Macedonian pharmaceutical bulletin, 69 (Suppl 1) 155 - 156 (2023)
Online ISSN 1857 - 8969
DOI: 10.33320/maced.pharm.bull.2023.69.03.076
Short communication

The influence of cation-exchange cartridge on quality of [^{18}F]NaF radiopharmaceutical

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Introduction

[^{18}F]Sodium fluoride is a positron emitting radiopharmaceutical used for imaging of metastatic bone disease and microcalcification (Ahuja et al., 2020). The radioisotope fluorine-18 in form of anion [^{18}F]F$^-$ is produced with proton irradiation of small volume oxygen-18 enriched water in targets. After the bombardment, the irradiated enriched water, not only [^{18}F]fluoride ion, but also contains other radioactive and nonradioactive ions (Köhler et al., 2013, Choi et al., 2016). According to the European Pharmacopoeia monograph, two common approaches are used to purify the produced fluoride-18 from target water, such us anion-exchange cartridges or electrochemical deposition and redissolution (Ph. Eur. 10, 01/2008:2100, 2020). By identifying the most appropriate type of SPE cartridges, this study aims to optimize the purification process and ensure the production of high-quality sodium [^{18}F]fluoride radiopharmaceutical for clinical use.

Materials and methods

The materials used in the study were: enriched water 18 (NUKEM isotopes), 0.9 % Sodium Chloride injection solution (Alkaloid Ad Skopje), water for injection (Alkaloid Ad Skopje), SCX SPE cartridge (S*Pure, Singapore) Sep-Pak Accell Plus QMA Plus Light Cartridge (Waters, United States), sterile filter 0.22 µm (Merck), sterile vials (Huayi isotopes), 10 ml Syringe (BTC Medical Europe), Sodium Fluoride standard (Sigma Aldrich), pH strips (Macherey Nagel), Sodium hydroxide solution 50-52 % for IC (Sigma Aldrich), Water-type 1 (Direct Q3, Millipore).

The radioisotope [^{18}F]F$^-$ was produced *via* the ^{18}O(p,n)^{18}F nuclear reaction, by irradiating the enriched ^{18}O water with protons in PET GeTrace 800 cyclotron (GE Healthcare, United States) with niobium target. For purification of the produced radioisotope [^{18}F]F$^-$ from the radionuclidic impurities present in the irradiated enriched water, two types of solid-phase extraction cartidges, were used, like quaternary methyl ammonium anion-exchange cartridge (QMA) and cation-exchange cartridge (Strong cation exchange cartridge - SCX).

The influence of cation-exchange cartridge on quality of [^{18}F]NaF radiopharmaceutical was investigated. To select the most appropriate cartridges for purification, three type of experiments (manual productions) were performed using the QMA and SCX cartridges in the following combinations:

Experiment 1 - QMA + SCX
Experiment 2 - SCX + QMA
Experiment 3 - QMA cartridge

The obtained [^{18}F]NaF samples were examined for several parameters to assess their quality. These parameters include: approximate pH value, chemical, radiochemical and radionuclidic purity. The parameters sterility and bacterial endotoxins defined in the Sodium Fluoride ^{18}F injection monograph were not executed due to the manual preparations of sodium [^{18}F]fluoride without final sterilization.

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Results and discussion

The results of the analyzed samples from the three experiments (QMA+SCX, SCX+QMA, only QMA), showed that the combination of QMA + SCX was not appropriate due to the result for the parameter approximate pH value that was not within the acceptance criteria. The results of other analyzed parameters, identification, chemical, radiochemical and radionuclide purity were in acceptance criteria (Table 1). On the radiochromatograms from the three experiments only one peak was observed, and the radiochemical purity was determined as 100% (Fig. 1).

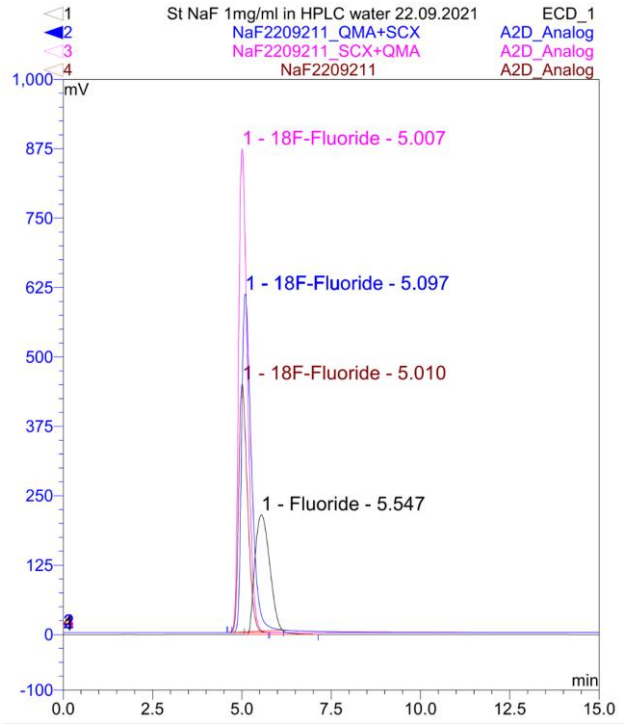

Fig.1 Radiochemical purity of [^{18}F]NaF samples

Table 1. Results of [^{18}F]NaF radiopharmaceutical

Test	QMA+SCX	SCX+QMA	QMA
Approximate pH	1	7	7
Half – life (hours)	1.81	1.84	1.82
Chemical purity (mg/mL)	< 0.425	< 0.425	< 0.425
Radiochemical purity (%)	100	100	100
Radionuclidic purity (%)	$1.02*10^{-05}$	$8.04*10^{-06}$	$1.34*10^{-05}$

The results from the experiment 2 (SCX+QMA) and experiment 3 (only QMA) differ only for the parameter radionuclide purity ($8.04*10^{-06}$% and $1.34*10^{-05}$% respectively). The radionuclidic purity of the final sample of experiment 3 expressed in percentage was in the order of 10^{-5}, which is ten thousand times (10^{4}) less than the defined acceptance criterion (10^{-1}%). Quality control results have shown that the use of an additional SPE cartridge (cation exchange) does not contribute to [^{18}F]NaF purification. Considering this, only the anion exchange cartridge was selected as the optimal cartridge solution for further production and analysis.

Conclusion

This study confirmed that the originally designed and in-house developed production method of sodium [^{18}F]fluoride can be successfully carried out using only a quaternary methyl ammonium anion-exchange cartridge (QMA) as purification cartridge, producing radiopharmaceutical with quality that meets the acceptance criteria defined in the European Pharmacopoeia monograph (Ph. Eur. 01/2008:2100).

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