18-[^{18}F]Fluoro-4-thia-palmitate

[^{18}F]FTP

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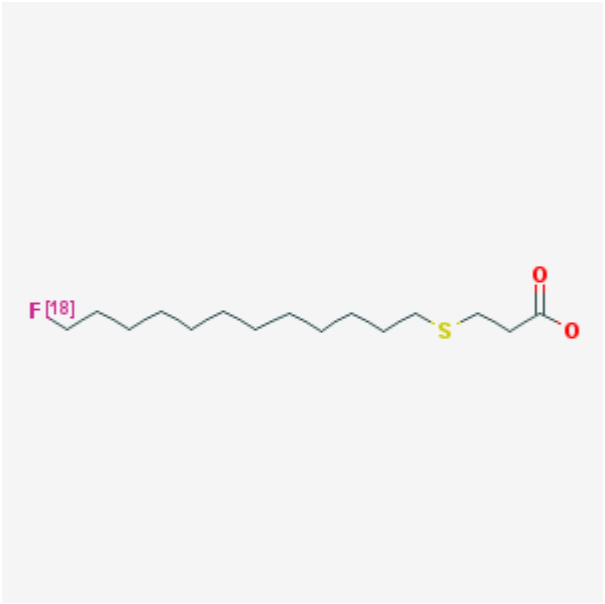
Chemical name:	18-[^{18}F]Fluoro-4-thia-palmitate
Abbreviated name:	[^{18}F]FTP
Synonym:	
Agent category:	Compound
Target:	Fatty acid oxidation (FAO) enzymes
Target category:	Enzyme
Method of detection:	Positron emission tomography (PET)
Source of signal:	^{18}F
Activation:	No
Studies:	• *In vitro* • Rodents • Non-primate non-rodent mammals



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Background

[PubMed]

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β-Oxidation of long-chain fatty acids is the major (60%–80%) aerobic process for energy production in the heart, liver, and skeletal muscle. Abnormalities of fatty acid oxidation (FAO) are associated with several cardiovascular diseases, neurodegeneration, fatty liver, and diabetes (1-5). Myocardium has a high mitochondrial content because of high energy usage. Carnitine palmitoyltransferases (CPT1 and CPT2) mediate transfer of fatty acids into the mitochondrial matrix for β-oxidation (6, 7). Various radiolabeled, thia-substituted, fatty acid analogs have been found to be metabolically trapped in the myocardial mitochondria (8-10). 4-Thia fatty acids are oxidized in the mitochondria to 4-thia-enoyl-CoAs, which cannot be further metabolized and trapped (protein-bound) in the mitochondria. DeGrado et al. (11, 12) have synthesized 18-[^{18}F]fluoro-4-thia-palmitate ([^{18}F]FTP) for evaluation as a positron emission tomography (PET) agent of FAO.

Related Resource Links:

- Chapters in MICAD
- Gene information in NCBI (CPT1)
- Articles in OMIM
- Clinical trials (CPT1)

Synthesis

[PubMed]

[^{18}F]FTP was prepared as described by DeGrado et al. (13). [^{18}F]Fluoride/Kryptofix 2.2.2/K_2CO_3 and methyl-16-iodo-4-thia-hexadecanoate were heated in acetonitrile for 15 min at 85°C, followed by hydrolysis with KOH for 4 min at 90°C. [^{18}F]FTP was purified with high-performance liquid chromatography with radiochemical yields of 25%–60% (decay-corrected) and a radiochemical purity of >99%. Specific activity of [^{18}F]FTP was >74.0 GBq/μmol (2.0 Ci/μmol) at the end of synthesis.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

DeGrado et al. (13) performed perfusion studies with isolated rat hearts (n = 5 per group) in normoxic (95% O_2) and hypoxic (35% O_2) conditions. [^{18}F]FTP was administered at the aortic root. The fractional tracer metabolic rate (FR_{FTP}) was 1.45 ± 0.39 mL/min per g under normoxic conditions and 0.73 ± 0.16 mL/min per g under hypoxic conditions. There was a reduction of 50% in the hypoxic group relative to the normoxic group. The FR_{FTP} was ~60% of the palmitate oxidation rate in these two conditions.

Animal Studies

Rodents

[PubMed]

DeGrado et al. (12) performed *ex vivo* biodistribution studies of [^{18}F]FTP in rats. [^{18}F]FTP accumulated mainly in the heart, liver, bone, and kidney with 0.32 ± 0.17% injected dose (ID)/g, 1.15 ± 0.16% ID/g, 0.24 ± 0.07% ID/g, and 0.25 ± 0.04% ID/g, respectively, at 30 min after injection. Retention of [^{18}F]FTP in the heart was moderate with 0.17 ± 0.05% ID/g at 120 min, whereas there was a slight washout in the liver and kidney. Bone accumulation was approximately one-fold higher at 120 min. Pretreatment with the CPT1 inhibitor etomoxir (40 mg/kg, 120 min before [^{18}F]FTP injection) reduced the radioactivity level in the heart by 82% at 30 min after injection with little inhibition in the other organs. Folch-type analysis of the excised hearts showed that 80% of [^{18}F]FTP radioactivity was protein-bound. Pretreatment with etomoxir reduced the protein-bound radioactivity to 10%. The heart/blood, heart/lung, heart/brain, and heart/muscle ratios were 7, 3, 10, and 10, respectively, at 120 min after injection.

Other Non-Primate Mammals

[PubMed]

Whole-body PET imaging in two swine showed that [^{18}F]FTP accumulated mainly in the heart, liver, and kidneys with low accumulation in the bone over an imaging period of 3 h (13). Good myocardial images were observed at 10–20 min after injection with little interference from the lung and liver. Myocardium/blood and myocardium/lung ratios were 7 and 8, respectively, at 20 min after injection. Myocardium clearance half-time of radioactivity was 5 h, whereas the clearance half-time was 50 min for the liver.

Non-Human Primates

[PubMed]

No publication is currently available.

Human Studies

[PubMed]

No publication is currently available.

NIH Support

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References

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