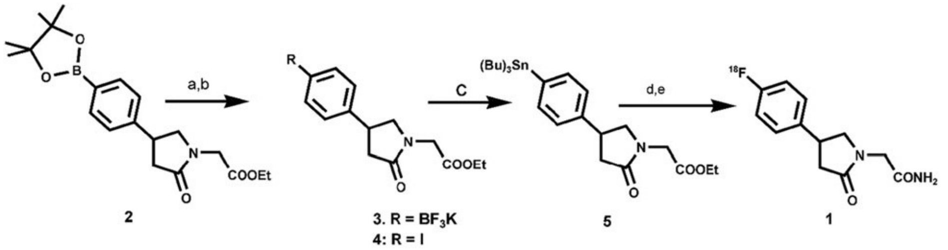

a. KHF_2, acetone-H_2O, r.t, 6 h, b: $FeCl_3$, NaI, CH_3CN, 16 h, 80 °C; c: Bu_6Sn_2, $Pd(PPh_3)_4$, toluene, reflux, 4h; d: [^{18}F]KF, KOTf, K_2CO_3, $CuOTf_2\,(Py)_4$, DMA, 130 °C, 30 min; e: NH_4OH, EtO, 70 °C, 12 min

Conclusions

An improved synthesis of 4-(4-[^{18}F]fluorophenyl)piracetam, **1**, a potential PET imaging agent for PD has been successfully accomplished in two steps from tin precursor **5**. The radiochemical yield was found to be 24% that is two times more than previously reported method. The radiochemical purity was determined to be >95%. The total reaction time was 50 min.

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Poster Category: Radiochemistry - ^{18}F

P-018 | A novel [^{18}F]fluoride relay reagent for radiofluorination reactions

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Objectives

Fluorine-18 is the most utilized radioisotope in Positron Emission Tomography (PET), but the wide application of fluorine-18 radiopharmaceuticals is hindered by its challenging labelling conditions. This necessitates production at centralized PET centres with highly specialized equipment including cyclotrons, hot cells, synthesizers, and HPLC capabilities, which ultimately limit the availability of fluorine-18 tracers to those whose production has a large marketing scale (e.g., [^{18}F]FDG). As such, many potentially important leads remain underutilized. Herein, we describe the use of [^{18}F]ethenesulfonyl fluoride (ESF) as a novel radiofluoride relay reagent that allows radiofluorination reactions to be performed in minimally equipped satellite nuclear medicine centres (Figure 1).

Methods

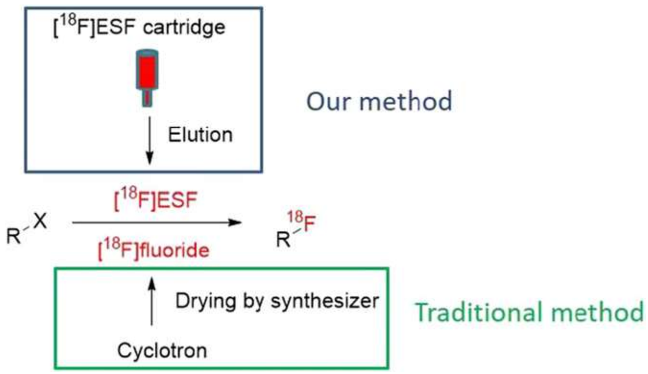
[^{18}F]ESF was produced from 2,4,6-trichlorophenylethenesulfonate using a microfluidic system and was stored on inert cartridges. The cartridges could be shipped remotely where trapped [^{18}F]ESF was liberated by chosen solvent to a vial containing precursor and additives. The reaction mixture was then stirred and heated using a heating block. Reaction conditions including temperature, time, precursor concentration, and additives were optimised, and the radiochemical yields (RCYs) were compared with those for traditional [^{18}F]fluoride method.

Results

We found that conditions of 1 mg/mL precursor, 0.5 mg/mL tetraethylammonium bicarbonate as additive, temperature of 100°C, and time of 15 min were useful to assess radiofluorination scope on commercially available precursors. The obtained RCYs were compared with those generated from traditional dried [^{18}F]fluoride source and no statically significant difference was observed for most precursors. Some differences on RCYs, both positive and negative, were noted when novel type of precursors (i.e., boronic acids, iodonium ylides) were tested.

Conclusions

We have developed a method to perform radiofluorinations using a new radiofluoride relay reagent, [^{18}F]ESF. Such method reduces the reaction equipment needed, in the simplest case to a simple heating block, single-use vials and magnetic stir bar. Notably, this new process is not only compatible with typical commercial precursors, but also feasible to accommodate emerging precursors with novel leaving groups.



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Poster Category: Radiochemistry - ^{18}F

P-019 | An improved method for preparing [^{18}F]AV-45 using solid-phase extraction purification

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Objectives

Alzheimer's disease (AD) is a neurodegenerative disease with a very significant social impact in aging population.[1] Accumulation of Aβ in the brain is one of the major factors in driving AD pathogenesis. [^{18}F]AV-45 (florbetapir f18, Amyvid) is the first ^{18}F-labeled PET imaging agent targeting β-amyloid plaques for the diagnosis of AD approved by FDA. It is now being used for patient selection prior to enrollment in drug trials specifically designed to reduce the accumulation of β-amyloid plaques in the brain.[2] In this preliminary work, instead of using HPLC purification, we proposed to take advantage a rapid and simple solid-phase extraction (SPE) purification method for preparation of [^{18}F]AV-45.[3] However, one of the main issues in using this SPE purification method was that the main chemical impurity, predominantly a hydroxyl derivative (AV-136), cannot be completely removed. We report herein an optimization of SPE purification method for preparation of [^{18}F]AV-45 to remove the majority of chemical impurities.

Methods

Radiosynthesis of [^{18}F]AV-45 was first initiated by azeotropic distillation with acetonitrile to obtain activated [^{18}F]KF/K222, after a nucleophilic substitution reaction with tosylate precursor (1 mL DMSO, 110, 120, 130, or 140°C), followed by acid hydrolysis (1 mL 3 M HCl or 1 mL 2 M H_2SO_4 acid solutions, 100°C) and neutralization. The crude product was passed through an Oasis cartridge (3cc, Waters), and the cartridge was rinsed with water (10 mL × 2). Then the Oasis cartridge was eluted with increasing concentration of ethanol (EtOH/water, 10%-70%) and acetonitrile (ACN/water, 10%-50%), respectively. Next, increasing volume of optimal combination of eluent (ACN/water or EtOH/water) to wash the cartridge was carried out. Finally, we also identified and quantified residual chemical impurities in the product by using LC/MS analysis and estimated quantity presenting in each HPLC peak by comparing with standard curves.

Results

As shown in Figure 1 (B, C), a majority of the pseudo-carrier, AV-136, was removed with ACN/water, while retaining the desired product, [^{18}F]AV-45. In order to make the SPE purification more efficient, we explored the optimal combination of eluent using EtOH/water or ACN/water (Figure 1D and 1E). The optimal elution conditions for SPE purification was identified as washing Oasis cartridge with 6 mL of 35% ACN/water (Figure 1D and 1E). With this SPE purification method, more than 95% of AV-136 was removed, while the loss of the desired product, [^{18}F]AV-45, was minimized to less than 10%. There were two other chemical impurities remaining in the SPE-purified product: 4 and 5 (Figure 1A). Under optimized conditions, the remaining two impurities, 4 and 5, were reduced. In summary, we have optimized and purified the desired, [^{18}F]AV-45, by using SPE purification via Oasis cartridge. Under an optimized condition, the remaining pseudo-carrier, AV-136, in the final product was 13.2 ± 1.2 μg (n = 3); the amount of impurity **4** was 3.4 ± 0.9 μg (n = 3), and the amount of impurity **5** was about 3.0 ± 2.5 μg (n = 3). It was observed that after the optimal SPE purification a total amount of chemical impurities remaining in the final product vial was less than 30 μg.

Conclusions

A rapid and simple SPE purification method for [^{18}F]AV-45 preparation was developed to remove majority of chemical impurities. This simplified preparation may be suitable for routine preparation in clinical studies.

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