the most important issues, which affects wider use of targeted α therapy in nuclear medicine, is the availability and the price of the radionuclides.

223Ra, as radium chloride, is the first commercially and widely used α-radiopharmaceutic. It is easily obtained from the 227Ac/223Ra generator. However, 223Ra is used mostly for treatment of bone metastases derived from primary prostate cancer, because 223Ra, as a member of Alkaline Earth
metals, forms very weak complexes. There is a lack of chelators which can effectively bind 223Ra for the purposes of receptor targeted therapy. In our studies we propose to use barium ferrite (BaFe12O19) nanoparticles as multifunctional carriers for 223Ra radionuclide for targeted α therapy and magnetic hyperthermia.

Barium hexaferrite nanoparticles labeled with 223Ra were synthesized by a modified autoclave method described by Drofenik et al [1]. The reaction mixture of FeCl3, BaCl2 and 223RaCl2 was alkalized with NaOH solution. Next, the reaction mixture was stirred in autoclave at 210 Celsius degrees for 5 h. Obtained radioactive, magnetic [223Ra]BaFe12O19 nanoparticles were washed with distilled water and hydrochloric acid (0.001 mol/L HCl). Yield of labeling was about 70% (for 100kBq 223Ra). Stability of the obtained radioactive nanoparticles was tested in various biological solutions: 0.01M PBS,0.9% NaCl and in human blood serum. It is confirmed that 223Ra was highly retained inside nanoparticles in every tested solution. Only about 20% of 211Pb (decay product of 223Ra) was released to the solution.

Obtained magnetic BaFe12O19 nanoparticles were characterized by transmission emission microscopy and dynamic light scattering. The diameter of synthesized nanoparticles was ~20 nm and the determined magnetization of nanoparticles in room temperature was about 42 emu/g.

In order to synthesize a radiobioconjugate having affinity to HER2 receptors, the monoclonal antibody trastuzumab was conjugated to the obtained barium ferrite nanoparticles. Firstly, the surface of barium ferrite nanoparticles was modified with 3-phosphonopropionic acid (CEPA) linker using a method described by Mohapatra et al [2], and then, the monoclonal antibodies were coupled to the barium ferrite nanoparticles using the carbodiimide chemistry. Synthesized bioconjugate was characterized by thermogravimetric analysis, dynamic light scattering and were tested for stability in biological fluids. The obtained [223Ra]BaFe12O19-CEPA-trastuzumab radiobioconjugate almost quantitatively retains 223Ra and majority of the daughter products. Radiobioconjugate has high receptor affinity towards HER2 receptors expressing on ovarian cancer cells and exhibits high cytotoxic effect in vitro.

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