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Preparation and Imaging of [^{124}I]IPT, [^{124}I]β-CIT, [^{124}I]FP-CIT

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1. Introduction

The dopamine transporter is a protein localized presynaptically on dopaminergic nerve terminals. The *in vivo* imaging of the dopamine transporter in the human brain with PET or single photon emission computer tomography (SPECT) may be useful for monitoring degenerative brain disorders such as Parkinson's disease. Within 10 years, several radioligands have been developed mainly for use in *in vitro* studies. For *in vivo* binding to the dopamine transporter, much attention has been given to the development of cocaine analogues based on the phenyltropane moiety, such as 2β-carbomethoxy-3β-(4-chlorophenyl)-8-([Z]-3-iodoprop-en-1-yl)nortropane (IPT)[1], 2β-carbomethoxy-3β-(4-iodophenyl)tropane (β-CIT)[2], *N*-3-fluoropropyl-2β-carbomethoxy-3β-(4-iodophenyl)nortropane (FP-CIT)[3] or the fluoro analogue β-CFT. The structure of β-CIT and FP-CIT allow labeling with ^{123}I in the aromatic ring and IPT allows labeling with ^{123}I in the olefin for SPECT studies or with ^{11}C ($t_{1/2}$ = 20 min) in the *N*-methyl group or with ^{18}F ($t_{1/2}$ = 109.7 min) in the *N*-fluoroalkyl group for PET studies. An advantage with radiolabeled β-CIT and FP-CIT are that direct comparisons can be made between the results of the two imaging techniques, whereas IPT can only be used for SPECT. A problem with the quantity of β-CIT and FP-CIT binding to the dopamine transporter is that the uptake of radioactivity in the dopamine-transporter rich striatum increases with time and does not reach equilibrium within the time of a PET examination[4]. By following the kinetics of [^{123}I]β-CIT with SPECT, a binding equilibrium in the striatum was not reached for more than 18 h. There is a need for a radioligand for the dopamine transporter that gives an equilibrium within the time limit of a PET study (90 to 120 min) and that can be used for quantity of dopamine transporters in the human brain with the high-resolution PET cameras. Recently, new long half-life radioisotope developed for PET such as I-124 ($t_{1/2}$ = 4.18 days). Therefore, our interest in applying I-124 labeling dopamine transporter instead of I-123 labeled for solving problem with the quantity of using SPECT dopamine transporter imaging agent and the kinetics of short half-life positron emission radioisotope for PET.

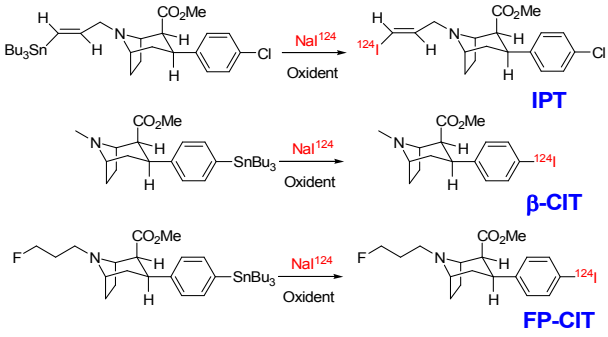
2. Methods and Results

2.1. Synthesis and purification

The precursor of [^{124}I]IPT, [^{124}I]β-CIT and [^{124}I]FP-CIT as well as the reference standard of IPT, β-CIT and FP-CIT use in HPLC was obtained from Future Chem. Radioiodinations of IPT, β-CIT and FP-CIT were electrophilic iododestamrylation. Iodine-124 was produced via the ^{125}Te(p, 2n) ^{124}I nuclear reactions on enriched ^{125}TeO$_2$, respectively, at the MC-50 cyclotron of KIRAMS.

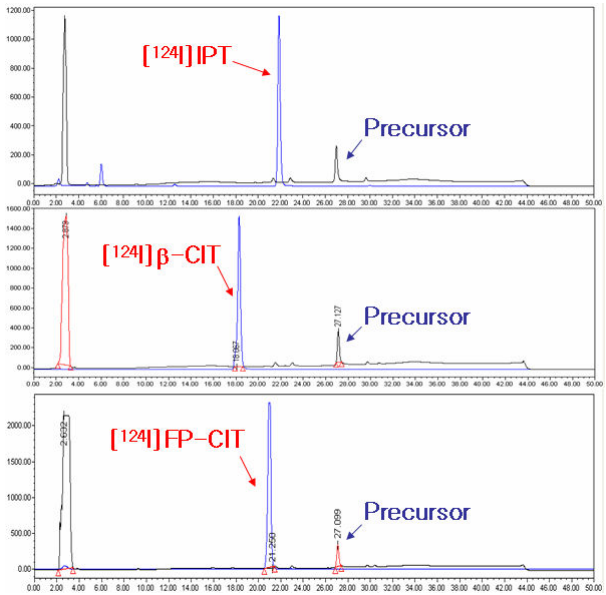
In analogy to a methodology about 20 mg of the tin-precursors were dissolved in 50 μL of EtOH and subsequently 100 μL of 1 N HCl, the radioiodide in 0.01 N NaOH, and 30 μL of 30% H_2O_2 were added and stirred for 3 minutes at room temperature. After 10 min, this reaction mixture was quenched with 100 μL of sat. $NaHSO_3$. Then this solution was pre-purified with using activated C-18 Sep-pack cartridge.

Scheme 1. Radiosynthesis of [^{124}I]IPT, [^{124}I]β-CIT and [^{124}I]FP-CIT



In each case identification and purification of the labelled product was performed by HPLC-separation on a μ-Bondapak C 18 10 μm column (7.8 mm x 300 mm) with 0.1% TEA contained water/EtOH (0-3 min ; 6:4, 3-30 min ; 0:10, 30-40 min ; 0:10, 254 nm, 4 mL/min, *R*t = 21.07 min([^{124}I]IPT), 18.29 min([^{124}I]β-CIT), 20.95 min([^{124}I]FP-CIT) as eluent. After evaporation of the solvent the radiophamaceuticals were dissolved in ethanol and buffer in order to formulate an injectable solution. The product was sterilized by filtration through a 0.2 μm filter. The radiochemical yields of [^{124}I]IPT, [^{124}I]β-CIT and [^{124}I]FP-CIT were 70-85% and the radiochemical purity was ~99 %.

Fig 1. [^{124}I]IPT, [^{124}I]β-CIT and [^{124}I]FP-CIT of HPLC



2.2. Small animal imaging

Brain image of [^{124}I]IPT, [^{124}I]β-CIT and [^{124}I]FP-CIT was studied in adult Sprague Dowley rat (240±10 g). Rat tail vein was catheterized with 24 gauge IV catheter. Catheterized rats were anesthesized with 1~1.5 % isoflurane using gas anesthesia system during PET scans. Following blockade of thyroid with injection of 1 mL perchlorate (5 mg/mL), catherized rat under anesthesia was placed on the bed of microPET R4 scanner. Immediately after the injection, IPT, CIT, FP-CIT (37 MBq respectively) up to 1 mL volume for 30 seconds by microinjector, PET acquisition was started for 3 hours. For finding a optimal imaging time, delayed image was acquired at a interval of 3~6 hours for one day.

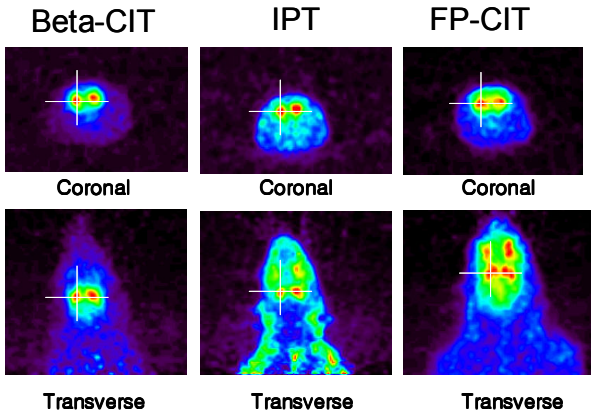


Fig 2. microPET R4 imaging of [^{124}I] -CIT, [^{124}I]IPT and [^{124}I]FP-CIT in normal rats. Image shows the coronal and transverse cross-section (The cross-hair is placed on the left striatum). Optimal scan time after injection of CIT, IPT and FP-CIT was 6, 2 and 2 hrs, respectively.

2.3. Results

Iodine-124 was produced 100 mCi/batch via the ^{125}Te(p, 2n) ^{124}I nuclear reactions on enriched $^{125}TeO_2$. The purification of the labelled product was performed by HPLC-separation. The radiochemical yields of [^{124}I]IPT, [^{124}I]β-CIT and [^{124}I]FP-CIT were 70-85% and the radiochemical purity was ~99 %.

In the adult normal rat brain imaging, both the left and right striatum were clearly visible. The optimal scan time of [^{124}I]IPT, [^{124}I]β-CIT and [^{124}I]FP-CIT were 2, 6, 2 hours after injection, respectively.

3. Conclusion

Production of Iodine-124 was 100 mCi/batch via the ^{125}Te(p, 2n) ^{124}I nuclear reactions on enriched $^{125}TeO_2$. Obtained very high radiochemical yields and purities through the HPLC purification. The preliminary results show that PET imaging with I-124 labeled radiotracer could be useful in pre-clinical study for new drug development and disease model evaluation.

REFERENCES

1. Goodman M. M., Kung M. P., Kabalka G. W., Kung H. F., Switzert R. *J. Med. Chem.*, **1994**, *37,* 1535-1542.
2. Coenen H.H., Dutschka K., Muller S.P., Geworski L., Farahati J., Reiners C. *Nucl. Med. Biol.*, **1995**, *22*, 977-984.
3. Chaly T., Dhawan V., Kazumata K, Antonini A., Margouleff C., Dahl J. R., Belakhlef A., Margouleff D., Yee A., Wang S., Tamqnan G., Neumeyer J. L., Eidelber D. *Nucl. Med. Biol.*, **1996**, *23*, 999-1004.
4. Farde L., Halldin C., Miiller L., Suhara T., Karlsson P. and Hall H. *Synapes*, **1994**, *16*, 93-103.