A "KIT" METHOD FOR THE PREPARATION OF A TECHNETIUM-TIN(II) COLLOID AND A STUDY OF ITS PROPERTIES

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In the course of evaluating the use of Sn(II) for technetium labeling of albumin, it was found that a ^{99m}Tc-Sn(II) colloid could be prepared without pH titration and radiochemical separation in the procedure (*1*). This communication describes a "kit" procedure for preparing the colloid using Sn(II) and albumin, presents evidence for technetium (VII) reduction in the procedure, and reports studies of properties of the colloid.

MATERIALS AND METHODS

Technetium generators were obtained from New England Nuclear Corp. Stock solutions of human serum albumin (HSA), 5–50 mg/ml, were prepared by diluting a 250-mg/ml solution (pH 7, Cutter) in saline. A stock 1-m*M* Sn(II) solution was prepared as follows: 189.6 mg of anhydrous $SnCl_2$ flakes (Matheson, Coleman, and Bell) was weighed into a 100-ml volumetric flask. After filling the flask with 100 ml of distilled water, the flask content was mixed by inversions of the flask. The resultant 10-m*M* Sn(II) solution was further diluted in distilled water to 1 m*M*. After bubbling N_2 through it for 5 min, the 1-m*M* Sn(II) solution was passed through a 0.22-micron Millipore filter into vented sterile glass vials, 1 ml per vial. Then the air inside the vial was purged for 1.5 min with N_2 passed through a 0.22-micron Millipore filter. The time from preparing the 10-m*M* Sn(II) solution to completing the purging of 3–6 vials with N_2 was 26–40 min in the preparation of ten lots on different days. These 1-ml portions of the 1-m*M* Sn(II) solution were then kept at 4°C in a refrigerator until use. Redox titration of the Sn(II) was performed before and after the filtration. Iodine dissolved in potassium iodide solution was used for the titration. When the volume of the filtration did not exceed 2 ml/cm^2 of the filter, passage of the Sn(II) was essentially quantitative.

To prepare the colloid, 5 ml of the generator eluate was added to the stock Sn(II) solution in the vial. The vial was gently agitated for 1 min and set aside for additional 4 min. Then 1 ml of the stock HSA solution (5, 25, or 50 mg HSA) was added dropwise to the vial with a gentle agitation of the vial. The resultant mixture was the colloid. The colloid was usually kept at 4°C in a refrigerator when not in use. The amount of Sn(II) used in preparing 7 ml of the colloid was 1 μmole (1 ml, 1 m*M*) in all studies described in this paper. The only exception was in studies evaluating the consequence of oxidation of Sn(II) prior to its use in preparing the colloid. In these studies, 0.5 μmole of Sn(II) (1 ml, 0.5 m*M*) was used in the preparation.

Biological properties of the colloid were evaluated in Sprague-Dawley rats (BW 180–250 gm). The tissue distribution of the technetium was determined following the intravenous administration of 0.2-ml doses of the colloid. Organs were removed and packed in containers. The organ sample was placed at varying distance under the crystal detector of a scintillation camera, assayed for radioactivity at varying window width at the photopeak, and compared to duplicated standards of corresponding mass thickness in similar containers. Low-activity samples were assayed for the activity in a well scintillation counter. Whole-body retention of the technetium in the rat was measured using the scintillation camera as a whole-body counter. Rats sacrificed 15 min after the administration and kept frozen served as the 100% standards.

Nine batches of the colloid were evaluated by Millipore filtration. This was done following standing the preparation for 16–72 hr after portions of it were used for the assay in rats. During the standing, it was kept at room temperature in a lighted room for 1–10 hr and at 4°C in the refrigerator for 15–62 hr.

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TABLE 1. TISSUE DISTRIBUTION OF TECHNETIUM IN RATS FOLLOWING ADMINISTRATION OF ^{99m}Tc-Sn(II) COLLOIDS PREPARED WITH VARYING TIME INTERVAL BETWEEN ADDING GENERATOR ELUATE AND ADDING HUMAN SERUM ALBUMIN (HSA) TO Sn(II)*

Interval between the additions (min)	Batch of colloid	% dose/organ 10 min after iv†				
		Liver	Spleen	Lungs	Kidneys	Stomach
2	A	91.3 ± 0.6	3.3 ± 0.5	0.76 ± 0.13	0.33 ± 0.02	0.040 ± 0.000
5	B	93.5 ± 0.8	3.9 ± 0.2	0.42 ± 0.05	0.11 ± 0.01	0.009 ± 0.000
10	C	93.5 ± 0.3	4.1 ± 0.2	0.37 ± 0.06	0.07 ± 0.01	0.011 ± 0.000

* HSA concentration of the colloid was 0.714 mg/ml.
† Mean ± SEM of 5 rats.

TABLE 2. TISSUE DISTRIBUTION OF TECHNETIUM IN RATS FOLLOWING ADMINISTRATION OF ^{99m}Tc-Sn(II) COLLOIDS AT VARYING pH

Colloid			No. of rats	% dose/organ 10 min after iv†				
HSA* conc (mg/ml)	pH	Batches		Liver	Spleen	Lungs	Kidneys	Stomach
0	4.1	D	5	91.1 ± 1.2	5.3 ± 0.4	0.62 ± 0.12	0.09 ± 0.00	0.009 ± 0.000
0.714	5.2	B,E,F,G	19	92.1 ± 0.5	4.4 ± 0.2	0.62 ± 0.08	0.14 ± 0.02	0.014 ± 0.000
3.57	6.5	H	5	91.6 ± 0.6	5.2 ± 0.4	0.25 ± 0.01	0.30 ± 0.01	0.027 ± 0.000
7.14	6.8	I,J	9	93.0 ± 0.8	4.3 ± 0.3	0.57 ± 0.06	0.20 ± 0.02	0.014 ± 0.000

* Human serum albumin.
† Mean ± SEM.

Two milliliters of the preparation was gently passed through a 0.22-micron filter, 0.4 ml/cm^2 of the filter. Technetium concentration of the preparation before and after the filtration was then measured in a well scintillation counter. The results were used to calculate the percent retained by the filter. The filter did not retain the pertechnetate of the generator eluate.

To evaluate the stability of the colloid against agitation, 7 ml of the preparation in the glass vial (25-ml capacity) was agitated in a shaking water bath (Precision Scientific Co., Cat. #66800). The preparation was then assayed in rats.

To evaluate the effect of ionic Al(III), the generator eluate was adulterated with aluminum chloride. Aluminum chloride hexahydrate was dissolved in saline to varying aluminum concentrations. The mixture of the generator eluate and the aluminum chloride solution in the ratio of 4:1 (v/v) was incubated for 1 hr at room temperature. Then 5 ml of the adulterated generator eluate was used for preparing the colloid in the usual fashion.

To evaluate adherence of the colloid to the container, a portion of the preparation was sampled for measuring the technetium concentration after the colloid had stood for varying time. The technetium concentration of the sample was expressed as percent, taking the technetium concentration of the generator eluate multiplied by 5/7 as 100%.

RESULTS

The development of a Sn(II) colloid following the addition of 5-ml saline to 1-ml, 1-m*M* Sn(II) solution was studied. The mixture was illuminated in a darkened room and inspected at right angle to the illumination. The mixture was initially watery clear but was barely opalescent in 5 min with a further increase in the opalescence over the next 10–15 min. This opalescence was minimal and could not be appreciated in a lighted room.

Minimum necessary time interval between adding the generator eluate and adding the HSA to the Sn(II) in preparing the Tc-Sn(II) colloid was evaluated. The interval was varied, and the colloid prepared was assayed in rats. Table 1 shows the results. For the interval, 2 min was adequate. However, allowing 5 or 10 min for the interval appeared to result in a better colloid. Accordingly, in all subsequent preparation of the colloid, 5 min was allowed for the interval.

The colloid at varying HSA concentrations was prepared according to the procedure described in Materials and Methods. The pH of the colloid was higher at higher HSA concentration of the colloid and was 4.1–6.8 corresponding to the HSA concentration 0–7.14 mg/ml. The colloid at pH 4.1, 5.2, 6.5, and 6.8 appeared watery clear when inspected in a bright room. Table 2 shows the results of assay

TABLE 3. TISSUE DISTRIBUTION OF TECHNETIUM IN RATS AS A FUNCTION OF TIME FOLLOWING ADMINISTRATION OF ^{99m}Tc-Sn(II) COLLOIDS CONTAINING HUMAN SERUM ALBUMIN 0.714 mg/ml*

Time after iv	Batches of colloid	No. of rats	% dose/organ†				
			Liver	Spleen	Lungs	Kidneys	Stomach
5 min	K	5	93.7 ± 0.9	4.4 ± 0.7	0.55 ± 0.09	0.07 ± 0.00	0.007 ± 0.000
10 min	B,E,F,G	19	92.1 ± 0.5	4.4 ± 0.2	0.62 ± 0.08	0.14 ± 0.02	0.014 ± 0.000
2 hr	L	6	91.5 ± 1.1	5.0 ± 0.5	0.27 ± 0.02	0.22 ± 0.03	0.011 ± 0.000
6 hr	M	5	90.2 ± 0.4	2.0 ± 0.2	0.59 ± 0.02	1.09 ± 0.13	0.024 ± 0.000
12 hr	M	5	85.8 ± 1.0	3.9 ± 0.2	0.23 ± 0.01	2.25 ± 0.20	0.032 ± 0.000
21 hr	N	5	78.2 ± 1.6	2.9 ± 0.3	0.09 ± 0.00	2.72 ± 0.21	0.038 ± 0.017
31 hr	O,P	8	78.6 ± 1.3	3.2 ± 0.2	0.10 ± 0.01	2.63 ± 0.23	0.033 ± 0.010
41 hr	N	4	59.9 ± 1.2	2.1 ± 0.1	0.09 ± 0.00	4.17 ± 0.13	0.095 ± 0.036
51 hr	N,P,k,l	13	55.3 ± 1.6	2.2 ± 0.1	0.06 ± 0.00	4.37 ± 0.18	0.041 ± 0.000

*Results from experiments involving nine lots of stock 1-mMSn(II) solution and 12 batches of the colloid are shown.
† Mean ± SEM.

of the colloid in rats. About 97% of the technetium was localized in the liver plus spleen 10 min after the intravenous administration of the colloid at any one of these four pH values. The range of this localization was 93.2–100.8% in the 38 rats.

Tissue distribution of the technetium was studied as a function of time following the intravenous administration of the colloid at HSA concentration 0.714 mg/ml. Table 3 shows the results. The uptake by the liver and the spleen was essentially complete in 5 min. Subsequently, there was a definite release of the technetium from these reticuloendothelial organs over the next 51 hr. The liver uptake decreased from 92.1% (range 89.2–96.1%) at 10 min to 85.8% (range 82.3–87.9%) at 12 hr. Simultaneously, the renal uptake sharply increased from 0.14% (range 0.05–0.23%) to 2.25% (range 1.93–3.02%) and the gastric uptake from 0.014% (range 0.006–0.027%) to 0.032% (range 0.016–0.063%). By 51 hr, the liver uptake further decreased to 55.3% (range 45.7–67.6%) and the renal uptake further increased to 4.37% (range 3.21–5.16%). In the 51-hr period, the spleen uptake decreased by approximately one-half of its initial value to 2.2% (range 1.5–3.0%). The pulmonary uptake was 0.62% (range 0.26–1.24%) at 10 min and then declined by about tenfold over the next 51 hr. In seven of the 13 rats sacrificed after 51 hr, whole-body retention of the technetium was measured. The retention was 82.3% (range 75.3–86.8%) at 24 hr and 64.2% (range 56.9–69.8%) at 51 hr. Comparison of these retention data with the distribution data shown in Table 3 indicated that most of the technetium released from the liver and the spleen was rapidly excreted.

The maximum possible content of free technetium in nine batches of the colloid at the HSA concentration 0.714 mg/ml was determined by Millipore filtration as described in Materials and Methods. Six different lots of the stock 1-m*M* Sn(II) solution varying from 0 to 14 days in storage were used in preparing these nine batches. Table 4 shows the results. The free technetium was on the order of 0.1% during the first day and about 1% or less after 2–3 days.

TABLE 4. MILLIPORE FILTRATION OF ^{99m}Tc-Sn(II) COLLOIDS CONTAINING HUMAN SERUM ALBUMIN 0.714 mg/ml

Hr in standing before filtration	Batch	% ^{99m}Tc retained by 0.22-micron filter*
16	L	100.0
23	Q	99.9
29	R	99.9
30	S	99.3
30	T	99.9
48	M	99.1
48	U	99.6
50	V	99.1
72	W	99.1

* See text.

The colloid at the HSA concentrations 0.714, 3.57, and 7.14 mg/ml showed no change in its physical appearance and seemed to be stable for over 10 hr. When the HSA was omitted from the preparation, the colloid tended to coagulate and settle. These data were confirmed by scintigraphic studies and by tissue-distribution studies in rats. Table 5 shows the results of the latter studies. The colloid at the HSA concentration 0.714 mg/ml was stable for over 10 hr. However, by 10 hr the colloid not containing the HSA had deteriorated. In this deteriorated preparation, the greatly increased lung-localizing forms of the technetium was evidently a result of the coagulation. In addition, there appeared to be a release of non-colloidal forms of the technetium in the preparation

TABLE 5. STABILITY OF ^{99m}Tc-Sn(II) COLLOIDS IN STANDING WITH AND WITHOUT HUMAN SERUM ALBUMIN (HSA) IN THE COLLOID*

Colloid				% dose/organ 10 min after iv†				
HSA conc (mg/ml)	Hr in standing	Batches	No. of rats	Liver	Spleen	Lungs	Kidneys	Stomach
0.714	0.3–2	B,E,F,G,U,X	29	92.4 ± 0.4	4.5 ± 0.1	0.62 ± 0.02	0.13 ± 0.01	0.013 ± 0.000
0.714	3–6	Q,S,T	14	93.8 ± 0.6	3.4 ± 0.2	0.42 ± 0.02	0.10 ± 0.01	0.014 ± 0.000
0.714	8–10	E,F	10	92.1 ± 0.3	4.3 ± 0.2	1.00 ± 0.08	0.14 ± 0.02	0.014 ± 0.000
0.714	10‡	Y	5	95.0 ± 1.1	4.0 ± 0.4	0.32 ± 0.04	0.07 ± 0.00	0.012 ± 0.000
0	0.5–1	D	5	91.2 ± 1.2	5.3 ± 0.4	0.62 ± 0.12	0.09 ± 0.00	0.009 ± 0.000
0	10‡	Z	5	74.9 ± 1.1	7.6 ± 0.4	11.8 ± 0.4	0.66 ± 0.08	0.086 ± 0.009

* Results from evaluating 12 batches of the colloid in terms of tissue distribution of the technetium in rats are shown.
† Mean ± SEM.
‡ The gas phase inside the container was deliberately replaced with air prior to the standing (1.5 hr at room temperature and 8.5 hr at 4°C).

TABLE 6. STABILITY OF ^{99m}Tc-Sn(II) COLLOIDS AGAINST AGITATION*

Colloid				% dose/organ 10 min after iv†				
HSA‡ conc (mg/ml)	Agitation¶	Batches	No. of rats	Liver	Spleen	Lungs	Kidneys	Stomach
0.714	control	B,E,F,G	19	92.1 ± 0.5	4.4 ± 0.2	0.62 ± 0.08	0.14 ± 0.02	0.014 ± 0.000
0.714	220 rpm 10 min	R,V	9	92.9 ± 0.5	3.8 ± 0.1	0.90 ± 0.07	0.07 ± 0.00	0.007 ± 0.000
7.14	control	I,J	9	93.0 ± 0.8	4.3 ± 0.3	0.57 ± 0.06	0.20 ± 0.02	0.014 ± 0.000
7.14	220 rpm 10 min	a,b	10	90.4 ± 0.5	3.9 ± 0.2	1.09 ± 0.06	0.30 ± 0.06	0.020 ± 0.000

* Results from evaluating ten batches of the colloid in terms of tissue distribution of the technetium in rats are shown.
† Mean ± SEM.
‡ Human serum albumin.
¶ See text.

causing a significant increase in the renal and the gastric uptake.

When the HSA solution and the colloid preparation containing the HSA were shaken to the extent of causing foaming in the material, a fine flocculation tended to occur in both. In one instance, lungs as well as the liver and the spleen were scintigraphically visualized with a shaken foamy preparation in rats. To evaluate the extent of agitation permissible, four batches of the colloid containing the HSA were studied as described in Materials and Methods. Table 6 shows the results. Agitation at 220 rpm for 10 min in a shaker did not alter the appearance of the colloid and caused only a minimal increase in the lung-localizing forms of the technetium from about 0.6% (range 0.26–1.24%) to about 1% (range 0.64–1.45%).

The 1-ml supplies of the stock 1-m*M* Sn(II) solution were stable for at least 20 days when they were kept under the condition described in Materials and Methods. This was demonstrated by preparing colloids using the supplies kept for up to 20 days. As shown in Table 7, there was no evidence of deterioration of the Sn(II) during the 20-day storage.

The consequence of exposing the Sn(II) to oxidants prior to its use in preparing the colloid was studied. A 0.5-m*M* Sn(II) solution was kept under air in a lighted room for 28 hr. By this time, it was found to be totally devoid of its original iodine-reducing power. When it was used after the 28 hr to prepare the colloid, a preparation with the following properties was obtained. First, only 7.1% of the technetium in the preparation was sedimented by a 10-min centrifugation at 23,000 g. In contrast, when a control colloid was prepared using a freshly made 0.5-m*M* Sn(II) solution and subjected to the same centrifugation, 97% of the technetium was sedimented. Second, when the preparation was administered to rats intravenously, the scintiphoto shown to the right of Fig. 1 was obtained. The scintiphoto resembled those of rats given $^{99m}TcO_4^-$ intravenously. The middle scintiphoto in Fig. 1 shows that

TABLE 7. STABILITY OF THE 1-mM Sn(II) SOLUTION IN STORAGE*

Sn(II) storage (day)	Batches of colloid prepared	No. of rats	% dose/organ 10 min after iv†				
			Liver	Spleen	Lungs	Kidneys	Stomach
0	B,E,F,G	19	92.1 ± 0.5	4.4 ± 0.2	0.62 ± 0.08	0.14 ± 0.02	0.014 ± 0.000
1	Q	5	92.3 ± 1.2	3.8 ± 0.3	0.48 ± 0.04	0.08 ± 0.00	0.018 ± 0.000
4	U	5	91.9 ± 1.0	4.6 ± 0.2	0.58 ± 0.10	0.13 ± 0.02	0.014 ± 0.000
7	X	5	93.9 ± 0.8	4.4 ± 0.4	0.64 ± 0.15	0.08 ± 0.00	0.007 ± 0.000
10	S	4	94.6 ± 0.3	2.5 ± 0.2	0.41 ± 0.04	0.16 ± 0.03	0.018 ± 0.000
14	T	5	94.7 ± 0.7	3.8 ± 0.4	0.37 ± 0.01	0.06 ± 0.00	0.006 ± 0.000
20	c	5	93.5 ± 0.6	5.8 ± 0.6	0.28 ± 0.03	0.18 ± 0.00	0.017 ± 0.000

* Results from evaluating ten batches of the colloid prepared using six lots of the stock 1-mM Sn(II) solution are shown in terms of tissue distribution of the technetium in rats. The prepared colloid contained human serum albumin 0.714 mg/ml.
† Mean ± SEM.

the addition of an excess H_2O_2 to a freshly prepared 0.5-m*M* Sn(II) solution had a similar effect as did the 28-hr standing under air. These findings indicated that the technetium in the preparation was largely in a free form and in Tc(VII) state when the Sn(II) was oxidized to a higher valency tin prior to preparing the colloid.

To study the effect of ionic Al(III), five batches of the colloid at the HSA concentration 0.714 mg/ml were prepared using generator eluate with added aluminum chloride as described in Materials and Methods. The final aluminum concentration was 2–20 μg/ml colloid. Inspection of the colloid revealed flocculation or coagulation in none of these five batches. To substantiate this visual impression, these five batches were analyzed in rats. Table 8 shows the results. Ionic Al(III) up to 20 μg/ml colloid did not cause an increase in the lung-localizing forms of the colloid activity. The pulmonary uptake was 0.4% (range 0.33–0.59%) at 10 min in the five rats receiving the colloid at aluminum concentration 20 μg/ml. In addition, the colloid containing aluminum up to 10 μg/ml produced the same high uptake in the liver plus spleen, 97% (range 94–99%), and a similarly low uptake in the kidneys or in the stomach as did the control colloid. When the aluminum concentration was further increased to 20 μg/ml, there was a slightly decreased localization in the liver plus spleen and an increased uptake in the kidneys and in the stomach.

Adhesion of the colloid to containers was studied. The fraction of the colloid activity adherent to containers was measured as described in Materials and Methods. Table 9 shows the results. When care was taken to avoid disturbing the colloid at the HSA concentration 0.714 mg/ml, a variable fraction (7–22%) of its activity was found to be adherent to the container 0.5–2 hr after it was prepared. Gentle inversions of the container just prior to the sampling for the activity measurement was found to remove some of the adherent activity off the container. Under the circumstances, 4–7% remained adherent after 0.5–2 hr, 6–8% after 5 hr, and 9–12% after 8–12 hr. When the HSA concentration of the colloid was increased to 7.14 mg/ml, the same inversion was found to remove the adherent activity, if any, almost quantitatively off the container even after 12 hr.

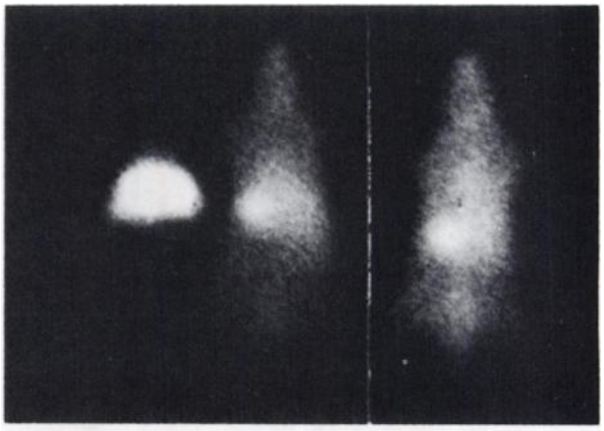

FIG. 1. Three in vivo scintiphotos of rats (posterior views) demonstrating failure to obtain technetium-labeled colloid when Sn(II) was oxidized under air or with H_2O_2 prior to its use in preparing ^{99m}Tc-Sn(II) colloids. Preparation used to obtain scintiphoto to right of figure was prepared using Sn(II) solution previously kept under air for 28 hr. That used to obtain middle scintiphoto was prepared using Sn(II) solution freshly made but with added excess H_2O_2. That used to obtain left scintiphoto was prepared using fresh Sn(II) solution to serve as reference. All three preparations were at same pH (5.1), same tin concentration (0.07 mM), and same albumin concentration (0.36 mg/ml). All three scintiphotos were obtained with Anger camera 7 min after intravenous administration of preparations.

Four batches of the colloid prepared from four individual lots of the stock Sn(II) were tested for sterility and pyrogenicity by standard methods. All were found to be sterile and nonpyrogenic.

DISCUSSION

All methods presently available for preparing technetium-labeled colloids involve chemical systems po-

TABLE 8. TISSUE DISTRIBUTION OF TECHNETIUM IN RATS FOLLOWING ADMINISTRATION OF ^{99m}Tc-Sn(II) COLLOIDS PREPARED USING GENERATOR ELUATE WITH AND WITHOUT ADDED IONIC Al(III)*

Colloid‡			% dose/organ 10 min after iv†				
Al conc (μg/ml)	Batches	No. of rats	Liver	Spleen	Lungs	Kidneys	Stomach
0	B,E,F,G	19	92.1 ± 0.5	4.4 ± 0.2	0.62 ± 0.08	0.14 ± 0.02	0.014 ± 0.000
2	d	5	94.0 ± 0.8	3.2 ± 0.2	0.32 ± 0.03	0.11 ± 0.02	0.008 ± 0.000
5	e ¶	5	89.3 ± 1.0	3.4 ± 0.2	0.41 ± 0.04	0.06 ± 0.00	0.009 ± 0.000
10	f,g	10	92.8 ± 0.7	4.0 ± 0.3	0.28 ± 0.02	0.12 ± 0.00	0.013 ± 0.000
20	h ¶	5	93.1 ± 1.0	2.9 ± 0.2	0.40 ± 0.05	0.37 ± 0.05	0.039 ± 0.000

* See text.
† Mean ± SEM.
‡ The colloid contained human serum albumin 0.714 mg/ml.
¶ Administered to rats following standing at room temperature for 10–11 hr after they were prepared.

TABLE 9. ADHERENCE OF ^{99m}Tc-Sn(II) COLLOIDS TO CONTAINERS

HSA conc (mg/ml)	Batch	Time in standing before sampling	Agitation just before sampling	% ^{99m}Tc not adherent to container*
0.714	i	30 min	—†	90
0.714	j	40 min	—	93
0.714	B	1 hr	—	81
0.714	G	2 hr	—	78
0.714	K	30 min	+‡	96
0.714	X	2 hr	+	95
0.714	R	2 hr	+	93
0.714	S	5 hr	+	94
0.714	T	5 hr	+	92
0.714	X	8 hr	+	91
0.714	K	12 hr	+	88
7.14	I	30 min	+	99
7.14	b	2 hr	+	101
7.14	I	12 hr	+	99

* Technetium concentration of the sample expressed as percent of the expected concentration calculated assuming that none of the technetium was adherent to the container.
† "—" represents no agitation.
‡ "+" represents inverting the container gently ten times.

tentially capable of reducing Tc(VII) (*2*). These include the acid-hydrogen sulfide system (*3*) and the acid-thiosulfate system (*4,5*) for Tc-S colloids, the acid-thiocyanate-ascorbate system (*6*) for a Tc-Fe colloid, and the acid-borohydride system (*7*) for a "TcO_2" colloid. In this study, it is shown that in preparing the Tc-Sn colloid, Sn(II) is effective but not a higher valency tin. This is considered an evidence for Tc(VII) reduction in preparing the Tc-Sn(II) colloid. It is analogous to the case of technetium labeling of albumin in a study (*1*) showing that Fe(II) without ascorbate is effective but not Fe(III) without ascorbate. In this earlier study, evidence was found for cationic forms of a lower valency technetium in a mixture of Sn(II) solution and generator eluate at an acidic pH. Possibly, this form of the technetium turns colloidal at a higher pH. Stannous salts form colloids at near neutral pH. It is likely that the presently described colloid represents a co-colloid of a lower-valency technetium and Sn(II) stabilized by hydrophilic albumin.

Preparation of technetium-labeled colloids using Sn(II) has been described by Maass, Alvarez, and Arriaga (*8*) and by Subramanian and McAfee (*9*). The present procedure differs from theirs in three respects. First, in the present procedure, an aqueous Sn(II) is made in water instead of in acid. This eliminates a pH adjustment step. Second, the present procedure employs HSA in place of gelatin. Desirability of HSA as a stabilizer for radiopharmaceutical colloids has been commended (*10*). In addition, heat-coagulation of the colloid could result in macroaggregates suitable for lung imaging. Studies are in progress to consolidate such a technique. On the other hand, HSA is denatured by violent shaking, and the possibility of a careless handling causing flocculation in the colloid may be a disadvantage. Third, the present procedure is in a "kit" form. The procedure for preparing the kit is quite simple. That for preparing the colloid from the kit is nearly an "instant" one. This may encourage a wide use of the colloid first proposed by Maass, Alvarez, and Arriaga (*8*).

The presently described colloid is of good quality and readily reproducible. Its biological property appears to be quite insensitive to pH in the range 5–7. The technetium distribution in rats at 10 min has been determined with 25 batches of the colloid at this pH range prepared from 10 lots of 1-m*M* Sn(II) supplies varying from 0 to 20 days in storage. The range of the uptake in the liver plus spleen was 93–102% (mean 97%) in 130 rats. The colloid is stable under either N_2 or air for over 10 hr. This stability is provided by the HSA. As with Tc-S colloid (*11,12*), omission of stabilizer causes settling of the colloid and release of noncolloidal technetium.

Haney, Ascanio, Gigliotti et al (*13*) have described a good Tc-S colloid prepared by a "kit" method using the acid-thiosulfate system. Reference to Table 2 in their study and to Table 3 in this study for a comparison between the Tc-S colloid and the present Tc-Sn(II) colloid suggests the following qualitative conclusions: First, initial uptake by the liver plus spleen appears to be somewhat faster, and possibly to a slightly greater extent with the Tc-Sn(II) colloid. Second, in terms of the renal and the gastric uptake at 5 and at 10 min, the free technetium content appears to be smaller in the Tc-Sn(II) colloid. Third, throughout the first 2 days, the pulmonary uptake is smaller with the Tc-Sn(II) colloid. This may be related to a greater abundance of particles exceeding colloidal range in the Tc-S colloid (*11,14*). Taplin, Johnson, Dore et al (*15*) have indicated that particles of a few microns in size exhibit an initial pulmonary retention, not necessarily by embolization. Difference in physical appearance between the two colloids is consistent with the above in vivo difference. The Tc-S colloid is more opalescent. Fourth, a little over one third of the initial uptake of the Tc-Sn(II) colloid in the liver plus spleen is released and excreted in 2 days. This release and excretion of the technetium is several times or more faster than that found for Tc-S colloids in the studies of Haney, Ascanio, Gigliotti et al (*13*) and Harper, Lathrop, and Gottschalk (*3*).

Certain technetium generator eluate has been found to contain contaminating ionic Al(III) to an aluminum concentration as high as 26 μg/ml (*16, 17*). This aluminum has been blamed as a cause of a variability of the Tc-S colloid preparation (*18*). Weinstein and Smoak (*19*) have indicated that more than 50% of the Tc-S colloid activity can be precipitated in the presence of certain amounts of added ionic Al(III). In the study of Haney, Ascanio, Gigliotti et al (*13*), ionic Al(III) added to the generator eluate to a concentration as little as 1 μg Al/ml colloid was shown to cause a flocculation in the Tc-S colloid not containing ethylenediaminetetraacetate. In the case of the Tc-Sn(II) colloid at the HSA concentration 0.714 mg/ml, the ionic Al(III) added to the generator eluate to a concentration as high as 20 μg Al/ml colloid did not cause flocculation when evaluated by inspection and by in vivo assay.

SUMMARY

A "kit" method for the preparation of a technetium-tin(II) colloid was presented. The entire procedure for preparing the colloid consisted of adding technetium generator eluate and albumin solution in that order to an aqueous tin(II) in a vial.

The aqueous tin(II) was made in water in a standardized fashion. The sterility of this aqueous tin(II) and its preservation in a "kit" form were accomplished by Millipore filtering the aqueous tin(II) into sterile vials and subsequent purging of the air inside the vial with Millipore-filtered nitrogen. When kept at 4°C under the nitrogen, the aqueous Sn(II) was stable for at least 20 days.

Ionic aluminum(III) added to the generator eluate to a concentration up to 10 μg Al/ml colloid did not have adverse effect on the quality of the coilloid. The aluminum at concentrations up to 20 μg Al/ml colloid failed to induce flocculation in the colloid when evaluated by inspection and by in vivo assay.

The colloid was reproducible. Its free technetium content was in the order of 0.1%. Ten minutes after its intravenous administration, the technetium uptake in the liver plus spleen was 97% with a range of 93–102% using 25 batches of the colloid in 130 rats. The technetium was not permanently retained by these reticuloendothelial organs. By 51 hr, a little over one third of the initial technetium uptake in these organs had been released and excreted.

The colloid was stable in standing either under nitrogen or under air for over 10 hr. It was also stable against agitation that would not cause foaming in the colloid.

In terms of the simplicity of its preparation procedure, its relative insensitivity to contaminating ionic aluminum(III), its low content of the technetium below and above the colloidal range, and the rate of release and excretion of the technetium following its initial localization in the liver and the spleen, the present technetium-tin(II) colloid appeared to compare favorably with technetium-sulfur colloids.

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