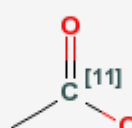


[¹¹C]Acetate

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Chemical name:	[¹¹ C]Acetate	
Abbreviated name:		
Synonym:	[¹¹ C]Acetic acid	
Agent Category:	Compound	
Target:	TCA cycle, fatty acid synthetase,	
Target Category:	Incorporation into membrane	
Method of detection:	PET	
Source of signal:	¹¹ C	
Activation:	No	
Studies:	<ul style="list-style-type: none"> <i>In vitro</i> Rodents Non-primate mammals Non-human primates Humans 	

Background

[PubMed]

Acetate is readily taken up by cells and is activated to acetyl-CoA in both the cytosol and mitochondria by acetyl-CoA synthetase. Acetyl-CoA is a common metabolic intermediate for synthesis of cholesterol and fatty acids, which are then incorporated into membrane (1). Acetyl-CoA is also oxidized in mitochondria by the tricarboxylic acid (TCA) cycle to carbon dioxide and water. Some of the acetate is converted to amino acids. In

normal myocardium, acetate is metabolized to CO₂ via the TCA cycle as the dominant pathway. In contrast, tumor cells convert most of the acetate into fatty acids by a key enzyme fatty acid synthetase (FAS), which is over-expressed in cancer cells (2). Acetate is predominantly incorporated into intracellular phosphatidylcholine membrane microdomains that are important for tumor growth and metastasis (3). [¹¹C]Acetate are used as a positron emission tomography (PET) tracer for studying myocardial oxidative metabolism and regional myocardial blood flow (4). [¹¹C]Acetate is a promising PET tracer for renal, pancreatic, and prostate tumors (5).

Synthesis

[PubMed]

[¹¹C]Acetate is commonly produced by a reaction of methylmagnesium bromide or chloride and [¹¹C]carbon dioxide. This method produces [¹¹C]acetate in a radiochemical yield of $72 \pm 12\%$ in 20 min and in high specific activity (>18.5 GBq/ μmol , 0.5 Ci/ μmol). The radiochemical purity of [¹¹C]acetate was found to be $> 95\%$ (6). Several automated systems provided radiochemical yields of 60 - 80% and radiochemical purity of 99% in 15 - 23 min (7-9)

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

Acetate uptake and metabolism were studied in four tumor cell lines and one fibroblast cell line with [¹⁴C]acetate. All four tumor cell lines showed higher accumulation of [¹⁴C] activity than the resting fibroblasts. Tumor-to-fibroblast ratios were larger than those of [³H]-2-deoxyglucose. [¹⁴C]Acetate was metabolized and incorporated into phosphatidylcholine and neutral lipids in proportionally to cellular proliferation rates. The remaining fraction of [¹⁴C]acetate was converted to amino acids, acetylCoA, and CO₂ (10). This was shown by extraction of tissue samples followed by analysis using thin layer chromatography and paper chromatography with authentic samples of possible metabolites.

Animal Studies

Rodents

[PubMed]

Tissue accumulation of [¹¹C]acetate was studied in mice with EMT-6 murine mammary carcinoma tumors and rats with 9L-glioma tumors at 1 h postinjection of the tracer (11). In the EMT-6 mice, the organ with the highest uptake was in the pancreas (2.49% injected dose/g (ID/g)), followed by the liver (1.42% ID/g), spleen (1.40% ID/g) and kidneys (1.18% ID/g). The tumor uptake was only 0.60% ID/g giving a tumor-to-blood ratio of 1.3. In the rats bearing 9L-glioma tumors, the organ with the highest uptake was in the pancreas (0.88% ID/g), followed by the spleen (0.42% ID/g), liver (0.35% ID/g), and kidneys (0.33% ID/g). The tumor uptake was only 0.42% ID/g giving a tumor-to-blood ratio of 3.2.

Oyama et al. reported that androgen ablation caused a decrease of 2-[¹⁸F] fluoro-2-deoxy-D-glucose ([¹⁸F]FDG) and [¹¹C]acetate uptake in the prostate in Sprague-Dawley male rats to monitor metabolic changes in normal prostate tissue. Dihydrotestosterone administration returned uptake of both tracers to that of the baseline level. Therefore, serum testosterone levels influence glucose and acetate metabolism in the prostate (12).

[¹¹C]Acetate has been used to study myocardial oxygen consumption rate (MVO₂) with the metabolic fate of the tracer in normoxic, hypoxic, and ischemic conditions in isolated perfused rat hearts. Model-estimated MVO₂ correlated well with experimentally measured MVO₂ for these conditions correlated strongly with the myocardial clearance rate determined from the tissue kinetics (13).

In a rat model of an occluded, acute left anterior descending (LAD) coronary artery, ^{60}Cu -ATSM was used to visualize hypoxic rat heart tissue using an *ex vivo* tissue slice imaging technique (14). In addition, $[^{11}\text{C}]$ acetate was used to monitor myocardial blood flow. Low $[^{11}\text{C}]$ acetate uptake (low blood flow) and high ^{60}Cu -ATSM uptake (hypoxia) were observed in mildly ischemic regions. In the center of severely ischemic regions with no blood flow, little accumulation of ^{11}C or ^{60}Cu radioactivity was observed.

Other Non-Primate Mammals

[PubMed]

$[^{11}\text{C}]$ Acetate PET was used to study cardiac output in a pig model (15). The tracer uptake in the right and left heart cavities was measured as well as in the lung. Myocardial output measured by $[^{11}\text{C}]$ acetate PET was linearly related to cardiac output by thermodilution. Lung uptake of $[^{11}\text{C}]$ acetate was also linearly related to stroke volume.

Non-Human Primates

[PubMed]

$[^{11}\text{C}]$ Acetate PET was studied in monkeys with coronary ligation. The infarct myocardial regions showed a decrease in tracer accumulation (16).

Human Studies

[PubMed]

Myocardial oxygen consumption can be estimated with PET from analysis of the myocardial turnover rate constant (k) after administration of $[^{11}\text{C}]$ acetate. $[^{11}\text{C}]$ Acetate was administered to five normal volunteers and six patients with myocardial infarction. Uptake of $[^{11}\text{C}]$ acetate by the myocardium was avid, and its clearance from the blood pool was rapid, yielding myocardial images of excellent quality. Regional k was homogeneous in the myocardiums of healthy volunteers. In patients, k in regions remote from the area of infarction was not different from values in the myocardiums of healthy human volunteers. In contrast, k in the center of the infarct region of necrotic myocardium was significantly reduced (17).

$[^{11}\text{C}]$ Acetate PET has been shown to have high sensitivity for detection of recurrent prostate cancer and metastases. It was reported that 27 of 46 prostate cancer patients were positive with $[^{11}\text{C}]$ acetate PET studies, whereas only eight $[^{18}\text{F}]$ FDG PET studies had positive detections (18). In another study, it was cautioned that acetate also accumulates in normal, hyperplastic, and benign prostate tissues. It was reported that the $[^{11}\text{C}]$ acetate standardized uptake values for normal prostate and benign prostate, overlap significantly with those for prostate cancer patients (19).

Human dosimetry was estimated in six healthy volunteers by intravenous injection of 525 MBq (14.2 mCi) of $[^{11}\text{C}]$ acetate (20). The organs receiving the highest absorbed doses were the pancreas (0.017 mGy/MBq or 62.9 mrad/mCi), bowel (0.011 mGy/MBq or 40.7 mrad/mCi), kidneys (0.0092 mGy/MBq or 34.0 mrad/mCi), and spleen (0.0092 mGy/MBq or 34.0 mrad/mCi). No urinary excretion of tracer was detected. The effective dose equivalent was 0.0062 mSv/MBq (22.9 mrem/mCi).

$[^{11}\text{C}]$ Acetate is rapidly taken up by myocardium and metabolized to CO_2 and water after intravenous injection. The uptake is indirectly dependent on blood flow (21). The clearance of the tracer is a direct reflection of TCA cycle activity, which is coupled to myocardial oxygen consumption [PubMed]. Rates of clearance from myocardium of $[^{11}\text{C}]$ acetate reflect oxidative metabolism (22). $[^{11}\text{C}]$ Acetate PET is used to evaluate ischemia and myocardial infarction [PubMed]. Many prostate, bladder, and renal cancer patients have been imaged with $[^{11}\text{C}]$ acetate PET to assess primary and metastatic tumors [PubMed].

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