^{99m}Tc-Galactosyl-methylated chitosan

^{99m}Tc-GMC

Kam Leung, PhD[1]

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Chemical name:	^{99m}Tc-Galactosyl-methylated chitosan	
Abbreviated name:	^{99m}Tc-GMC	
Synonym:		
Agent category:	Compound	
Target:	Asialoglycoprotein receptors (ASGP-Rs)	
Target category:	Receptor	
Method of detection:	Single-photon emission computed tomography (SPECT), gamma planar imaging	
Source of signal/contrast:	^{99m}Tc	
Activation:	No	
Studies:	• Rodents	Click on protein, nucleotide (RefSeq), and gene for more information about ASGP-R.

Background

[PubMed]

Asialoglycoprotein (ASGP) is specifically taken into mammalian hepatocytes by binding to ASGP receptors (ASGP-Rs) (1). The galactosyl moiety of ASGP is recognized on the surface of hepatocytes and is bound by ASGP-R. The ASGP–ASGP-R complex on the cell surface is subsequently taken into cytoplasm by endocytosis and transferred to lysosomes. ASGP-R is then dissociated from ASGP and recycled to the cell surface. ASGP is degraded in the lysosomes and excreted into the bile. The number of ASGP-Rs on the hepatocytes of individuals with liver disease decreases and is thus considered a good indicator for the evaluation of liver function. Because ASGP-R recognizes galactose, ^{99m}Tc-

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

Corresponding author.

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diethylenetriamine pentaacetic acid-galactosyl-human serum albumin (^{99m}Tc-GSA) (2, 3) and ^{99m}Tc-galactosyl-neoglycoalbumin (^{99m}Tc-NGA) (4) are ASGP-R probes that accumulate specifically in the liver and are used for liver scintigraphy to determine liver mass and function. Chitosan is a linear polysaccharide composed of D-glucosamine and *N*-acetylglucosamine subunits with numerous amine groups of D-glucosamine for ligand conjugation. Kim et al. (5) conjugated galactose (*via* lactobionic acid) to methylated chitosan for radiolabeling with ^{99m}Tc to form ^{99m}Tc-galactosyl-methylated chitosan (^{99m}Tc-GMC) for imaging ASGP-R expression in the liver.

Synthesis

[PubMed]

Deacetylated chitosan (5 kDa) was incubated with lactobionic acid, 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide hydrochloride, and *N*-hydroxysuccinimide for 72 h at room temperature (5). The resulting galactosylated chitosan was purified with dialysis and incubated with excess methyl iodide in the presence of sodium hydroxide for 1 h at ~60°C. GMC was isolated by precipitation with ethanol and centrifugation. GMC was incubated with 111 MBq (3 mCi) ^{99m}Tc-sodium pertechnetate, tricine, and stannous chloride for 30 min at room temperature. ^{99m}Tc-GMC conjugates were prepared with a labeling efficiency of >95%. ^{99m}Tc-GMC conjugates were stable in saline up to 6 h. The stability in human serum was >81% up to 2 h. The amount of galactose in galactosylated chitosan was 7.5 mol%. The composition of tri-, di-, and mono-methylation was 9, 46, and 35 mol%, respectively.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

No publication is currently available

Animal Studies

Rodents

[PubMed]

Kim et al. (5) performed *ex vivo* biodistribution studies in normal mice (n = 5/group) after intravenous injection of ^{99m}Tc-GMC at 10, 60, and 120 min. The initial tracer accumulation in the liver was 11.2% injected dose per gram (ID/g) at 10 min, 14.0% ID/g at 60 min, and 14.1% ID/g at 120 min after injection. The kidneys had the highest accumulation with 27.3%, 22.0%, and 19.6% ID/g at these time points, respectively. ^{99m}Tc-GMC was largely cleared by the kidneys. The stomach, intestine, heart, lung, muscle, blood, and spleen all showed relatively low accumulation (<4% ID/g). Single-photon emission computed tomography scintigraphic imaging was performed in mice after intravenous injection of 18.5 MBq (0.5 mCi) ^{99m}Tc-GMC at 10, 30, 60, and 120 min

after injection. High accumulation was observed in the liver and kidneys within a few minutes after injection. The urinary bladder was also highly visualized. Injection of ^{99m}Tc-methylated chitosan (non-galactosylated) showed high accumulation in the kidneys and urinary bladder with low radioactivity in the liver. 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.

References

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