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technical note

Isolation of Cyclotron Produced ^{205}Bi, ^{206}Bi and ^{203}Pb using a Lead-selective Extraction Chromatographic Resin

GJERMUND HENRIKSEN and PER HOFF

Department of Chemistry, University of Oslo, Oslo, Norway

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The lead-selective extraction chromatographic resin Pb-SpecTM has been evaluated for the separation of Bi-radioisotopes from cyclotron irradiated lead targets. The objective of the work was to obtain sources of ^{205,206}Bi which could be used in the chemical and biological evaluation of Bi-compounds intended for use in targeted radiotherapy. It was found that two consecutive separations using Pb-SpecTM provide a simple and rapid procedure for the preparation of ^{205,206}Bi sources of the desired quality. The procedure may also be used for the production of ^{203}Pb sources. © 1998 Elsevier Science Ltd. All rights reserved

Introduction

The use of α-emitting radionuclides for cancer therapy has been suggested for several reasons (Kozak *et al.*, 1990; Macklis *et al.*, 1988; Zalutsky *et al.*, 1989). The α-emitting Bi-isotopes ^{212,213}Bi (half-lives 60.6 and 45.6 m, respectively) are two of the candidates which have been proposed for this application. Both *in vitro* studies and *in vivo* experiments in animals with ^{212}Bi bound to anti-leukemia monoclonal antibodies have clearly shown a potential for the treatment of highly vascularised cancers (Kozak *et al.*, 1986; Ruegg *et al.*, 1990). For solid disease, ^{212,213}Bi may have a potential if the radionuclide is bound to small, function specific molecules, e.g. bone-seeking agents (Hassfjell *et al.*, 1997). Successful experiments with intraperitoneal administration in an ovarian cancer model have also been reported (Rotmensch *et al.*, 1989).

The ^{212}Pb/^{212}Bi system may possibly be used as an *in vivo* isotope generator, where the very weakly radiotoxic precursor ^{212}Pb decays to the α-emitter ^{212}Bi. The half-life of ^{212}Pb is 10.6 h, which is much more favorable for most applications. For this strategy to be applicable, it is a prerequisite that the ^{212}Pb is incorporated in a compound sufficiently stable to avoid loss of activity during the nuclear transition ^{212}Pb$\rightarrow$^{212}Bi. The compounds tested in this respect so far have not fulfilled the requirement (Mirzadeh *et al.*, 1993; Ruegg *et al.*, 1990).

Due to the relatively short half-lives of ^{212,213}Bi and ^{212}Pb, Bi- and Pb-labelled compounds intended for targeted radiotherapy are more easily evaluated using the longer-lived radionuclides ^{203}Pb ($t_{1/2}$ = 51.9 h), ^{205}Bi ($t_{1/2}$ = 15.31 d) and ^{206}Bi ($t_{1/2}$ = 6.24 d). The Bi-radioisotopes are most easily produced through (p,xn) reactions on lead targets. To ensure high specific activities of the final Bi-labelled compounds, a reproducible and effective method for separation of Bi-radioisotopes from macro amounts of Pb is needed. In the present work we show that the Pb-SpecTM resin may be used for this purpose, and also to produce sources of ^{203}Pb. This latter radionuclide may be separated from irradiated lead by first isolating ^{203}Bi which is then left to decay to ^{203}Pb.

Experimental

Irradiations

Proton irradiations were carried out using the cyclotron (Scanditronix MC 35) at the Section for Nuclear Physics, Department of Physics, University of Oslo. The target consisted of a 1.8 mm thick layer of natural lead with > 99.999% purity (Fluka, Buchs, Switzerland) melted onto a circular cavity, diameter 25.4 mm, depth 2 mm in a 42 × 40 × 3 mm^3 aluminium target backing. The proton energy was 29–30 MeV with beam intensities of 2.5–3.5 μA/h. The target was cooled with water on the back of the aluminium plate and irradiated for periods of up to 7 h. The theoretical yield (Lagunas-Solar *et al.*, 1987) with this combination of proton beam energy and target thickness is 34–35 MBq/μAh for ^{206}Bi and 8–8.5 MBq/μAh for ^{205}Bi. ^{203}Bi ($t_{1/2}$ = 11.22 h) and ^{204}Bi ($t_{1/2}$ = 11.24 h) are also produced, but these Bi-isotopes are less interesting for direct use in labelling experiments due to their shorter half-lives. However, ^{203}Bi is useful as a precursor for ^{203}Pb.

Radionuclide detection

Radioactivity measurements were performed with energy- and efficiency-calibrated HPGe detectors (Canberra, Meriden, CT, U.S.A.) coupled to multichannel analyzers and data collection software.

Reagents

All water used was obtained from a Milli-Q water purification system (Millipore, Bedford, MA, U.S.A.). The reagents used were of analytical grade and were used as received unless otherwise noted.

Column preparation

The extraction chromatographic material containing 50–100 μm particles consisted of bis-4,4′(5′)-[tert-butylcyclohexano]-18-crown-6 in isodecanol impregnated on a polymeric substrate, commercially available as Pb-SpecTM from EIChroM Industries (Darien, IL, U.S.A.). The material has high ability to retain lead efficiently and selectively from nitric acid solutions (Horwitz *et al.*, 1994). The sorbed lead may be recovered by elution with complexing agents. The Pb-SpecTM was pretreated (Horwitz *et al.*, 1994) to remove traces of lead in the Pb-SpecTM, by stirring with a Teflon coated magnetic bar in a vessel containing 0.2 M H_2SO_4. The clean Pb-SpecTM was then transferred to a 4 × 60 mm^2 column fitted with filtering disks to retain the resin. The column was then eluted with 5 ml of 0.2 M H_2SO_4, and washed to neutrality with water, and finally with 10 ml of 3 M HNO_3.

Target treatment and separations

One to two hours post-irradiation the lead targets were treated using the procedure described by Lagunas-Solar *et al.* (1987) with minor modifications. The irradiated Pb was detached mechanically from the Al-backing and dissolved in 7 M HNO_3 at 90°C. The resultant solution was evaporated to a volume of 1–2 ml, and after cooling, 5 ml of concentrated HNO_3 were added to ensure almost complete precipitation of $Pb(NO_3)_2$ while keeping the bismuth isotopes in solution. The $Pb(NO_3)_2$ precipitate formed was then removed by filtration through a 0.2 μm