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FIRST SYNTEHSIS OF FLT AT CANNIZZARO HOSPITAL OF CATANIA

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BACKGROUND-AIM

^{18}F-Fluoro Thymidine (FLT) is a fluorinated thymidine analog used in PET for the diagnosis and grading of brain tumors, such as gliomas and glioblastomas. In vivo, FLT is phosphorylated by thymidine kinase-1 and is resistant to degradation, being trapped into DNA chains. It is used as a marker of cell proliferation assuming that its trapping is a representation of thymidine incorporation into DNA.
Up to now our center produces FDG and 11C-Methionine for PET/CT brain studies. Since FLT uptake in the normal brain tissue is very low, FLT-PET shows a low background brain image, providing a better tumor/background ratio compared to FDG, and presenting the advantage of a longer half-life compared to ^{11}C-labelled tracers as Methionine.

METHODS

FLT has been synthesized by means of GE FastLab synthesis module, using their commercial cassette. ^{18}F is produced by IBA Cyclotron 18/9. Quality Controls (QCs) are performed on Varian Gas Chromatograph, Dionex HPLC, using radiochemical, UV and electrochemical detectors according to Pharmacopoeia methods and evidences of literature. Synthesis takes place as follows: Cyclotron produced ^{18}F-Fluoride is trapped on an anion exchange resin, washed with carbonate and dried in acetonitrile/water mixture. Addition of precursor (3-N-BOC-5'-O-dimethoxytrityl-3'-O-nosyl-thymidine) and subsequent acetonitrile removal by azeotropic distillation completes the reaction, with a cartridge purification to provide the final product. Sterilization by filtration is used to obtain the injectable solution ready for use.

RESULTS

Three synthesis have been completed in our lab, in order to validate the method. Total synthesis time was around 1 hour, and yield varied from 6,5 to 10,5% EOS. No synthesis failed, nor Radiochemical purity in all the synthesis was higher than 99,5%, being the main contaminant not-bound fluoride. As expected, the main cold impurities detected were cold FLT (Alovudine) and hydrolyzed precursor Stavudine, whose amount however was lower than 0,1 mg/V and 0,1mg/V (being V the maximum injectable volume) respectively. Residual phase-transfer catalyst TBAOH was present in amount under 2,6 mg/V. Acetonitrile content was lower than 0,6 mg/V, while Ethanol (used as excipient) around 6%. a constant pH value of 7 was recorded. All these values were compliant with EU Pharmacopoeia.

CONCLUSION

Preliminary results show a reliable synthesis system, easy to use and able to produce the radiopharmaceutical compound with appropriate quality in a relatively long time. This aspect is not modifiable, therefore it will be necessary to increase cyclotron beam time to obtain higher amount of starting Fluoride (and consequently of FLT). Further tests have to be conducted in order to improve the yield and to fully validate the system. However the encouraging results we obtained show that it will be possible, in the next future, to implement our lab with the production of this new tracer, providing a powerful tool for diagnosis and stading of brain tumors.