Quantum dot 800–mercaptopropionic acid

QD800-MPA

Kam Leung, PhD[1]

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Chemical name:	Quantum dot 800–mercaptopropionic acid	
Abbreviated name:	QD800-MPA	
Synonym:		
Agent category:	Compound	
Target:	Non-targeted	
Target category:	Non-targeted	
Method of detection:	Optical, near-infrared fluorescence (NIR)	
Source of signal:	Quantum dot (QD)	
Activation:	No	
Studies:	• *In vitro* • Rodents	Structure is not available in PubChem.

Background

[PubMed]

Optical fluorescence imaging is increasingly used to monitor biological functions of specific targets in small animals (1-3). However, the intrinsic fluorescence of biomolecules poses a problem when fluorophores that absorb visible light (350–700 nm) are used. Near-infrared (NIR) fluorescence (700–1,000 nm) detection avoids the background fluorescence interference of natural biomolecules, providing a high contrast between target and background tissues. NIR fluorophores have wider dynamic range and minimal background as a result of reduced scattering compared with visible fluorescence detection. They also have high sensitivity, resulting from low infrared background, and high extinction coefficients, which provide high quantum yields. The NIR region is also

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

Corresponding author.

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compatible with solid-state optical components, such as diode lasers and silicon detectors. NIR fluorescence imaging is becoming a noninvasive alternative to radionuclide imaging in small animals (4).

Fluorescent semiconductor quantum dots (QDs) are nanocrystals made of CdSe/CdTe/ZnS with radii of 1–10 nm (5-7). They can be tuned to emit fluorescence signals in a range of wavelengths by changing their sizes and composition, thus providing broad excitation profiles and high absorption coefficients. They have narrow, symmetric emission spectra with long, excited-state lifetimes (20–50 ns) compared with those of fluorescent dyes (1–10 ns). They process good quantum yields of 40%–90% and possess high extinction coefficients. They are more photo-stable than conventional organic dyes. They can be coated and capped with hydrophilic materials for additional conjugation with biomolecules, such as peptides, antibodies, nucleic acids, and small organic compounds, which have been tested *in vitro* and *in vivo* (7-11). Although many cells have been labeled with QDs *in vitro* with little cytotoxicity, there are limited studies of long-term toxicity of QDs in small animals (12-20); little is known about the toxicity and the mechanisms of clearance and metabolism of QDs in humans.

QDs that do not contain Cd (non-Cd QDs) have been prepared as an alternative to the more toxic Cd-based QDs. These newly developed non-Cd QDs exhibit improved blood half-life and minimal reticuloendothelial system (RES) accumulation with rapid renal clearance (21). These QDs easily extravasate leaky tumor blood vessels because of the enhanced permeability and retention effect. Mercaptopropionic acid (MPA)-coated InAs/InP/ZnSe QDs (QD800-MPA) have been evaluated for NIR fluorescence imaging tumor in mice (21, 22).

Related Resource Links:

- Chapters in MICAD (QDs)

Synthesis

[PubMed]

Non-Cd QDs (InAs/InP/ZnSe) (QD800, 1 nmol In) with an emission maximum at 800 nm was mixed with 5 mM MPA (pH 8) in chloroform for 4 h. QD800-MPA was isolated with centrifugation to remove excess MPA (22). QD800-MPA had a hydrodynamic diameter of 8.2 nm. QD800 ITK carboxyl (QD800-COOH) was purchased from Invitrogen as a control; it is composed of Cd/Te/ZnS and has a hydrodynamic diameter of 25 nm. QD800-MPA-HSA was prepared by mixing 1,000 nmol QD800-MPA with 15 nmol human serum albumin (HSA). QD800-MPA-HSA had a hydrodynamic diameter of 18 nm.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

Xie et al. (21) showed that QD800-MPA (10 nM, In) was less toxic than QD800-COOH (10 nM) to RAW 264.7 mouse macrophage cells after incubation for 24 h at 37°C. QD800-MPA exhibited 10% cytotoxicity, whereas QD800-COOH showed 50% cytotoxicity. Cell cytotoxicity for QD800-MPA and QD800-COOH increased to 50% and 65% at 48 h, respectively.

Animal Studies

Rodents

[PubMed]

Gao et al. (22) performed tumor-imaging studies with QD800-MPA in nude mice (n = 3/group) bearing 22B or LS174T tumors. Whole-body small animal images were obtained with reflectance planar fluorescence after intravenous injection of QD800-MPA (0.2 nmol), QD800-COOH (0.2 nmol), or QD800-MPA-HSA (0.1 nmol). Intense tumor signals were obtained in both tumors (passive targeting by enhanced vascular permeability) at 1 h after injection of QD800-MPA with low signal intensity from other organs. Tumor intensity increased over time with good fluorescence contrast at 4 h. *Ex vivo* biodistribution was studied at 4 h with mice bearing 22B tumors. Tumor accumulation was 11.0 ± 2.0% injected dose/gram (ID/g). The tissue with the highest accumulation was the liver (42.6 ± 6.4% ID/g), followed by the kidney (18.9 ± 1.9% ID/g), spleen (10.2 ± 2.9% ID/g), and lung (3.2 ± 1.4% ID/g). The tumor/background ratios were ~4 at 0.5, 1, and 4 h and decreased to 1.1 at 24 h. The biodistribution pattern obtained with region of interest fluorescence analysis was similar. Histological analysis of tumor sections showed that QD800-MPA was present in the interstitial space and tumor vessels. On the other hand, QD800-COOH showed tumor/background ratios of ~1 from 0.5 h to 24 h after injection. QD800-COOH showed one-fold higher accumulation in the liver and four-fold lower accumulation in the kidney than QD800-MPA at 4 h after injection. Tumor accumulation of QD800-MPA-HSA at 4 h after injection was 23.0 ± 2.4% ID/g; liver accumulation was 27.0% ID/g at 4 h after injection, and spleen accumulation was 5% ID/g at the same time point. QD800-MPA-HSA was considered to be more suitable than QD800-MPA as an imaging agent because it exhibited lower RES accumulation and higher tumor accumulation. QD800-MPA-HSA and QD-MPA were eliminated mainly by renal clearance. Xie et al. (21) determined that the circulation half-life of QD800-MPA in normal nude mice was 110 min, whereas the half-life for QD800-COOH was only 6 min.

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.

NIH Support

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