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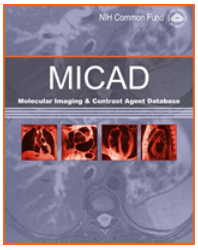

^{111}In-Diethylenetriaminepentaacetic acid-cyclo(CTTHWGFTLC)

^{111}In-DTPA-CTT

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Chemical name:	^{111}In-Diethylenetriaminepentaacetic acid- cyclo(CTTHWGFTLC)	
Abbreviated name:	^{111}In-DTPA-CTT	
Synonym:		
Agent category:	Peptide	
Target:	Gelatinases (MMP-2 and MMP-9)	
Target category:	Enzyme	
Method of detection:	Single-photon emission computed tomography (SPECT), gamma planar imaging	
Source of signal:	^{111}In	
Activation:	No	
Studies:	• *In vitro* • Rodents	Structure is not available in PubChem.

Background

[PubMed]

Extracellular matrix (ECM) adhesion molecules consist of a complex network of fibronectins, collagens, chondroitins, laminins, glycoproteins, heparin sulfate, tenascins, and proteoglycans surrounding connective tissue cells, and they are mainly secreted by fibroblasts, chondroblasts, and osteoblasts (1). Cell substrate adhesion molecules are considered essential regulators of cell migration, differentiation, and tissue integrity and remodeling. These molecules play a role in inflammation, but they also participate in the process of invasion and metastasis of malignant cells in the host tissue (2). Invasive tumor cells adhere to the ECM components, which provide a matrix environment for their permeation through the basal lamina and underlying interstitial stroma of the connective tissue by matrix metalloproteinases (MMPs), which degrade the basement membrane and ECM (3).

Gelatinase family is a subgroup of MMPs consisting of gelatinase A (MMP-2) and B (MMP-9) (4). Gelatinase expression in normal cells, such as trophoblasts, osteoclasts, neutrophils and macrophages, is highly regulated. Elevated level of gelatinases has been found in tumors associated with a poor prognosis in cancer patients (5). A

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cyclic decapeptide, cCTTHWGFTLC (CTT), was found to be a potent and selective inhibitor of MMP-2 and MMP-9 (6). The HWGF motif is important for the inhibitory activity. Diethylenetriaminepentaacetic acid was conjugated to an amino group of the N-terminal cysteine of the CTT peptide for radiolabeling with ^{111}In. ^{111}In-DTPA-CTT is being developed for single-photon emission computed tomography (SPECT) imaging of gelatinase activity in metastatic tumors.

Related Resource Links:

- Chapters in MICAD (MMP)
- Gene information in NCBI (MMP2, MMP9)
- Articles in Online Mendelian Inheritance in Man (OMIM) (MMP2, MMP9)
- Clinical trials (MMP)
- Drug information in FDA (MMP)

Synthesis

[PubMed]

A mixture of 3.7-7.4 MBq (0.1-0.2 mCi) $^{111}InCl_3$ and DTPA-CTT (10 μg) was incubated in 0.1 M acetic acid for 30 min at room temperature (7). ^{111}In-DTPA-CTT was purified by high-performance liquid chromatography to have a radiochemical purity of >95%. The specific activity was >400 MBq/μmol (10.8 mCi/μmol).

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

Hanaoka et al. (7) reported that In-DTPA-CTT inhibited the proteolytic activity of MMP-2 with an IC_{50} value of 1026 μM, whereas CTT had an IC_{50} value of 283 μM. ^{111}In-DTPA-CTT was ~85% intact in murine serum for 3 h at 37°C.

Animal Studies

Rodents

[PubMed]

Hanaoka et al. (7) performed biodistribution studies in nude mice (n = 4-5) bearing human breast carcinoma MDA-MB-231 (high gelatinase expression) or MDA-MB-435S (low gelatinase expression) xenografts. ^{111}In-DTPA-CTT cleared rapidly from the blood with 0.09 ± 0.01% injected dose (ID)/g for the MDA-MB-231 and 0.16 ± 0.04% ID/g for the MDA-MB-435S tumors at 3 h. The tumor/blood ratio was 2.81 and 0.94 at 3 h, respectively. Accumulation of radioactivity was low in the liver (0.12-0.23% ID/g) and muscle (<0.01% ID/g). The majority of the radioactivity was excreted via the kidneys (7.8-9.19% ID/g at 3 h) into urine. There is a significant correlation (r = 0.801) between tumor accumulation and gelatinase activity. No blocking experiment was performed.

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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