2-[*methyl*-^{11}C]Methoxyestradiol

[^{11}C]2-ME

Kam Leung, PhD[1]

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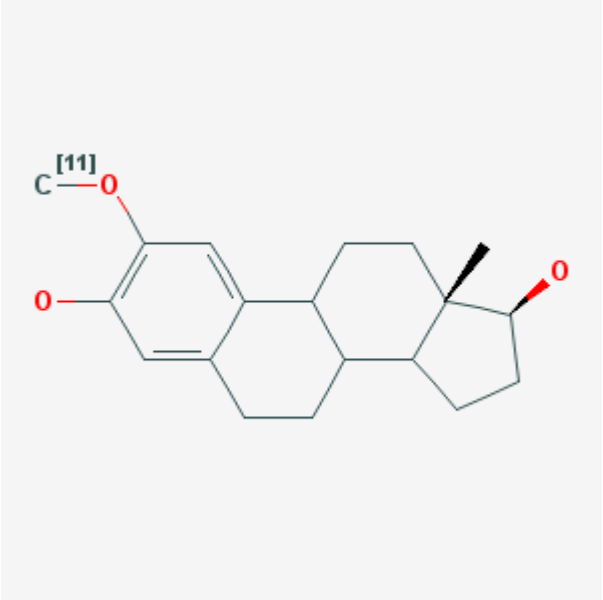
Chemical name:	2-[*methyl*-^{11}C]Methoxyestradiol
Abbreviated name:	[^{11}C]2-ME
Synonym:	
Agent Category:	Compound
Target:	Superoxide dismutase
Target Category:	Enzyme binding
Method of detection:	Positron emission tomography (PET)
Source of signal:	^{11}C
Activation:	No
Studies:	• *In vitro* • Non-human primates



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Background

[PubMed]

Endothelial cells are important cells in angiogenesis (1). Tumor growth requires the formation of new blood vessels. Potent angiogenic factors (e.g., vascular endothelial growth factor and basic fibroblast growth factor) induce proliferation, sprouting, migration, and tube formation of endothelial cells (2). 2-Methoxyestradiol (2-ME), an

[1] National Center for Biotechnology Information, NLM, NIH, Bethesda, MD; Email: micad@ncbi.nlm.nih.gov.

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endogenous metabolite of 17β-estradiol, inhibits proliferating tumor cells and angiogenesis *in vitro* and *in vivo* (3, 4). It also inhibits the proliferation of endothelial cells and has low affinity for estrogen receptors. Huang et al. (5) demonstrated that the anti-proliferation effect of 2-ME may be the result of its inhibition of superoxide dismutase (SOD) and induction of apoptosis. Inhibition of SOD leads to free radical–mediated damage to mitochondrial membranes resulting in apoptosis. 2-[*methyl*-^{11}C]Methoxyestradiol ([^{11}C]2-ME) has been evaluated as an imaging probe to study angiogenesis (6).

Synthesis

[PubMed]

[^{11}C]2-ME was synthesized from its precursor, 2-hydroxy-3,17β-estradiol-3,17-bis(methoxymethyl)ether, by *O*-methylation by use of ^{11}C-methyl iodide (NaH, 80°C for 6 min), followed by acid hydrolysis (HCl, 80°C for 6 min) (6). [^{11}C]2-ME was purified by reverse-phase high-performance liquid chromatography. The radiochemical yields (decay-corrected) on the basis of [^{11}C]CH_3I were 25–34%, and the specific activities were 34–38 GBq/μmol (0.92–1.03 Ci/μmol) at the end of synthesis. The total synthesis time was 60–65 min.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

Fotsis et al. (3) reported that 2-ME (10 μM) inhibited proliferation of human umbilical vein endothelial cells (HUVECs) by >85%. Lee et al. (6) showed that [^{11}C]2-ME accumulated in HUVECs with 2.96% injected dose (ID) at 5 min, 4.74% ID at 15 min, 6.51% ID at 30 min, and 7.10% ID at 60 min. 2-ME (10 μM) inhibited the uptake at 60 min by 70%.

Animal Studies

Rodents

[PubMed]

Lee et al. (6) performed biodistribution studies of [^{11}C]2-ME in mice bearing a Lewis lung carcinoma tumor in the right flank. The organs with the highest accumulation of [^{11}C]2-ME (% ID/g) were the liver (9.34 ± 2.12), lung (3.36 ± 0.09), and kidneys (3.26 ± 0.55) at 60 min after injection. The tumor (1.04 ± 0.27% ID/g) exhibited a tumor/muscle ratio of 2.36, which would provide a good contrast for tumor imaging. No blocking experiment was performed. In normal mice, [^{11}C]2-ME showed a distribution half-life ($t_{1/2}\alpha$) and an elimination half-life ($t_{1/2}\beta$) of 0.36 and 19 min, respectively.

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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