^{11}C-Labeled 1,7β,10β-trihydroxy-9-oxo-5β,20-epoxytax-11-ene-2α,4,13α-triyl 4-acetate 2-benzoate 13-{(2*R*,3*S*)-3-[(tert-butoxycarbonyl)amino]-2-hydroxy-3-phenylpropanoate}

[^{11}C]-Docetaxel

Arvind Chopra, PhD[1]

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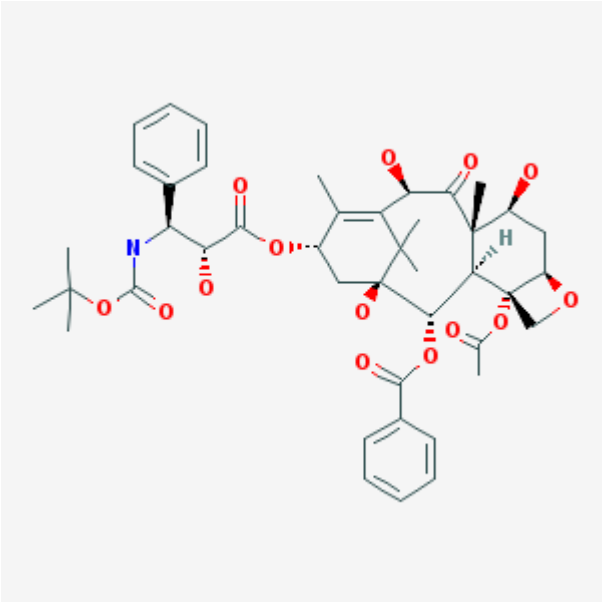
Chemical name:	^{11}C-Labeled 1,7β,10β-trihydroxy-9-oxo-5β,20-epoxytax-11-ene-2α,4,13α-triyl 4-acetate 2-benzoate 13-{(2*R*,3*S*)-3-[(*tert*-butoxycarbonyl)amino]-2-hydroxy-3-phenylpropanoate}
Abbreviated name:	[^{11}C]-Docetaxel
Synonym:	
Agent Category:	Compound
Target:	Tubulin (microtubules)
Target Category:	Other (cytoskeleton)
Method of detection:	Positron emission tomography (PET)
Source of signal / contrast:	^{11}C
Activation:	No



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Studies:	• *In vitro* • Rodents • Humans	Click on above structure of docetaxel for additional information in PubChem.

Background

[PubMed]

Docetaxel is a diterpine (taxane) anti-mitotic agent that binds to free tubulin and leads to the assembly of stabilized microtubule bundles, inhibition of the cell cycle, and cell death due to apoptosis (1). This drug has been approved by the United States Food and Drug Administration as a single-agent treatment of metastatic breast cancer, metastatic androgen-independent prostate cancer, and advanced non-small cell lung cancer (NSCLC), and as an adjuvant in combination with doxorubicin and cyclophosphamide for the treatment of early-stage breast cancer (2). Patients treated with docetaxel often experience drug-related toxicity (due to myelosuppression) and show limited or no response to the treatment (3). To some extent, the response to an anti-neoplastic drug, including docetaxel, depends on attaining a sufficiently high concentration in the cancerous lesions, so it is important to quantify the uptake of an anti-cancer agent by the affected tissues to assess the efficacy of a drug. Therefore, measuring the amount of radionuclide-labeled docetaxel that has accumulated in cancerous tumors can be of prognostic value to predict patient response to the treatment (4). For this, ^{11}C-labeled docetaxel ([^{11}C]-docetaxel) was synthesized (5), and in a preliminary study its biodistribution was investigated in normal rats (4). In another study, the biodistribution and radio-dosimetry of [^{11}C]-docetaxel was investigated in cancer patients (6), and recently the kinetics of [^{11}C]-docetaxel was studied using positron emission tomography (PET) in lung cancer patients (3).

Related Resource Links

Microtubule inhibitors in PubMed

Anti-mitotic agents in PubMed

1 National Center for Biotechnology Information, NLM, Bethesda, MD 20894; Email: micad@ncbi.nlm.nih.gov.

NLM Citation: Chopra A. ^{11}C-Labeled 1,7β,10β-trihydroxy-9-oxo-5β,20-epoxytax-11-ene-2α,4,13α-triyl 4-acetate 2-benzoate 13-{(2*R*,3S)-3-[(tert-butoxycarbonyl)amino]-2-hydroxy-3-phenylpropanoate}. 2011 Jul 22 [Updated 2011 Aug 25]. In: Molecular Imaging and Contrast Agent Database (MICAD) [Internet]. Bethesda (MD): National Center for Biotechnology Information (US); 2004-2013.

Clinical trials with docetaxel

Synthesis

[PubMed]

The radiosynthesis of [^{11}C]-docetaxel has been described by van Tilburg et al. (5). The decay-corrected radiochemical yield (RCY) of the reaction was 10 ± 1% (n = 5 reactions). The radiochemical purity (RCP), specific activity, and stability of the final product were not reported.

[^{11}C]-Docetaxel was also synthesized as described by van Tilburg et al. with a semi-automated method compliant with good manufacturing practices (7). The total synthesis time was 67 min, with a decay-corrected RCY of 10 ± 2%, an RCP of >98%, and a SA of 9–17 GBq/ μmol (0.24–0.46 Ci/μmol) (n = 7 reactions).

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

The concentration of non-radiolabeled docetaxel that inhibits the proliferation of human SKOV-3 ovarian tumor cells by 50% (IC_{50}) after 72 h drug exposure was reported by Lu et al. to be $3.4 \times 10{-}^{3}$ μM (8).

Animal Studies

Rodents

[PubMed]

In a letter to the editor (no data presented), van der Velt et al. reported preliminary results obtained from a study to investigate the biodistribution of [^{11}C]-docetaxel in normal rats (4, 5). The investigators reported that >99% of the injected [^{11}C]-docetaxel was cleared from blood circulation in <5 min. The spleen showed the highest uptake of the labeled drug, followed by the urine, lung, and liver. Lowest uptake was observed in the brain and the testis of the animals.

Other Non-Primate Mammals

[PubMed]

No reference is currently available.

Non-Human Primates

[PubMed]

No reference is currently available.

Human Studies

[PubMed]

The biodistribution and radiation dosimetry of [^{11}C]-docetaxel was studied in seven cancer patients with advanced solid tumors (five individuals had NSCLC, one had malignant pleural mesothelioma, and one had prostate cancer) as described by van der Veldt et al. (6). The patients were given dexamethasone before the administration of a single intravenous bolus of 178 ± 79 MBq (4.8 ± 2.1 mCi) [^{11}C]-docetaxel. Four whole-body serial PET scans were then acquired from each patient within 1 h, and the duration of each scan was 6.9 ± 1.2, 12.6 ± 2.3, 18.3 ± 3.3, and 24.0 ± 2.3 min, respectively. Regions of interest (ROI) were drawn on the PET scans for each organ, including the tumors, and the mean standardized uptake value (SUV) normalized to the body weight and the percent of the injected dose (% ID) for each organ were calculated as described elsewhere (6). High uptake of [^{11}C]-docetaxel was observed in the liver (47 ± 9% ID) and the gall bladder (7.2 ± 3.6% ID), and the highest accumulated amount was observed in the gall bladder (SUV_{mean} 96 ± 49), followed by the liver (SUV_{mean} 24 ± 3) and upper large intestines (SUV_{mean} 9 ± 6). The lowest activity was detected in the brain (SUV_{mean} 0.05 ± 0.03) and the lungs (SUV_{mean} 0.7 ± 0.2). The clearance of [^{11}C]-docetaxel from circulation was very rapid, and the amount of label in the blood was reported to decrease to <0.001% ID/ml within 30 min after injection.

Time-activity curves were generated from the ROI on the PET scan of one tumor from each patient, and the SUV for the tumor was calculated as detailed elsewhere (6). The highest SUV was 5.1 for a primary NSCLC tumor, and the lowest SUV was ~1.2 for a metastasized NSCLC tumor.

The liver and gall bladder had the highest estimated absorbed radiation doses of 35.2 ± 6.6 and 34.6 ± 9.9 μGy/MBq (μGy/27 μCi), respectively (6). The mean effective dose of [^{11}C]-docetaxel was estimated to be 4.7 ± 0.2 μSv/MBq (μSv/27 μCi).

From this study, the investigators concluded that, because the lungs showed a low uptake of [^{11}C]-docetaxel, this tracer could be used to detect tumors in the thoracic region of cancer patients (6).

In another study, the quantification of [^{11}C]-docetaxel with dynamic PET-computed tomography (CT) was assessed in 34 lung cancer patients (3). The effects of tumor size, tumor perfusion, and pre-administration of dexamethasone in the patients on [^{11}C]-docetaxel kinetics were also investigated in this study. Results from this study showed that the quantification of [^{11}C]-docetaxel with non-invasive imaging techniques such as PET/CT is possible. The investigators were able to identify 32 lesions in the various patients, and the net variable influx rate of [^{11}C]-docetaxel in these lesions was in the range of 0.0023–0.0229 mL/cm^{-3} per min^{-1}. From this study, the investigators concluded that perfusion (Spearman's p = 0.815, $P < 0.001$) and not size (Spearman's p = –0.14, $P < 0.446$) affected the tumor uptake of [^{11}C]-docetaxel. It was observed that tumors in patients pretreated with dexamethasone (n = 24 individuals) showed a lower

accumulation of the tracer ($P = 0.013$). In addition, in a sub-group of patients treated with docetaxel, a high tumor uptake of [^{11}C]-docetaxel correlated with an improved response to the drug.

From these studies, the investigators concluded that [^{11}C]-docetaxel kinetics can be studied with non-invasive imaging techniques in a clinical setting, and that such investigations can reveal the sensitivity of lung cancer to therapy with this drug (3).

Supplemental Information

[Disclaimers]

No information is currently available.

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