Quality evaluation of RIKEN ^{67}Cu for labeling peptide compound

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Copper-67 (^{67}Cu) with a half-life of 2.58 days is one of the promising RIs for both diagnosis and therapy in nuclear medicine. We have been developing a technology for producing ^{67}Cu via the ^{70}Zn$(d, \alpha n)^{67}$Cu reaction using the RIKEN AVF cyclotron and distributing purified ^{67}Cu products (RIKEN ^{67}Cu) to the general public through the Japan Radioisotope Association.[1] In this work, we investigated the availability of RIKEN ^{67}Cu for radiolabeling a peptide compound.

DOTA-Substance P (DOTA-SP) is DOTA-peptide that has been studied as a candidate radiopharmaceutical for glioblastoma.[2,3] In the present study, we selected DOTA-SP as a model compound.

The labeling method of ^{67}Cu-DOTA-SP is as follows.

Step 1: RIKEN ^{67}Cu chloride (2.6 MBq) was dissolved in 0.05 M hydrochloric acid to prepare a ^{67}Cu-stock solution (80 MBq/mL). The radioactivity of ^{67}Cu was determined using a germanium semiconductor detector.

Step 2: DOTA-SP was dissolved in 0.75 M sodium acetate buffer at pH5.0 to prepare 14×10^{-5}, 4.6×10^{-5}, and 0.92×10^{-5} M DOTA-SP solutions.

Step 3: 2.0 μL of the ^{67}Cu-stock solution was added to 1.0 μL of each DOTA-SP solution. The mixture of the ^{67}Cu-stock solution and DOTA-SP solutions of 14×10^{-5}, 4.6×10^{-5}, and 0.92×10^{-5} M resulted in 1.2, 3.5, and 17 MBq/nmol solutions, respectively.

Step 4: The mixture in Step 3 was heated at 97°C for 10 min and kept at a room temperature for 5 min.

Step 5: Labeling yields of ^{67}Cu-DOTA-SP were determined using the thin-layer chromatography (TLC) method with a C18 reversed-phase TLC plate (NAGEL PR-18W/UV254) and eluted with a mixture of acetonitrile, 0.5 M ammonium acetate, methanol, and tetrahydrofuran in a volume ratio of 4:3:2:1.

Figure 1 shows the labeling yield (%) as a function of the specific radioactivity of ^{67}Cu-DOTA-SP. RIKEN ^{67}Cu was used to label DOTA-SP with the highest yield at 1.2 MBq/nmol. The yield decreased with an increase of the specific radioactivity.

In previous research using another DOTA-peptide, DOTA-TATE, the labeling yield with ^{64}Cu was reported to be 97% at a specific radioactivity of 7 MBq/nmol.[4] ^{64}Cu is a radionuclide with a half-life of 12.7 h. We can convert thereported specific radioactivity of 7 MBq/nmol for ^{64}Cu into 1.4 MBq/nmol for ^{67}Cu. This is comparable with our result at 1.2 MBq/nmol in DOTA-SP and might be applicable to other compounds with such a specific radioactivity of RIKEN ^{67}Cu. This specific radioactivity was considered to be sufficient for use in studies such as *in vitro/in vivo* studies to examine candidate radiopharmaceuticals.

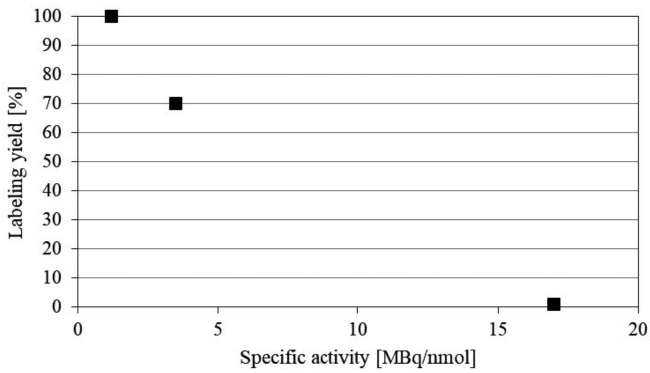

Fig. 1. Relation between specific activity (MBq/nmol) and labeling yield (%) of ^{67}Cu-DOTA-SP.

In this study, we evaluated the quality of RIKEN ^{67}Cu through DOTA-SP labeling and revealed that RIKEN ^{67}Cu has a high and sufficient quality to label compounds such as DOTA-peptides for studies on radiopharmaceuticals.

References
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