T1-3

SIGNIFICANCE OF PH CONTROL IN DETERMINATION OF RADIOCHEMICAL PURITY OF F-18 LABELED TRACERS USING LIQUID CHROMATOGRAPHY

Csaba Hámori, Cintia Anna Balogh, István Jószai*

Department of Nuclear Medicine, Clinical Center, University of Debrecen

INTRODUCTION: Synthesis of [^{18}F]FDG as well as [^{18}F]FET is based on participation of [^{18}F] fluoride ions in S_N2 nucleophile reaction. However, liquid chromatographic methods may used in quality control of these radiopharmaceuticals are not useful for detection of [^{18}F]fluoride ions. Determination of free radioactive fluoride could be achieved using additional TLC method. The aim of this work was to examine the effect of pH of the eluent for elution of [^{18}F]fluoride ions to determine the total radiochemical purity by single HPLC method.

METHODS: Composition of the applied HPLC system was as follows: Jasco autosampler, degasser, low pressure gradient valve, pump, radioactivity detector. Waters I-Class system was applied for UPLC measurements. The used analytical columns were Acquity UPLC, BEH Amide 1.7 μm, 3.0 × 100 mm (Waters), LiChroCART NH_2, 5 μm, 250 × 4 mm, (Merck), LiChroCART RP18, 5 μm, 250 × 4 mm, (Merck). Reference materials were prepared either on synthesis modules or manually [1].

RESULTS: In quality control of [^{18}F]FDG the separation of active ingredient from the intermedier [^{18}F]TAG is possible on LiChroCART NH_2 column with MeCN/H_2O (95/5 V/V%). On the other hand, the elution of [^{18}F]fluoride ions is only possible using buffer solution with pH7. The following gradient method is could be applied for determination of total radiochemical purity of [^{18}F]FDG. The elution started with acetonitrile/phosphate buffer (pH7; 5 mM) in the ratio of 85/15 V/V%. To elute [^{18}F]fluoride eluent composition is to be changed to acetonitrile/phosphate buffer (pH7; 5 mM) in the ratio of 5/95 V/V%. Gradient profile: 0 min 100% *A* — 0% *B*, 2 min 100% *A* — 0% *B*, 3 min 0% *A* — 100% *B*, 7 min 0% *A* - 100% *B*. At 2 mL/min flow rate the measurement time was 7 minutes. Retention times: 1.303 min [^{18}F]TAG, 2.485 min [^{18}F] FDG, [^{18}F]fluoride ion 5.143 min. The resolution between [^{18}F]TAG and [^{18}F]FDG was 4.2 and between [^{18}F]FDG and [^{18}F]fluoride was 10.2. The developed method was successfully transferred to UPLC system. In case of UPLC procedure Amide column was applied. The elution started with acetonitrile/ammonium acetate buffer (pH5; 50 mM) in the ratio of 90/10 V/V%. To elute [^{18}F]fluoride eluent composition was changed to ammonium acetate buffer (pH10; 50 mM) in the ratio of 10/90 V/V%. Gradient profile: 0 min 100% *A* — 0% *B* 1.2 mL/min, 1.20 min 100% *A* — 0% *B* 1.2 mL/min, 1.25 min 0% *A* — 100% *B* 0.6 mL/min, 1,50 min 0% *A* — 100% *B* 0.4 mL/min, 5.00 min 0% *A* — 100% *B* 0.4 mL/min. Retention times: [^{18}F]TAG 0.393 min, a [^{18}F]FDG 1.024 min, a [^{18}F]fluoride 3.045 min. The resolution between [^{18}F]TAG and [^{18}F]FDG was 2.8 and between [^{18}F]FDG and [^{18}F]fluoride was 6.9. In case of [^{18}F]FET we implemented the elution of [^{18}F]fluoride ions on LiChroCART RP18 column with pH7 phosphate buffer. The recovery of [^{18}F]fluoride ions was higher than 95%.

CONCLUSION: This work gives recommendations on determination of total radiochemical purity of [^{18}F]FDG as well as [^{18}F]FET using liquid chromatographic technique. Single analytical method could simplify the quality control of tracers as well as to increase the productivity of Q.C. management.

1. Hamacher K, Coenen H, Stöcklin G. J Nucl Med. 1986; 27: 235–238.