(*R*)-3-[^{18}F]Fluoro-2-methyl-2-*N*-(methylamino)propanoic acid

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

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Chemical name:	(*R*)-3-[^{18}F]Fluoro-2-methyl-2-*N*-(methylamino)propanoic acid
Abbreviated name:	(*R*)-[^{18}F]*N*MeFAMP
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]

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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 (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/background ratio (8, 9). (*R*)-3-[^{18}F]Fluoro-2-methyl-2-*N*-(methylamino)propanoic acid ((*R*)-[^{18}F]*N*MeFAMP) 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*)-3,4-dimethyl-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 66% for (*R*)-[^{18}F]*N*MeFAMP at the end of bombardment (10). 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]*N*MeFAMP exhibited a rapidly increasing uptake into L9 rat gliosarcoma tumor cells with 7.08 ± 0.47% (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 54%, 92%,

and 89% inhibition, respectively. (*S*)-[^{18}F]*N*MeFAMP (3.87 ± 0.22% ID/5 × 10^5 cells) exhibited a lower uptake than (*R*)-[^{18}F]*N*MeFAMP. The uptake was blocked by the presence of BCH, MeAIB, and ACS with 29%, 79%, and 58% inhibition, respectively.

Animal Studies

Rodents

[PubMed]

Yu et al. (10) performed *ex vivo* biodistribution studies of (*R*)-[^{18}F]*N*MeFAMP in rats (*n* = 5) implanted intracerebrally with a 9L gliosarcoma. The uptake in the brain (0.04% ID/g) was low at 30 min after injection and decreased slightly to 0.02% ID/g at 120 min. The uptake in the tumor was 1.46% ID/g at 15 min and increased to 2.78% ID/g at 120 min after injection. Most of the other tissues showed lower radioactivity levels at 120 min than at 15 min. The tissues with the highest accumulation at 30 min were the pancreas (2.72% ID/g) and kidney (8.91% ID/g). The tumor/brain ratios were 25.0, 53.2, 58.2, and 115.4 at 15, 30, 60, and 120 min, respectively. The radioactivity in the bone was low (0.44% ID/g at 120 min). (*S*)-[^{18}F]*N*MeFAMP exhibited lower tumor accumulation but slightly higher pancreas and kidney accumulation than (*R*)-[^{18}F]*N*MeFAMP. The tumor/brain ratios were 20.4, 30.2, 28.7, and 35.4 at 15, 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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