^{68}Ga labeling of DOTMP using freeze-dried kit for the imaging of bone metastasis

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1. Introduction

Bone is a favorable site of metastasis and is invaded common primary tumors such as prostate, breast, and lung. Due to the progressive pain and mortality of the bone metastasis, effort has been focused on the detection of bone metastasis in the field of nuclear medicine (Mitterhauser, Toegel et al. 2007, Mirzaei, Jalilian et al. 2015). In designing suitable imaging agents for bone metastasis, multidentate polyaminophosphonate are regarded as the most promising candidates as carrier ligands owing to their high bone affinity, selective localization in skeletal lesions and ability to form metal chelates with high in-vivo stability (Chakraborty, Das et al. 2008). 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetramethylene phosphonic acid (DOTMP) which is one of the multidentate polyaminophosphonate has been labeled with ^{153}Sm, ^{166}Ho and ^{177}Lu to treat bone metastasis (Liu and Edwards 2001, Chakraborty, Das et al. 2008, Jaime, F. et al. 2012). However, the study using ^{68}Ga for imaging of bone metastasis has not reported yet. The present study describes ^{68}Ga labeling of DOTMP using freeze-dried kit.

2. Methods and Results

2.1 Radiolabeling of DOTMP with ^{68}Ga

The DOTMP (OXCHEM, CA, USA) shown in Fig. 1 was used to be labeled with ^{68}Ga produced from ^{68}Ge/^{68}Ga generator (ITG, Germany).

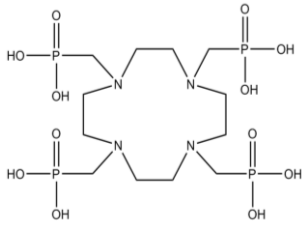
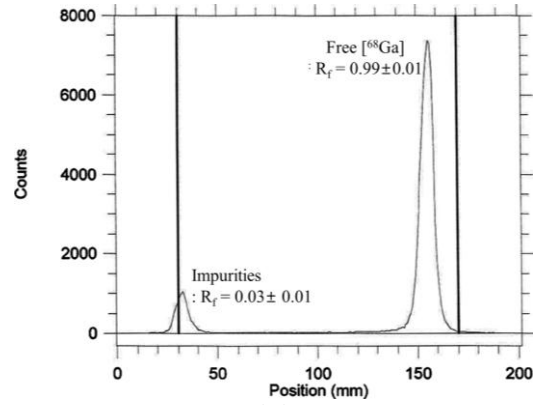


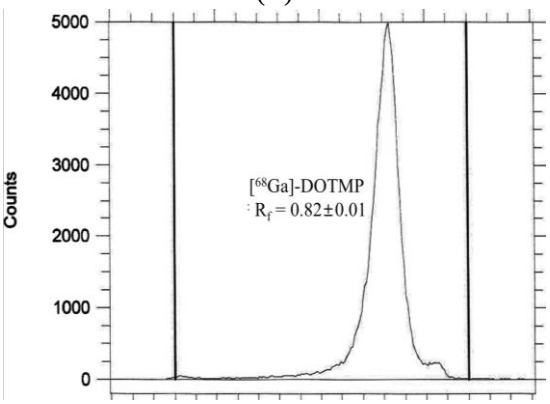
Fig. 1 The molecular structure of DOTMP

The ^{68}Ga was concentrated and purified using a NaCl based ^{68}Ga-concentration method as described by Mueller et al. (Mueller, Klette et al. 2012). The radiolabeling yield was determined by TLC method, using 0.5 M sodium citrate buffer (pH4.5) as the eluting solvent.

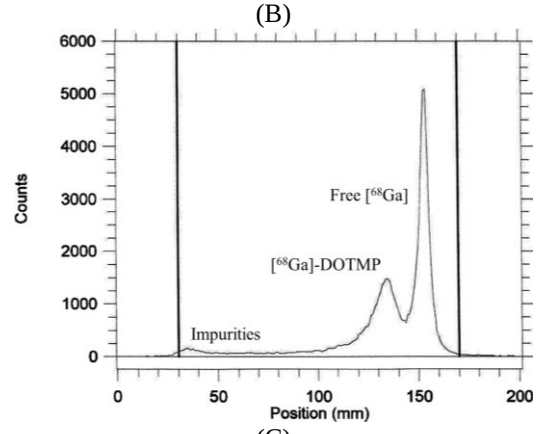
As shown in Fig. 2(A), the eluted ^{68}Ga solution contained 5~10% of impurities, and was successfully purified by NaCl method. The purified ^{68}Ga was reacted with DOTMP by heating at temperatures of 100 ℃ for 7 min. The ^{68}Ga-labeled DOTMP was found in the middle of the TLC plate (R_f=0.8), and the incorporation yield was over 98% (Fig. 2(B)). Fig. 2(C) showed the each peak of eluted ^{68}Ga and ^{68}Ga-labeled DOTMP.



(A)



(B)

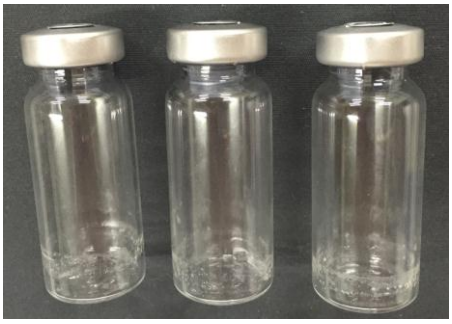


(C)

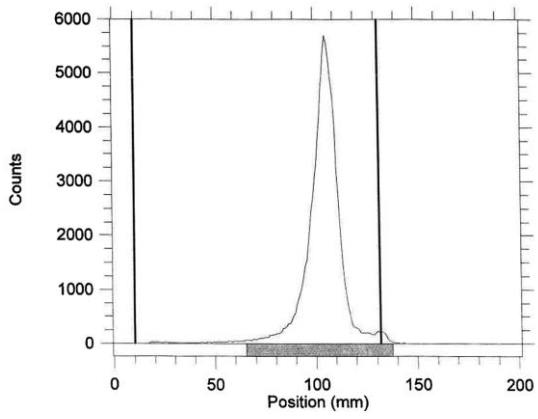
Fig. 2 Typical iTLC profiles of eluted ^{68}Ga (A), ^{68}Ga-labeled DOTMP (B), and mixture of eluted ^{68}Ga and ^{68}Ga-labeled DOTMP (C). Mobile phase was pH4.5 0.5M sodium citrate buffer.

2.2 Formulation of freeze-dried DOTMP kits for labeling DOTMP with ^{68}Ga

Freeze-dried DOTMP kit vial was consist of 400 μg of DOTMP, 19.27 mg of ammonium acetate and 17.62 mg of ascorbic acid. All the preparative steps were carried out under aseptic conditions, and the prepared kit vials were shown in Fig. 3(A).
The lyophilized DOTMP powder in the kit was dissolved by 0.5 ml of DDW, and 0.5 ml of concentrated 555 MBq of ^{68}Ga was added to the vial. The vial was heated at 100 ℃ for 7 min for the radiolabeling, and the radiolabeling yield was evaluated by TLC. The incorporation yield was over 98%, and further purification was not needed.



(A)



(B)

Fig. 3 Freeze-dried DOTMP kit vials for ^{68}Ga radiolabeling (A), and the preparation of 555 MBq of ^{68}Ga-DOTMP using the freeze-dried kit (B).

3. Conclusions

In this study, we described the ^{68}Ga labeling of DOTMP using a freeze-dried kit. The ready-to-use DOTMP kit could be labeled with ^{68}Ga, in consistently high labeling yield (>98%) within twenty minutes. The easy and efficient labeling of this kit with ^{68}Ga make them suitable for preparing ^{68}Ga-DOTMP for imaging of bone metastasis.

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