

GENERATOR OF ACTINIUM-225

V. TSOUPOKO-SITNIKOV, YU. NORSEEV, V. KHALKIN

Joint Institute for Nuclear Research, Laboratory of Nuclear Problems,
141980 Dubna, Moscow Region (Russia)

(Received October 4, 1995)

Dependence upon pH of Ac and Th distribution coefficients between the cation exchange resin and buffer citrate solutions had been investigated; the optimal conditions are suggested for effective separation of the elements in this system. These results are in successful accordance with such conditions calculated on the basement of Ac and Th citrate complex formation constants.

The generator method for ^{225}Ac periodical separation from ^{229}Th samples is developed. ^{229}Th storage in solution between separations excludes the contamination of actinium final solution with radiolysis products and provides 100-% yield of this isotope and its high radiochemical purity. The parent nuclide loss after continuous use of the generator does not take place.

The nuclear physical properties of ^{225}Ac ($T_{1/2} = 10$ days) and its short-lived daughters (Fig. 1) make it promising for radiotherapy of tumours. Used in the form of tumortropic radiopharmaceuticals based on monoclonal antibodies, it would allow avoiding radiation effects on the organism in general while providing high radiation load on the tumour tissue. This is due to the fact that the chain members do not emit hard γ -radiation being at the same time sources of very intense high-energy α -

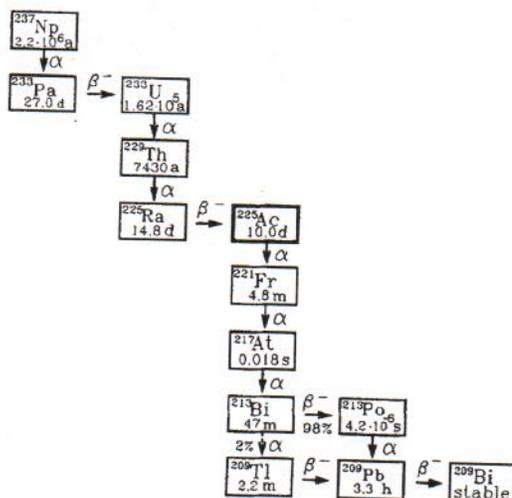


Fig. 1. Radioactive family of neptunium-237.

radiation (4 α -emitting nuclides, $\overline{E}_\alpha = 6.9$ MeV). The radiation load time distribution is not very rough because of relatively long half-life of the isotope, so the intoxication of organism can be avoided. A possibility of making these preparations is proved by their existence for rare-earth elements [1].

At the same time interest in studying properties of nuclei in the so-called transition regions between spherical and deformed ones is none the lower at present. Static octupole deformation predicted for light actinides with mass numbers $220 < A < 230$ [2] stimulates nuclear spectroscopic investigation of actinium-225 and its decay products, which implies obtaining high-quality α - and γ -spectra, conversion electron spectra, studying (α - γ) and (γ - γ) coincidences. It is desirable to follow variations in properties on going from one nucleus to another and establish decay schemes for each radionuclide. This task requires preparations of ^{225}Ac and short-lived members of the chain purified of mother and daughter nuclides as much as possible [3,4]. A decisive point in studying α -spectra and conversion electron spectra is quality of radiation sources. Their production requires additional methodical investigations.

The above points show the necessity of developing a simple and reliable method for production of radiochemically pure actinium-225 preparations to be used in the fields mentioned.

The simplest way to produce ^{225}Ac is to use thorium-229 ($T_{1/2} = 7340$ years). In one month 1 mCi (4.7 mg) of this radionuclide yields 0.74 mCi of ^{225}Ra and 0.53 mCi of ^{225}Ac ; in 15 days one can isolate 0.32 mCi more of ^{225}Ac from radium (Fig. 2). However, this isotopic generator has not been described in the literature yet, i.e. no technique has been developed for periodic reproducible isolation of radium and actinium ultramicro-quantities from milligramme quantities of thorium. A variety of methods for separation of thorium and actinium are found in publications [e.g. 5-9], yet the majority of them are intended for single use and any repeat is either completely impossible or requires labour-consuming operations that result in loss of the mother isotope.

The difficulty in developing the method are aggravated by the fact that the classical isotope generator scheme (constant fixation of the mother nuclide on the sorbent) is

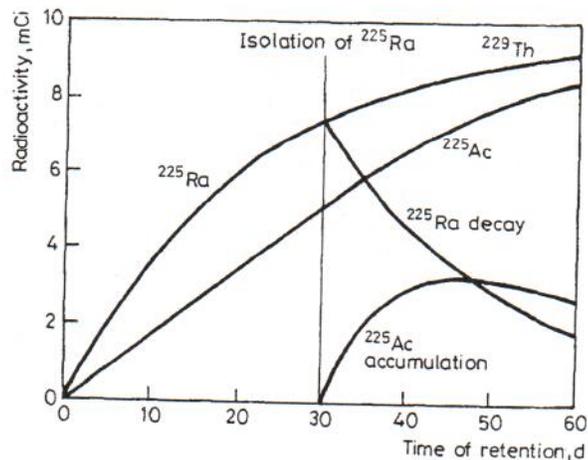


Fig.2. Kinetics of Ra-225 and Ac-225 accumulation from 10 μCi of Th-229; decay of isolated Ra-225; accumulation of Ac-225 in Ra-225 separated.

not suitable, in our opinion, for work with chains of α -emitting radioisotopes because the sorbent is subject to strong radiolytic destruction. It applies both to synthetic organic ion-exchangers, which lose a noticeable part of their capacity at radiation doses 10^7 – 10^9 rad [10], and to inorganic sorbents [1, 11]. The separation process is also complicated by reduction in the yield of the desired radionuclide because of "hammering" recoil ^{225}Ra nuclei in the sorbent matrix during thorium-229 decay. All this makes it necessary to find a new approach to development of a ^{229}Th -based ^{225}Ac generator. We think that the generator technique for actinium-225 production must meet the following requirements:

- 1) maximum yield of the desired radioisotope with minimum contamination of final actinium samples by the mother isotope and radiolysis products;
- 2) losses of the of mother thorium-229 per separation cycle below few fractions of per cent;
- 3) reproducible and simple operations, low time and labour consumption.

In the present paper we propose a method for periodical separation of daughter radionuclides from macroquantities of ^{229}Th , which we think meets the above requirements.

Experimental

Preliminary notes

The method we have chosen for separation of radionuclides is cation exchange chromatography with an organic complexing agent. In most cases complex compounds of thorium with organic ligands are far more stable than those of actinium. It allows high-quality separation with a properly chosen complexing agent. An advantage of this method is that the final thorium solution can be prepared for repeat separation by simply changing its pH. Among most popular complexing agents employed in separation like that citric acid seems to have the optimum properties because difference in stability constants between citrate complexes of actinium and thorium is especially large. Thorium form bonds with citrate ions to produce two types of complex ions. $\text{Th}(\text{Cit})^+$ and $\text{Th}(\text{Cit})_2^{2-}$. Their stability constants are $K_1 = 10^{13.0}$ and $K_2 = 10^{8.0}$ respectively [12], where

$$K_{1\text{Th}} = \frac{[\text{ThCit}^+]}{[\text{Th}^{4+}][\text{Cit}^{3-}]}, \quad K_{2\text{Th}} = \frac{[\text{ThCit}_2^{2-}]}{[\text{ThCit}^+][\text{Cit}^{3-}]} \quad (1)$$

Stability constants of complexes AcCit^0 and $\text{Ac}(\text{Cit})_2^{3-}$ are approximately equal [13] amounting to

$$K_{1\text{Ac}} = \frac{[\text{AcCit}]}{[\text{Ac}^{3+}][\text{Cit}^{3-}]} = (9.6 \pm 0.5) \times 10^6.$$

Comparing values of the constants one can see that it is possible in principle to separate actinium and thorium on a cationite using a citrate-containing elutriator.

Using the above stability constant values we can estimate the degree of complexing α of actinium and thorium in a citrate solution:

$$\alpha_{Ac} = \frac{[AcCit]}{[Ac^{3+}]} = K_{1Ac}[Cit^{3-}], \quad (2)$$

$$\alpha_{Th} = \frac{[ThCit^+]}{[Th^{4+}]} = K_{1Th}[Cit^{3-}],$$

where

$$[Cit^{3-}] = \frac{cK_1K_2K_3}{[H^+]^3 + [H^+]^2K_3 + [H^+]K_2K_3 + K_1K_2K_3}, \quad (3)$$

$$K_n = \frac{[H_nL]}{[H^+][H_{n-1}L]}$$

are the stepwise protonation constants of the citrate ion, $\log K_1 \approx 5.5$, $\log K_2 \approx 4.4$, $\log K_3 \approx 3.06$ [12].

Assuming that only hydrated cations Ac^{3+} and Th^{4+} are sorbed by the cationite from aqueous solutions and complex compounds exist only in the aqueous phase, we can write down equations for distribution of elements between the ion exchanger and solution as

$$D_{gAc}^k = \frac{\{Ac^{3+}\}}{[AcCit^+] + [Ac^{3+}]}, \quad D_{gTh}^k = \frac{\{Th^{4+}\}}{[ThCit^+] + [Th^{4+}]} \quad (4)$$

where D_g^k is the mass coefficient of distribution of an element between the sorbent and solution in the presence of a complexing agent; in braces there are mass concentrations of elements in the ion exchanger. According to the data from some publications, including the monograph [14], at $pH \geq 1$

$$\log D_{gTh}^k = \log \frac{\{Th^{4+}\}}{[Th^{4+}]} \approx 5; \quad \log D_{gAc}^k = \log \frac{\{Ac^{3+}\}}{[Ac^{3+}]} \approx 4 \quad (5)$$

where D_g is the mass coefficient of distribution of an element between the sulphocationite and aqueous solution without a strong complexing agent. Jointly solving (4) and (5) with calculated α_{Ac} and α_{Th} (see (2)) one can estimate D_{gAc}^k and D_{gTh}^k . Their calculated dependencies on pH of a 0.25M citrate solution are shown in Fig. 3

Simple computation allows a conclusion that in a 0.25M citrate solution with pH ranging from 1.5 to 3.0 (a typical concentration for this kind of separation is taken) thorium and actinium are easily separated by the method of successive elutriation.

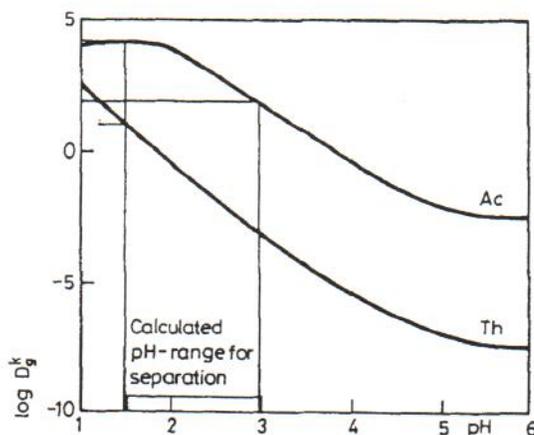


Fig.3. Calculated dependence of coefficients of Ac and Th distribution between sulphocationite and 0.25M solution of ammonia citrate on the pH of the solution.

Apparatus and reagents

Eluate radioactivity was controlled by means of a simple radiochromatographic apparatus consisting of a scintillation γ -detector (NaI crystal, photomultiplier), a spectrometric amplifier and an analysing interface card incorporated in IBM PC. Special software allowed radiochromatograms in the "volume of flowing elutriator - relative radioactivity of eluate" coordinates.

Radioactivity of the samples was measured by a γ -spectrometer with a Ge-Li detector.

pH of eluting solutions was corrected by a concentrated ammonia solution and measured by a digital pH-meter MV-870 to ± 0.03 units.

Analytical-grade, chemically pure and highly pure reagents were used.

Procedure

Model separation of radioelements and determination of their coefficients of distribution between the ion exchanger and solution were carried out in glass columns filled with cationites Aminex-A5 (grains $13 \pm 2 \mu\text{m}$ in size, exchange capacity 5 mg-eq/g) and Dowex-50W-X8 (200-400 mesh) in NH_4^+ and H^+ form at $(20 \pm 2)^\circ \text{C}$. Dynamic coefficients of distribution of elements were calculated by the equation

$$D_g = \frac{V_{\text{max}} - V_0}{m}$$

where D_g is in $[\text{ml/g} = \text{l/kg}]$, V_{max} is the element retention volume, V_0 is the free volume of the chromatographic column, m is the mass of dry cation exchanger in the column.

Results and Discussion

Preliminary experiments showed that large-grained cationite Dowex is unsuitable for working with macroquantities of thorium. With this cationite the chromatographic zone of thorium has an irregular shape (delayed pulse decay and "tails" are observed) in a wide range of elutriator concentrations and pH. Cationite Aminex-A5 did not show an effect like this and it was used in development of the method. Figure 4 depicts the experimental dependence of dynamic coefficients of actinium and thorium distribution between the cation exchanger and 0.25M solution of ammonia citrate on pH of the solution.

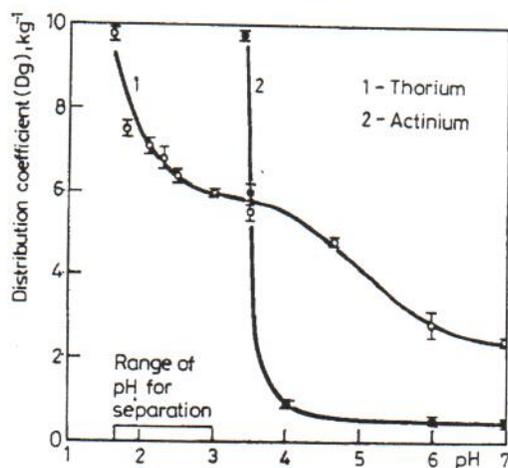


Fig. 4. Dynamic coefficients of Ac and Th distribution between Aminex-A5 and 0.25M solution of ammonia citrate as a function of a solution pH. A $\varnothing 4 \times 40$ mm column.

It is seen that the optimum pH interval for separation of the elements is the interval 1.8-2.5, where distribution coefficients of the elements differ by several orders of magnitude (simple extrapolation). This interval is in good agreement with the calculated result, though the shape of the $\text{pH}-D_g$ relation in weakly acid solutions is greatly distorted as compared with the calculated curve. It might be explained by formation of poorly soluble basic citrates and thorium hydroxide in the resin phase at high pH. The relative behaviour of elements at low pH can be considered correctly calculated. Citrate complexes of radium are far less stable, so its coefficients D_g are very large under the same conditions. This element can be washed out by a 4M solution of nitric acid after successive elutriation of thorium and actinium by citrate solutions. Using the data obtained, we have developed the following method for periodical separation of actinium-225 from the mother isotope (see also the scheme in Fig. 5):

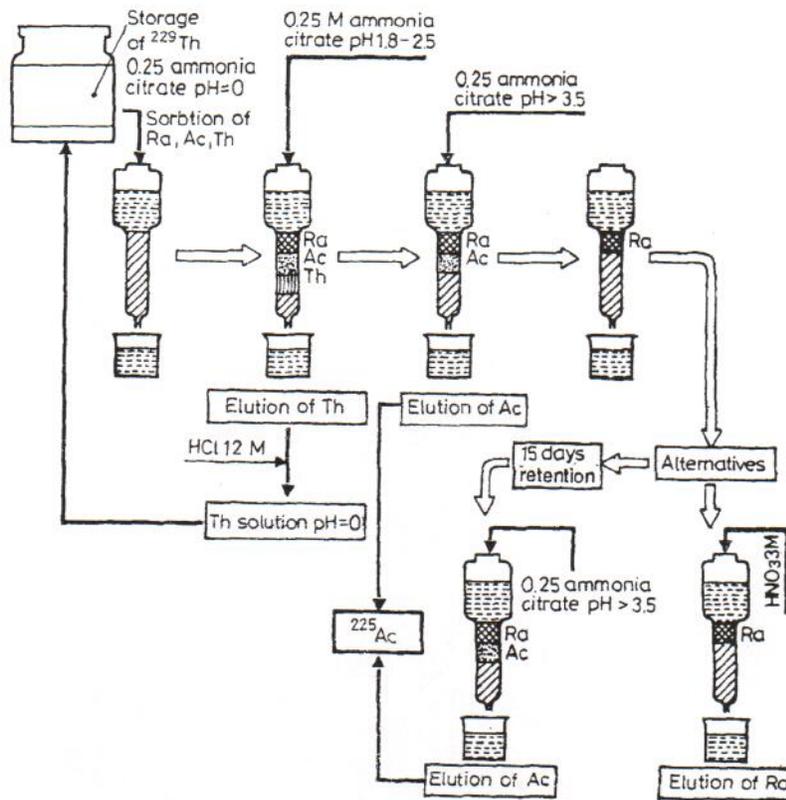


Fig. 5. Scheme of the generator of actinium-225.

The initial solution (about 3 ml) contains milligramme quantities of thorium-229 and decay products in equilibrium. The ammonia citrate concentration is 0.25M, pH of the solution is below 1. The solution is passed through a chromatographic column 4 mm in diameter and 40 mm long, filled with cationite Aminex-A5 (grains $13 \pm 2 \mu\text{m}$ in size). The outgoing solution is rejected. After deposition thorium is quantitatively eluted from the column by a 0.25M solution of ammonia citrate with $\text{pH} = 2.0-2.5$; the thorium fraction volume can vary between 0.5 and 3.0 ml in accordance with the radionuclide amount used. There are no noticeable ($> 0.1\%$) losses of thorium during deposition and elutriation. Actinium is washed out by 1 ml of the citrate solution with $\text{pH} > 4.0$. Then Ra is eluted by 1 ml of the 4M solution of nitric acid. The thorium-229 solution collected at the beginning of the separation is acidified to $\text{pH} < 1$ and stored as for 1-2 months. Then separation is repeated by the given scheme.

In Fig. 6 there is a radiochromatogram obtained in separation of 5 mg of thorium and ultramicroquantities of actinium and radium by the proposed method. Thorium-232 (amount 5 mg) is used to be a carrier for $10 \mu\text{Ci}$ of ^{229}Th . After repeated treatment of $60\text{-}\mu\text{Ci}$ thorium-229 by this method no losses of the mother radionuclide were detected in precise γ -spectrometric measurements by a semiconductor detector. Examination of the produced ^{225}Ac samples by γ -spectroscopic and precise α -spectroscopic methods did not reveal the presence of mother radionuclides in them.

Conclusion

In our opinion, the main positive features of the proposed generator method are:

1. Continuous storage of the mother isotope in a solution, which prevents radiolytic

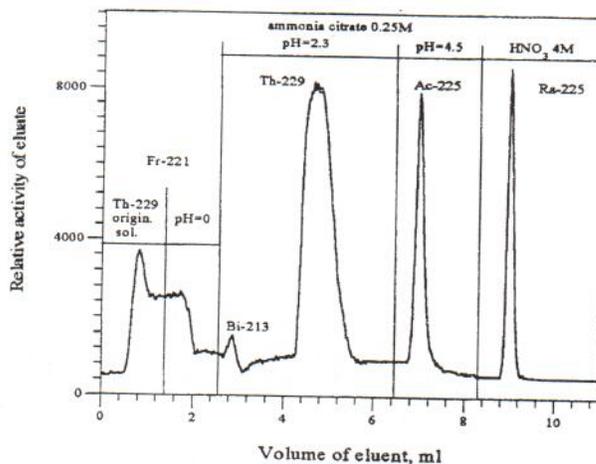


Fig.6. Radiochromatogram obtained in separation of 5 mg of thorium and Th-229 daughter products (column $\varnothing 4 \times 40$ mm Aminex-A5).

destruction of the sorbent to be used in separation and contamination of actinium samples by radiolysis products, removes "hammering effect".

2. Simplicity in preparation of the purified thorium solution for the next separation cycle (pH correction of the final citrate solution of the isotope).
3. Absence of mother isotope losses and 100% yield of the daughter radionuclide in separation.

*

The authors express their deep gratitude to S.S.Eliseev and V.G. Chumin for helpful discussions and α -spectrometric measurements, as well as to D.V.Bosenko and T.A.Furjaev for assistance in script preparation.

References

1. O.A.GANSOW, ACS Symposium, ser.241, Symposium at the 185-th Meeting of ACS, Seattle Washington, March 20-25, 1983. ACS. Wash. D.C. - 1984, p. 215.
2. R.R.CHASMAN, Phys. Lett., 96B (1980) 7.
3. O.EL SAMAD, J.DALMASSO, G.BARCI-FUNEL, G.GARDISSON, Radiochim. Acta, 62 (1993) 65.
4. F.ABDUL-HADI, V.BARCI, B.WEISS, H.MARIA, G.GARDISSON, M.HUSSONNOIS, O.CONSTANTINESCU, Phys. Rev., C47 (1993) 94.

5. Z.K.KARALOVA, B.F.MJASOEDOV, *Analiticheskaja khimija elementov: actinij*, Nauka, Moscow, 1982.
6. A.R.SANI, *J.Radioanal. Chem*, 4 (1970) 127.
7. R.W.ATCHER, J.J.HINES, A.M.FRIEDMAN, *J.Radioanal. Nucl. Chem., Letters*, 117(1987) 155.
8. A.K.DAS, J.C.PAL, S.BANERJEL, *Anal. Chem. Acta*, 42 (1969) 162.
9. G.J.BEYER, E.HERRMAN, F.MOLNAR, V.J.RAJKO, H.TYROFF, *Radiochim. Radioanal. Lett.*, 12 (1972) 259.
10. V.A.SOKOLOV, *Generatori Korotkozivuschih Radioaktivnih Isotopov*, Atomizdat, Moscow, 1975.
11. M.MONSECOUR, P. DE REGGE, A.DEMILDT, *Radiochem. Radioanal. Lett.*, 14 (1973) 365.
12. *Stability Constants of Metall-Ion Complexes*, Suppl. 1 (spec.publ #25), pt.2, London, 1971.
13. T.P.MAKAROVA, G.S.SINITINA in: *Compleksoobrazovanie i ekstraktsija lantanoidov i aktinoidov*, Nauka, Leningrad, 1974.
14. M.MARHOL, *Ion exchangers in analytical chemistry*, Academia, Prague, 1982.