8° OBI
Workshop sobre Órgãos Artificiais, Biomateriais e Engenharia de Tecidos
October 29-31 | Fortaleza, CE - Brazil

Dedicated Micro-Cartridge for Radionuclide Concentration in Radiopharmaceutical Development and Production

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Keywords: Micro-cartridge; Microfluidic; Radiopharmaceutical; Fluorine-18;

Introduction and objective: Fluorine-18 is a radionuclide widely used in the synthesis of radiopharmaceuticals for Positron Emission Tomography (PET), a non-invasive clinical imaging exam with high sensitivity and specificity in the diagnosis and staging of cancer. However, conventional processes, which involve an aqueous solution with a high percentage of water during the elution step of fluorine-18 and its azeotropic distillation for anhydrous nucleophilic synthesis, negatively impact the radiochemical production yield. Microfluidics offers advantages in the synthesis of radiopharmaceuticals, such as shorter reaction times and surface-to-volume ratio. In this work, we present an alternative synthesis of fluorine-18 radiolabelling without azeotropic drying.

Experimental Procedure: The micro-cartridge is filled with the anion exchange resin Quaternary Methyl Ammonium (QMA), used to trap fluorine-18 (^{18}F). The amount of QMA used was (7.6 ± 0.8) mg (1/16 of the conventional cartridge). The recovery step used an aqueous solution containing only 5% water, with an eluent volume of 100 µL, which is 6 to 10 times less than in the conventional process. The recovered ^{18}F was then used directly in the radiolabelling synthesis of [^{18}F]Fluoromisonidazole ([^{18}F]FMISO) without the need for an azeotropic drying step.

Results and discussion: The micro-cartridge, without the need for preconditioning, showed a trapping efficiency (TE) of (92.1 ± 1.6) % and recovery efficiency (RE) of (94.1 ± 0.6) % using activities above 120 GBq of ^{18}F, which is the first report of RE for a micro-cartridge with such activities. In the nucleophilic fluorination synthesis of ^{18}F to form THP-protected [^{18}F]FMISO without the need for azeotropic drying, a radiochemical conversion (RCC) of 100% was achieved in only 10 minutes of synthesis. In the automated module for the synthesis of [^{18}F]FMISO, the estimated time for the azeotropic drying process and radiolabelling of [^{18}F]FMISO is 22 minutes [1]. It is important to note that in addition to the RCC result, a significant time reduction was achieved in this process compared to the traditional synthesis time.

Conclusions: Therefore, all the results are not only unprecedented in Brazil, but also represent a significant contribution to the entire scientific community, as it is the first report of this radiolabelling synthesis with 100% RCC without the drying step. In this way, the new micro-cartridge represents an innovative tool that paves the way for the future integration of microfluidic chips into conventional cassettes, facilitating the efficient production of radiopharmaceuticals.

References:

[1]T. Kniess et al. “Synthesis of [18F]FMISO, a hypoxia-specific imaging probe for PET, an overview from a radiochemist’s perspective,” *EJNMMI Radiopharm. Chem.*, vol. 8, no. 1, 2023.

Acknowledgments: CNPq INCT-465763/2014-6, Sisfóton 440228/2021-2 and GD 174673/2023-0