S-[^{11}C]Methyl-L-cysteine

[^{11}C]MCYS

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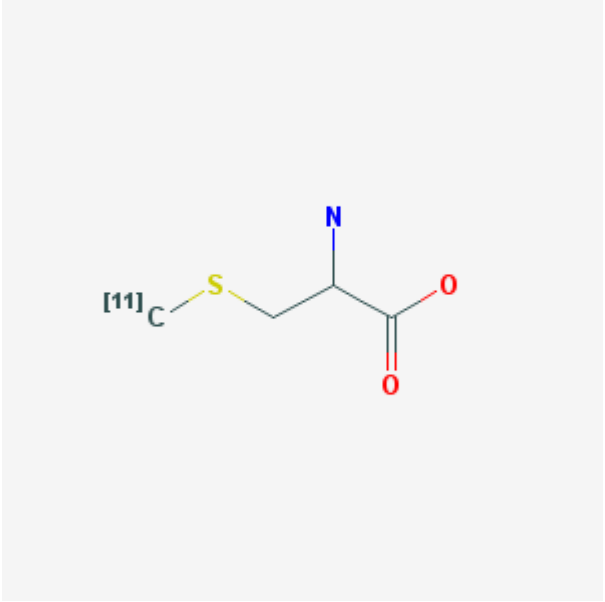
Chemical name:	*S*-[^{11}C]Methyl-L-cysteine
Abbreviated name:	[^{11}C]MCYS
Synonym:	
Agent category:	Compound
Target:	L-type amino acid transporter 1 (LAT1)
Target category:	Neutral amino acid uptake and protein synthesis
Method of detection:	Positron emission tomography (PET)
Source of signal:	^{11}C
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 tissues (3). These amino acids are composed of naturally occurring amino acids, such as L-[^{11}C]leucine, *S*-[^{11}C]methyl-L-methionine ([^{11}C]MET), 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. ^{123}I-Labeled amino acids are also used in oncological imaging (1, 4, 5).

Some 20 amino acid transporter systems have been identified (1). Most amino acids are taken up by tumor cells through an energy-independent L-type amino acid transporter system, a Na-dependent transporter system A, or a Na^+-dependent system B^0 (6). They are retained in tumor cells due to their metabolic activities, including incorporation into proteins, which are higher than most normal cells (1). Malignant transformation increases the use of amino acids for energy, protein synthesis, and cell division. Tumor cells have been found to have overexpressed transporter systems (7). L-[^{11}C]MET, [^{18}F]fluorotyrosine, L-[^{11}C]leucine, and [^{18}F]fluoro-α-methyl tyrosine have been widely used in the detection of tumors (2, 6) but are not approved by the United States Food and Drug Administration. These agents are moved into cells by various amino acid transporters and are incorporated into proteins. The fraction of radiolabeled amino acid that is incorporated into protein is usually small compared to the total amount taken up into the cell except for leucine which is quantitatively incorporated into proteins. These natural amino acid images are based on amino acid transport and protein incorporation.

[^{11}C]MET has been widely used in the detection of brain, head and neck, lung, and breast cancers as well as lymphomas (2) [PubMed]. [^{11}C]MET can cross the blood–brain barrier, and while it is incorporated mainly into proteins, but [^{11}C]MET is also incorporated into lipid, RNA, and DNA. [^{11}C]MET PET imaging is more sensitive to radiotherapy compared to [^{18}F]FDG and is useful for monitoring treatment of cancer. *S*-[^{11}C]Methyl-L-cysteine ([^{11}C]MCYS), an analog of [^{11}C]MET, was evaluated as a PET tumor imaging agent (8).

Related Resource Links:

- Chapters in MICAD (Amino acid transporters)
- Gene information in NCBI (L-type amino acid transporter 1, L-type amino acid transporter 2, A-type amino acid transporter)
- Articles in Online Mendelian Inheritance in Man (OMIM) (Amino acid transporters)
- Clinical trials (Amino acid transporters, L-[^{11}C]methionine)
- Drug information in FDA (Amino acid transporters, L-[^{11}C]methionine)

Synthesis

[PubMed]

A continuous flow procedure was automated for the synthesis of [^{11}C]methyl iodide from [^{11}C]CO_2 and [^{11}C]MCYS by ^{11}C-meythylation of the desmethyl precursor L-cysteine with [^{11}C]methyl iodide (8). The preparation was completed in 12 min after the end of bombardment, with a yield of >50% based on [^{11}C]methyl iodide. The radiochemical purity of [^{11}C]MCYS was >99%, with >90% enantiomeric purity. The specific activity of [^{11}C]MCYS was not reported.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

Deng et al. (8) showed that [^{11}C]MCYS accumulation in Hepa1-6 mouse hepatocellular carcinoma cells was reduced by 80% in the presence of 2-aminobicyclo[2.2.1]heptane-2-carboxylic acid (BCH, an L-type transporter inhibitor). The accumulation of [^{11}C]MCYS was not affected by the presence of Na^+ ions. On the other hand, no inhibition was observed in the presence of *N*-methyl-α-aminoisobutyric acid (an A-type transporter inhibitor) and L-alanine/serine/cysteine (System ASC). Specific transport of [^{11}C]MCYS in Hepa1-6 cells was mediated mainly by System L and was independent of sodium ions.

Animal Studies

Rodents

[PubMed]

Ex vivo tissue accumulation of [^{11}C]MCYS was studied in normal mice at 5, 10, 20, 30, and 60 min after injection of 0.74–1.48 MBq (0.02–0.04 mCi) of the tracer (8). The tissue with the highest uptake at 5 min was the liver (1.97% injected dose (ID)/g)), followed by the blood (1.03% ID/g), stomach (0.99% ID/g), heart (0.94% ID/g), small intestine (0.92% ID/g), lung (0.91% ID/g), kidney (0.89% ID/g), brain (0.72% ID/g), and muscle (0.61% ID/g). All tissues showed moderate to rapid washout. At 30 min, the radioactivity levels were 0.86%, 0.21%, 0.44%, 0.40%, 0.46%, 0.38%, 0.32%, 0.18%, and 0.17% ID/g in the liver, blood, stomach, heart, small intestine, lung, kidney, brain, and muscle, respectively.

Deng et al. (8) performed whole-body PET imaging studies at 60 min after intravenous injection of 10 MBq (0.27 mCi) [^{11}C]MCYS, [^{18}F]FDG, or [^{11}C]MET in female nude mice (n = 5/group) bearing Hepa1-6 tumors and turpentine-induced inflammation. The tumor accumulation of radioactivity was 4.58 ± 0.65% ID/g, 4.32 ± 0.47% ID/g, and 3.03 ± 0.79% ID/g for [^{11}C]MCYS, [^{18}F]FDG, and [^{11}C]MET, respectively. The tumor/muscle ratios were 7.27, 5.08, and 4.26 for [^{11}C]MCYS, [^{18}F]FDG, and [^{11}C]MET, respectively. *Ex vivo* tissue analysis at 30 min after injection showed that >99% of [^{11}C]MCYS was not incorporated into proteins in the tumor, pancreas, brain, and blood . [^{11}C]MCYS was >90% intact in these tissues. The inflammation accumulation of radioactivity was 1.02 ± 0.18% ID/g, 3.30 ± 0.23% ID/g, and 1.62 ± 0.68% ID/g for [^{11}C]MCYS, [^{18}F]FDG, and [^{11}C]MET, respectively. The inflammation/muscle ratios were 1.62, 3.88, and 2.28 for [^{11}C]MCYS, [^{18}F]FDG, and [^{11}C]MET, respectively. [^{11}C]MCYS exhibited a higher

tumor/muscle ratio and a lower inflammation/muscle ratio than did [^{18}F]FDG and [^{11}C]MET. 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]

[^{11}C]MCYS and [^{18}F]FDG PET brain imaging scans were performed in a 45-year-old male patient with grade IV glioma (8). [^{18}F]FDG exhibited heterogeneous radioactivity in patches, whereas [^{11}C]MCYS showed high radioactivity accumulation in the tumor lesion, which was confirmed with histopathological examination. Specific uptake was not determined.

References

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