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Fully Automated Radiosynthesis of 18F-16-α-Fluoroestradiol ([18F]FES) With Solid Phase Extraction Cartridge Purification by Sep Pak® Plus ALOX N

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Background of the Study:

The utility of [18F]Fluoroestradiol ([18F]FES), a fluorinated steroidal tracer for determining the tissue estrogen receptor level of breast cancer patients is clinically proven. This radiotracer is thus used in prior prediction of the response of antiestrogen therapy of primary, recurrent or metastatic breast cancer. A fully-automated, high-yield synthesis procedure is the key requirement for its availability in large scale, ensuring its widespread clinical use.
The radiosynthesis of [18F]FES is carried out starting from MMSE (3-methoxymethyl-16α, 17β-epiestriol-O-cyclic sulfone) precursor. The low yield of [18F]FES obtained from this precursor is attributed to difficulties in the hydrolysis and purification steps after the first step radiofluoriation.
Herein, we report an improved fully automated and optimized radiosynthesis procedure of 18F-16-α-Fluoroestradiol ([18F]FES) from MMSE precursor, involving hydrolysis with 2N HCl and subsequent purification using Sep-Pak® Plus ALOX-N cartridge. The method is reliable, with considerably improved yield of the product with acceptable radiochemical purity.
Methodology:
18F–produced in the medical cyclotron [18O (p, n) 18F] was trapped in perfectly conditioned and dried QMA cartridge and TBA18F was eluted by 0.6 ml 75mM TBAHCO3. 1.2 ml dry acetonitrile was added followed by azeotropic distillation for obtaining extra dry TBA18F. MMSE precursor (2mg/0.8 ml dry MeCN) was added and radio-fluorination was carried out at 120˚C for 15 minutes. Hydrolysis of the radiofluorinated MMSE precursor was carried out at 115˚C for 12 min using 0.7 ml of HCl (2N). The reaction mixture was cooled and around 2 ml of pharmacopeia grade ethanol was added into the reaction vessel, under stirring condition. The reaction mixture was then passed through a stand of four perfectly conditioned SepPak® Plus ALOX-N cartridges discarding the eluent and subsequently dried by-passing helium. Finally, [18F]FES was eluted with 12 ml of 15% ethanol containing water in the product vial. 1.5 ml of 10% NaCl and 0.5 ml of 1(M) NaH2PO4 were added at the beginning of the synthesis in order to maintain acceptable pH and isotonicity of the product.
[18F]FES was then dispensed through 0.2μ filter into sterile and bacterial endotoxin free vials. Including its physical properties, radiochemical purity was ascertained by radio-TLC. The product formation is confirmed by comparison of its TLC with that of the authenticated reference standard [19F]FES.
Results:
The non-decay corrected radiochemical yield was found to be ~ (35±5) % (n = 3) within 60±2 mins. The radiochemical purity (> 95 %) was confirmed by radio-TLC using freshly prepared 95/5 MeOH/NH3 solvent. While [18F]FES has Rf of 0.7, free [18F]F- exhibits Rf of 0.01 and that of the radiofluorinated MMSE precursor is around 0.15. The radiochemical purity of [18F]FES was confirmed by comparing with the authenticated reference standard [19F]FES. [18F]FES obtained was clear, colourless and free of any suspended particle, with pH ~ 6.

Conclusion:
[18F]FES has been successfully synthesized and purified in good yield using the fluorination module in the medical cyclotron under optimized condition which is identical in principle with GE TRACERLABFX-FDG.

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