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Production of ^{114m}Indium in Triga Mark IPR-R1 reactor and evaluation for radionuclide therapy application

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1. Introduction

Targeted radionuclide therapy, also called endoradiotherapy, is an attractive alternative to external beam radiotherapy because it attempts to exploit anatomical or biochemical features in order to enhance the specificity of tumour-cell cytotoxicity. An advantage of targeted radiotherapy is that radionuclides are available which emit radiation with a wide variety of emission types and energies. Thus, it is possible to select a radionuclide whose radiation is most appropriate for the treatment of a certain type of tumour. Radionuclide therapy has involved β-emitting radionuclides such as ^{131}I and ^{90}Y which deposit their energy over several millimetres. Auger electron emitters and α emitters are two alternatives to β-emitters. These corpuscular radiations have a high ionization power and high Relative Biological Effectiveness (RBE) when they are emitted in contact with the cell [1].

Although ^{111}In is commonly used for cancer diagnosis, it is under study for therapeutical application due to a good relative biological efficiency ascribed to Auger electrons emission, causing damage to DNA and its subsequent cell death, being more appropriate for smaller tumors [2]. A number of efficient tumor-seeking pharmaceuticals have been developed and labeled with ^{111}In [3, 4, 5]. By replacing ^{111}In with ^{114m}In, some of these molecules may be useful for therapy. Recent studies show that ^{114m}In, with an energy of 190keV, can be used as radiopharmaceutical for therapy because its high-energy beta particles and Auger electrons are attractive for larger tumors [6].

In this work we have studied the activated indium in the Triga Mark reactor – IPR-R1, where the produced radio-indium isotopes were characterized by the energy emitted in their decay. Subsequently, radiochemical purity tests were carried out with thin layer chromatography and the radionuclide therapy potential was evaluated by measuring absorbed dose in vitro.

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2. Methodology

2.1 Production of radioactive nuclides

Standard indium aliquots (ranging from 100 to 1000µg) and liquid indium sample of $In(NO_3)_3$ (Sigma-Aldrich 207398-97-8) with 38% of indium were subjected to neutron activation in Triga Mark IPR-R1 reactor with a power of 100kW under neutron fluxes of $4.1x10^{12}$ $n.cm^{-2}.s^{-1}$ and $6.6x10^{11}$ $n.cm^{-2}.s^{-1}$ for 4-8h of irradiation.

2.2 Characterization of the produced indium nuclides

The identification and quantification of isotopes induced by irradiation of the samples, as well as the activation yield, was performed by gamma spectrometry in a Hyper Pure Germanium (HPGe) detector, Canberra brand, GC2520, nominal efficiency of 25% coupled to an acquisition system and analysis with Genie 2000 software.

2.3. Specific Activity

For this calculation, the activity obtained at the end of the neutron activation of the sample containing natural indium on the activated mass was used. The standard indium aliquots were varied precisely to verify whether the specific activity would increase with the amount of the sample.

2.4 Radiochemical quality control

Radiochemical quality control was carried out by thin layer chromatography (TLC) using as stationary phase silica gel with a 10cm front and with different mobile phases: 0.2M EDTA and pH 5.0; 0.1M sodium citrate and pH 5.0; 10% methanol/sodium acetate. According to the literature, the Rf using 10% methanol/sodium acetate as mobile phase for $^{111}InCl_3$ is 1; for sodium citrate the Rf of $^{111}InCl^3$ is 0.8-0.9 [7]. And with the mobile phase being EDTA the Rf for the unbound ^{111}In is 0.6-0.8 [8].

2.5 Radionuclide therapy potential

Radionuclide therapy potential was evaluated by dosimetric study.

3. Results and Discussion

^{114m}In was successfully produced with insignificant amounts of ^{116m}In and ^{115m}In isotopes after cooling time when ^{114m}In isotope became the predominant isotope (Table I). Specific activity obtained at the end of bombardment was 4.01MBq/mmol.

Table I: Indium isotopes three days after the end of bombardment (EOB).

Nuclide	Energy (keV) (intensity)	% in relation to total índium energies
^{114m}In	190,55 (100)	100%
	559,23 (4)	

	726,3 (4)	
^{115m}In	336,7	0%
^{116m}In	1293,4(100)	0%

^{114m}In was obtained with high purity as shown in Table II.

Table II - Thin layer chromatography with activated indium sample.

Stationary phase	Mobile phase	Retention factor (Rf)	% Bq of ^{114m}In
Sílica Gel	EDTA	0,9	71
	Citrato de Sódio	0,4	48
	Metanol /Acetato de Sódio 10%	0	83

^{114m}In indium samples at micromolar concentrations delivered up to 570 µGy on the exposed TLD's dosimeters (Table III) arguing in favour of its high therapeutic potential.

Table III: Dosimetry of activated Indians.

Radio-indium (concentration µM)	Bq	Exposure time	Dose (µGy)
1	18,5	4h	130
		24h	190
		48h	270
5,5	28,4	24h	340
		48h	570

^{114m}In indium samples at micromolar concentrations delivered up to 570 microGy on the exposed TLD's dosimeters Table 3. This is strong evidence of its high therapeutic potential. Indeed we have shown the antitumoral radionuclide therapy potential of molecules labelled with ^{114m}In elsewhere Oliveira *et al.*, 2017 [8].

4. Conclusions

Therefore, this work focused on the production of ^{114m}In from natural indium activated in the Triga Mark IPR-R1 reactor with a power of up to 100kW, which presents high radionuclide therapeutic potential.

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