Quality confirmation of RIKEN ^{186}Re using bifunctional chelating agents and derivatives

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Rhenium-186 (half-life $T_{1/2} = 3.7186$ days) and ^{188}Re ($T_{1/2} = 17.003$ hours) emit beta rays appropriate for targeted radiotherapy use. These radioactive Re isotopes are used according to the tumor size and form radiotheranostic pairs with ^{99m}Tc for radiodiagnosis.[1] However, ^{186}Re has not been investigated as well as ^{188}Re has.[2] One of the possible reasons is that it is difficult to obtain no-carrier-added ^{186}Re through the classical production method of the ^{185}Re$(n,\gamma)^{186}$Re reaction, while no-carrier-added ^{188}Re can be obtained using a ^{188}W/^{188}Re generator.[1,3] At RIKEN, we started to produce no-carrier-added ^{186}Re (RIKEN ^{186}Re) in the ^{186}W$(d,2n)^{186}$Re reaction at the RIKEN AVF cyclotron. In this study, we selected DADT, ECD, MAG3, and DMSA (Fig. 1) as model compounds, which had already been reported in many articles,[4–7] and evaluated radiolabeling efficiencies for these compounds to confirm the quality of RIKEN ^{186}Re, especially in terms of its usefulness as a radioisotope (RI) material for bifunctional chelating agents and derivatives.[8,9]

In this report, the method for DADT radiolabeling is described below as the representative among the model compounds.

Step 1: RIKEN ^{186}Re (3.8 MBq) was dissolved in 0.05 M hydrochloric acid to prepare a ^{186}Re stock solution (138 MBq/mL). The radioactivity of ^{186}Re was determined using a germanium semiconductor detector and a dose calibrator.

Step 2: 2.2 μL of the ^{186}Re stock solution in Step 1 was added to 63.8 μL of saline to prepare a ^{186}Re solution.

Step 3: 3.0 μL of the ^{186}Re solution in Step 2 was mixed with 2.5 μL of DADT (1.0 μg), 1.4 μL of tin (II) dichloride dihydrate (10 μg), and 2.0 μL of L-tartaric acid (200 μg) aqueous solution.

Step 4: The mixture in Step 3 was heated to 99°C and held for 15 min.

Step 5: The radiolabeling yield of ^{186}Re-DADT was determined using the TLC method with a C18 reversed-phase TLC plate (NAGEL RP-18W/UV254) and eluted with acetone and 0.5 M ammonium acetate in a volume ratio of 13:7.

As a result, the radiolabeling yield of ^{186}Re-DADT at the specific radioactivity of 4.3 GBq/mmol was 86%. In Ref. 4), 88% of the radiolabeling yield of ^{188}Re-DADT at the specific radioactivity of 23 GBq/mmol was reported. To compare these results, each activity of ^{186}Re and ^{188}Re was converted to the amount of substance.

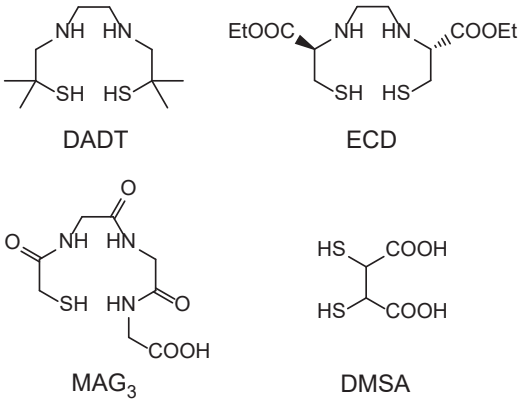

Fig. 1. Chemical structures of DADT, ECD, MAG_3, and DMSA.

Both 4.3 GBq of ^{186}Re and 23 GBq of ^{188}Re correspond to 3.3 nmol. This indicates that the ratio of the amount of DADT to that of $^{186/188}$Re was constant. Therefore, it was regarded that our result of labeling yield corresponded to that of ^{188}Re in Ref. 4). In a previous *in vivo* and *in vitro* evaluation, the radiolabeling of 222-MAMA(*N*-6-Ahx-OEt) with ^{186}Re was performed on 6.1 GBq/mmol.[10] It was suggested that RIKEN ^{186}Re is useful as an RI material for *in vivo* and *in vitro* studies.

Regarding the radiolabeling efficiencies for ECD, MAG_3, and DMSA, the radiolabeling yields were 51%, 46%, and 95%, respectively. It was revealed that these compounds are also able to form ^{186}Re complexes, although these are preliminary results.

In conclusion, our study revealed the availability of RIKEN ^{186}Re for radiolabeling and its feasibility as an RI material with bifunctional chelating agents and derivatives. By optimizing the labeling conditions in the future, RIKEN ^{186}Re is expected to be applied to targeted radiotherapy using bifunctional chelating agents, such as a peptide moiety in their structures.[11]

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