(*R*)-2-Amino-3-[^{18}F]fluoro-2-methylpropanoic acid

(*R*)-[^{18}F]FAMP

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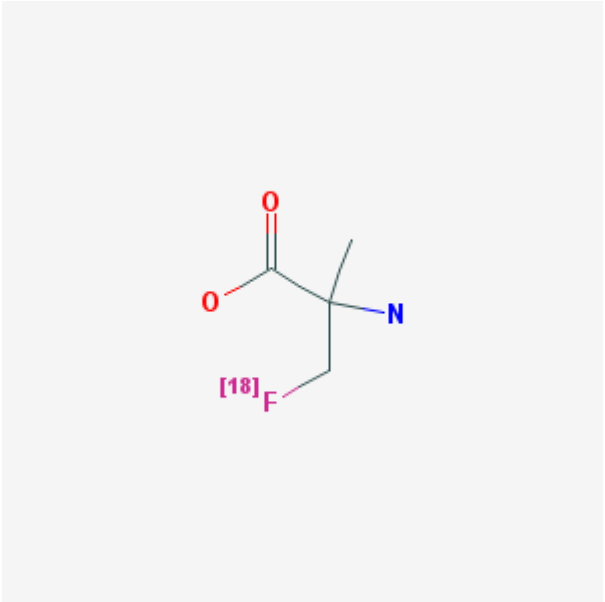
Chemical name:	(*R*)-2-Amino-3-[^{18}F]fluoro-2-methylpropanoic acid
Abbreviated name:	(*R*)-[^{18}F]FAMP
Synonym:	
Agent category:	Compound
Target:	L-type and A-type amino acid transporter
Target category:	Transporter
Method of detection:	Positron emission tomography (PET)
Source of signal:	^{18}F
Activation:	No
Studies:	• *In vitro* • Rodents



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Background

[PubMed]

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 (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, and [^{11}C]1-aminocyclobutane-1-carboxylic acid. There are also ^{123}I-labeled amino acids 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 metabolic pathways, including incorporation into proteins, than most normal cells (4). L-[^{11}C]Methionine and [^{18}F]fluorotyrosine have been widely used in the detection of tumors. On the other hand, the non-natural amino acids are not metabolized. Their uptakes are through both the L-type transporter and the energy-dependent A-type transporter (7). Therefore, they can accumulate intracellularly in high concentrations. [^{11}C]Aminoisobutyric acid was shown to have a high tumor/brain ratio (8, 9). (*R*)-2-Amino-3-[^{18}F]fluoro-2-methylpropanoic acid ((*R*)-[^{18}F]FAMP) is a fluorinated analog of [^{11}C]α-aminoisobutyric acid (AIB) that is being evaluated as a useful tracer in PET tumor imaging (10).

Related Resource Links:

- Chapters in MICAD
- Gene information in NCBI (Amino acid transporter)
- Articles in OMIM
- Clinical trials (Amino acid transporter)

Synthesis

[PubMed]

Nucleophilic fluorination of (*R*)3-(tert-butoxycarbonyl)-4-methyl-1,2,3-oxathiazolidine-4-carboxylic acid tert-butyl ester 2,2-dioxide with K[^{18}F]F/Kryptofix2.2.2 and subsequent hydrolysis and purification provided a radiosynthesis yield (decay-corrected) of 52% for (*R*)-[^{18}F]FAMP at the end of bombardment. A radiochemical purity of 99% was obtained. The total synthesis time was 85 min. The specific activity was ~1.85 GBq/μmol (50 mCi/μmol).

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

(*R*)-[^{18}F]FAMP exhibited a rapidly increasing uptake into L9 rat gliosarcoma tumor cells with 13.06 ± 0.23% (n = 3) injected dose (ID)/5 × 10^5 cells at 30 min of incubation (10). The uptake was blocked by the presence of L-type transporter inhibitor BCH (2-amino-bicyclo[2.2.1]heptane-2-carboxylic acid), A-type transporter inhibitor MeAIB (*N*-methyl-AIB), and system ASC inhibitor ACS (alanine-cysteine-serine) with 67%, 58%, and 87% inhibition, respectively. (*S*)-[^{18}F]FAMP (4.77 ± 0.73% ID/5 × 10^5 cells) exhibited a lower uptake than (*R*)-[^{18}F]FAMP. The uptake was blocked by the presence of BCH, MeAIB, and ACS with 75%, 31%, and 72% inhibition, respectively.

Animal Studies

Rodents

[PubMed]

Yu et al. (10) performed *ex vivo* biodistribution studies of (*R*)-[^{18}F]FAMP in rats implanted intracerebrally with a 9L gliosarcoma. The uptake in the brain (0.06% ID/g) was low at 30 min after injection and increased slightly to 0.09% ID/g at 120 min. The uptake in the tumor was 2.42–2.82% ID/g at 30–120 min after injection. Most of the other tissues showed lower radioactivity levels at 120 min than at 30 min. The organs with the highest accumulation at 30 min were the pancreas (2.96% ID/g) and kidney (3.47% ID/g). The tumor/brain ratios were 38.2, 28.6, and 27.5 at 30, 60, and 120 min, respectively. The radioactivity in the bone was low (0.26% ID/g at 120 min). (*S*)-[^{18}F]FAMP exhibited lower tumor accumulation (1.38–2.13% ID/g) but higher pancreas and kidney accumulation than (*R*)-[^{18}F]FAMP. The tumor/brain ratios were 21.1, 30.9, and 27.7 at 30, 60, and 120 min, respectively. No blocking experiments were performed. The specificity of uptake, especially given the disruption of the blood brain barrier, was not studied.

Other Non-Primate Mammals

[PubMed]

No publication is currently available.

Non-Human Primates

[PubMed]

No publication is currently available.

Human Studies

[PubMed]

No publication is currently available.

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