[^{11}C]Triphenylmethylphosphonium

[^{11}C]TPMP

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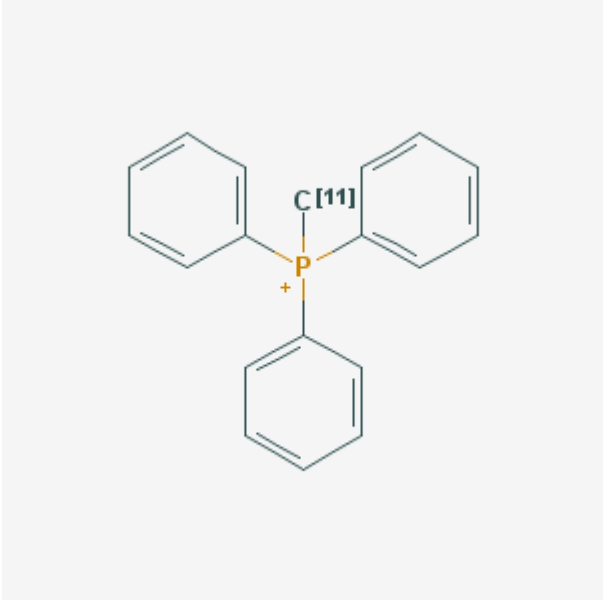
Chemical name:	[^{11}C]Triphenylmethylphosphonium
Abbreviated name:	[^{11}C]TPMP
Synonym:	
Agent category:	Compound
Target:	Mitochondria
Target category:	Lipophilic cation, membrane potential
Method of detection:	PET
Source of signal:	^{11}C
Activation:	
Studies:	• Rodents • Non-primate non-rodent mammals



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Background

[PubMed]

Lipophilic cations are capable to pass through biological membranes by passive diffusion into the cytoplasm and mitochondria of cells in response to a large negative plasma- and mitochondrial- membrane potentials. ^{99m}Tc-2-methoxyisobutylisonitrile (^{99m}Tc-MIBI)

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and ^{99m}Tc-tetrofosmin are delocalized lipophilic cations, which are rapidly taken up into cells being driven by metabolic demand and membrane potential (1-4). They are used as myocardial perfusion single photon emission computed tomography (SPECT) as well as tumor imaging agents. However, the high accumulation of technetium tracers in the lung and liver may hinder the detection of flow abnormalities in the myocardium.

Triphenylmethylphosphonium is a lipophilic cation and has been used to measure membrane potentials of cells *in vitro* (5). [^{11}C]Triphenylmethylphosphonium ([^{11}C]TPMP) has been investigated as a positron emission tomography (PET) agent for myocardial and tumor imaging to provide a better temporal and spatial resolution than SPECT.

Related Resource Links:

- Chapters in MICAD (Lipophilic cation)
- Clinical trials (^{99m}Tc-MIBI)
- Drug information in FDA (^{99m}Tc-MIBI)

Synthesis

[PubMed]

[^{11}C]TPMP was prepared by reacting [^{11}C]methyl iodide with triphenylphosphonium with a radiochemical yield of 9-13% (based on [^{11}C]CO_2) and specific activities of 15-33 GBq/μmol (400-900 mCi/μmol) at end of synthesis (6). The total synthesis time was 30 min.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

No publication is currently available.

Animal Studies

Rodents

[PubMed]

Biodistribution studies in rats injected with 0.037-0.111 MBq (1-3 μCi) [^{14}C]TPMP were performed by Fukuda et al. (6) showing high accumulation of radioactivity in the heart (3.05 ± 0.16% injected dose (ID) at 2 min and 4.14 ± 0.83%ID at 60 min post injection. The bulk of accumulation was in the lungs, liver, intestine, and kidneys at 2 min. Clearance of radioactivity occurred at 60 min for all tissues except the heart. The heart/blood ratios were 31 at 2 min, 50 at 10 min, 93 at 30 min and 154 at 60 min. *Ex vivo* whole-body autoradiographic studies of rats at 30 and 120 min showed high radioactivity

in the myocardium, small intestine and urinary bladder with little radioactivity in the heart cavity, brain and spinal cord.

Other Non-Primate Mammals

[PubMed]

Fukuda et al. (6) performed PET imaging measurements of [^{11}C]TPMP binding in the heart of one dog injected intravenously with 666 MBq (18 mCi) of [^{11}C]TPMP. PET scans showed distinct accumulation of [^{11}C]TPMP in the myocardium. Within the time interval between 20 and 60 min after injection, the radioactivity retained in the heart was 0.045%ID/ml and 0.049%ID/ml, respectively. The heart/blood ratios were 40 at 20 min and 74 at 60 min.

Krause et al. (7) performed PET imaging in 4 mongrel dogs to study extraction fraction and uptake measurements of [^{11}C]TPMP. Under normal flow conditions [^{11}C]TPMP uptake reached a maximum within the first 10 min after injection and remained constant during the entire observation period of 80 min. Over the same time period, the heart/blood ratio was 46-106, and the heart/lung ratio 14. Following permanent occlusion of the left anterior descending coronary artery, [^{11}C]TPMP uptake in the normally perfused myocardium also reached a maximum at 10 minutes after injection, whereas in the infarcted area there was no significant accumulation of [^{11}C]TPMP. For a time period of 80 min the noninfarcted/infarcted myocardium ratio was 12. Extraction was measured in dogs with a double isotope method using ^{99m}Tc-HSA as the reference tracer. The extraction fraction was 91% at a flow of 0.69 ml/min/g. As flow increased to five-fold (3.42 ml/min/g) following administration of adenosine, extraction fell to 61%. Following coronary artery occlusion, the [^{11}C]TPMP content in the myocardium was highly correlated ($r = 0.93$, $p < 0.01$) with the microsphere determined regional myocardial blood flow.

Madar et al. (8) performed [^{11}C]TPMP PET imaging in 3 mongrel dogs bearing glioma tumor cells in the brain. [^{11}C]TPMP exhibited enhanced uptake and prolonged retention in canine brain glioma tumor cells within 20-95 min. ^{68}Ga-EDTA exhibited an enhanced uptake and a gradual washout from the tumor tissue, indicating that the blood-brain barrier was not intact. The tumor/normal brain uptake ratio at 55 to 95 min after injection was 47.5 ± 17.6 for [^{11}C]TPMP and 8.1 ± 1.9 for ^{68}Ga-EDTA. Qualitative comparison with histological sections showed that [^{11}C]TPMP enhanced uptake was restricted to the tumor area.

Non-Human Primates

[PubMed]

No publication is currently available.

Human Studies

[PubMed]

No relevant publication is currently available.

References

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