World Academy of Science, Engineering and Technology
International Journal of Pharmacological and Pharmaceutical Sciences
Vol:12, No:03, 2018

Implementation of Synthesis and Quality Control Procedures of ^{18}F-Fluoromisonidazole Radiopharmaceutical

Authors : Natalia C. E. S. Nascimento, Mercia L. Oliveira, Fernando R. A. Lima, Leonardo T. C. do Nascimento, Marina B. Silveira, Brigida G. A. Schirmer, Andrea V. Ferreira, Carlos Malamut, Juliana B. da Silva

Abstract : Tissue hypoxia is a common characteristic of solid tumors leading to decreased sensitivity to radiotherapy and chemotherapy. In the clinical context, tumor hypoxia assessment employing the positron emission tomography (PET) tracer ^{18}F-fluoromisonidazole ([^{18}F]FMISO) is helpful for physicians for planning and therapy adjusting. The aim of this work was to implement the synthesis of 18F-FMISO in a TRACERlab® MXFDG module and also to establish the quality control procedure. [^{18}F]FMISO was synthesized at Centro de Desenvolvimento da Tecnologia Nuclear (CDTN/CNEN/Brazil) using an automated synthesizer (TRACERlab® MXFDG, GE) adapted for the production of [^{18}F]FMISO. The FMISO chemical standard was purchased from ABX. 18O- enriched water was acquired from Center of Molecular Research. Reagent kits containing eluent solution, acetonitrile, ethanol, 2.0 M HCl solution, buffer solution, water for injections and [^{18}F]FMISO precursor (dissolved in 2 ml acetonitrile) were purchased from ABX. The [^{18}F]FMISO samples were purified by Solid Phase Extraction method. The quality requirements of [^{18}F]FMISO are established in the European Pharmacopeia. According to that reference, quality control of [^{18}F]FMISO should include appearance, pH, radionuclidic identity and purity, radiochemical identity and purity, chemical purity, residual solvents, bacterial endotoxins, and sterility. The duration of the synthesis process was 53 min, with radiochemical yield of (37.00 ± 0.01) % and the specific activity was more than 70 GBq/µmol. The syntheses were reproducible and showed satisfactory results. In relation to the quality control analysis, the samples were clear and colorless at pH 6.0. The spectrum emission, measured by using a High-Purity Germanium Detector (HPGe), presented a single peak at 511 keV and the half-life, determined by the decay method in an activimeter, was (111.0 ± 0.5) min, indicating no presence of radioactive contaminants, besides the desirable radionuclide (^{18}F). The samples showed concentration of tetrabutylammonium (TBA) < 50µg/mL, assessed by visual comparison to TBA standard applied in the same thin layer chromatographic plate. Radiochemical purity was determined by high performance liquid chromatography (HPLC) and the results were 100%. Regarding the residual solvents tested, ethanol and acetonitrile presented concentration lower than 10% and 0.04%, respectively. Healthy female mice were injected via lateral tail vein with [^{18}F]FMISO, microPET imaging studies (15 min) were performed after 2 h post injection (p.i), and the biodistribution was analyzed in five-time points (30, 60, 90, 120 and 180 min) after injection. Subsequently, organs/tissues were assayed for radioactivity with a gamma counter. All parameters of quality control test were in agreement to quality criteria confirming that [^{18}F]FMISO was suitable for use in non-clinical and clinical trials, following the legal requirements for the production of new radiopharmaceuticals in Brazil.

Keywords : automatic radiosynthesis, hypoxic tumors, pharmacopeia, positron emitters, quality requirements
Conference Title : ICRR 2018 : International Conference on Radiopharmacy and Radiopharmaceuticals
Conference Location : Madrid, Spain
Conference Dates : March 26-27, 2018