^{99m}Tc-Tricarbonyl–labeled aspartic-*N*-monoacetic acid (ASMA)

[^{99m}Tc](CO)$_3$(ASMA)

Arvind Chopra, PhD[1]

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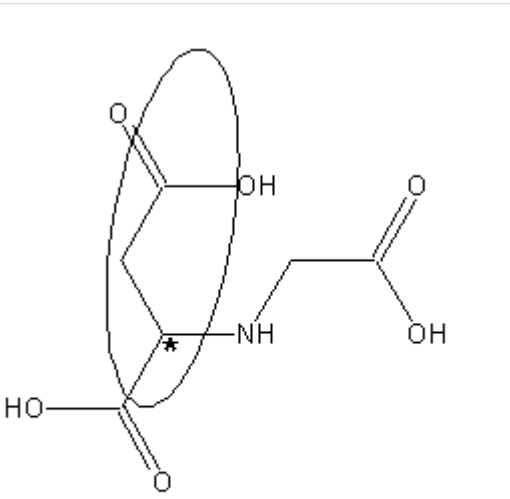
Chemical name:	^{99m}Tc-Tricarbonyl–labeled aspartic-*N*-monoacetic acid (ASMA)
Abbreviated name:	[^{99m}Tc](CO)$_3$(ASMA)
Synonym:	
Agent Category:	Compound
Target:	Organic anion transporter 1 (OAT1)
Target Category:	Transporter
Method of detection:	Single-photon emission computed tomography (SPECT); gamma planar imaging
Source of signal / contrast:	^{99m}Tc
Activation:	No
Studies:	• *In vitro* • Rodents



Structure of ASMA (1)

Background

[PubMed]

Ortho-[^{131}I]-iodohippurate ([^{131}I]-OIH) is considered to be the gold standard for the noninvasive imaging of kidney function and the detection of nephro-urological diseases

[1] National Center for Biotechnology Information, NLM, Bethesda, MD 20894; Email: micad@ncbi.nlm.nih.gov.

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in humans (2). However, because [^{131}I]-OIH can deliver a high dose of radiation to the kidneys and the thyroid, especially in patients with an impaired renal function, this radiolabeled compound is no longer available for clinical use in many countries (1). In the United States, ^{99m} Tc-labeled mercaptoacetylglycylglycylglycine ([^{99m}Tc]-MAG_3) is often used with gamma planar imaging to assess renal function in individuals, but this tracer generates a low signal/background ratio from the kidneys due to a differential attenuation of the ^{99m}Tc-gamma radiation between the two organs (3). In addition, data generated from these scans do not allow accurate quantification of kidney function because the renal clearance of [^{99m}Tc]-MAG_3 is only 50%–60% that of [^{131}I]-OIH (1).

A ^{99m}Tc-tricarbonyl–labeled nitrilotriacetic acid (NTA)–based renal imaging agent ([^{99m}Tc]$(CO)_3$(NTA)) was shown to be equivalent to [^{131}I]-OIH for the assessment of kidney function in normal rats (4) and human volunteers (5). However, the use of [^{99m}Tc]$(CO)_3$(NTA) in patients with a clinically diminished renal capacity has not been evaluated. In an effort to develop a radiolabeled imaging agent that can be used to assess impaired renal function, an isomer of [^{99m}Tc]$(CO)_3$(NTA), [^{99m}Tc]$(CO)_3$(aspartic-*N*-monoacetic acid) ([^{99m}Tc]$(CO)_3$(ASMA)), was developed, and the biodistribution of [^{99m}Tc]$(CO)_3$(ASMA) was investigated in normal rats and a rats that model of renal failure (1).

Related Resource Links

Related chapters in MICAD

References for [^{131}I]-iodohippurate in PubMed

References for [^{99m}Tc]-MAG_3 in PubMed

Clinical trials with [^{99m}Tc]-MAG_3

Synthesis

[PubMed]

A racemic mixture of the D- and L-isomers of ASMA (*rac*-ASMA) and the enantiomerically pure L-ASMA were synthesized as described elsewhere (1). The ^{99m}Tc-tricarbonyl complexes of *rac*-ASMA ([^{99m}Tc]$(CO)_3$(*rac*-ASMA)) and L-ASMA ([^{99m}Tc]$(CO)_3$(L-ASMA)) were prepared as detailed by Lipowska et al. (1). The radiochemical purity (RCP) of the two radiolabeled compounds was >99% as determined with high-performance liquid chromatography (HPLC). The radiochemical yields (RCY) and specific activities of [^{99m}Tc]$(CO)_3$(*rac*-ASMA) and [^{99m}Tc]$(CO)_3$(L-ASMA) were not reported.

The source, RCY, RCP, and specific activity of [^{131}I]-OIH, which was used in the biodistribution studies for comparison purposes, were not reported (1).

In this chapter, the term [^{99m}Tc]$(CO)_3$(ASMA) has been used as a general reference to the [^{99m}Tc]$(CO)_3$(*rac*-ASMA) and [^{99m}Tc]$(CO)_3$(L-ASMA) complexes.

In Vitro Studies: Testing in Cells and Tissues

[PubMed]

The stability of the [^{99m}Tc](CO)$_3$(ASMA) tracers was evaluated by incubating the radiochemicals with or without cysteine or histidine in phosphate buffer (pH 7.4) for up to 24 h (1). HPLC analysis of aliquots obtained at various time points from the mixtures showed there was no decomposition of the radiochemical complexes for at least 4 h.

Animal Studies

Rodents

[PubMed]

The biodistribution of [^{99m}Tc](CO)$_3$(ASMA) was investigated in normal rats (Group A) and a group of rats that modeled renal failure (Group B; the renal pedicles in these animals were ligated so that no urine was produced) (1). The rats (n = 4 anesthetized animals/group) were injected with a mixture of 0.74 MBq (20 μCi) [^{99m}Tc](CO)$_3$(ASMA) and 185 kBq (5 MCi) [^{131}I]-OIH through the tail vein. Group A rats were euthanized at 10 min postinjection (p.i.) and at 60 min p.i., and the Group B animals were euthanized at 60 min p.i. to determine the amount of radioactivity accumulated in the tissues and organs of interest. Urine was also collected from these animals for the duration of the study as described by Lipowska et al. (1). The amount of radioactivity present in the various tissues and urine of the animals was presented as a percent of injected dose (% ID) as shown in Table 1. With both [^{99m}Tc](CO)$_3$(ASMA) preparations, the amount of radioactivity in the blood of Group A rats was comparable to that with [^{131}I]-OIH (P = 0.07) at 10 min p.i.; however, at 60 min p.i. the amount of ^{99m}Tc in the blood with both ^{99m}Tc tracers was significantly lower ($P < 0.003$) than radioiodide. At 10 min p.i., the amount of radioactivity from the ^{99m}Tc tracers in the urine was comparable to that from [^{131}I]-OIH ($P > 0.1$). At 60 min p.i., the elimination of ^{99m}Tc through the urine was significantly faster ($P < 0.001$) than that of ^{131}I. The urinary ^{99m}Tc/^{131}I ratios at 10 min p.i. and 60 min p.i. were 106 ± 6 and 100 ± 3, and 106 ± 0 and 107 ± 2 for [^{99m}Tc](CO)$_3$(*rac*-ASMA) and [^{99m}Tc](CO)$_3$(L-ASMA), respectively. With the ^{99m}Tc-labeled compounds, very low levels of radioactivity were detected in the other organs (only data for liver is presented in Table 1).

Table 1: Biodistribution of tracer from [^{99m}Tc](CO)$_3$(ASMA) presented as % ID in select tissues of normal rats (Group A) and rats with renal failure (Group B) (1).

Tissue, organ, or fluid	Group A				Group B
	^{99m}Tc-*rac*-ASMA	^{99m}Tc-L-ASMA	^{99m}Tc-*rac*-ASMA	^{99m}Tc-L-ASMA	^{99m}Tc-*rac*-ASMA
	Time p.i.				

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	10 min		60 min		
Blood	5.2 ± 1.7 (6.7 ± 1.9)	4.7 ± 0.9 (5.1 ± 1.0)	0.2 ± 0.0 (0.7 ± 0.1)	0.3 ± 0.1 (0.8 ± 0.1)	17.9 ± 1.1 (16.7 ± 1.3)
Liver	2.5 ± 0.3 (3.7 ± 0.6)	3.7 ± 1.2 (2.9 ± 0.3)	0.2 ± 0.1 (0.7 ± 0.1)	0.3 ± 0.0 (0.6 ± 0.2)	6.2 ± 0.6 (7.9 ± 0.5)
Kidney	6.7 ± 1.0 (6.5 ± 0.7)	4.3 ± 2.2 (4.0 ± 1.8)	0.2 ± 0.1 (0.3 ± 0.1)	0.7 ± 0.3 (0.7 ± 0.3)	0.6 ± 0.2 (0.5 ± 0.2)
Urine	51.3 ± 6.2 (48.3 ± 4.9)	51.1 ± 7.3 (50.9 ± 6.0)	94.4 ± 1.0 (89.1 ± 0.9)	95.1 ± 4.1 (88.8 ± 2.7)	–
% Urinary ^{99m}Tc/^{131}I ratio	106 ± 6	100 ± 3	106 ± 0	107 ± 2	–

Values in parentheses represent % ID of radioactivity from [^{131}I]-OIH. ID: injected dose; p.i., postinjection.

Because the biodistribution of [^{99m}Tc](CO)$_3$(*rac*-ASMA) and [^{99m}Tc](CO)$_3$(L-ASMA) was similar in the normal rats, only [^{99m}Tc](CO)$_3$(*rac*-ASMA) was used for the biodistribution study in rodents with renal failure (Group B) (1). The Group B animals showed an increased accumulation of radioactivity in the liver and intestine both with [^{99m}Tc](CO)$_3$(*rac*-ASMA) and [^{131}I]-OIH at 60 min p.i. Accumulation of the tracer was significantly higher with [^{131}I]-OIH compared with [^{99m}Tc](CO)$_3$(*rac*-ASMA) (P = 0.032 and P = 0.019 for liver and intestine, respectively). This indicated that, compared with the ^{99m}Tc-labeled tracer, the excretion of radioactivity from the ^{131}I-labeled compound was primarily through the hepatobiliary route under renal failure conditions. In addition, the retention of label in the blood was significantly higher (P = 0.017) with [^{99m}Tc](CO)$_3$(*rac*-ASMA) than with [^{131}I]-OIH.

From these studies, the investigators concluded that the biodistribution of the [^{99m}Tc](CO)$_3$(ASMA) complexes was quite similar to that of [^{131}I]-OIH in normal rodents (1).

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.

Supplemental Information

[Disclaimers]

No information is currently available.

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