Production of [18F]F-Py-TFP as a secondary labelling precursor on a cassette based synthesis unit towards a GMP-compliant and convenient fluoroarylation of [18F]-peptides and [18F]-peptidomimetics

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Aim: The synthesis and purification of prosthetic groups for the radiofluorination of peptides are sophisticated and therefore difficult to translate into routine production. The aim is to transfer the synthesis of [18F]F-Py-TFP (6-[18F]fluoronicotinic acid 2,3,5,6-tetrafluorophenyl ester) as reported by Olberg et al. onto a cassette-based radiosynthesizer for large-scale GMP-compliant automated production ready for subsequent labelling of peptides. Materials and Methods: An aqueous solution containing [18F]fluoride was obtained by nuclear reaction (18O(p,n)18F) from a Scanditronix MC32NI cyclotron, transferred to a Trasis AllinOne synthesis module, trapped on and eluted from a QMA cartridge using TBA-HCO3 in water and acetonitrile as the eluent. After azeotropic drying, 10 mg of precursor N,N,N-trimethyl-5-((2,3,5,6-tetrafluorophenoxy)- carbonyl)pyridin-2-aminium trifluoromethanesulfonate in 1.2 mL tert.- BuOH and 0.3 mL acetonitrile was added and heated. The reaction mixture was cooled down to room temperature and diluted with 5 mL of water. The crude mixture was trapped on a pre-conditioned Oasis MCX SPE cartridge and rinsed with 10 mL of water. Impurities were removed from the cartridge using the first fraction of acetonitrile. [18F]F-Py-TFP was obtained by further elution with acetonitrile and dried using a SepPak Dry Sodium Sulfate cartridge. [18F]F-Py-TFP was then used to label the novel PSMA-ligand PSMA-1007 in a mixture of DMSO, acetonitrile and N,N-diisopropylethylamine at elevated temperature. The radiolabelled peptidomimetic was purified by HPLC and diluted with PBS buffer and sterile-filtered. Results and Conclusion: The secondary labelling precursor [18F]F-Py-TPF was obtained within 30 minutes in dry acetonitrile and radiochemical yields higher than 25% (d.c.) on an automated cassette based synthesis module. The radiochemical purity of the product after simple cartridge extraction was sufficiently high and further investigations on the major impurity resulting from hydrolysis are in progress. Nevertheless, [18F]F-Py-TPF was used on the same radiosynthesizer for direct radiolabeling of a wide range of peptides including the novel small PSMA-ligand PSMA-1007 which was obtained in high radiochemical purity. Hence, this fully automated procedure represents a step forward towards the GMP-compliant production of promising F-18 labelled peptides and peptidomimetics.