

Labeling and stability studies of ^{44}Sc -DOTATOC

N. Loktionova¹, M. Pruszyński², A. Majkowska², P. Riß¹, F. Rösch¹

¹ Institute of Nuclear Chemistry, University of Mainz, Mainz, Germany; ² Institute of Nuclear Chemistry and Technology, Warszawa, Poland

Introduction: The radioisotope ^{44}Sc is a positron emitter, which is of interest for medical imaging using PET radiopharmaceuticals because of its 3.93 h half-life and 94% β^+ branching. The aim of this work was to find the optimum conditions for labeling a DOTA-conjugated octreotide (DOTATOC) with ^{44}Sc and to check the stability of obtained conjugate.

Experimental: The ^{44}Sc was eluted from the recently developed $^{44}\text{Ti}/^{44}\text{Sc}$ generator and on-line post-processed on the AG 50W-X8 resin [1]. Finally around 160 MBq ^{44}Sc was obtained in 3 ml of 0.25 M ammonium acetate buffer, pH = 4.0. This solution was used for labeling of DOTATOC directly. Optimisation of the reaction conditions was performed varying period and temperature of heating, addition of various amounts of DOTATOC and pH of the reaction mixture. The influence of microwave heating on the time and radiolabeling of DOTATOC with ^{44}Sc was determined under the optimal conditions found during the optimization experiments. Radiochemical analysis of ^{44}Sc -DOTATOC was accomplished using silica-coated TLC plates (Silica-gel 60) and 4 different developing solutions:

- 0.1 M sodium citrate pH = 4.0;
- 0.1 M sodium acetate pH = 4.0
- 5 % NaCl / MeOH (3:1);
- 5 % NaCl / MeOH / 25 % NH_3 (3:1:1).

^{44}Sc -DOTATOC was purified on a C-18 cartridge and eluted with 400 μl of pure ethanol. Stability of ^{44}Sc -DOTATOC was checked at room temperature and at 37 °C in EtOH, 0.9 % NaCl, PBS (pH=7.4) and in the presence of the metal cations Fe^{3+} , Ca^{2+} , Mg^{2+} and Cu^{2+} at 10^{-2} M concentration. The purified ^{44}Sc -peptide was diluted at least 20 times by the solution in which stability was checked.

Results: The overall radiolabeling yield was >96 % when 30 μl (21.1 nmol) of DOTATOC was added to 3 ml of the ^{44}Sc eluate (pH = 4.0) and heated in the oil-bath for 25 minutes at 95 °C. Changing the pH below 3 or increasing to > 5 resulted in a drop of labeling yield. Microwave-assisted labeling speeded up ^{44}Sc complexation with DOTATOC. After 1 minute of microwave heating reaction, the yield was >95 % and increased up to 98 % during next 2 min. Purification on the 30 mg C-18 cartridge recovered the ^{44}Sc -conjugate in 400 μl of pure EtOH with the radiochemical purity higher than 99 %.

Stability studies of about 160 MBq ^{44}Sc -DOTATOC in 400 μl of EtOH showed high stability of the labeled conjugate during at least 7 h. ^{44}Sc -DOTATOC was also stable during 8 h studies in 0.9 % NaCl and PBS at 37 °C. The obtained ^{44}Sc -DOTATOC seems to be kinetically very inert. It was stable even after 25 h incubation at 37 °C in the presence of metal cations at concentration 10^{-2} M.

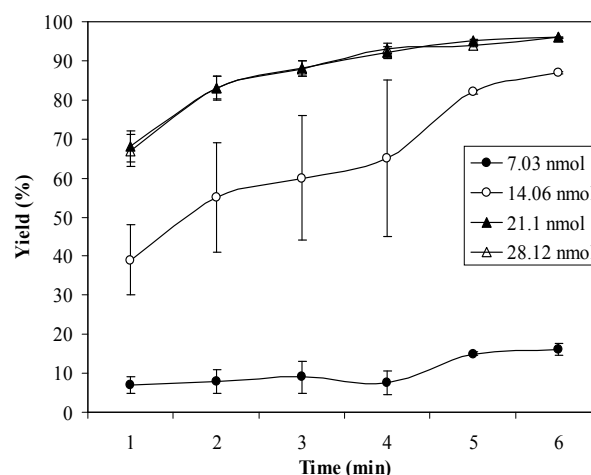


Figure 1. The labeling yield of ^{44}Sc -DOTATOC at 95 °C.

Conclusions: Optimum labeling of DOTATOC with ^{44}Sc in >96 % yield were obtained for 24.5 nmol of DOTATOC and 3 ml of ^{44}Sc eluate at pH = 4.0. The studies show high stability of the obtained ^{44}Sc -DOTATOC conjugate in different media. The potential diagnostic radiopharmaceutical was obtained after purification with more than 99% radiochemical purity. After membrane sterilization and dilution in saline it is ready for further cell and animal studies.

References:

- [1] N. Loktionova, D.V. Filosofov, M. Pruszyński, F. Rösch, Post-processing of $^{44}\text{Ti}/^{44}\text{Sc}$ -radionuclide-generator for medical application, 2008

Acknowledgement:

This work was financially supported by DFG grant RO 985/18.