jnm/ RADIOCHEMISTRY AND RADIOPHARMACEUTICALS

^{99m}Tc-Thiomalic Acid Complex: A Nonstannous Chelate for Renal Scanning

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Thiomalic acid (monomercaptosuccinic acid) has been labeled with ^{99m}Tc without the use of an intermediary reducing agent. Tissue distribution studies in rats following the injection of ^{99m}Tc-tagged thiomalic acid (^{99m}Tc-TMA) showed 40–48% of the injected dose in the kidneys. Renal incorporation of this compound was influenced by various parameters such as pH, quantity of thiomalic acid, heating time, and the preparation–injection interval. Scintigrams of a midline kidney slice showed that the ^{99m}Tc activity concentrated mainly in the renal cortex. As a proposed renal-imaging agent, ^{99m}Tc-TMA compared favorably with ^{99m}Tc-Sn-dimercaptosuccinate and ^{99m}Tc-penicillamine regarding the percent incorporation into the kidney and was superior in this respect to ^{99m}Tc-Sn-glucoheptonate and ^{99m}Tc-Sn-diethylenetriamine pentaacetic acid. The ^{99m}Tc-TMA was also shown to be highly stable through 24 hr. The reagent can be made available in kit form and is easily combined with ^{99m}Tc in two steps. Finally, the absence of stannous ion in the ^{99m}Tc-TMA complex should avoid the problem of interference with other procedures involving pertechnetate $^{99m}TcO_4^-$ as the imaging agent.

J Nucl Med 18: 353–359, 1977

Most technetium-labeled renal-scanning agents require the presence of stannous ion or other reducing substances in their preparation (*1–4*). Experience with ^{99m}Tc-penicillamine (^{99m}Tc-PEN) (*5,6*) has shown that a technetium chelate may be prepared without an intermediate reductant. Although ^{99m}Tc-PEN possesses outstanding renal-imaging properties, its widespread use has been limited by its somewhat tedious method of preparation. Because of this disadvantage, we undertook an investigation aimed at developing a comparable agent that would be easier to prepare and still possess the useful characteristics of ^{99m}Tc-PEN. The introduction of ^{99m}Tc-Sn-dimercaptosuccinate (^{99m}Tc-Sn-DMSA) (*4*) led us to investigate the labeling of thiomalic acid, a compound known to form stable chelates with a variety of metals (*7–9*). This report summarizes our preliminary investigation toward the formation of a nonstannous ^{99m}Tc chelate of thiomalic acid (^{99m}Tc-TMA) which shows promise as a radiopharmaceutical for renal cortical imaging.

MATERIALS AND METHODS

Initially, a stock solution of thiomalic acid (100 mg/cc) was prepared using sterile water for injection. Then 1-cc aliquots were transferred to 5-cc sterile reaction vials by passage through a 0.22-μm Millipore filter.

Preparation of ^{99m}Tc-TMA. The optimal formulation for this tracer was derived by investigating the effects of pH, heating time, and TMA concentration

Received Feb. 4, 1976; revision accepted Oct. 26, 1976.

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on the labeling efficiency and organ distribution of the finished product. The initial TMA concentration (100 mg/cc) was varied by adding incremental volumes of $^{99m}TcO_4^-$ in normal saline to the reagent vial. The acidity of the reagent was adjusted by dropwise addition of 1 *N* HCl or NaOH. All pH determinations were performed with a pH meter. The labeling procedure was completed by heating the solution at 100°C in a constant-temperature oil bath.

The stability and labeling efficiency of ^{99m}Tc-TMA was investigated chromatographically in several solvent systems using both ascending thin-layer and ascending paper techniques. The prepared compound was spotted 10 min after preparation and then at varying intervals up to 24 hr. For purposes of comparison, chromatography was performed with one system for each of the other renal agents studied in this set of experiments. The effect of oxygen on the stability of the ^{99m}Tc-TMA was studied by bubbling O_2 through the solution for 10 min at room temperature after initial chromatographic analysis, followed by repeat chromatography in the same system. The effect of high-activity labeling and ingrowth of generator were also explored.

Tissue distribution studies were performed on Sprague–Dawley rats, weighing 250–400 gm. Microcurie quantities of ^{99m}Tc-TMA (1.6 mg) were injected through the tail vein into the ether-anesthetized animals. At the appropriate time after injection, the rats were reanesthetized, blood samples drawn by cardiac puncture, and the animals killed in an ether atmosphere. The liver, one kidney, and a gastrocnemius muscle were removed, washed once in water, twice in 10% formalin, blotted dry, and wet-weighed on an analytic balance. They were then counted in an automatic gamma-counting system. The percent of administered dose incorporated into the tissues was calculated using a standard prepared from the injected material. For purposes of calculating the organ uptake of the radiopharmaceutical, blood was taken to represent 7% and muscle 40% of the body weight. The concentrations in the kidney and liver were determined using actual organ weight. Each data point represents the mean value for four animals and is reported to two significant figures. The data are presented as percent dose/organ, percent mean body concentration (MBC) (*10*), and as ratios of the MBC. The distribution of ^{99m}Tc-TMA in the renal parenchyma was determined by gamma scintigraphy of a midline kidney slice using methods previously described (*5*).

In order to evaluate ^{99m}Tc-TMA for renal scanning, it was compared to ^{99m}Tc-PEN, ^{99m}Tc-Sn-DMSA, ^{99m}Tc-Sn-glucoheptonate (^{99m}Tc-Sn-GH),

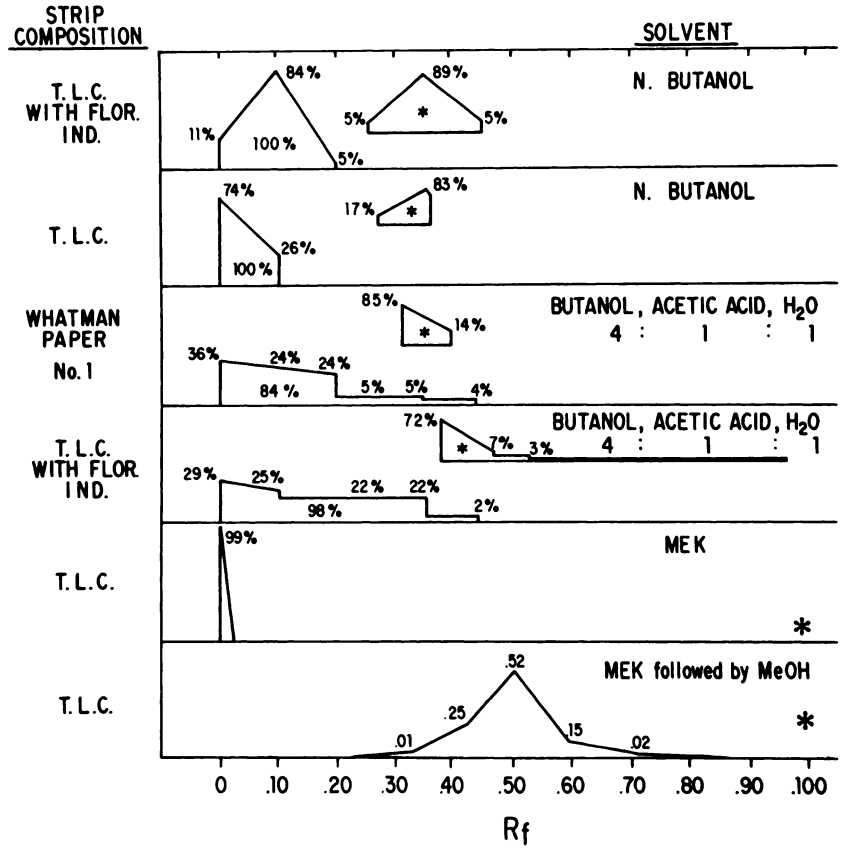

FIG. 1. Chromatography studies. Areas with asterisks represent range of $^{99m}TcO_4^-$ spread. Percentage marks indicate magnitude of migration to selected R_f. Enclosures without asterisks indicate similar data for ^{99m}Tc-TMA. Percentages within enclosures indicate quantity of applied radioactivity encompassed by that range. $^{99m}TcO_4^-$ and ^{99m}Tc-TMA were developed on separate strips, and at no time was there more than 5% free $^{99m}TcO_4^-$ present in ^{99m}Tc-TMA preparation.

and ^{99m}Tc-Sn-diethylenetriaminepentaacetic acid (^{99m}Tc-Sn-DTPA) in the same animal model using the same procedure. ^{99m}Tc-PEN was prepared in our laboratory by the addition of 2 cc of pertechnetate solution (1–2 mCi) to 60 mg of D-penicillamine, adjusting the pH to 8.6, and autoclaving for 15 min at 100°C. The other pharmaceuticals were obtained as commercial kits and labeled with $^{99m}TcO_4^-$ from a generator* in accordance with the manufacturer's instructions.

RESULTS

Chromatographic results. Figure 1 illustrates the results of the useful solvent systems studied. The most favorable separation of labeled compound from $^{99m}TcO_4^-$ was achieved with methyl ethyl ketone (MEK) on silica gel TLC. When this was followed by the development of the strip in 85% methanol, there resulted a migration of radioactivity that resolved into a single activity peak. The R_f of ^{99m}Tc-TMA was significantly separated from the R_f of free pertechnetate. In no chromatographic system did we find evidence of ^{99m}Tc activity that migrated differently from pertechnetate or the labeled compound. In all systems the amount of free pertechnetate was less than 5%.

Neither bubbling oxygen through the ^{99m}Tc-TMA solution for 10 min nor allowing the prepared compound to sit for as long as 24 hr caused a breakdown to pertechnetate or a change in the chromatographic patterns described. In the solvent systems employed, ^{99m}Tc-Sn-DTPA, ^{99m}Tc-Sn-GH, and ^{99m}Tc-Sn-DMSA remained at the origin; there was less than 5% free $^{99m}TcO_4^-$, and no evidence of breakdown followed oxygenation for 10 min.

Mass effect. Table 1 shows the effect of the varying TMA concentration on the organ distribution of ^{99m}Tc-TMA. Clearly, the presence of TMA in the preparation results in the formation of a technetium complex that shows a propensity for kidney uptake remarkably unlike that of $^{99m}TcO_4^-$. As the TMA concentration during labeling was increased from 10 mg/cc, a significant rise in renal uptake of ^{99m}Tc resulted, with about 33 mg/cc being most effective. The levels of liver and muscle radioactivity rose slightly with increasing concentration, while the blood concentration remained relatively constant. The kidney-to-tissue ratios indicate that excellent images could be obtained over a wide range of TMA concentrations.

pH effect. To determine the effect on the behavior of ^{99m}Tc-TMA the product was prepared by adding 2 cc of $^{99m}TcO_4^-$ to 1 cc of stock solution (100 mg/cc) and adjusting the solution to the desired pH level by adding 1 *N* HCl or NaOH. The labeling procedure was completed by heating for 10 minutes at 100°C. Table 2 shows the change in organ distribution of ^{99m}Tc-TMA with these variations in pH. Peak kidney concentrations occurred between pH 1.5 and 2.5, dropping significantly above or below that range. Likewise the ratios between kidney and blood, liver, and muscle generally appeared maximal in this same pH range.

Effect of heating time. The product was made by adding 2 cc $^{99m}TcO_4^-$ to 1 cc TMA reagent (100 mg/cc) and heating at 100°C for 0, 5, 10, and 15 min. Table 3 shows that heating the product for 10 min gave the highest renal uptake. Significant kidney accumulation of ^{99m}Tc-TMA also occurred when the product was not exposed to heating. This suggests that the formation of a Tc-TMA complex proceeds

TABLE 1. ORGAN DISTRIBUTION OF ^{99m}Tc-TMA COMPARED WITH ORIGINAL TMA CONCENTRATION

	PERCENT DOSE/ORGAN $\bar{x} \pm$ s.d.					
Concentration (mg/cc):	0	10	20	33	50	75
Blood	11 ± 0.53	10 ± 1.3	8.8 ± 0.59	11 ± 1.8	11 ± 1.6	12 ± 0.57
Liver	3.8 ± 0.24	3.2 ± 0.13	3.0 ± 0.75	4.3 ± 0.064	4.8 ± 0.29	6.6 ± 1.1
Kidney	0.48 ± 0.057	10 ± 1.7	13 ± 2.2	17 ± 1.9	18 ± 1.9	18 ± 0.48
Muscle	6.4 ± 0.48	4.3 ± 0.63	4.0 ± 0.61	6.1 ± 1.1	5.5 ± 0.54	4.8 ± 0.68
	MEAN BODY CONCENTRATION (%) $\bar{x} \pm$ s.d.					
Concentration (mg/cc):	0	10	20	33	50	75
Blood	160 ± 7.6	140 ± 18	110 ± 28	160 ± 26	150 ± 23	180 ± 8.1
Liver	110 ± 7.8	77 ± 8.0	71 ± 15	120 ± 3.3	100 ± 15	170 ± 18
Kidney	140 ± 7.5	2900 ± 630	3600 ± 630	4700 ± 400	5100 ± 250	5200 ± 390
Muscle	16 ± 1.2	11 ± 1.6	10 ± 1.5	15 ± 2.3	14 ± 1.3	12 ± 1.7
	TISSUE RATIOS					
Kidney/Blood	0.88	21	33	29	34	29
Kidney/Liver	1.3	38	51	39	51	31
Kidney/Muscle	8.8	260	360	310	360	430

even at room temperature and that heat simply accelerates the reaction.

Thus, our optimal preparation consists of 1 cc of TMA (100 mg/cc), 2 cc of $^{99m}TcO_4^-$ in normal saline (which brings the pH to about 2.0), and a 10-min heating at 100°C. This solution is then cooled to room temperature for injection.

^{99m}Tc-TMA stability. To evaluate the effect of time on the biologic distribution of the prepared compound, in vivo distribution studies were performed at varying time intervals after preparation. Table 4 shows that with increasing time after preparation, the renal concentration of ^{99m}Tc actually increased while the blood levels fell, thereby increasing the kidney-to-blood ratios.

Comparison study. A study was performed to compare the renal concentration and body distribution of ^{99m}Tc-TMA to ^{99m}Tc-Sn-DMSA, ^{99m}Tc-PEN, ^{99m}Tc-Sn-GH and ^{99m}Tc-Sn-DTPA. Tables 5–7 show the results obtained with each freshly prepared compound at 0.5, 1, and 2 hr after injection. The time periods selected for study were chosen on the basis of possible clinical requirements. The highest renal concentrations for any of the scanning agents were achieved with ^{99m}Tc-TMA and ^{99m}Tc-Sn-DMSA, with no significant difference noted with variation of time. The next highest renal concentration was achieved with ^{99m}Tc-PEN, followed by ^{99m}Tc-Sn-GH and ^{99m}Tc-Sn-DTPA. Those compounds with the highest concentrations in the kidney exhibited the

TABLE 2. ORGAN DISTRIBUTION OF ^{99m}Tc-TMA COMPARED WITH LABELING pH

	PERCENT DOSE/ORGAN $\bar{x} \pm$ s.d.						
pH	1.0	1.5	2.0	2.5	3.0	5.3	7.0
Blood	13 ± 0.82	12 ± 0.65	11 ± 1.8	9.1 ± 1.8	11 ± 0.82	9.0 ± 0.89	7.9 ± 1.1
Liver	7.2 ± 0.46	5.0 ± 0.28	4.3 ± 0.064	4.3 ± 0.32	2.7 ± 0.49	2.9 ± 0.17	5.0 ± 0.32
Kidney	9.9 ± 1.1	17 ± 1.8	17 ± 1.9	17 ± 1.1	9.6 ± 1.9	4.6 ± 0.24	3.1 ± 0.18
Muscle	6.0 ± 0.62	12 ± 2.9	6.1 ± 1.1	7.8 ± 0.46	5.2 ± 1.5	5.2 ± 0.69	4.7 ± 1.1
	MEAN BODY CONCENTRATION (%) $\bar{x} \pm$ s.d.						
pH	1.0	1.5	2.0	2.5	3.0	5.3	7.0
Blood	180 ± 12	170 ± 9.3	160 ± 26	130 ± 25	150 ± 12	130 ± 13	110 ± 16
Liver	190 ± 13	120 ± 7.7	120 ± 3.3	100 ± 20	57 ± 11	66 ± 2.2	130 ± 18
Kidney	2800 ± 420	4700 ± 550	4700 ± 400	5000 ± 660	2800 ± 600	1300 ± 69	820 ± 77
Muscle	15 ± 1.5	31 ± 7.2	15 ± 2.3	20 ± 1.1	13 ± 3.9	13 ± 1.7	12 ± 2.7
	TISSUE RATIOS						
Kidney/Blood	16	27	29	39	19	10	7.5
Kidney/Liver	15	39	39	50	49	20	6.3
Kidney/Muscle	190	150	310	250	220	100	68

TABLE 3. DISTRIBUTION OF ^{99m}Tc-TMA COMPARED WITH HEATING TIME AT 100°C

	PERCENT DOSE/ORGAN $\bar{x} \pm$ s.d.			
Heating time (min)	0	5	10	15
Blood	9.1 ± 1.2	12 ± 1.6	12 ± 1.2	11 ± 1.2
Liver	4.5 ± 1.2	4.6 ± 0.25	4.5 ± 0.43	5.3 ± 0.55
Kidney	7.5 ± 0.79	16 ± 0.93	22 ± 2.0	20 ± 1.6
Muscle	5.4 ± 0.56	6.0 ± 0.40	5.3 ± 0.81	4.4 ± 0.16
	MEAN BODY CONCENTRATION (%) $\bar{x} \pm$ s.d.			
Heating time (min)	0	5	10	15
Blood	130 ± 18	170 ± 22	170 ± 17	160 ± 18
Liver	87 ± 19	93 ± 4.9	120 ± 9.8	120 ± 16
Kidney	2000 ± 170	4400 ± 340	6000 ± 730	5500 ± 940
Muscle	14 ± 1.4	15 ± 0.99	13 ± 2.0	11 ± 0.41
	TISSUE RATIOS			
Kidney/Blood	15	26	35	34
Kidney/Liver	23	47	50	46
Kidney/Muscle	140	290	460	500

TABLE 4. DISTRIBUTION OF ^{99m}Tc-TMA ONE HOUR POSTINJECTION COMPARED WITH TIME POSTPREPARATION

PERCENT DOSE/ORGAN $\bar{x} \pm$ s.d.			
Time after preparation (hr):	0.5	3	5
Blood	12 ± 1.0	8.3 ± 1.5	7.0 ± 0.20
Liver	5.6 ± 0.87	8.0 ± 0.33	8.5 ± 0.58
Kidney	22 ± 2.5	26 ± 2.8	27 ± 0.83
Muscle	5.8 ± 0.47	7.6 ± 1.6	4.8 ± 0.71
MEAN BODY CONCENTRATION (%) $\bar{x} \pm$ s.d.			
Time after preparation (hr):	0.5	3	5
Blood	170 ± 14	120 ± 21	100 ± 2.9
Liver	140 ± 22	220 ± 23	270 ± 24
Kidney	5800 ± 890	7800 ± 1000	8200 ± 200
Muscle	14 ± 0.18	19 ± 4.1	12 ± 1.8
TISSUE RATIOS			
Kidney/Blood	34	65	82
Kidney/Liver	41	36	30
Kidney/Muscle	410	410	680

slowest blood clearance rates, and vice versa. We have noted a curious feature of ^{99m}Tc-Sn-DMSA: at each time period, the percentage of the injected dose incorporated into and remaining in the liver is greater than that for any other compound studied by our group. This finding appears to be at variance with those reported in the literature (*4*). This inordinate liver uptake was found to be reproducible in subsequent in vivo studies. An explanation for the inconsistency was sought but has not been found. Examination of the tissue ratios show that among the agents studied, ^{99m}Tc-Sn-GH obtained the highest ratios at every time period, along with low blood, liver, and muscle values. The quantity of this compound in the kidney, however, varied from ½ to ⅓ of that obtained by the cortical labeling agents. The least desirable ratio was achieved by ^{99m}Tc-Sn-DTPA.

DISCUSSION

Several useful Tc-labeled renal-scanning agents are available commercially, but they contain either stannous ion or another reducing agent. The efficacy of the labeled products formed using these reductants may be influenced by oxidation or hydrolysis. For example, one manufacturer recommends that their preparation (^{99m}Tc-Sn-DMSA) be used within 0.5 hr of the time of formulation. To this potential problem, it was recommended that the reductants be used in excess or the product stored under nitrogen to minimize degradation (*11*). Furthermore, stannous ion in a reaction medium may cause high tissue background in a subsequent radioactive study involving $^{99m}TcO_4^-$ (*12*). It appears that in the case of the ^{99m}Tc-chelates, the elimination of the need for an exogenous reducing agent would be a useful achievement. Two chelates discussed here (^{99m}Tc-TMA and ^{99m}Tc-PEN) are prepared without added reducing agents and do not appear to present problems of instability.

The parent compound, thiomalic acid, is a stable reagent, has a molecular weight of 150, is water-

TABLE 5. COMPARATIVE ORGAN DISTRIBUTION OF VARIOUS Tc-LABELED COMPOUNDS AT 0.5 HR POSTINJECTION

PERCENT DOSE/ORGAN $\bar{x} \pm$ s.d.	^{99m}Tc-TMA	^{99m}Tc-PEN	^{99m}Tc-Sn-DMSA	^{99m}Tc-Sn-GH	^{99m}Tc-Sn-DTPA
Blood	18 ± 2.0	33 ± 4.9	17 ± 2.4	4.0 ± 0.98	4.8 ± 0.46
Liver	5.9 ± 1.5	6.0 ± 1.2	25 ± 1.8	1.7 ± 0.30	1.03 ± 0.19
Kidney	18 ± 1.1	11 ± 2.2	17 ± 1.5	8.8 ± 0.52	1.1 ± 0.27
Muscle	8.7 ± 1.6	8.6 ± 2.5	5.2 ± 0.36	4.8 ± 1.5	4.1 ± 0.70
MEAN BODY CONCENTRATION (%) $\bar{x} \pm$ s.d.					
	^{99m}Tc-TMA	^{99m}Tc-PEN	^{99m}Tc-Sn-DMSA	^{99m}Tc-Sn-GH	^{99m}Tc-Sn-DTPA
Blood	260 ± 29	460 ± 90	240 ± 34	57 ± 14	68 ± 6.6
Liver	130 ± 26	150 ± 16	460 ± 48	39 ± 8.7	25 ± 3.5
Kidney	4800 ± 790	2900 ± 550	4000 ± 350	2500 ± 180	330 ± 84
Muscle	22 ± 3.9	22 ± 6.1	13 ± 0.89	12 ± 3.8	10 ± 1.7
TISSUE RATIOS					
Kidney/Blood	19	6.3	17	44	4.8
Kidney/Liver	37	19	8.7	64	13
Kidney/Muscle	220	130	310	210	33

TABLE 6. COMPARATIVE ORGAN DISTRIBUTION OF VARIOUS Tc-LABELED COMPOUNDS AT ONE HOUR POSTINJECTION

	^{99m}Tc-TMA	^{99m}Tc-PEN	^{99m}Tc-Sn-DMSA	^{99m}Tc-Sn-GH	^{99m}Tc-Sn-DTPA
PERCENT DOSE/ORGAN $\bar{x}$ ± s.d.					
Blood	12 ± 2.0	21 ± 2.1	14 ± 2.2	1.9 ± 0.31	1.9 ± 0.50
Liver	7.2 ± 0.66	4.0 ± 0.27	17 ± 3.7	1.3 ± 0.25	0.57 ± 0.09
Kidney	20 ± 1.3	16 ± 1.5	20 ± 1.4	9.1 ± 1.1	0.66 ± 0.10
Muscle	6.0 ± 1.0	9.0 ± 1.2	4.5 ± 1.4	1.9 ± 0.45	1.5 ± 0.37
MEAN BODY CONCENTRATION (%) $\bar{x}$ ± s.d.					
Blood	180 ± 29	300 ± 30	200 ± 32	27 ± 4.5	27 ± 7.2
Liver	220 ± 30	100 ± 3.7	310 ± 86	33 ± 7.7	17 ± 3.0
Kidney	6600 ± 1100	4100 ± 730	5300 ± 380	2500 ± 260	220 ± 51
Muscle	15 ± 2.7	22 ± 2.9	11 ± 3.5	4.7 ± 1.1	3.8 ± 0.84
TISSUE RATIOS					
Kidney/Blood	37	14	27	93	8.1
Kidney/Liver	30	41	17	76	13
Kidney/Muscle	440	190	480	530	58

TABLE 7. COMPARATIVE ORGAN DISTRIBUTION OF VARIOUS Tc-LABELED COMPOUNDS AT TWO HOURS POSTINJECTION

	^{99m}Tc-TMA	^{99m}Tc-PEN	^{99m}Tc-Sn-DMSA	^{99m}Tc-Sn-GH	^{99m}Tc-Sn-DTPA
PERCENT DOSE/ORGAN $\bar{x}$ ± s.d.					
Blood	8.3 ± 0.70	14 ± 2.4	11 ± 0.72	0.96 ± 0.02	0.18 ± 0.03
Liver	8.7 ± 0.59	3.4 ± 0.54	11 ± 3.2	0.98 ± 0.08	0.38 ± 0.03
Kidney	24 ± 2.1	17 ± 2.6	27 ± 1.1	8.7 ± 0.29	0.46 ± 0.14
Muscle	4.5 ± 0.58	7.4 ± 0.91	4.4 ± 0.39	1.2 ± 0.37	0.33 ± 0.08
MEAN BODY CONCENTRATION (%) $\bar{x}$ ± s.d.					
Blood	120 ± 10	210 ± 35	150 ± 10	14 ± 0.32	2.5 ± 0.45
Liver	200 ± 16	86 ± 16	250 ± 43	23 ± 1.2	9.2 ± 1.6
Kidney	5800 ± 540	4300 ± 510	7100 ± 640	2300 ± 94	110 ± 31
Muscle	11 ± 1.5	18 ± 2.3	11 ± 0.98	3.0 ± 0.93	0.82 ± 0.20
TISSUE RATIOS					
Kidney/Blood	48	21	47	160	44
Kidney/Liver	29	50	28	100	12
Kidney/Muscle	530	240	650	770	130

soluble and nontoxic in low dosage, and is a known chelating agent. In its reaction with such transition metals as Zn and Ni (*7–9*), there is evidence that it forms complexes having 1:1 and 2:1 ligand-to-metal ratios, respectively. Titration curves of thiomalic acid in the presence of equivalent amounts of metal ion show the displacement of three protons/molecule, indicating that the metal may be coordinated through the sulfur of the mercapto group as well as the carbonyl groups (*7*). The transition-metal chelates formed vary in their stability constants; one proposed hierarchy being Hg > Zn > Ag > Ni > Co (*7*).

The structure of ^{99m}Tc-TMA is not known, but its method of preparation is similar to that for the ^{99m}Tc-pyridoxal reported by Baker, Bellen, and Ronai (*11*). As in their synthesis, the quantity and duration of heat applied, the pH of the environment, and the quantity of compound used in the reaction were all important contributors to the labeling efficiency. Unlike their parent compound, the thiomalic acid molecule (as well as D-penicillamine) contains a sulf-

hydryl group and is a straight-chain compound instead of a ring structure. It is devoid of an imino site, yet complexing occurs under similar conditions.

As our data indicate, thiomalic acid in the presence of heat and an acid environment probably forms a complex with technetium that is stable for at least 24 hr after preparation. The blood clearance of ^{99m}Tc-TMA is slow relative to ^{99m}Tc-Sn-DTPA or ^{99m}Tc-Sn-GH. The target organs are the kidneys and liver. The quantity of ^{99m}Tc-TMA that concentrates in rat kidney compares well with that of ^{99m}Tc-Sn-DMSA. Our data suggest that, once prepared, ^{99m}Tc-TMA would be sufficiently stable to be used throughout the work day.

The radiation dose to the kidneys was calculated to be 0.8 rad/mCi of ^{99m}Tc-TMA injected (*14*), and is similar in this respect to the estimate for ^{99m}Tc-Sn-DMSA. These values are greater than for the other compounds studied, due primarily to greater uptake and retention of the former complexes by the kidney. Gamma scintigraphy of a kidney slice following injection of ^{99m}Tc-TMA located nearly all of the activity in the cortical portion of the kidney, just as with ^{99m}Tc-PEN. For scanning purposes, provided a perfusion study is not required, the appropriate dose of ^{99m}Tc-TMA should be about the same as for ^{99m}Tc-PEN or ^{99m}Tc-Sn-DMSA. Ingrowth generator time and high activity labeling did not affect the preparation of ^{99m}Tc-TMA in our work.

ACKNOWLEDGMENT

This study was supported by MRIS Grant 3376.

FOOTNOTE

* New England Nuclear, North Billerica, Mass.

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