Extraction of astatine isotopes for development of radiopharmaceuticals using a 211Rn–211At generator

Title - Extraction of astatine isotopes for development of radiopharmaceuticals using a ^{211}Rn-^{211}At generator

Names - E. Maeda[1], A.Yokoyama[2,*], T. Taniguchi[1], K. Washiyama[3] and I. Nishinaka[4]

Affiliations – [1]Grad. School Nat. Sci., Tech. Kanazawa Univ., [2]Inst. Sci. Eng., Kanazawa Univ. [3]Inst. Med. Pharma. Health Sci., Kanazawa Univ. [4]ASRC, Japan Atomic Energy Agency

Corresponding author, *E-mail:yokoyama@se.kanazawa-u.ac.jp

Abstract – In order to utilize a ^{211}At isotope, a promising α-emitter for radionuclide therapy, the chemical properties of astatine isotopes are studied. We have examined wet chemistry methods through the distribution ratios of astatine in liquid-liquid extraction. The astatine isotopes have been found to be well extracted into DIPE and MIBK. We observed that the distribution ratio of astatine isotopes increases with concentrations of HCl greater than 3 M, while it decreases with the HCl concentration less than 2 M. The results will be useful for development of the ^{211}Rn-^{211}At generator.

Introduction

Highly energetic α-particles are expected to suppress tumor cell growth efficiently with a low level of damage to surrounding tissues because of their short path lengths in tissues (<100 μm) and high linear energies

transferred (~100 keV/μm). Among α radionuclides, ^{211}At has gathered attention as a promising α-emitter for radionuclide therapy due to its physical half-life of 7.2 h. Astatine isotopes must be produced via nuclear reactions and separated from irradiated targets with high purity. But, the chemical properties of astatine are not well known for that purpose. In order to determine appropriate procedures in preparation of astatine used in radiopharmaceuticals, we produced astatine isotopes by the reaction of ^{nat}Pb(^{7}Li,xn)$^{209\text{-}211}$At and evaluated chemical separations of the isotopes from target materials. Solvent extraction has been considered one of the effective methods for that purpose [1]. We report dependence of the distribution ratio in solvent extraction of astatine on the polarity of organic solvents and on the concentration of HCl. In addition, we produced a radon isotope to determine the behavior of astatine isotopes generated in the decay from radon precursors and examined feasibility of that chemical procedure. Additionally, we used a bismuth radiotracer to research the behavior of bismuth atoms from the target material in chemical separations of the astatine isotopes.

Experimental

A lead target (0.74 mg/cm^2) was irradiated with 50 MeV ^{7}Li beam with a current of 120~200 nA using the JAEA-Tokai tandem accelerator, to

produce astatine isotopes by the reaction of $^{nat}Pb(^{7}Li, xn)^{209-211}At$. The irradiated target was put into a test tube and heated up to 650 ℃ and let stand for about 20 min in an electric furnace. Then carrier-free astatine was separated by distillation from the lead target. Then astatine isotopes were trapped in 8 M HCl solution. Astatine was extracted from the 8 M HCl solution into equal volumes of several organic solvents with varing polarity by shaking for 5 minutes. The γ-activity of each phase in extraction was measured by a HPGe detector to obtain the distribution ratio of astatine isotopes.

Subsequently, the dependence of the distribution ratio of astatine on the concentration of HCl was investigated after astatine isotopes were produced and distilled as in the experiment described above. In the procedure, astatine isotopes were trapped in 4 M HCl solution, which was then adjusted to several HCl concentrations between 1 M and 8 M, and subsequently subjected to the extraction process of astatine isotopes with an equal volume of DIPE for 5 minutes. The distribution ratios were obtained in the same way as the experiment described above.

In addition, the behavior of astatine generated in the decay from the radon precursor was investigated by irradiation of bismuth targets (3~5 mg/cm^{2}) with 60 MeV ^{7}Li beam and a current of 200 nA using the JAEA-Tokai tandem accelerator. We produced radon isotopes by the reaction of $^{209}Bi(^{7}Li,5n)^{211}Rn$. The irradiated target was soaked in dodecane solution in a vial and then dissolved in 6 M HNO$_{3}$ solution added to the vial. After dissolving the bismuth material, extraction of

the radon precursor was performed by shaking for 1 minute. Both of the phases from the extraction as well as the irradiated target were subjected to γ-ray spectrometry.

A lead target (2 mg/cm^2) was also irradiated with 22 MeV proton beam at a current of 1000 nA using the AVF cyclotron of RCNP in Osaka university, producing bismuth isotopes by the reaction of $^{nat}Pb(p,xn)^{205-206}Bi$. The irradiated target was put into a vial with an organic solvent, then it was dissolved by the addition of the 6 M HNO$_3$. After removal of the dissolved target, vials are extracted by shaking for 1 minute. The distribution ratios were obtained in the same way as the experiment described above.

Results

The astatine isotopes were efficiently extracted into diisopropyl ether (DIPE) and methyl isobutyl ketone (MIBK), but no significant extraction was observed in toluene and decane as show in Fig. 1. It is assumed that the extraction process of astatine is related to polarity of the organic solvent.

Dependence of the distribution ratio on the concentration of HCl was observed for DIPE as show in Fig. 2. Increases in concentration of HCl provided higher distribution ratios. In addition, the distribution ratios were increased at concentrations lower than 2M HCl. In Fig. 3 is shown the γ-ray spectrum of the irradiated target including ^{211}Rn from the reaction of $^{209}Bi(^7Li,5n)^{211}Rn$, and the γ-ray spectra of organic and aqueous phases from the extraction are shown in Fig. 4 and Fig. 5,

respectively, where radon isotopes are well extracted into the organic phase and isolated from the other elements such as astatine and polonium. The experiment with the bismuth radiotracer suggested that very small quantities of bismuth isotopes, if any, are extracted into organic solvent from 6 M HNO_3 because its distribution ratio are $(4.5 \pm 0.2) \times 10^{-4}$ and $(45.3 \pm 0.6) \times 10^{-4}$ for decane and dodecane, respectively.

Discussion

The distribution ratio of astatine was previously found to depend on the polarity of the organic solvent [2], and that is generally consistent with our results. The results suggest that astatine compounds have an electric polarization, so that they are easily extracted into the polar organic solvents such as DIPE and MIBK. Therefore, we focused on the extraction with DIPE here.

Because of the results shown in Fig.2, it appears that astatine isotopes are extracted into DIPE depending on the concentration of the chloride ion in HCl between 4 M to 8 M. There was a previous report about the same chloride ion concentration dependence. [3] Their results appear to be inconsistent with our results at the concentrations of HCl under 2 M. The reason of disagreement is not still clear. We repeated the same experiment to confirm the results. Around the concentrations of HCl examined astatine is expected to form a cationic ion [4], so astatine ions are neutralized with the coordination of chloride ions and extracted into organic phase. On the other hand, at concentrations of

HCl between 0.1 M to 2 M, the hydrolysis of astatine species makes them neutralized with the hydroxide ion.

Solvent extraction is considered as one of the most effective methods to separate radon isotopes from many by-products from the results of Figs.3 to 5. The astatine isotopes generated in the decay from radon precursor can be back-extracted into other solvents.

We have confirmed that extremely small quantities of bismuth ions are extracted into organic solvent in the chemical procedure examined. This suggests that the bismuth atom is in the form of a cation like Bi^{3+}, so that it has a strong affinity to the water phase with a higher polarity. Our results show that it is possible to remove the contaminating bismuth atoms of the target material during the isolation of radon isotopes from the irradiated targets.

We believe the results from this study will be useful for development of a ^{211}Rn-^{211}At generator.

References

[1] Neumann H M (1957) SOLVENT DISTRIBUTION STUDIES OF THE CHEMISTRY OF ASTATINE. Inorg Nucl Chem 4:349-353

[2] Alliot C, Chérel M, Barbet J, Sauvage T, Montavon G (2009) Extraction of astatine-211 in diisopropylether (DIPE). Radiochim Acta 97:161-165

[3] Nayak D, Lahiri S (2003) Extraction separation of No-carrier-added astatine from bismuth target. Radiochim Acta 91:159-161

[4] Champion J, Sabatié-Gogova A, Bassal F, Ayed T, Alliot C, Galland N, Montavon G (2013) Investigation of Astatine(Ⅲ) Hydrolyzed Species: Experiments and Relativistic Calculations. J Phys Chem A 117:1983-1990

Figure caption

Fig. 1 Distribution ratios for different polarities of organic solvent with

8M HCl.

Fig. 2 Distribution ratios for several concentrations of HCl with DIPE.

Fig. 3 Gamma-ray spectrum of ^{211}Rn produced by the reaction of

^{209}Bi(^{7}Li,5n)^{211}Rn.

Fig. 4 Gamma-ray spectrum of organic phase in dodecane after

extraction.

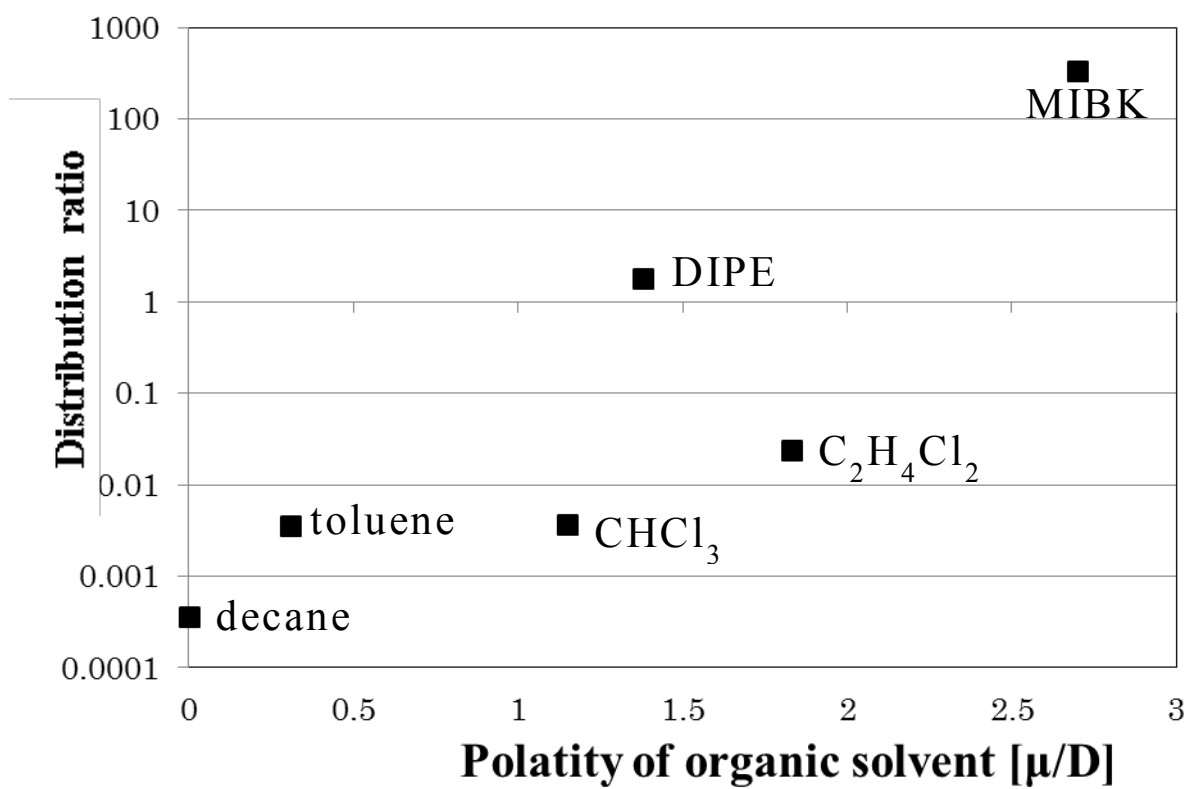Fig. 5 Gamma-ray spectrum of aqueous phase after extraction.
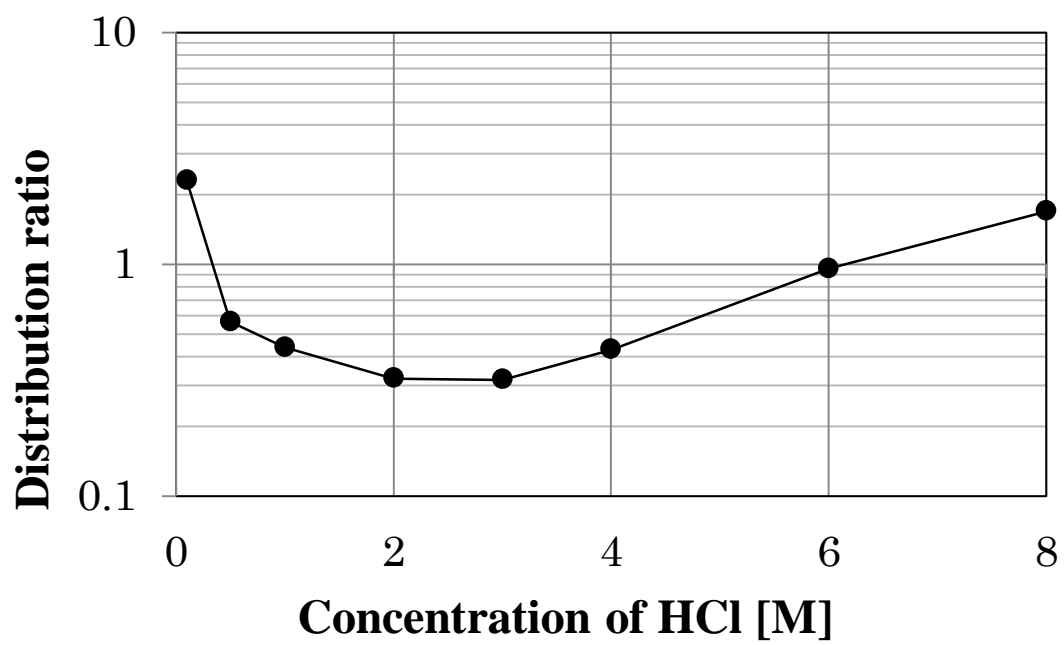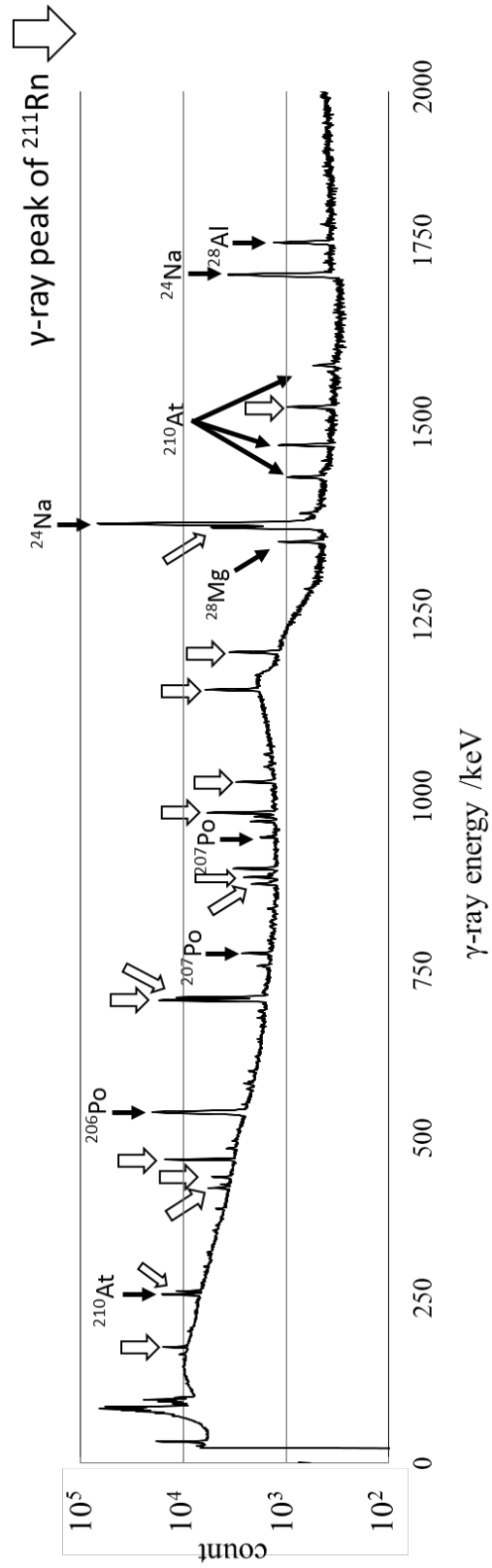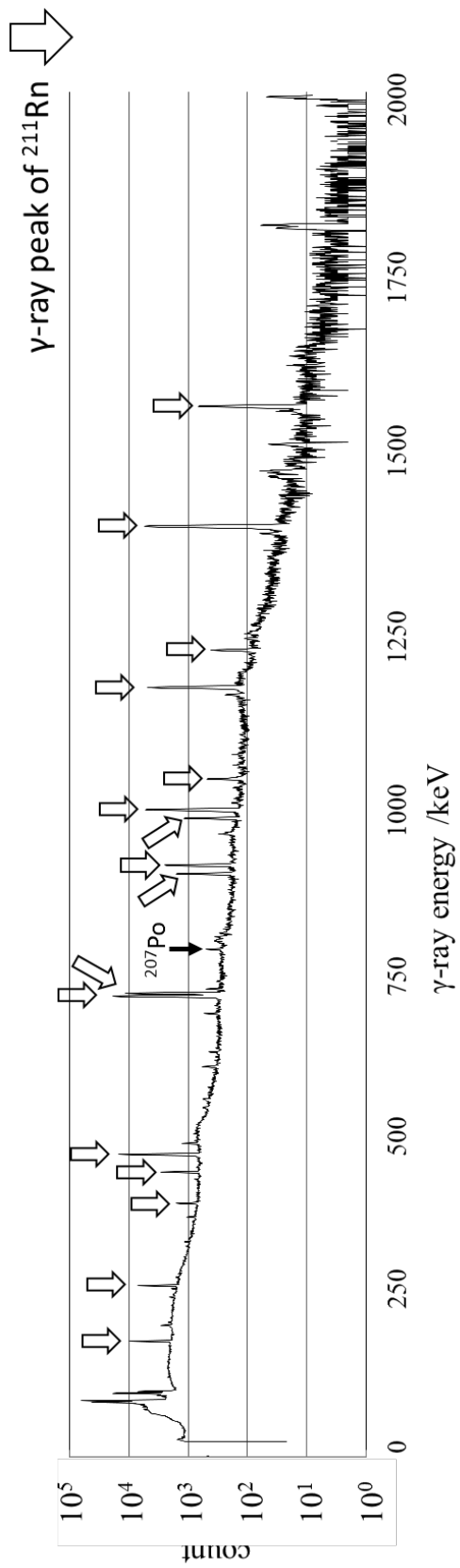
Figure.1

Figure.2

Figure.3

Figure.4

Figure.5