Abstract

^{18}F-Labeled aromatic amino acids became more and more important for molecular imgaging with Positron Emission Tomography (PET). Several examples have emerged showing higher specificity in imaging disorders in neurological processes or tumors. The essential amino acid tryptophan is an important precursor in the serotonergic system and the kynurenine pathway, reported to be of significance in the metabolism of some tumors. Therefore, ^{18}F-labeled derivatives of tryptophan are of major interest for the investigation of neurological and oncological behavior via PET. In this work, new [^{18}F]fluorotryptophan derivatives were synthesized by a novel copper-mediated radiofluorination method which was also amenable to automation.

In an initial step, the reactivity of the different substitution positions in the indole motif was examined using the copper-mediated radiofluorination. The highest reactivity was found in position 6; therefore, an appropriate precursor for the radiosynthesis of 6-[^{18}F]fluoro-L-tryptophan (6-[^{18}F]FTrp) was synthesized in a 6-step synthesis with 40 % overall yield. Using this precursor, the radiosynthesis was improved by using less concentrated base, a different drying method, other solvents and a new acidic hydrolysis. The overall radiochemical yield was 16 % within 110 min, an enantiomeric excess (*e.e.*) of 89 % and a molar radioactivity up to 240 GBq/µmol. In a next step, a new designed appropriate precursor for 5-[^{18}F]fluoro-L-tryptophan (5-[^{18}F]FTrp) was synthesized using protecting groups which are easier to hydrolyze. Furthermore, the copper-mediated radiofluorination was modified by using different alcoholic solvents. After studying several parameters of the new alcohol-enhanced method, the radiosynthesis of 5-[^{18}F]FTrp gave a radiochemical yield of 53 % in 105 min, an *e.e.* of >99 % and a molar radioactivity of up to 180 GBq/µmol. As last derivative, a precursor for 4[^{18}F]fluoro-L-tryptophan (4-[^{18}F]FTrp) was synthesized and radiofluorinated using the same parameters as for 5-[^{18}F]FTrp. It was obtained in a RCY of 39 % whithin 104 min, an *e.e.* of >99 % and a molar radioactivity up to 95 GBq/µmol. The radiosyntheses of all three [^{18}F]FTrp derivatives were amenable to automation. They were thus produced in quantities sufficient for *in vivo* animal-PET studies in rats. Every [^{18}F]fluorotryptophan derivative showed a different *in vivo* behavior. In summary, a practical radiosynthesis for three ^{18}F-labeled tryptophan-derivatives was established giving sufficient radiochemical yields and purities for *in vivo* investigations and the procedure shows adaptility for automation.