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Nucleophilic synthesis of [18F]FDOPA by using an automated module : A summary of the results of 18 batches

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Background

6-[18F]Fluoro-L-DOPA, ([18F]FDOPA) or simply FDOPA is a radiopharmaceutical used for targeting dopamine receptors by using positron emission tomography. FDOPA is useful for differential diagnosis of Parkinson's disease and other degenerative disorders of the central nervous system. FDOPA PET is also useful for detection and staging of endocrine and brain tumors. FDOPA is conventionally produced via electrophilic substitution by using fluorine-18 prepared by irradiating neon gas using deuteron beam. However, results in the production of low specific activity tracer. Nucleophilic substitution reaction using fluoride has been developed for the synthesis of FDOPA which results in the production of high specific activity tracer. Cassette based synthesis in automated module using novel precursors are now commercially available. Considering the high demand for FDOPA, we are routinely carrying out the production of FDOPA under GMP. The results are presented in this paper.

Methodology

No carrier added 18F was produced by 11 MeV Siemens HP cyclotron. Production of FDOPA was carried out using NEPTIS automated synthesizer procured from Neptis, Belgium installed in clean room with class B area. Radioactivity measurements were done using capintec dose calibrator. Oxygen-18 enriched water and FDOPA cassettes, including all chemicals were procured from ABX, Germany. The precursor (S)–N-Trityl–5–formyl-4-methoxy-methylene-2-nitro-phenylalanine tert-butyl ester is used in the cassette in addition to all other chemicals and purification cartridges. TLC was performed using AR2000 TLC scanner procured from Erkect and Ziegler. The mobile phase used for TLC is glacial acetic acid and methanol (9:1). Residual solvents were analyzed by Agilent Gas chromatography.

Results and discussion

The FDOPA was prepared in four step synthesis in a Neptis synthesizer. Followed by the steps of nucleophilic fluorination, oxidation of intermediates and hydrolysis, FDOPA was trapped on HR-P cartridge and eluted with phosphate buffer, passed through a C-18 and Oasis Wax cartridges to remove non-polar and solid impurities. The product is collected in a 30 mL vial connected to a 0.22 ⍰ millipore filter. The above series of purification avoids the need for HPLC purification. The total duration of FDOPA production was 90 minutes. The radiochemical yields of FODPA (n=18) are 6 ± 1.2% (decay uncorrected) and 10.5 ± 2.2% (decay corrected). The radiochemical purity was always >94 % and 97.2±1.6 % (n=18) and was retained > 92% upto 7 h. FDOPA was used in multiple nuclear medicine departments for PET-CT and PET-MR studies. The images were found to be highly useful for clinical evaluation of patients suffering from neurological disorders as well as neuroendocrine tumors.

Conclusion

Consistent production of FDOPA was achieved using a cassette based nucleophilic synthesis in a Neptis automated synthesizer under GMP conditions. Though the final decay uncorrected yields were low (˜6%), the product was found to be clinically useful for PET-CT and PET-MR studies.

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