

Synthesis and neutron activation of Lu₂O₃ nanoparticles functionalized with target specific peptides

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Background

The preparation of ¹⁷⁷Lu-peptides for targeted radionuclide therapy requires the use of lutetium-177 from medium to high specific activity (from 400 to 3000 GBq/mg), which cannot be obtained in low flux research nuclear reactors [1,2]. However, the synthesis of ¹⁷⁶Lu in the form of injectable nanoparticles functionalized with target-specific peptides, would allow to irradiate in the TRIGA (Training, Research, Isotopes, General Atomics) Mark III reactor a mass of lutetium enough to obtain radiopharmaceuticals with activities suitable for direct medical use.

Objective

To synthesize and characterize, Lu₂O₃ nanoparticles functionalized with the RGD peptide, as well as to study the effect on their structural properties after neutron irradiation in the Triga Mark III reactor.

Methodology

Lu₂O₃ tablets were prepared and immersed in an injectable solution containing the DOTA-RGD peptide. The sample was irradiated in a Nd:YAG laser equipment (Q-Smart-100, quantel laser)(50 mJ) with a repetition rate of 10 Hz (irradiance of 16 Watts/cm²), producing instantaneously a turbid solution containing the lanthanide oxide nanoparticles with the peptide (Lu₂O₃-NPs-peptide) attached on their surface. The solution was purified and concentrated by ultracentrifugation and filtered through a 0.22 μm membrane (Millipore). The nanosystem was analyzed by TEM, DLS, UV-Vis and IR techniques. The Lu₂O₃-NPs-peptide solution (1 mg/mL), contained in a sealed vial of pharmaceutical grade plastic, was irradiated in the Triga Mark III reactor (3x10¹³ n.cm⁻².s⁻¹) for 20 h. After decay, the sample was reanalyzed by TEM, DLS, UV-Vis and IR techniques.

Results and discussion

TEM, DLS, UV-Vis and IR analyses of the Lu₂O₃-NPs-peptide sample, showed that the method of synthesis by laser irradiation (thermo-reduction) is suitable for the preparation of nanosystems based on lutetium oxide functionalized with target-specific peptides (size from 2 to 100 nm), which were not significantly affected when subjected to neutron irradiation in the Triga Mark III reactor. The irradiation of the Lu₂O₃-NPs-peptide (sterile solution) for 20 h, yielded 9.2 GBq useful for direct clinical use. The Lu₂O₃-NPs-RGD system could potentially be applied in targeted radiotherapy of intrahepatic carcinomas. In order to produce significant amounts of Lu₂O₃-NPs, other methods of synthesis can be applied, such as for example the thermo-reduction by calcination.

Conclusions

Laser irradiation is suitable for the synthesis of lutetium oxide nanoparticles functionalized with target-specific peptides, which are not significantly affected after neutron irradiation. The Lu₂O₃-NPs-RGD nanosystem is potentially useful for targeted radiotherapy purposes.

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Primary authors: Ms ANCIRA-CORTÉS, Alejandra (Instituto Nacional de Investigaciones Nucleares, Universidad Autónoma del Estado de México); Dr OCAMPO-GARCÍA, Blanca (INSTITUTO NACIONAL DE INVESTIGACIONES NUCLEARES); Dr MORALES-AVILA, Enrique (Universidad Autónoma del Estado de México); Dr LUNA-GUTIÉRREZ, Myrna (INSTITUTO NACIONAL DE INVESTIGACIONES NUCLEARES); Dr JIMÉNEZ-MANCILLA, Nallely (CONACyT. Instituto Nacional de Investigaciones Nucleares)

Presenter: Ms FERRO-FLORES, Guillermina

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