Preparation of biodegradable microbeads containing Dysprosium for ^{166}Dy/^{166}Ho *in vivo* generator application

Bo-Bae Cho, Kanghyuk Choi*

[1]*Korea Atomic Energy Research Institute, P. O. Box 105, Yusung, Daejeon 305-600, Republic of Korea*

The microbeads containing radionuclides are interesting materials, which can be applied in the treatment of liver malignancies. Their proper size of 20-50 μm allow them to stay in and around a tumor, and the radionuclides induce tumor apoptosis. Holmium-166(^{166}Ho), which a lanthanide, is a potential therapeutic radiopharmaceutical that is already used in radiotherapeutic medical fields such as bone marrow ablation and radiation synovectomy owing to its high-β radiation energy [$T_{1/2}$=26.6 h, E^{β}_{max}=1855 keV (51%), E^{β}_{av}=666 keV]. ^{166}Ho can be produced using direct (^{165}Ho(n, γ)^{166}Ho) and indirect (^{164}Dy(2n, γ)^{166}Dy→^{166}Ho) methods. Between production systems, Dy/Ho nuclides of an indirect method can be applied to the *in vivo* generator concept. In an *in vivo* generator, the parent nuclide, as an example of ^{166}Dy ($T_{1/2}$=81.5 h, E^{β}_{max}=486.8 keV, E^{β}_{av}=130 keV), with a long-half life is delivered to the target tumor, and then *in vivo* decay to form a daughter nuclide (^{166}Ho) with a short lived and high decay energy then occurs. In this study, we produced microbeads including Dy, as a parent nuclide, for ^{166}Dy/^{166}Ho *in vivo* generator application.

The Dy-microbeads were synthesized using O/W and W/O/W suspension polymerization from the starting material, $DyCl_3 \cdot 6H_2O$. In addition, the synthesized Dy-microbeads consist of a biodegradable polymer such as Poly-L-lactic acid (PLLA) and Polycaprolactone (PCL). The morphologies were confirmed using a Jeol JSM-7100 F field-emission scanning electron microscope (FE-SEM). The chemical structures were identified using a Fourier transform infra-red (FT-IR) and Maldi-TOF mass spectrometer. The metal contents of the microbeads were determined using Atomic Adsorption Spectroscopy. To evaluate the cytotoxicity of Dy and Ho ions released from biodegradable polymers, the cell viability of Dy and Ho ions against a liver cancer cell line (Hep G 2) and lung cancer cell line (A 549) were studied.

Based on a O/W suspension polymerization, the Dy-microbeads show a spherical appearance with a size of 20-30 μm. The size and surface shape are affected by the stirring speed and contents of Dy-ACAC, intermediate material, respectively. The Dy-microbeads obtained through W/O/W suspension polymerization with PLLA show many holes on the surface. Compared to PLLA, microbeads with PCL have a smooth surface. The results of a cytotoxicity assay show that Hep G 2 and A 549 exhibit high viability toward Dy and Ho ions, where both ions represent have an excellent bio-compatibility property. These detailed studies established the idea that Dy-microbeads have a potential application for ^{166}Dy/^{166}Ho *in vivo* generator systems.

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