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Abstract

Sulfur [^{18}F]Fluoride Exchange Reaction Enables Rapid Access to ^{18}F-Labeled PET Tracers †

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Abstract: Efficient ^{18}F-fluorination procedures for the production of radiopharmaceuticals are urgently needed to satisfy the increasing demand for clinical diagnostics using positron emission tomography (PET). However, the development of PET tracers is often a time-consuming and challenging process. This work examines the applicability of the recently described sulfur [^{18}F]fluoride exchange ([^{18}F]SuFEx) chemistry as a fast screening approach towards a number of clinically relevant PET tracer preparations. The preparation of a number of ^{18}F-labeled compounds commenced with [^{18}F]fluoride loading onto a quarternary methylammonium (QMA) cartridge, which was eluted with a methanolic solution containing a base, followed by solvent removal under reduced pressure. Thereafter, the radiolabeling precursors in MeCN were added to the reaction vessels, and allowed to react via [^{18}F]SuFEx at room temperature for 5 min. The radiofluorination reactions were quenched by water dilution followed by C18 cartridge purification. The ^{18}F-labeled products were isolated by elution from the cartridge with EtOH and the identities of the products were confirmed by radio-ultra high performance liquid chromatography (UHPLC). The optimized preparations of ^{18}F-labeled prostate-specific membrane antigen (PSMA) inhibitor, Programmed death-ligand 1 (PD-L1) ligand, cyclooxygenase-2 inhibitor (COXIB), and Fibroblast activation protein alpha inhibitor (FAPI) were achieved with high non-decay corrected isolated activity yields (AY) of 33–57% (n = 12) and >95% radiochemical purity (RCP) in 25 min. The automated radiosynthesis procedures afforded the radiolabeled products in an unoptimized 8–15% AY (n = 5), with >95% RCP in 40 min. The ultra-fast [^{18}F]SuFEx reaction permitted several structurally diverse ^{18}F-labeled compounds for potential imaging to be rapidly achieved in excellent isolated AYs and high RCP. Presently, optimization of the automated radiosynthesis and biological assessment of the ^{18}F-labeled products is underway.

Keywords: fluorine-18; positron emission tomography (PET); 18F-fluorination; [18F]SuFEx; PSMA; FAPI; PD-L1; COX-2 inhibitor

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