Comparison of ^{211}At recovery rates in glass vials and plastic tubes

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Targeted alpha therapy (TAT) using alpha-emitting radionuclides as cytotoxic reagents has emerged as a promising cancer therapy modality in recent decades. With the increased demand for preclinical studies and the interest in TAT, the supply of alpha-ray emitters has become increasingly important. Several groups at the Isotope Science Center at University of Tokyo are working on TAT research using the alpha emitter ^{211}At supplied by the RIBF, RIKEN. Each month, we are conducting therapeutic or imaging experiments using xenograft animal models and ^{211}At-labeled monoclonal antibodies (mAbs).

In our ^{211}At drug delivery system, we label mAbs conjugated with N-Succinimidyl 3-Trimethylstannylbenzoate (m-MeATE) using a modified method based on that described in Refs. 1) and 2). The radiolabeling protocol is explained here briefly. First, a freeze-dried m-MeATE/mAb conjugate stock is redissolved in 115 μL of 0.2 M acetate buffer (pH 5.5) and adjusted to 200 μL to obtain mAb concentration of 1 mg/mL. The m-MeATE/mAb solution is then added with ^{211}At dissolved in a 15-μL solution mixture of N-iodosuccinimide (NIS)/methanol/1% acetic acid (20 μg/mL), and incubated for 1 min. The incubated solution is further mixed with 3 μL of NIS (1 mg/mL) in methanol/1% acetic acid and 5 μL of 0.25 M ascorbic acid, and then applied to a pre-equilibrated PD SpinTrap G25 column with PBS for buffer exchange.

After the buffer exchange, we measure the activities of the [^{211}At]At-m-MeATE-mAb solution using a spin column, vials or tubes, and a dose calibrator, and calculate the radiochemical yield (RCY). The RCY typically ranges from 10% to 40%. In the ^{211}At radiolabeling experiments conducted so far, we have frequently observed that a significant portion of ^{211}At not incorporated into m-MeATE/mAb conjugates is retained in the reaction vials. To reduce the amount of ^{211}At adsorbed to reaction vials and in turn to increase the ^{211}At RCY, we investigated the ^{211}At recovery rates of several glass vials and a plastic tube.

As shown in Fig. 1, 240 μL of ^{211}At obtained from RIKEN was diluted in chloroform. Then, 20 μL was dispensed into four low-adsorption glass vials and one plastic tube. All these vials and tube were air-dried from chloroform with nitrogen gas. After approximately 3 hours, 150 μL of ethanol was added to each vial to dissolve the ^{211}At, and it was transferred to another plastic tube for activity measurement. The ^{211}At activities of the tubes before and after transfer, the low-adsorption glass vials, and the pipette tips used were measured.

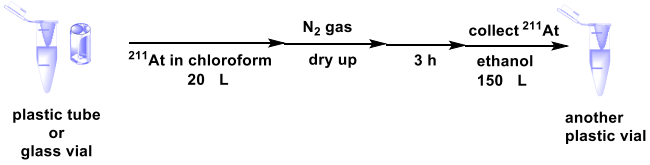

Fig. 1. Scheme of the experiment.

The recovery rates were then calculated as follows:

$$\frac{(^{211}\text{At activity after recovery} + {}^{211}\text{At activity of used pipette tips})}{^{211}\text{At activity immediately before ethanol dilution}} \times 100(\%)$$

We also calculated the unrecovered rates as follows:

$$\frac{(^{211}\text{At activity in an original vial})}{^{211}\text{At activity immediately before ethanol dilution}} \times 100(\%)$$

The tested plastic tube UFC510096 (Merck Millipore) showed only 37.8% of a ^{211}At recovery rate, which was significantly lower than the average of the glass vials (85.6%) (Table 1); this corresponds to a difference of approximately a factor of 2.3. The glass vial 1.1-STVGN (Thermo Fisher Scientific) and the plastic tube UFC510096 exhibited the highest (95.5%) and lowest (37.8%) recovery rates, respectively.

Table 1. Results of ^{211}At adsorption test.

Entry	Vial information Model number Maker	Material	Recovery rate (%)	Uncollected rate (%)
1	1.1-STVGN Thermo Fisher Scientific	glass	95.5	5.9
2	6PSV9-TR1 Thermo Fisher Scientific	glass	81.2	19.5
3	11092275 GL Science	glass	80.4	21.8
4	9512S-OCV-TRS Tomsic	glass	85.3	15.0
5	UFC510096 Merck Millipore Ltd.	plastic	37.8	59.8

All the glass vials examined resulted in higher ^{211}At recovery rates than that of the plastic tube. The highest recovery rate was observed in the 1.1-STVGN glass vial (Thermo Fisher Scientific). Using glass vials can reduce ^{211}At activity loss during radiolabeling and potentially increase the ^{211}At RCY.

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