1-[^{18}F]Fluoro-3,6-dioxatetracosane

[^{18}F]SteP2

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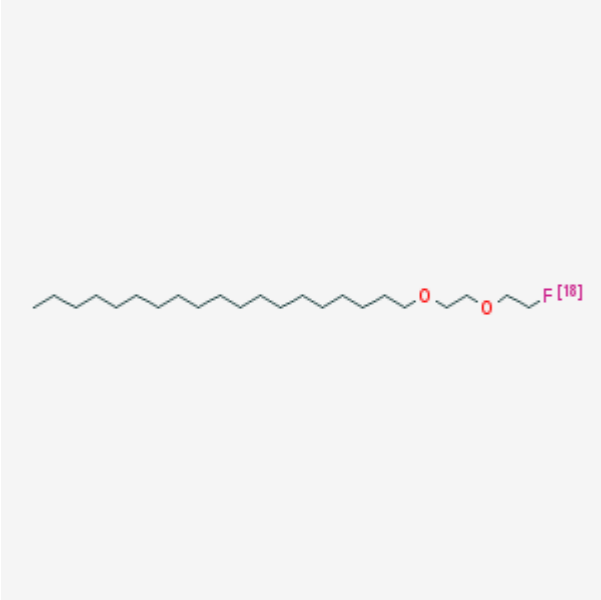
Chemical name:	1-[^{18}F]Fluoro-3,6-dioxatetracosane
Abbreviated name:	[^{18}F]SteP2
Synonym:	[^{18}F]7a
Agent Category:	Compound
Target:	Liposomes
Target Category:	Non-targeted
Method of detection:	Positron emission tomography (PET)
Source of signal / contrast:	^{18}F
Activation:	No
Studies:	• *In vitro* • Rodents



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Background

[PubMed]

Liposomes may be characterized as artificial vesicle-like structures possessing an inner hydrophilic core surrounded by one or more outer hydrophobic bilayer membrane(s) that are composed of various natural or synthetic lipids, including phospholipids (1).

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Liposomes are used as drug delivery vehicles because the hydrophilic core can entrap a variety of compounds such as anti-cancer, anti-fungal, or photoactive drugs, or even nucleic acids and their derivatives for gene therapy (2-4). Therefore, it is important to evaluate the distribution of these drug delivery vesicles in an *in vivo* system using a non-invasive technique. 2-[^{18}F]-2-Deoxy-2-fluoroglucose has been used to investigate the *in vivo* biodistribution of liposomes in tumor-bearing mice with the use of photon emission tomography (PET), but the synthesis of these labeled liposomes was inefficient and required much handling by the operator (5). More recently, Marik et al. investigated the biodistribution of liposomes encapsulating [^{18}F]fluorodipalmitin, but the method used to generate the labeled liposomes is not suitable to label preformed liposomes (6). Urakami and colleagues developed a solid-phase transition method to generate a novel ^{18}F-labeled probe, 1-[^{18}F]fluoro-3,6-dioxatetracosane ([^{18}F]SteP2 or [^{18}F]7a), which can be used in a single-step process for the rapid labeling of preformed liposomes, and the investigators used PET to study the biodistribution of [^{18}F]SteP2 in normal mice (7). In another study, the distribution of [^{18}F]SteP2-labeled, liposome-encapsulated hemoglobin (LEH) in rat brains under ischemic conditions was investigated by Urakami and colleagues (8).

Synthesis

[PubMed]

The synthesis of [^{18}F]SteP2 was described by Urakami and colleagues (7). Briefly, compound 7a was prepared from the corresponding alcohol of 3,6-dioxatetracosane using (diethylamino)sulfur fluoride (7). The agent was labeled with [^{18}F] using a nucleophilic substitution reaction by refluxing the sulfonate of compound 7a with a mixture of [^{18}F]potassium fluoride, 4,7,13,16,21,24-Bexaoxa-1,10-diazabicyclo[8,8,8]hexacosane, and acetonitrile using a method modified from that of Harada et al. (9) as described by Urakami and colleagues (7). The radiochemical yield, purity, storage conditions, and specific activity of [^{18}F]SteP2 were not reported.

Liposomes of three different sizes (90, 170, and 570 nm) were labeled with [^{18}F]SteP2 by the solid-phase transition method (7). To achieve this, [^{18}F]SteP2 was dried into a thin film in a test tube. The three different liposomes were respectively added to the dried compound at a molar ratio of 100:1 (lipid:[^{18}F]SteP2) and incubated for 15 min at 65°C. The labeled liposomes were ultracentrifuged to remove any unincorporated [^{18}F]SteP2, and the various fractions (labeled liposomes, supernatant, and any precipitate) were quantified with high-performance liquid chromatography. On the basis of four separate determinations, the liposome labeling efficiency with [^{18}F]SteP2 was ~85%.

The stability of [^{18}F]SteP2-labeled liposomes was determined by exposing them to 50% fetal bovine serum for 1 h at 37°C (7). Under these conditions, amphiphilic compounds such as [^{18}F]SteP2 that are incorporated to the lipid bilayer through weak hydrophobic interactions are known to transfer from the liposome to the high-density lipoproteins present in the serum. The liposomes and the lipoproteins in the serum were fractionated with gel filtration chromatography, and the amount of label remaining bound to the

liposomes was determined. Under these experimental conditions, ~90% of the label was reported to be bound to the liposomes.

In another study, [18F]SteP2-labeled LEH was prepared and labeled using the procedures described above (8). Labeling efficiency for LEH was reported to be 46.4 ± 4.8%, but the radiochemical purity, stability, and specific activity of [18F]SteP2 LEH were not reported.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

No references are currently available.

Animal Studies

Rodents

[PubMed]

The biodistribution of [18F]SteP2-labeled liposomes of different sizes was studied in normal mice (7). The animals (number of animals per group was not reported) were respectively injected with free [18F]SteP2 and the labeled liposomes through the tail vein. Whole-body imaging of the injected animals was performed at various time points between 1 and 60 min after the injection. Whole-body imaging showed that the larger the size of the labeled liposome, the higher the radioactivity that accumulated in the spleen. With free [18F]SteP2, the radioactivity accumulated primarily in the kidneys immediately after the injection and was subsequently excreted in the urine.

To investigate accumulation of the labeled liposomes in various organs of the animals, the mice were euthanized after imaging, and the radioactivity accumulated in all the major organs was determined. This study revealed that radioactivity from free [18F]SteP2 and the labeled liposomes had accumulated mainly in the blood (~25% of injected dose/gram tissue (% ID/g)), liver (~20% ID/g), spleen (10–15% ID/g), and kidneys (~2.5% ID/g) at 60 min after administration of the radiotracers.

In another study, Urakami and colleagues investigated the distribution of [18F]SteP2-labeled LEH in rat brains under ischemic conditions (8). To confirm absence of blood flow in the ischemic region of the rat brains under *in vivo* conditions, imaging was performed after the administration of radioactive oxygen–labeled water. Twenty minutes after the ischemic conditions were confirmed, the animals were injected with labeled LEH and dynamic imaging was performed continuously for the next 60 min. Initially, little signal was observed in the ischemic brain area; however, during the next 60 min the radioactivity gradually increased in the cerebral cortex, but no detectable signal was obtained from the basal ganglia ischemic core, which indicated that, compared with the basal ganglia, the cerebral cortex was selectively protected. With results obtained from these studies, the investigators concluded that PET imaging could be used to investigate the distribution of [18F]SteP2-labeled, liposome-encapsulated drugs in small animals (8).

Other Non-Primate Mammals

[PubMed]

No references are currently available.

Non-Human Primates

[PubMed]

No references are currently available.

Human Studies

[PubMed]

No references are currently available.

Supplemental Information

[Disclaimers]

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