

AUTOMATED PRODUCTION OF [¹⁸F]ALDOVIEW – FIRST TRANSLATION OF A SULFONIUM SALT PRECURSOR TO GMP

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Objectives

Fluorine-18 labelled AldoView is a novel PET tracer for imaging of aldosterone-producing adenomas (APAs) in patients with Primary Hyperaldosteronism [1]. The tracer was initially labelled hands-on by reacting the corresponding dibenzothiophenium salt (DBT) precursor with [¹⁸F]fluoride under conventional conditions with kryptofix 222 and potassium bicarbonate as the base [2]. The objective of this study was to establish automated production of [¹⁸F]AldoView according good manufacturing practice (GMP) in order to allow first-in-human PET studies.

Methods

The DBT precursor for labelling was obtained in two steps from the corresponding bromide. Coupling of the bromide with the protected biaryl thiol gave the corresponding thioether. Subsequent treatment with calcium hypochlorite triggered ring-closing of the biaryl thioether to give the DBT leaving group. The GMP grade precursor was obtained by custom synthesis. Automated labelling was established on a Trasis AllInOne synthesis module using a programme and cassette previously optimized for production of [¹⁸F]DPA-714. The DBT precursor (2-4 mg in 0.8 mL DMSO) was allowed to react with [¹⁸F]fluoride for 15 min at 115°C. After labelling, [¹⁸F]AldoView was purified by HPLC and formulated in a solution of saline for injection.

Results

The synthetic yields for the coupling step and ring-closing reaction were 94% and 32% respectively. Automated labelling provided [¹⁸F]AldoView in 29% ± 4% (non-decay corrected, *n* = 6) radiochemical yield, with a radiochemical purity of >99%, and a synthesis time of 75 min. The molar activity was 308 ± 23 GBq/μmol (*n* = 3) when starting from 16 - 23 GBq of [¹⁸F]fluoride. The formulated product passed all GMP release criteria.

Conclusions

Translation of [¹⁸F]AldoView from hands-on labelling to automated GMP tracer production was readily achieved using standard methods and equipment for direct labelling of ¹⁸F-labelled PET tracers under GMP. The radiochemical yields, radiochemical purity and molar activity obtained with the automated method compared favorably to the results obtained with hands-on labelling. This study demonstrates that sulfonium salts allow seamless translation from hands-on labelling to automated GMP tracer production and are therefore ideally suited for translational PET studies.

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