3-β-(4-Iodophenyl)tropane-2-β-carboxylic acid 2-[^{18}F]fluoroethyl ester

[^{18}F]FE@CIT

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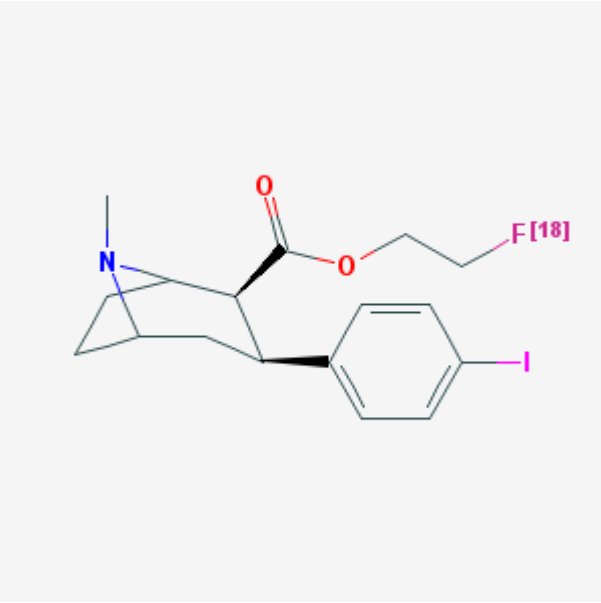
Chemical name:	3-β-(4-Iodophenyl)tropane-2-β-carboxylic acid 2-[^{18}F]fluoroethyl ester
Abbreviated name:	[^{18}F]FE@CIT
Synonym:	
Agent Category:	Compound
Target:	Dopamine transporter
Target Category:	Binding
Method of detection:	PET
Source of signal:	^{18}F
Activation:	No
Studies:	• *In vitro* • Rodents



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Background

[PubMed]

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Dopamine, a neurotransmitter, plays an important role in the mediation of movement, cognition, and emotion. Parkinson's disease (PD) is associated with a loss of dopamine-containing neurons in the striatum, resulting in a loss of dopamine transporters (DAT) in the presynaptic nerve terminals (1, 2). Reduced DAT density is inversely correlated with the severity of motor dysfunction in PD patients. Several cocaine analogs have been developed for the evaluation of DAT density in the neurons of PD patients. Radiolabeled 2-β-carboxymethoxy-3-β-(4-iodophenyl)tropane (β-CIT) and *N*-(3-fluoropropyl)-2β-carbomethoxy-3β-(4-iodophenyl)nortropane (FP-CIT) have been used for brain imaging (3-6). Because of the short physical half-life of ^{11}C-labeled analogs, equilibrium conditions are difficult to achieve in positron emission tomography (PET) measurements. [^{123}I]β-CIT was studied with single-photon emission computed tomography (SPECT), which showed slow tracer uptake kinetics (7, 8). This led to the development of 3-β-(4-iodophenyl)tropane-2-β-carboxylic acid 2-[^{18}F]fluoroethyl ester ([^{18}F]FE@CIT) for PET brain imaging in PD patients (9).

Synthesis

[PubMed]

[^{18}F]FE@CIT was synthesized by reaction of 3-β-(4-iodophenyl)tropane-2-β-carboxylic acid with 2-bromo-1-[^{18}F]fluoroethane ([^{18}F]BFE) for 20 min at 150°C (9). [^{18}F]BFE was prepared by nucleophilic fluorination of 2-bromoethyl triflate using the standard [^{18}F]KF Kryptofix complex for 10 min at 100°C. The radiochemical yields of [^{18}F]FE@CIT were >90% (based on [^{18}F]BFE) with a radiochemical purity of >99% and specific activity of >416 GBq/μmol (11.2 Ci/μmol) at the end of synthesis.

In Vitro studies: Testing in Cells and Tissues

[PubMed]

In vitro [^{18}F]FE@CIT autoradiography of frozen brain sections obtained from rats was performed by Ettlinger et al. (10) The striatum exhibited a higher radioactivity level than the cortex. Gu et al. (11) showed that binding affinities (K_i) of FE@CIT at DAT, serotonin transporter (SERT), and norepinephrine transporter (NET) were 0.93, 4.02, and 116 nM, respectively. FE@CIT exhibited a higher DAT affinity than FP-CIT for DAT (8.29 nM) and more selective affinity for DAT over SERT and NET.

Animal Studies

Rodents

[PubMed]

Mitterhauser et al. (9) performed biodistribution studies in rats (n = 4/group) at 5, 15, 30, 60, and 120 min after injection of 1.25–2.23 MBq (0.033–0.06 mCi). At 60 min after injection, the radioactivity in the striatum was 1.23% injected dose/g (ID/g), which was

greater than the thalamus (0.42% ID/g) and cerebellum (0.33% ID/g). The highest striatum/cerebellum ratio was 3.73, and the highest thalamus/cerebellum ratio was 1.65. The other organs with high accumulation were the kidney (3.86% ID/g), liver (3.06% ID/g), and lung (0.86% ID/g), whereas the bowels (0.54% ID/g), bone (0.14% ID/g), blood (0.15% ID/g), and muscle (0.16% ID/g) exhibited little or low accumulation at 60 min. There were continuous increases in radioactivity in the kidneys and liver from 5 min to 120 min. No blocking experiments were performed.

Other Non-Primate Mammals

[PubMed]

No publication is currently available.

Non-Human Primates

[PubMed]

No publication is currently available.

Human Studies

[PubMed]

No publication is currently available.

Human Studies

MH34006, MH47370, NS40587

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