^{99m}Tc-Diethylenetriaminepentaacetate-deoxyglucose

^{99m}Tc-DTPA-DG

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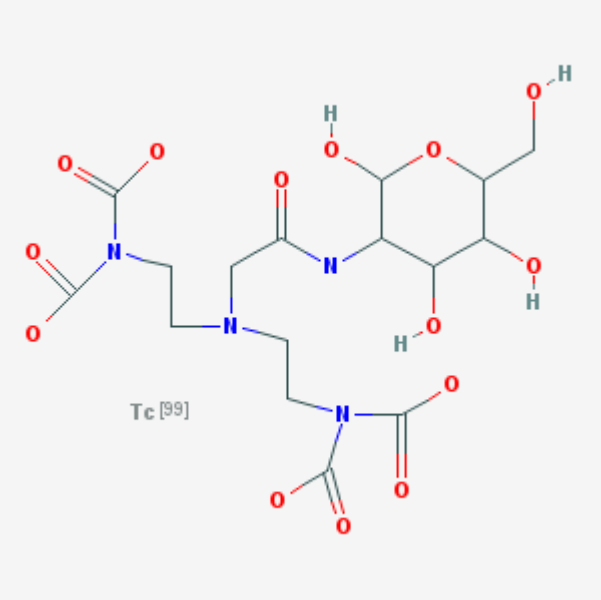
Chemical name:	^{99m}Tc-Diethylenetriaminepentaacetate-deoxyglucose	
Abbreviated name:	^{99m}Tc-DTPA-DG	
Synonym:	^{99m}Tc-Deoxyglucose	
Agent Category:	Compound	
Target:	Glucose transporter and hexokinases	
Target Category:	Specific binding and phosphorylation	
Method of detection:	Single-Photon Emission Computed Tomography (SPECT) , Planar gamma imaging	
Source of signal / contrast:	^{99m}Tc	
Activation:	No	
Studies:	• *In vitro* • Rodents	Click on the above structure for additional information in PubChem.

Background

[PubMed]

^{99m}Tc-diethylenetriaminepentaacetate-deoxyglucose (^{99m}Tc-DTPA-DG) is a radioligand developed for single-photon emission computed tomography (SPECT) of glucose utilization rates in normal and pathologic diseases that reflect tumor cell proliferation activities and viability (1). ^{99m}Tc is a gamma emitter with a physical half-life ($t_{½}$) of 6.02 h.

Movement of glucose into and out of cells is mediated by one or more members of the transport protein family of glucose transporters (2). There are different classes of glucose transporters for two forms of glucose transport. SGLT1 and SGLT2 are sodium glucose cotransporters involved in secondary active transport, and GLUT1 to GLUT13 are facilitated glucose transporters (3). They are similar in that they have a polypeptide chain of 500 amino acids. After glucose enters a living cell, phosphorylation catalyzed by hexokinase transforms the molecule to glucose-6-phosphate (G-6-P). There are four hexokinase isoforms (HKI to HKIV) that exist in mammalian tissues (4). The G-6-P isomerase then converts G-6-P into fructose-6-phosphate (F-6-P) by rearranging the carbonyl group from the C-1 to the C-2 position in the ring structure to enter further metabolic pathways. Cancer cells are known to have accelerated metabolism, high glucose consumption, and increased glucose uptake (5). In humans, high levels of GLUT expression in tumors have been associated with poor survival. Increased HK activities have also been associated with metastatic disease.

Molecular imaging with glucose analogs is a useful tool in the detection, staging, and therapy response monitoring of various malignant neoplasms (6, 7). 2-[^{18}F]Fluoro-2-deoxy-2-D-glucose ([^{18}F]FDG) was the first successful radiolabeled glucose analog developed for clinical positron emission tomography (PET) applications (8). [^{18}F]FDG, like glucose, is transported into cells by glucose transporters and is a substrate for hexokinase. However, it is converted to [^{18}F]FDG-6-phosphate ([^{18}F]FDG-6-P), which cannot be further metabolized. [^{18}F]FDG-6-P is not a substrate for the G-6-P isomerase and therefore is metabolically trapped in the cell. The trapping of [^{18}F]FDG-6-P within cells and tissues allows *in vivo* PET imaging of glucose utilization rates in normal and pathologic tissues. Because of the short $t_{½}$ of ^{18}F and the requirement of cyclotron production, it is desirable to develop a gamma-emitter for SPECT imaging (9). Early ^{123}I-labeled glucose analogs were either chemically unstable or poor substrates for hexokinase

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(6, 10, 11). Bayly et al. (12) reported the successful synthesis of a glucosamine labeled with the tricarbonyls of ^{99m}Tc(I). Yang et al. (13, 14) also demonstrated the feasibility of synthesis and imaging of ^{99m}Tc-ethylenedicysteine-deoxyglucose in rodents bearing tumors. These studies did not attempt to determine whether these glucose analogs actually followed the key steps in glucose metabolism. Chen et al. (1) developed a one-step ^{99m}Tc-DTPA-DG kit and showed tumor accumulation of ^{99m}Tc-DTPA-DG in nude rats bearing MCF-7 human mammary tumors. However, the mechanism of tumor uptake was not investigated.

Synthesis

[PubMKed]

Chen et al. (1) reported the synthesis of ^{99m}Tc-DTPA-DG from commercially available D-glucosamine hydrochloride. Briefly, thionyl chloride was first added dropwise to DTPA with stirring at 0°C. The mixture was then continuously stirred in boiling water for 3 h and refluxed for 20 h. The mixture was distilled to remove excess thionyl chloride, and then dianhydride acylchloride, dimethyl sulfoxide, pyridine, and D-glucosamine hydrochloride were added. The reaction mixture was stirred in a boiling water bath for 24–48 h. DTPA-DG was isolated by dialysis or gel chromatography. Radiolabeling with ^{99m}Tc was performed by first preparing DTPA-DG reaction kits that contained 25 mg DTPA-DG and 0.5 mg stannous chloride. The pH was adjusted to 6.0. The shelf life of the kit lasted at least 3 months at 4°C. At the time of radiolabeling, ~200–300 MBq (5.4–8.1 mCi) ^{99m}Tc pertechnetate was added to each kit, gently mixed, and incubated at room temperature for 30 min. The radiochemical purity was 99.2% at 30 min and remained >98.6% after 6 h.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

In vitro cellular uptake assay of ^{99m}Tc-DTPA-DG was performed with the MCD-7 cell line, with ^{99m}Tc-DTPA and [^{18}F]FDG serving as the controls (1). Both ^{99m}Tc-DTPA-DG and [^{18}F]FDG had significantly increased radioactivity localized in the cancer cells when compared with ^{99m}Tc-DTPA (P<0.05). At 4 h after incubation, 0.5% of ^{99m}Tc-DTPA-DG radioactivity was localized in the cells. In comparison, >0.6% [^{18}F]FDG radioactivity was taken up by the cells.

Animal Studies

Rodents

[PubMed]

Chen et al. (1) injected 0.037–0.111 MBq (1–3 μCi) ^{99m}Tc-DTPA-DG intravenously into nude rats bearing MCF-7 tumors (right leg muscle ~6 mm in diameter) for

biodistribution studies. ^{99m}Tc-DTPA-DG was rapidly cleared from the blood and excreted by the kidneys. The tumor radioactivity levels (n = 3) were 5.12 ± 1.43 (10 min), 3.10 ± 0.87 (1 h), 2.10 ± 0.02 (2 h), 1.59 ± 0.04 (4 h), and 1.69 ± 0.03 (8 h). The tumor/blood ratios were 0.45 ± 0.09 (10 min), 1.29 ± 0.26 (1 h), 3.13 ± 0.63 (2 h), 3.24 ± 0.65 (4 h), and 3.38 ± 0.68 (8 h). The kidney radioactivity levels were 28.86 ± 8.88 (10 min), 10.63 ± 4.35 (1 h), 4.45 ± 0.98 (2 h), 4.22 ± 2.00 (4 h), and 1.99 ± 0.12 (8 h). The liver radioactivity levels were 5.20 ± 0.93 (10 min), 2.68 ± 0.32 (1 h), 2.76 ± 1.05 (2 h), 1.67 ± 0.29 (4 h), and 1.37 ± 0.47 (8 h). No significant radioactivity accumulation was found in other organs. In comparison, [^{18}F]FDG had tumor radioactivity levels of 2.84 ± 1.03 (10 min), 1.43 ± 0.65 (2 h), and 1.42 ± 0.12 (4 h). The tumor/blood ratios of [^{18}F]FDG were 1.58 ± 1.65 (10 min), 5.73 ± 2.78 (2 h), and 7.12 ± 2.12 (4 h).

Planar gamma imaging was conducted in nude rats bearing MCF-7 tumors. An i.v. dose of 11.1 MBq (0.3 mCi) ^{99m}Tc-DTPA-DG was administered to each rat. There was a marked increase in tumor radioactivity that enabled good visualization of the tumors at 2 and 4 h. The region of interest (ROI) ratios for tumor/nontumor were 2.46 ± 1.02 and 3.54 ± 1.36 at 0.5 and 2 h, respectively. The kidneys, liver, and bladder were also visualized. Little radioactivity was observed in the thyroid gland and stomach, and the authors suggested that this indicated good *in vivo* stability of ^{99m}Tc-DTPA-DG. In comparison, the tumor/nontumor ratios for ^{99m}Tc-DTPA were 1.16 ± 0.02 and 1.14 ± 0.03 at 0.5 and 2 h, 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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