Auger-Emitting Lanthanides for Radiobiological Studies

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Introduction

Recently FDA approved radiopharmaceuticals, $^{177}$Lu-PSMA-617 (Pluvicto®) and $^{177}$Lu-DOTATATE (Lutathera®), have attracted interest into radiouclide decay needs of $^{177}$Lu. $^{177}$Yb is similar in chemical structure but differs in its co-emission of 12-13 conversion and Auger electrons (CAEs) per decay. Radiobiological investigations into the advantages of CAEs are necessary for radiopharmaceuticals.

However, the short half-life of primarily CAE emitting lanthanides, such as $^{167}$Er (t$_{1/2}$=10.36 h, 7.8 CAEs/decay), can be a limiting factor. Separation of the radioisotope from the bulk target material may be difficult requiring the separation of adjacent lanthanides. In order to aid these radiobiological studies, yield calculations of two nuclear reactions producing longer-lived radionuclides, $^{167}$Tm (t$_{1/2}$=9.25 d, 13-14 CAEs/decay) and $^{169}$Yb (t$_{1/2}$=32.03 d, 29-30 CAEs/decay), with a low-energy cyclotron were performed. Additionally, a lanthanide quantification method was tested on holmium solutions. The results indicate a possible application in rapidly assaying holmium concentration in fractions produced during chromatographic separation of lanthanides.

Materials and methods

Yield Calculation

A Microsoft EXCEL based calculator was created using SRIM stopping range values and TALYS-calculated excitation functions to calculate the yield of the $^{167}$Ho(10,p)n$^{167}$Er reaction and these yields were compared to the IAEA Medical Isotope Browser. This calculator was then adapted to calculate the yields of the nuclear reactions, Yb,2p$n^{3}$Lu,9β$^{3}$Yb$^{167}$Tm (with a natural Yb target and an enriched $^{169}$Yb$^{167}$O$_{3}$ target) and $^{169}$Yb(n,p$^{169}$Yb). The activities of the desired iso closest produced from these reactions were then weighed against the activities of long-lived isotopes produced alongside them and their ratio assessed.

Lanthanide Quantification

Arsenazo III (AIII) is a dye often used for spectrophotometric studies. In the past, it has shown use in its ability to complex lanthanides and allow for absorbance measurements. Various concentrations of samples of holmium in nitric acid (0.3 M, 130 µL) were prepared and aliquots of phosphate buffer (0.5 M, 1.1 mL) and ArII dye (20 – 2000 ppm, 65 µL) in buffer solution were added. These samples were then analyzed by UV-Vis (Tecan Spark! Microplate Reader) in 96-well plates to achieve a high throughput. Different parameters including the pH of the buffer, well volume, dye concentration, and time of analysis were tested in the process of determining the best method for lanthanide quantification.

Results

Yield Calculation

Calculations of the $^{167}$Ho(p,n)$^{167}$Er reaction at 12.5 MeV and varying target thicknesses were compared to the IAEA Yield Calculator and experimental yield values (Figure 3). The yield from irradiating (14 MeV, 1 µA, 1 h) a natural 300 µm thick Yb target has a ratio of $^{167}$Tm to $^{167}$Lu on the order of 10$^{9}$ whereas 90-98% enriched $^{169}$Yb targets of the same thickness have ratios between 1 – 10 (Figure 4). According to the Microsoft EXCEL yield calculator and using an excitation function from Nuclear Data for Selected Therapeutic Radioisotopes, a 16 MeV proton irradiation of a thick Tm target can produce a maximum of 1.3 MBq µA$^{-1}$ h$^{-1}$ of $^{169}$Yb (Figure 5).

Lanthanide Quantification

Assays containing different AIII dye concentrations in buffer solution show that 2000 ppm dye led to higher error in lower holmium concentration assays and 20 ppm dye in the assays resulted in a slope too insignificant for accurate quantification (Figure 6). Buffer solutions of different pH values show that a pH of 3.5 resulted in less deviation and a higher linear correlation of absorbance values in comparison to a buffer solution with a pH of 2.7 (Figure 7). 200 µL, 350 µL, and 400 µL aliquots per well (corresponding to absorbance pathlengths of 0.6, 1.0, and 1.1 cm) were compared. A well volume of 400 µL shows the smallest deviation and highest linear correlation compared to the other well volumes tested (Figure 8). Several dried samples were run again after initial absorbance measurement. The absorbance decreased significantly after an hour, indicating that the complex may not be stable in solution.

Conclusions

Yield Calculation

The yields calculated by the Microsoft EXCEL-based calculator and the IAEA Medical Isotope Browser for the $^{167}$Ho(p,n)$^{167}$Er reaction were within 1-3% of each other. The experimental yields were 50% of theoretical calculated values. This may be attributed to beam diameters larger than the target. Product yield ratios of the Yb,2p$n^{3}$Lu,$^{3}$Yb$^{167}$Tm reaction have a very low 30$^{8}$Tm-to-$^{167}$Lu ratio in natural Yb targets but $^{169}$Yb enrichment effects in much higher ratio. The $^{169}$Yb(n,p$^{169}$Yb) reaction produces only 1.30 MBq µA$^{-1}$ h$^{-1}$ of activity at 16 MeV, making its production not ideal for a low-energy cyclotron.

Literature cited


Further Work

- A method for target fabrication and recycling of enriched Yb$_{2}$O$_{3}$ targets needs to be developed.
- A method for the radiochemical separations needs to be theorized and tested.
- Other lanthanides involved in radiochemical separations need quantification methods investigated.
- The buffer capacity of the phosphate buffer needs testing for more concentrated acidic lanthanide solutions.
- The concentrations calculated using UV-Visible absorbance values need to be cross-checked with ICP-OES or MP-AES values.

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