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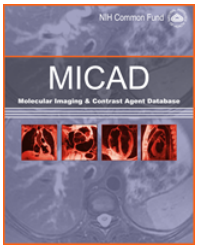

Gadolinium-Diethylenetriamine pentaacetic acid-poly(lactic-co-glycolic acid) microbubbles

Gd-DTPA-PLGA

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Chemical name:	Gadolinium-Diethylenetriamine pentaacetic acid-poly(lactic-co-glycolic acid) microbubbles	
Abbreviated name:	Gd-DTPA-PLGA, Gd-PLGA	
Synonym:		
Agent category:	Compound	
Target:	Non-targeted	
Target category:	Non-targeted	
Method of detection:	Multimodality imaging: magnetic resonance imaging (MRI), ultrasound (US)	
Source of signal:	Gadolinium (Gd), microbubbles	
Activation:	No	
Studies:	• *In vitro* • Non-primate non-rodent mammals	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 to create images because of their abundance in water molecules, which comprise >80% of most soft tissues. The contrast of proton MRI images depends mainly on the density of nuclear 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 contrast between normal and diseased tissues requires the use 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 and other iron oxide formulations affect T2 primarily and lead to a decreased signal. On the other hand, paramagnetic T1 agents such as gadolinium (Gd^{3+}) and manganese (Mn^{2+}) accelerate T1 relaxation and lead to brighter contrast images.

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Ultrasound is the most widely used imaging modality in clinical medicine (2) and its role in noninvasive molecular imaging is expanding with ligand-carrying microbubbles (3). Microbubbles are spherical cavities filled by a gas and encapsulated in a shell. The shells are made of phospholipids, surfactant, denatured human serum albumin, or synthetic polymer. Ligands and antibodies can be incorporated into the shell surface of microbubbles. Microbubbles are usually 1–8 μm in size and provide a strongly reflective interface and resonate to ultrasound waves. They are used as ultrasound contrast agents in imaging of inflammation, angiogenesis, intravascular thrombus, and tumors (4-6). They can also potentially be used for drug and gene delivery (7). Ao et al. (8) used poly(lactic-co-glycolic acid) (PLGA) as an encapsulating agent to form a multimodality imaging agent composed of gadolinium-diethylenetriamine pentaacetic acid (Gd-DTPA) (for MRI) and fluorocarbon-filled microbubbles (for ultrasound). Gd-DTPA-PLGA has been evaluated with *in vivo* imaging of the liver in rabbits, exhibiting enhanced MRI and ultrasound signals.

Related Resource Links:

- Chapters in MICAD
- Clinical trials (Gd-DTPA)
- Drug information in FDA (Gd-DTPA)

Synthesis

[PubMed]

Gd-DTPA-PLGA microbubbles were prepared with a double-emulsion method as described by Ao et al. (8). Laser particle-size analysis showed that the mean diameter of the microbubbles in saline solution (10^8 microbubbles/ml) was 1.47 ± 0.38 μm. The mean Gd concentration in the microbubbles was 25 ± 2 μg/mg.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

Longitudinal relaxation rates (ms^{-1}) of Gd-DTPA-PLGA at 0, 0.025, 0.05, and 0.075 mM Gd-DTPA were 7.13, 19.14, 21.73, and 23.19, respectively, measured at 1.5 T (8). Echo signal was detected in solution containing Gd-DTPA-PLGA with ultrasound scans (10 MHz).

Animal Studies

Rodents

[PubMed]

No publication is currently available.

Other Non-Primate Mammals

[PubMed]

Ao et al. (8) performed *in vivo* ultrasound imaging in rabbits after injection of ~2×10^{10} Gd-DTPA-PLGA microbubbles/kg (100 mg/kg) *via* the ear vein. The liver was the region of interest (20 mm^2). The echo intensities of the liver parenchyma were 16.2 ± 0.7, 25.2 ± 0.4, 24.9 ± 0.5, 24.1 ± 0.4, 23.6 ± 0.3, 21.9 ± 0.8, 20.1 ± 0.5, and 19.2 ± 1.5 at 0, 5, 10, 15, 20, 25, 30, and 35 min after injection, respectively. The echo intensity reached a maximum value at 5 min and thereafter decreased gradually. Increased echo intensities were observed in the hepatic artery, portal vein, and hepatic vein. T1-Weighted MRI imaging of the liver was performed at 0, 2, 15, 30, and 60 min after injection of Gd-DTPA-PLGA (200 mg/kg), and the signal intensities were 257 ± 15, 420 ±

32, 476 ± 42, 509 ± 42, and 411 ± 68, respectively. The microbubbles had no effect on the functions of the kidney and liver up to 30 days after injection.

Non-Human Primates

[PubMed]

No publication is currently available.

Human Studies

[PubMed]

No publication is currently available.

References

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