Gadolinium-diethylenetriamine pentaacetic acid-carboxymethylarabinogalactan

Gd-DTPA-CMAG-A_2

Kam Leung, PhD[1]

Created: November 15, 2008; Updated: January 6, 2009.

Chemical name:	Gadolinium-diethylenetriamine pentaacetic acid-carboxymethylarabinogalactan	
Abbreviated name:	Gd-DTPA-CMAG-A_2	
Synonym:		
Agent category:	Polysaccharide	
Target:	Hepatic asialoglycoprotein receptor (ASGP-R)	
Target category:	Receptor	
Method of detection:	Magnetic resonance imaging (MRI)	
Source of signal/contrast:	Gadolinium, Gd	
Activation:	No	
Studies:	• *In vitro* • Rodents	No structure is available in PubChem.

Background

[PubMed]

Magnetic resonance imaging (MRI) maps information about tissues spatially and functionally. Protons (hydrogen nuclei) are widely used in imaging because of their abundance in water molecules. Water comprises ~80% of most soft tissue. The contrast of proton MRI depends primarily on the density of the nucleus (proton spins), the relaxation times of the nuclear magnetization (T1, longitudinal; T2, transverse), the magnetic environment of the tissues, and the blood flow to the tissues. However, insufficient

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

NLM Citation: Leung K. Gadolinium-diethylenetriamine pentaacetic acid-carboxymethylarabinogalactan. 2008 Nov 15 [Updated 2009 Jan 6]. In: Molecular Imaging and Contrast Agent Database (MICAD) [Internet]. Bethesda (MD): National Center for Biotechnology Information (US); 2004-2013.

contrast between normal and diseased tissues requires the development of contrast agents. Most contrast agents affect the T1 and T2 relaxation times of the surrounding nuclei, mainly the protons of water. T2* is the spin–spin relaxation time composed of variations from molecular interactions and intrinsic magnetic heterogeneities of tissues in the magnetic field (1). Cross-linked iron oxide (CLIO) nanoparticles and other iron oxide formulations affect T2 primarily and lead to decreased signals. On the other hand, paramagnetic T1 agents such as gadolinium (Gd^{3+}) and manganese (Mn^{2+}) accelerate T1 relaxation and lead to increased contrast images.

Gd, a lanthanide metal ion with seven unpaired electrons, has been shown to be very effective in enhancing proton relaxation because of its high magnetic moment and water coordination (2, 3). Gd-labeled diethylenetriaminepentaacetic acid (Gd-DTPA) was the first intravenous MRI contrast agent used clinically, and a number of similar Gd chelates have been developed in an effort to further improve clinical use. However, these low molecular weight Gd chelates have short blood and tissue retention times, which limit their use as imaging agents in the vasculature and in cancer tissues. Furthermore, they are largely nonspecific. Arabinogalactan, a polysaccharide, binds specifically to hepatocytes *via* asialoglycoprotein receptor (ASGP-R) (4-6). Li et al. (7) prepared aminated carboxymethylarabinogalactan (CMAG-A_2) to link with Gd-DTPA to form Gd-DTPA-CMAG-A_2 for imaging the liver *via* ASGP-R.

Synthesis

[PubMed]

DTPA-CMAG-A_2 was prepared by incubation of DTPA succinimide ester (~14 mmol) and CMAG-A_2 (0.51 mmol) (pH 10) at room temperature for 24 h (7). $GdCl_3$•6 H_2O was added to the solution of DTPA-CMAG-A_2 (1.2:1 molar ratio) and incubated at room temperature for 18–20 h. The product, Gd-DTPA-CMAG-A_2, was isolated with column chromatography. DTPA-CMAG-A_2 had 0.51 mmol of DTPA/g.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

Gd-DTPA-CMAG-A_2 and Gd-DTPA exhibited T1 relaxivity r_1 values (0.47 T) of 7.9 and 5.4 $mM^{-1}s^{-1}$ at 37°C in buffer containing bovine serum albumin, respectively (7). The r_1 value of Gd-DTPA-CMAG-A_2 was not affected by the addition of equal molar of Ca^{2+} or ethylenediaminetetraacetic acid.

Animal Studies

Rodents

[PubMed]

Li et al. (7) performed dynamic T1-weighted MRI imaging (4.7 T) studies in rats (n = 3) after injection of Gd-DTPA-CMAG-A_2 (79 nmol/kg) or Gd-DTPA (96 nmol/kg). The mean enhancement of the liver parenchyma and kidney was 38.7 ± 6.4% and 69.4 ± 4.4% for Gd-DTPA-CMAG-A_2 at 10–30 min, respectively. On the other hand, the mean enhancement of the liver parenchyma and kidney was 21.9 ± 4.5% and 53.8 ± 4.8% for Gd-DTPA at 10–30 min, respectively. The hepatic uptake rate of Gd-DTPA-CMAG-A_2 (half-life ($t_{1/2}$), 0.8 min) was faster than that of Gd-DTPA ($t_{1/2}$, 16.7 min), whereas the liver excretion rate of Gd-DTPA-CMAG-A_2 ($t_{1/2}$, 129.8 min) was slower than that of Gd-DTPA ($t_{1/2}$, 52.4 min). The renal uptake rate of Gd-DTPA-CMAG-A_2 ($t_{1/2}$, 0.1 min) was faster than that of Gd-DTPA ($t_{1/2}$, 4.6 min), whereas the renal excretion rate of Gd-DTPA-CMAG-A_2 ($t_{1/2}$,153.8 min) was slower than that of Gd-DTPA ($t_{1/2}$, 86.1 min). Rats receiving Gd-DTPA-CMAG-A_2 exhibited increases in the MR signal intensity in the liver comparing with Gd-DTPA at 10-90 min after injection. 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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