Polyethylene glycol-gold nanoparticles

PEG-AuNPs

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Chemical name:	Polyethylene glycol-gold nanoparticles	
Abbreviated name:	PEG-AuNPs	
Synonym:		
Agent Category:	Metal	
Target:	Phagocytes and tumor cells	
Target Category:	Phagocytosis, blood pool retention	
Method of detection:	X-ray, computed tomography (CT)	
Source of signal:	Au	
Activation:	No	
Studies:	• *In vitro* • Rodents	No structure is currently available in PubChem.

Background

[PubMed]

X-Ray imaging, or computed tomography (CT), visualizes tissue density differences that provide the image contrast produced by X-ray attenuation between soft tissues and electron-dense bone (1). Radiopaque X-ray contrast agents are needed to enhance the degree of contrast between diseased tissues and normal tissues. Water-soluble X-ray contrast agents are generally based on small tri-iodobenzene compounds such as monomers or dimers (2), which can be ionic (high osmolality) or nonionic (low osmolality). When injected intravenously, commonly *via* intra-arterial catheterization, these agents exhibit highly nonspecific vascular permeation and rapid renal excretion, which limits their targeting performance.

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Gold has not been used as an X-ray contrast agent *in vivo*. Gold has a higher atomic number and a higher absorption coefficient than iodine, providing 2.7-fold greater contrast/weight than iodine (3). Furthermore, imaging gold at 80–100 keV reduces interference from bone absorption and provides lower soft tissue absorption, which would reduce radiation to patients. Hainfeld et al. (3) used gold nanoparticles (AuNPs; 1.9 nm in diameter, ~50 kDa) as a CT contrast agent in mice; these experiments showed enhanced CT contrast of the vasculature, kidneys, and tumor in mice. However, plasma proteins in blood adsorb onto the surface of bare AuNPs, which produces large aggregates (4) that may result in altered pharmacokinetics and biodistribution of AuNPs (5). Polyethylene glycol (PEG) is found to minimize nonspecific adsorption of proteins onto NPs and to reduce their uptake by the liver (5). PEG-AuNPs are being studied as cancer CT imaging and photothermal agents (6).

Synthesis

[PubMed]

Cai et al. (6) prepared AuNPs by the citrate reduction of chloroauric acid. First, 500 ml of 0.254 mM chloroauric acid was heated to 100°C. Then 17.5 ml of 1% citric acid was added to the solution to produce AuNPs. AuNPs were incubated with methoxy PEG sulfhydryl solution at room temperature for 12 h. PEG-AuNPs were ~38 nm in diameter as measured with transmission electron microscopy (TEM) images and dynamic light-scattering experiments.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

Chithrani et al. (7) showed that AuNPs between 14 and 74 nm in diameter entered cultured HeLa tumor cells in medium containing 10% serum and were shown with TEM to be trapped in vesicles in the cytoplasm. The cellular uptake of the AuNPs increased for the first 2 h and gradually reached a plateau at 4–7 h. The uptake half-life was 2.10, 1.90, and 2.24 h at a rate of 622, 1,294, and 417 NPs/h for NPs 14, 50, and 74 nm in diameter, respectively.

Cai et al. (6) performed *in vitro* cytotoxicity assays in human WI-38 embryonic, human HepG2 hepatoma, and mouse macrophage RAW 264.7 cell lines. PEG-AuNPs (1.25–40 mM) showed little effect on cell viability after 24 h at 37°C.

Animal Studies

Rodents

[PubMed]

Cai et al. (6) performed biodistribution studies of PEG-AuNPs (2.5 μmol Au/g PEG-AuNPs) administered to normal mice *via* intravenous injection. The plasma half-life of PEG-AuNPs was 14.8 ± 3.3 h. The tissue with the highest AuNP accumulation was the liver (64.4% injected dose (ID)) at 3 d, followed by the spleen (9.7% ID), small intestine (4.3% ID), lymph nodes (1.9% ID), large intestines (1.6% ID), muscle (1.3% ID), and kidneys (~1% ID). There was minimum accumulation in the brain, heart, and lung. PEG-AuNPs were taken up by the reticuloendothelial system and by phagocytes in the liver, spleen, lymph nodes, and bone marrow as measured with optical microscopy of the tissues and cells. TEM images of the liver Kupffer cells showed intracellular accumulation of NPs in the cytoplasm. The mice showed normal hematology and blood chemistry at days 3 and 14. Histological examination of nine major organs and tissues 3 days after injection showed no evidence of inflammatory cell infiltration, cell swelling, or tissue necrosis in any mice. No signs of sickness were observed in the mice up to 6 months. CT imaging of mice bearing HT-1080 fibrosarcoma tumors showed good contrast enhancement in the right ventricle (~2-fold), inferior vena cava (~2-fold), spleen (~2-fold), liver (<1-fold), and kidney (<0.5-fold) from 0.1 h up to 24 h. There was a gradual accumulation of NPs in the liver up to 3 h, which then stayed almost constant up to 72 h, whereas there was a continuous accumulation in the spleen even after 48 h. All major blood vessels were well visualized as well as vessels leading to the tumor; contrast returned to background levels by 72 h.

Kim et al. (8) performed CT imaging in rats bearing a hepatoma tumor in the liver after intravenous injection of 40 mg PEG-AuNPs (31 nm in diameter). Good contrast enhancement (~2-fold) was observed in the hepatoma *versus* the surrounding normal liver from 5 min to 24 h after injection. The heart and major vessels were clearly visualized for at least 4 h. There was a gradual accumulation of NPs by the liver for up to 2 h, whereas there was a continuous accumulation in the spleen even after 24 h.

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.

References

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