Contribution ID: **321** Type: **Verbal**

18F]Flumazenil, Radioligand of the Central Benzodiazepine Receptors: A Systematic Study of Synthesis and Purification Parameters

Thursday, May 15, 2014 9:20 AM (20 minutes)

Positron emission tomography (PET) is an imaging modality that allows in-vivo studies of physiological and biochemical processes on molecular level. Radiolabeled flumazenil analogues are important radiopharmaceuticals for the assessment of the central benzodiazepine receptors (cBZR) density by PET. These receptors play an important role in many neurological and psychiatric disorders, such as epilepsy, panic disorder, dementia, acute stroke, alcoholism. [11C]Flumazenil is a gold standard radioligand for cBZR, however due to the short half-life of carbon-11 (20.4 min) its application is limited by cyclotron-equipped centers.

The fluorine-18 labeled analogue, [18F]flumazenil ([18F]FMZ) presents an advantage due to a longer half-life of radionuclide (109.8 min). Synthesis of [18F]flumazenil by nucleophilic substitution of nitro group of Ro 15-2344 with [18F]fluoride in the presence of phase transfer catalyst (PTC) has been suggested. Using 6-8 mg of labeling precursor provided by Hoffmann La Roche the 18F-incorportaion rate achieved 60% (DMF, 180oC, 30 min) [1]. Selective binding of [18F]flumazenil to cBZR in monkey and human brain has been further demonstrated [1,2]. The factors limiting clinical application of [18F]FMZ belong to relatively low 18F incorporation yield using commercially available nitro-precursors and the losses on the HPLC purification and post-formulation steps, both lowering the radioactivity produced. The aim of this study was to investigate 18F-fluorination step under different conditions and suggest the SPE purification method avoiding time-consuming HPLC purification. [18F]Fluoride was produced via 18O (p,n)18F nuclear reaction in [18O]H2O water target of GE PETtrace cyclotron and synthesis was operated by home-made remote controlled apparatus. [18F]Flumazenil was prepared by heating of 1-4 mg of Ro 15-2344 (Syncom, the Netherlands) in DMF, DMSO or o-DCB at 140-160oC in the presence of different PTC and bases (kryptofix 2.2.2/K2CO3, kryptofix 2.2.2BB/K2CO3 or TBAHCO3). The highest incorporation rate of more than 40% was obtained using kryptofix 2.2.2/K2CO3 (DMF, 15 min) and only 1 mg of Ro 15-2344. In the attempted study using combination of different commercially available SPE cartridges/resins and solvents the conditions to separate both radiochemical and chemical impurities have been identified. As a result the principal possibility to replace HPLC purification with more attractive for automated SPE procedure has been demonstrated. At present the substitution of HPLC by suitable SPE approaches can be considered as a milestone for PET radiochemistry Work is now in progress to optimize all the developed procedures.

[1]. Ryzhikov N.N. et al. Nucl Med and Biol., 2005:32, 109-116.
[2]. Odano I. et al. NeuroImage, 2009:45, 891-902.

Primary author: Dr GOMZINA, Natalia (N.P.Bechtereva Institute of the Human Brain, Russian Academy of Sciences (IHB RAS), St. Petersburg, Russia)

Co-authors: Mrs VAULINA, Daria (N.P.Bechtereva Institute of the Human Brain, Russian Academy of Sciences (IHB RAS), St. Petersburg, Russia); NASIRZADEH, Morteza (N.P.Bechtereva Institute of the Human Brain, Russian Academy of Sciences (IHB RAS), St. Petersburg, Russia); KUZNETSOVA, Olga (N.P.Bechtereva Institute of the Human Brain, Russian Academy of Sciences (IHB RAS), St. Petersburg, Russia)

Presenter: Dr GOMZINA, Natalia (N.P.Bechtereva Institute of the Human Brain, Russian Academy of Sciences (IHB RAS), St. Petersburg, Russia)

Session Classification: Radiopharmaceutical Chemistry, Labelled Compounds 2

Track Classification: Radiopharmaceutical Chemistry, Labelled Compounds