

SPE-BASED PURIFICATION OF [¹⁸F]F-JK-PSMA-7: A ROBUST ALTERNATIVE TO HPLC FOR SIMPLIFIED RADIOTRACER PRODUCTION

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Introduction

[¹⁸F]F-JK-PSMA-7 is a fluorine-18-labelled PSMA-targeting radiotracer widely used for PET imaging of prostate cancer, enabling accurate detection, staging, and therapy monitoring due to its high specificity and affinity for PSMA.^[1] Its current production relies on nucleophilic aromatic substitution followed by acidic deprotection and purification by high-performance liquid chromatography (HPLC). However, HPLC represents a critical bottleneck due to limited module availability and potential technical failures. This study aims to develop an alternative purification strategy based on solid-phase extraction (SPE), replacing HPLC to simplify the workflow and reduce overall synthesis time.

Materials and Methods

[¹⁸F]F-JK-PSMA-7 was synthesized using a Trasis All-In-One (AIO) module following the standard protocol up to the crude reaction stage. The reaction mixture was then subjected to off-line purification. Various SPE cartridges (C18, HLB, and CM) were evaluated. Washing protocols and fractionated ethanol and acidic elution conditions were tested. The purified products were analyzed by HPLC and thin-layer chromatography (TLC) to determine synthesis yield, radiochemical purity (RCP) and chemical purity, and were compared with the crude reaction mixture before purification.

Results

HPLC of the crude product showed multiple impurities, including free [¹⁸F]fluoride and by-products. Among the tested strategies, a combined C18–HLB SPE approach performed best. HLB cartridges efficiently retained the product, while diluted ethanol washes removed impurities. Elution with 50% ethanol gave ~55% recovery, increasing to ~70% when saline replaced water. Additional purification with a long C18 cartridge improved RCP but did not fully eliminate radiochemical impurities. To address this, an alternative acidic elution protocol (H₃PO₄/ACN), adapted from the HPLC method,^[1] was implemented on the HLB purification. This approach enabled efficient elution of [¹⁸F]F-JK-PSMA-7 with minimal chemical and radiochemical impurities. Subsequent conversion on a short C18 cartridge and final elution in 50% saline/ethanol yielded an RCP >95% and chemical purity compliant with the European Pharmacopoeia specifications.^[2]

Conclusions

SPE-based purification represents an available GMP-compliant alternative to HPLC for the production of [¹⁸F]F-JK-PSMA-7. This approach simplifies the synthesis process, reduces operator dependency, and improves production reliability while significantly shortening synthesis time. Ongoing work focuses on process automation and scale-up to enable multi-dose production and facilitate broader clinical implementation.

References: [1] B. D. Zlatopolskiy et al., *J Nucl Med*, **2019**, 60:6 [2] EU Pharmacopoeia Mon: 3205, **2025**.