N-[*N*-[(*S*)-1,3-Dicarboxypropyl]carbamoyl]-4-[^{18}F]fluorobenzyl-L-cysteine

^{18}F-DCFBC

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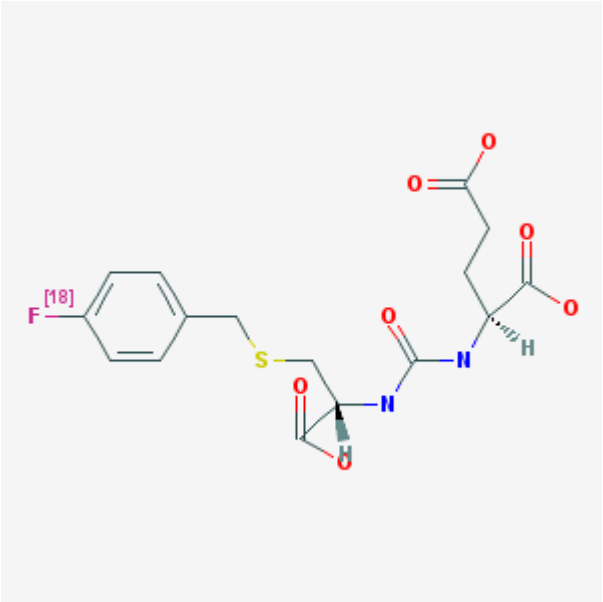
Chemical name:	*N*-[*N*-[(*S*)-1,3-Dicarboxypropyl]carbamoyl]-4-[^{18}F]fluorobenzyl-L-cysteine
Abbreviated name:	[^{18}F]DCFBC
Synonym:	
Agent category:	Compound
Target:	Prostate-specific membrane antigen (PSMA), or N-acetyl α-linked acidic dipeptidase (NAALADase)
Target category:	Receptor
Method of detection:	PET
Source of signal:	^{18}F
Activation:	No
Studies:	• *In vitro* • Rodents



Click on the above structure for additional information in PubChem.

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Background

[PubMed]

Prostate-specific membrane antigen (PSMA) is a cell-surface glycoprotein with a molecular weight of ~100 kDa. It is a unique, type II, transmembrane-bound glycoprotein that is overexpressed on prostate tumor cells and in the neovasculature of most solid prostate tumors, but not in the vasculature of normal tissues (1, 2). It has also been detected in other tissues such as the kidney, the proximal small intestine, and the salivary glands, with minimal expression in the brain (2). PSMA was found to have *N*-acetyl α-linked acidic dipeptidase (NAALADase) or glutamate carboxypeptidase II (GCPII) activity (3). PSMA may play an important role in the progression of prostate cancer, glutamatergic neurotransmission, and in the absorption of folate (4). In the central nervous system, PSMA metabolizes *N*-acetyl-aspartyl-glutamate (NAAG), and in the proximal small intestine PSMA removes γ-linked glutamates from poly-γ-glutamate folate and folate hydrolase (2). PSMA can be used as a marker for the detection of metastatic cancers with imaging agents. Although the commercially available monoclonal antibody [^{111}In]-Capromomab pendetide (^{111}In-CYT-356) is in clinical use for the detection of prostate cancer, the results obtained with this antibody are not entirely reliable (5). In addition, the antibody has limited access to tumors and may produce low signal/noise ratios because the target is the intracellular domain of PSMA (6, 7). *N*-[*N*-[(*S*)-1,3-dicarboxypropyl]carbamoyl]-*S*-[^{11}C]methyl-L-cysteine ([^{11}C]DCMC) was evaluated for the positron emission tomography (PET) imaging of PSMA-positive tumors in an *in vivo* rodent model for prostate cancer (8). However, the potential widespread use of [^{11}C]DCMC is limited by the short half-life of ^{11}C (20 min). *N*-[*N*-[(*S*)-1,3-Dicarboxypropyl]carbamoyl]-4-[^{18}F]fluorobenzyl-L-cysteine ([^{18}F]DCFBC), an analog of DCMC, has also been studied (9).

Synthesis

[PubMed]

(*S*)-2-[3-[(*R*)-1-Carboxy-2-mercaptoethyl]ureido]-pentanedioic acid was used as a precursor for the synthesis of [^{18}F]DCFBC (9). 4-[^{18}F]Fluorobenzyl bromide ([^{18}F]FBB) was added to a solution of the precursor in ethanol/ammonia and heated for 10 min at 60°C. [^{18}F]DCFBC was purified with high-performance liquid chromatography. However, the radiochemical purity was not reported. The time for synthesis was ~123 min from [^{18}F]KF. The average non-decay-corrected yield of [^{18}F]DCFBC was 16 ± 6% (n = 8) from [^{18}F]FBB , with a specific radioactivity of 52 GBq/μmol (1.49 Ci/μmol) at the end of synthesis.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

The binding affinity of DCFBC for PSMA was determined with the use of the NAAG peptidase assay in membranes isolated from Chinese hamster ovary cells transfected with rat GCPII (10). In this assay, 4 μM NAAG that contained trace amounts of ^{3}H-NAAG was incubated with the membranes in the presence of 1–100 nM DCFBC. A 50% inhibition concentration value of 13.9 nM was determined for DCFBC (9).

Animal Studies

Rodents

[PubMed]

Mease et al. (9) performed biodistribution studies of [^{18}F]DCFBC in nude mice bearing PSMA-positive PC-3 PIP tumor and PSMA-negative PC-3 FLU tumor xenografts. The maximum PIP tumor uptake was 8.2 ± 2.6% injected dose per gram (ID/g) at 60 min after injection, which decreased to 4.7 ± 0.9% ID/g at 120 min. The PIP/muscle ratio was 20 at 120 min. On the other hand, FLU tumors accumulated <1% ID/g at 60 and 120 min. The organ with the highest accumulation at 60 min after injection was the kidney (41.6% ID/g), followed by the urinary bladder (6.65% ID/g), liver (5.1% ID/g), blood (1.8% ID/g), and bone (1.7% ID/g). The washout from these organs was faster than the PIP tumors. The whole-body distribution of [^{18}F]DCFBC was also assessed with PET imaging 20–120 min after injection. The highest radioactivity levels were visualized in the kidneys, urinary bladder, liver, and PIP tumors; FLU tumors were barely visualized. No blocking experiment was performed although the use of tumors that are PSMA positive or PSMA negative is consistent with specific binding.

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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