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Evaluation of specific activity and stable impurities in 225Ac derived from ISAC and 229Th decay.

Introduction

Targeted Alpha Therapy (TAT) is a promising method for the treatment of cancer, due to the high Linear Energy Transfer (LET) of alpha particles resulting in a short range and dense ionization tracks in tissue. 225Ac (half-life 9.92 d) in particular was identified as one of the most favorable candidates for TAT due to its half-life, multiple alpha decays and favourable chelation chemistry. [1,2] To validate its potential, various studies have demonstrated the effectiveness of 225Ac treatments of metastatic and late-stage cancers. [1-3] The current supply of 225Ac for clinical studies has mainly come from 229Th generators obtained from 233U. The available supply from these sources, however, is not enough to support large-scale clinical studies, limiting the development of 225Ac-based radiopharmaceuticals.

Methods

The Life Sciences group at TRIUMF works in collaboration with Canadian Nuclear Laboratories (CNL) to establish and test various methods of production of 225Ac. This includes production using the ISAC facility, spallation reaction on thorium, and decay of 229Th (provided by CNL). A comparison study was performed using ISAC-produced and CNL-produced 225Ac to compare the specific activity and presence of stable contaminants that may affect radiolabeling with chosen chelators. The aim of this study was to establish the quality and applicability of 229Th-generated 225Ra/225Ac from CNL to enable future use of material in important chelation studies with novel ligands. If high purity and high specific activity 225Ac can be readily available through the collaboration with CNL, TRIUMF has the opportunity to make significant contributions to the chelation chemistry and in vivo use of 225Ac.

Experimental

The comparison study was designed to replicate a concentration dependence experiment, where the radiolabeling of 2-[4,7,10-tris(carboxymethyl)-1,4,7,10-tetrazacyclododec-1-yl]acetic acid (DOTA) and N,N'-bis[(6-carboxy-2-pyridil)methyl]-4,13-diaza-18-crown-6 (macropa) with various sources of 225Ac (ISAC and CNL) were tested. [4] Results of this study lead to changes in the separation procedure of 225Ra/225Ac from 229Th at CNL. The collaboration continues to work to optimize the purification process and work toward using the obtained 225Ac with higher specific activity for chelation studies that will translate to further in vitro and in vivo testing.

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