(R,S)-anti-1-Amino-2-[^{18}F]fluorocyclopentyl-1-carboxylic acid

anti-2-[^{18}F]FACPC

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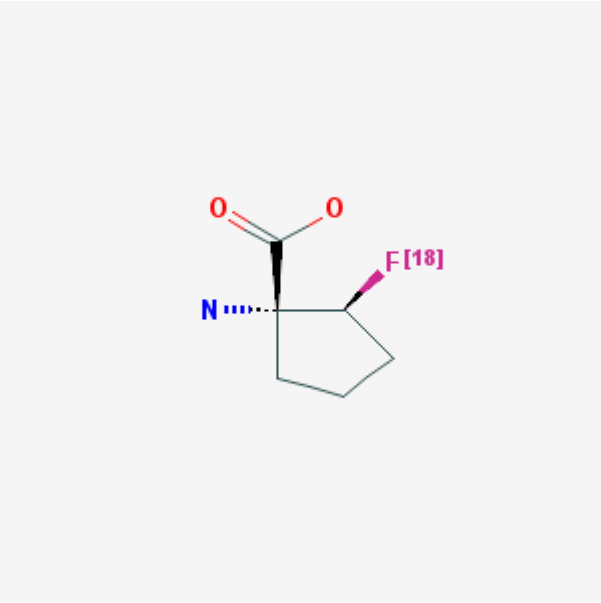
Chemical name:	*(R,S)-anti*-1-Amino-2-[^{18}F]fluorocyclopentyl-1-carboxylic acid
Abbreviated name:	*anti*-2-[^{18}F]FACPC, [^{18}F]FACPC
Synonym:	
Agent category:	Compound
Target:	L-type and A-type amino acid transporters
Target category:	Amino acid transporters
Method of detection:	Positron emission tomography (PET)
Source of signal:	^{18}F
Activation:	No
Studies:	• *In vitro* • Rodents • Humans



Click on the above structure for additional information in PubChem.

Background

[PubMed]

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A variety of ^{11}C- and ^{18}F-labeled amino acids have been studied for potential use in positron emission tomography (PET) oncology (1, 2). Most brain tumors show an increased uptake of amino acids as compared with normal brain tissue (3). These amino acids are composed of naturally occurring amino acids, such as L-[^{11}C]leucine, L-[^{11}C]methionine, and L-[^{11}C]tyrosine, and non-natural amino acids, such as [^{11}C]aminoisobutyric acid, [^{11}C]1-aminocyclopentane-1-carboxylic acid ([^{11}C]ACPC), and [^{11}C]1-aminocyclobutane-1-carboxylic acid. ^{123}I-Labeled amino acids are also used in imaging in oncology (4-6). The natural amino acids are taken up by tumor cells through an energy-independent L-type amino acid transporter system and retained in tumor cells because of their higher than normal metabolic pathways, including incorporation into proteins (4). L-[^{11}C]Methionine and [^{18}F]fluorotyrosine have been widely used in the detection of tumors, but are not approved by the FDA. On the other hand, the non-natural amino acids are not metabolized but are taken up through both the L-type transporter and the energy-dependent A-type transporter (7). Therefore, they can accumulate intracellularly in high concentrations. In this chapter, *(R,S)-anti*-1-Amino-2-[^{18}F]fluorocyclopentyl-1-carboxylic acid (*anti*-2-[^{18}F]FACPC), a fluorinated analog of [^{11}C]ACPC, was shown to have a high tumor/brain ratio in mice (8). However, *anti*-2-[^{18}F]FACPC exhibited unfavorable imaging characteristics for detection of pelvic recurrent prostate carcinoma in five patients because of high blood level at 5 min and high urinary bladder level at 20 min (9).

Related Resource Links:

- Chapters in MICAD
- Gene information in NCBI (L-type amino acid transporter, A-type amino acid transporter)
- Articles in Online Mendelian Inheritance in Man (OMIM) (Amino acid transporters)
- Clinical trials (Amino acid transporters)
- Drug information in FDA (Amino acid transporters)

Synthesis

[PubMed]

Nucleophilic fluorination of *syn*-3-(*N*-(tert-butoxycarbonyl)amino)-4-cyclopentane-1,2,3-oxathiazolidine-4-carboxylic acid tert-butyl ester 2,2-dioxide with K[^{18}F]F/Kryptofix2.2.2 was performed for 10 min at 110°C (8). Subsequent acid hydrolysis for 10 min at 110°C and purification provided a radiosynthesis yield of 39 ± 8% (decay-corrected, $n = 4$) of *anti*-2-[^{18}F]FACPC at the end of synthesis. A radiochemical purity of 99% was obtained. The total synthesis time was 60 min from the end of bombardment. The specific activity of *anti*-2-[^{18}F]FACPC was not reported.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

anti-2-[^{18}F]FACPC showed a fast uptake into rat 9L gliosarcoma tumor cells in culture with 6.33 ± 0.47% injected dose (10)/5 × 10^5 cells (n = 3) at 30 min of incubation (8). The uptake was reduced by 71%, 38%, and 65% by the presence of 10 mM 2-aminobicyclo[2.2.1]heptane-2-carboxylic acid (L-type transporter inhibitor), *N*-methyl-α-aminoisobutyric acid (A-type transporter inhibitor), and a mixture of alanine, cysteine, and serine (ACS), respectively. The data suggest that *anti*-2-[^{18}F]FACPC is a predominantly L-type transporter substrate with some affinity to the A-type transporter.

Animal Studies

Rodents

[PubMed]

Ex vivo biodistribution studies of *anti*-2-[^{18}F]FACPC were performed in rats (n = 5/group) implanted intracerebrally with 9L gliosarcoma (8). Accumulation of *anti*-2-[^{18}F]FACPC in the tumors was 0.57, 1.68, 1.24, and 0.98% ID/g at 15, 30, 60, and 120 min after injection, respectively. The accumulation in the contralateral brain tissue was ~0.11% ID/g at these time points. The tissue with the highest accumulation at 30 min after injection was the kidney (3.44% ID/g), followed by the pancreas (2.91% ID/g), lung (1.13% ID/g), and liver (0.63% ID/g). The accumulation in other tissues (heart, spleen, muscle, bone) was low (<0.5% ID/g). The tumor/brain and tumor/muscle ratios were 10–13 and ~5 at 30 min and 120 min, respectively. [^{18}F]FDG exhibited a tumor/brain ratio of 0.84 at 60 min in the same tumor model (11). No blocking studies were performed.

Other Non-Primate Mammals

[PubMed]

No publication is currently available.

Non-Human Primates

[PubMed]

No publication is currently available.

Human Studies

[PubMed]

Savir-Baruch et al. (9) studied five patients with elevated PSA after curative therapy for prostate carcinoma underwent 60-min dynamic PET/CT of the pelvis after injection of 193-340 MBq (5.2-9.3 mCi) *anti*-2-[^{18}F]FACPC. Average standard uptake value (SUV) of

malignant lesions was 4.1 ± 1.3 and 2.6 ± 1.0 at 5 and 20 min, respectively. The lesion/blood ratios were 1.4 ± 0.5 at 5 min, whereas lesions/urinary bladder ratio was 0.3 ± 0.8 at 20 min. It was concluded that *anti*-2-[^{18}F]FACPC exhibited unfavorable imaging characteristics for detection of pelvic recurrent prostate carcinoma because of high blood level at 5 min and high urinary bladder level at 20 min. On the other hand, *anti*-[^{18}F]FACBC exhibited the lesion/blood and lesion/urinary bladder ratios of 3.0 ± 0.9 at 5 min and 2.3 ± 1.4 at 20 min, respectively.

NIH Support

R01 CA129356

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