2-[2-([*O*-^{11}C]Tolyl)ethyl]-4,5-dihydro-1*H*-imidazole

[^{11}C]TEIMD

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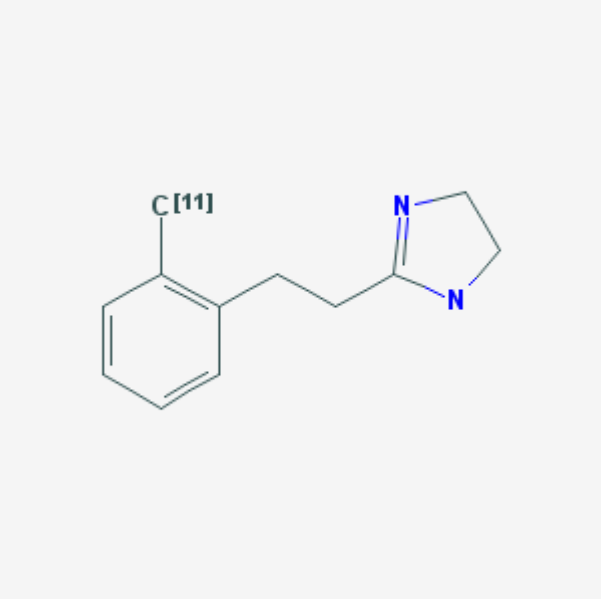
Chemical name:	*2*-[2-([*O*-^{11}C]Tolyl)ethyl]-4,5-dihydro-1*H*-imidazole
Abbreviated name:	[^{11}C]TEIMD
Synonym:	
Agent category:	Compound
Target:	I_2-imidazoline receptor (I_2R)
Target category:	Receptor
Method of detection:	Positron emission tomography (PET)
Source of signal:	^{11}C
Activation:	No
Studies:	• *In vitro* • Rodents



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Background

[PubMed]

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Two major imidazoline binding sites (I_1R and I_2R) have been identified (1, 2). The I_1R and I_2R exhibit high affinities for clonidine and idazoxan, respectively. Clonidine and its analogs mediate effects independent of α_2-adrenoceptor at the IR receptors. IR receptors are widely distributed in the central and peripheral nervous systems and in various organs such as the pancreas, liver, kidney, lung, and heart (3-6). I_1R is associated with hypertension (7), whereas I_2R is associated with depression (8), Alzheimer's disease (9), Parkinson's disease (10), Huntington's disease (10), and glial cell tumors (11). High densities of I_2R have been observed in the arcuate nucleus, interpeduncular nucleus, pineal gland, and ventricles in human brain (12). The I_2R gene has not been identified. Tesson et al. (13) showed that I_2R is localized to the mitochondrial outer membrane of the human and rabbit liver. Gentili et al. (14) showed that *2*-[2-(*O*-tolyl)ethyl]-4,5-dihydro-1*H*-imidazole (TEIMD) has a high and selective affinity for I_2R. *2*-[2-([*o*-^{11}C]Tolyl)ethyl]-4,5-dihydro-1*H*-imidazole ([^{11}C]TEIMD) was evaluated as a PET probe for imaging of I_2R in the peripheral tissues (15).

Related Resource Links:

- Chapters in MICAD (Imidazoline receptors)
- Gene information in NCBI (I_1R, α_2-adrenoceptors)
- Articles in OMIM (I_1R, α_2-adrenoceptors)
- Clinical trials (Clonidine)
- Drug information in FDA (Clonidine)

Synthesis

[PubMed]

[^{11}C]TEIMD was synthesized remotely via a reaction of [^{11}C]methyl iodine (produced from [^{11}C]CO_2) with the tributylsannyl precursor in the presence of tris(dibenzylideneacetone)dipalladium(0), $CuCl_2$, potassium carbonate and tri(*O*-tolyl)phosphine in dimethylformamide at 80°C for 5 min (14). [^{11}C]TEIMD was purified with high-performance liquid chromatography with a radiochemical yield of 13.6 ± 4.4% (n = 3) from [^{11}C]CO_2 at end of bombardment (EOB). The radiochemical purity was >95%, and the specific activity was 79 ± 40 GBq/μmol (2.1 ± 1.1 Ci/μmol) at end of synthesis. Total time of synthesis was 30 min from EOB.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

On the basis of *in vitro* competition binding studies, Gentili et al. (14) reported inhibition constant (K_i) values for TEIMD of 1.7 nM for I_2R, >2,000 nM for I_1R and 560 nM for α_2-adrenoceptor. cLogD (pH 7.4) value for TEIMD was 1.73.

Animal Studies

Rodents

[PubMed]

Ex vivo biodistribution of 9.1-13.4 MBq (0.25-0.36 mCi) [^{11}C]TEIMD was studied in normal mice (n = 4/group) at 5, 15, 30 and 60 min after injection (15). The tissue with the highest accumulation at 5 min after injection was the liver (10% injected dose/gram (ID/g)), followed by the lung (6% ID/g), kidney (5% ID/g), small intestine (5% ID/g), pancreas (5% ID/g), heart (3% ID/g), spleen (2% ID/g), muscle (2% ID/g), blood (1% ID/g), and brain (0.1% ID/g). All these tissues showed moderate to rapid washout. Co-injection of I_1R inhibitor moxonidine (1 mg/kg) and I_2R inhibitor BU224 (1 mg/kg) resulted with little inhibition of radioactivity in the liver and pancreas at 30 min after injection. Hence, [^{11}C]TEIMD is not suitable as a PET agent for imaging I_2R in the peripheral tissues.

Other Non-Primate Mammals

[PubMed]

No publications are currently available.

Non-Human Primates

[PubMed]

No publications are currently available.

Human Studies

[PubMed]

No publications are currently available.

References

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