Adsorption of ^{99m}Tc-Radiopharmaceuticals onto Injection Vials and Syringes

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Many groups have reported the adsorption or retention of ^{99m}Tc-radiopharmaceuticals on injection vials and disposable plastic syringes. Such an enormously high loss of radioactivity would result in poor images, radiation exposure, waste, and economic burdens. We therefore decided to investigate the extent of adsorption or retention of several ^{99m}Tc-radiopharmaceuticals on injection vials, rubber stoppers, and plastic syringes. These radiopharmaceuticals are produced as lyophilized kits in our department and supplied to various hospitals practicing nuclear medicine in Pakistan. **Methods:** A vial containing lyophilized material was reconstituted with 3 mL of freshly eluted $Na^{99m}TcO_4$. A 1-mL aliquot of the resulting solution was withdrawn into a syringe at 0.25, 0.5, 1, 3, and 5 h after preparation. All preparations were stored at room temperature (~22°C). After each withdrawal, the vial was reweighed and the activity remaining in the vial was measured using a radioisotope calibrator. The sample was reinjected into the vial. From the original weight and activity of solution in the vial, the initial activity per gram was calculated. From the weight and activity remaining in the vial after withdrawal of the sample, the activity per gram of the sample was calculated. From the difference between the initial activity per gram and the activity per gram of the sample, the percentage of ^{99m}Tc adsorbed on the vial was calculated. All preparations were kept in the syringe for 15 min, and the activity was measured before and after the syringe was emptied. The needle and plunger of the syringe were separated, and activity in the needle and plunger was also measured. **Results:** The labeling efficiency of all radiopharmaceuticals used during these studies was more than 95%. In most cases, the activity of ^{99m}Tc found on the rubber stopper was less than 1%. Adsorption of ^{99m}Tc onto vials increased gradually with storage time. Adsorption was minimal at the initial stages, whereas maximum retention was noted after 5 h. Nearly 5% adsorption of activity was observed after 5 h of storage time on vials of sestamibi, mercaptoacetyltriglycine, dextran, ciprofloxacin, and dimercaptosuccinic acid (III and V). Retention of activity on needles ranged from 1% to 2% for all preparations studied. Plungers did not show any significant retention of radioactivity; in most cases, retention was less than 0.5%. The maximum retention of radioactivity on plastic syringe bodies was more than 3% for sestamibi, dimercaptosuccinic acid, dextran, pyrophosphate, and phytate. **Conclusion:** The results revealed that losses of radioactivity from ^{99m}Tc-radiopharmaceuticals in these objects (glass vial, rubber stopper, plastic syringes, plungers, and needles) are not alarming in our setup.

Key Words: ^{99m}Tc-generator; ^{99m}Tc-radiopharmaceuticals; freeze-dried kits; quality assurance

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The physical and biologic properties of ^{99m}Tc make it an ideal radioisotope for scintigraphy. A wide variety of radiopharmaceuticals are being prepared from generator-produced ^{99m}Tc for scanning of different organs. By far the greatest numbers of preparations are those associated with kits. A radiopharmaceutical kit may be defined as a prepacked set of sterile ingredients that have undergone full quality assurance checks by the manufacturer. Containers for injectable preparations are made from materials that are sufficiently transparent to permit visual inspection of the contents and that do not diffuse into the preparation, causing deterioration, or introduce foreign substances into the preparation. The bottle or vial is made of glass. Glass vials are fitted with suitable closures, which ensure a good seal, prevent contamination, and permit withdrawal of a portion of the contents without removal of the closure. The rubber of which the closure is composed must be compatible with the preparation and be sufficiently firm and elastic to allow passage of a needle with minimal shedding of particles and to ensure that the puncture is resealed when the needle is withdrawn. In hospitals, radiopharmaceuticals are prepared from kits simply by injecting sodium pertechnetate solution into the vial of lyophilized reagent. The compound forms almost instantaneously. Occasionally, a boiling step is necessary. It is common practice to dispense radiopharmaceuticals into empty sterile vials for dispatch to the departments where they are to be administered. Disposable (single-use) plastic syringes are routinely used to administer ^{99m}Tc-radiopharmaceuticals to patients for imaging. The dose should be enough to provide an adequate study yet be consistent with "as low as reasonably achievable" principles and should be measured by a radioactivity calibration system immediately before being administered to the patient. Some groups have already reported the adsorption of various radiopharmaceuticals onto glass vials and single-use plastic syringes. Adhesion of various colloids on glass vials was investigated by

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TABLE 1
Formulation of ^{99m}Tc-Radiopharmaceuticals

Kit	Ingredients	pH	Imaging
Diisopropyl iminodiacetic acid	Diisopropyl iminodiacetic acid (20.0 mg), $SnCl_2{\cdot}2H_2O$ (0.2 mg)	~5.5	Hepatobiliary
DMSA (III)	DMSA (1.0 mg), $SnCl_2{\cdot}2H_2O$ (0.60 mg), ascorbic acid (0.70 mg), inositol (50 mg)	~2.2	Kidney
Diethylenetriaminepentaacetic acid	Diethylenetriaminepentaacetic acid (10 mg), $SnCl_2{\cdot}2H_2O$ (0.4 mg)	~7	Kidney/brain
Heptagluconate	Calcium heptagluconate (100 mg), $SnCl_2{\cdot}2H_2O$ (0.12 mg)	~6	Kidney/brain
Mercaptoacetyltriglycine	Mercaptoacetyltriglycine (1 mg), $SnCl_2{\cdot}2H_2O$ (0.1 mg), calcium heptagluconate (20 mg), lactose (20 mg)	~4.25	Kidney
Methylene diphosphonate	Methylene diphosphonate (7.5 mg), $SnCl_2{\cdot}2H_2O$ (0.36 mg), ascorbic acid (1.8 mg), NaCl (2.0 mg)	5.8–6	Bone
Phytate	Phytic acid (25.0 mg), $SnCl_2{\cdot}2H_2O$ (1.0 mg)	~6.8–7	Liver/spleen
Pyrophosphate	Pyrophosphate (10 mg), $SnCl_2{\cdot}2H_2O$ (2.5 mg)	~6.5	Red blood cell labeling, bone, heart infarct
Dextran	Dextran (50 mg), $SnCl_2{\cdot}2H_2O$ (0.013 mg)	6	Lymph
Sestamibi	Sestamibi (1 mg), $SnCl_2{\cdot}2H_2O$ (0.075 mg), L-cysteine (1 mg), sodium citrate (2.6 mg), mannitol (20 mg)	~5.4–5.9	Heart
Ciprofloxacin	Ciprofloxacin (3.8 mg), $SnCl_2{\cdot}2H_2O$ (0.39 mg), NaCl (4.4 mg)		Infection
Exametazime	d,l-exametazime (0.5 mg), $SnCl_2{\cdot}2H_2O$ (7.5 μg), NaCl (6.75 mg)	~10–11	Brain
DMSA (V)	DMSA (1.8 mg), $SnCl_2{\cdot}2H_2O$ (1.12 mg)	8.5	Medullary thyroid carcinoma
$Na^{99m}TcO_4$	0.9% NaCl, $Na^{99m}TcO_4$ (nanogram levels)	6–7	Thyroid

Elliott et al. (*1*) and Porter et al. (*2*). The adsorption behavior of some radiopharmaceuticals on glass vials has been studied (*3,4*). The adsorption of ^{99m}Tc-methylene diphosphonate, ^{99m}Tc-sestamibi, ^{99m}Tc-tetrofosmin, ^{99m}Tc-furifosmin, and ^{99m}Tc-macroaggregated albumin on plastic syringes has also been reported (*5,6*).

The Kit Production Group at the Pakistan Institute of Nuclear Science and Technology (PINSTECH) manufactures a large number of cold kits for ^{99m}Tc-radiopharmaceuticals for use in nuclear medical centers in different parts of Pakistan. Hence, compatibility between vials and radiopharmaceuticals was investigated. Adsorption of ^{99m}Tc-radiopharmaceuticals onto the disposable syringes generally used for administration at medical centers was also studied.

MATERIALS AND METHODS

All kits were products of the Kit Production Group of PINSTECH. Most of the precursors for these kits are purchased from commercial suppliers, whereas diisopropyl iminodiacetic acid, exametazime, mercaptoacetyltriglycine, and sestamibi are synthesized and char-

TABLE 2
Adhesion (%) of ^{99m}Tc-Radiopharmaceutical on Vials and Rubber Stoppers

Radiopharmaceutical	Activity (MBq)	Vial					Stopper (0 h)
		0.25 h	0.5 h	1 h	3 h	5 h	
$Na^{99m}TcO_4$	~3,700	0.2 ± 0.1	0.2 ± 0.1	0.2 ± 0.1	0.2 ± 0.1	0.2 ± 0.1	0.2 ± 0.1
Diisopropyl iminodiacetic acid	~3,700	0.5 ± 0.2	0.5 ± 0.1	0.7 ± 0.2	1.2 ± 0.3	2.2 ± 0.5	0.3 ± 0.1
DMSA (III)	~3,700	0.8 ± 0.3	1.2 ± 0.3	2.5 ± 0.5	3.5 ± 0.5	4.7 ± 0.8	0.4 ± 0.2
Diethylenetriaminepentaacetic acid	~3,000	0.4 ± 0.1	0.8 ± 0.2	1.2 ± 0.3	1.5 ± 0.3	1.8 ± 0.2	0.2 ± 0.1
Heptagluconate	~3,000	0.6 ± 0.3	1.0 ± 0.4	1.2 ± 0.3	1.8 ± 0.5	2.2 ± 0.6	0.3 ± 0.1
Mercaptoacetyltriglycine	~3,000	1.0 ± 0.2	1.2 ± 0.2	1.7 ± 0.3	2.5 ± 0.5	2.5 ± 0.6	1.1 ± 0.3
Methylene diphosphonate	~3,700	0.2 ± 0.1	0.4 ± 0.2	0.9 ± 0.4	1.5 ± 0.5	1.9 ± 0.5	0.4 ± 0.2
Phytate	~3,700	0.9 ± 0.3	1.2 ± 0.4	1.8 ± 0.5	2.5 ± 0.7	3.2 ± 0.6	0.3 ± 0.1
Pyrophosphate	~3,000	0.5 ± 0.2	0.8 ± 0.4	1.9 ± 0.4	2.7 ± 0.5	3.2 ± 0.4	0.3 ± 0.1
Dextran	~3,000	1.2 ± 0.3	1.2 ± 0.3	1.7 ± 0.5	3.7 ± 0.4	4.2 ± 0.4	0.3 ± 0.1
Sestamibi	~3,000	0.8 ± 0.2	1.2 ± 0.3	1.9 ± 0.7	3.9 ± 0.7	4.5 ± 0.4	0.9 ± 0.3
Ciprofloxacin	~3,700	1.2 ± 0.4	1.7 ± 0.4	2.9 ± 0.6	4.2 ± 0.5	4.4 ± 0.5	0.3 ± 0.2
Exametazime	~3,700	0.9 ± 0.2	—	—	—	—	0.3 ± 0.2
DMSA (V)	~2,500	1.2 ± 0.3	1.5 ± 0.3	2.2 ± 0.6	2.9 ± 0.8	4.2 ± 0.8	0.9 ± 0.3

TABLE 3
Adhesion (%) of ^{99m}Tc-Radiopharmaceutical on Different Parts of Syringes

Radiopharmaceutical	Activity (MBq)	Syringe type	Syringe body	Plunger	Needle
$Na^{99m}TcO_4$	925	A	1.2 ± 0.5	0.4 ± 0.1	1.5 ± 0.5
		B	1.4 ± 0.8	0.3 ± 0.1	1.2 ± 0.8
		C	1.1 ± 0.5	0.3 ± 0.2	1.0 ± 0.5
Diisopropyl iminodiacetic acid	296	A	1.9 ± 0.4	0.3 ± 0.2	1.5 ± 0.5
		B	2.2 ± 0.7	0.4 ± 0.1	1.2 ± 0.8
		C	2.5 ± 0.4	0.2 ± 0.1	1.0 ± 0.5
DMSA (III)	185	A	2.5 ± 0.4	0.4 ± 0.2	1.8 ± 0.8
		B	2.2 ± 0.4	0.3 ± 0.1	1.5 ± 0.8
		C	2.0 ± 0.4	0.4 ± 0.1	1.3 ± 0.6
Diethylenetriaminepentaacetic acid	925	A	1.9 ± 0.6	0.3 ± 0.1	1.4 ± 0.7
		B	1.8 ± 0.3	0.3 ± 0.1	1.4 ± 0.8
		C	2.2 ± 0.5	0.4 ± 0.1	1.4 ± 0.7
Heptagluconate	925	A	1.5 ± 0.5	0.4 ± 0.1	1.5 ± 0.5
		B	1.2 ± 0.6	0.4 ± 0.2	1.2 ± 0.8
		C	1.4 ± 0.5	0.3 ± 0.1	1.7 ± 0.5
Mercaptoacetyltriglycine	185	A	2.5 ± 0.4	0.4 ± 0.1	1.0 ± 0.3
		B	2.2 ± 0.5	0.4 ± 0.1	1.2 ± 0.5
		C	2.0 ± 0.5	0.3 ± 0.1	1.0 ± 0.5
Methylene diphosphonate	925	A	2.5 ± 0.4	0.4 ± 0.2	1.1 ± 0.5
		B	2.2 ± 0.5	0.4 ± 0.2	1.2 ± 0.8
		C	1.9 ± 0.2	0.4 ± 0.1	1.4 ± 0.6
Phytate	740	A	2.7 ± 0.5	0.4 ± 0.1	1.2 ± 0.3
		B	2.2 ± 0.8	0.3 ± 0.1	1.2 ± 0.8
		C	2.7 ± 0.5	0.4 ± 0.2	1.0 ± 0.5
Pyrophosphate	925	A	2.9 ± 0.4	0.4 ± 0.2	1.7 ± 0.6
		B	2.1 ± 0.7	0.3 ± 0.1	1.1 ± 0.5
		C	1.6 ± 0.6	0.3 ± 0.1	1.3 ± 0.5
Dextran	740	A	2.8 ± 0.6	0.3 ± 0.1	1.0 ± 0.4
		B	2.2 ± 0.3	0.4 ± 0.2	1.2 ± 0.7
		C	2.8 ± 0.3	0.4 ± 0.1	1.3 ± 0.6
Sestamibi	925	A	2.9 ± 0.5	0.3 ± 0.1	1.2 ± 0.4
		B	3.2 ± 0.5	0.3 ± 0.1	1.2 ± 0.6
		C	3.9 ± 0.4	0.3 ± 0.2	1.0 ± 0.2
Ciprofloxacin	740	A	1.9 ± 0.4	0.4 ± 0.1	1.6 ± 0.4
		B	1.8 ± 0.5	0.3 ± 0.1	1.0 ± 0.5
		C	2.5 ± 0.4	0.4 ± 0.2	1.0 ± 0.5
Exametazime	740	A	1.5 ± 0.5	0.3 ± 0.2	1.0 ± 0.7
		B	1.2 ± 0.8	0.2 ± 0.1	1.1 ± 0.6
		C	1.0 ± 0.5	0.1 ± 0.05	1.1 ± 0.6
DMSA (V)	740	A	3.5 ± 0.7	0.3 ± 0.2	1.5 ± 0.7
		B	3.3 ± 0.6	0.4 ± 0.1	0.9 ± 0.4
		C	2.5 ± 0.5	0.5 ± 0.1	1.4 ± 0.5

acterized locally. ^{99m}Tc was obtained from a locally produced fission-based PAKGEN ^{99}Mo/^{99m}Tc generator (PINSTECH). All chemicals were of analytic reagent grade and purchased from E. Merck. Ascending paper chromatography was performed using Whatman paper (no. 1 or 3), and instant thin-layer chromatography silica gel strips were obtained from Gelman Sciences. The distribution of radioactivity on chromatographic strips was measured using a 2π scanner (Berthold), or the strips were cut into 1-cm segments and counted in a γ-counter. The activity of the ^{99m}Tc was measured using a dose calibrator (Capintec). The disposable plastic syringes were the products of 3 different commercial manufacturers (Becton Dickinson Worldwide, Inc. [syringe A]; Safti syringes, Zafra International, Ltd., in collaboration with Boin Medica Co., Ltd. [syringe B]; and Shandong Qiaopai Group Co., Ltd. [syringe C]), and the injection vials and rubber stoppers were purchased from SCHOTT Glass Malaysia and Helvoet Pharma, respectively. All 3 types of syringes were 2.5 mL.

To study the rate of adsorption of ^{99m}Tc-radiopharmaceuticals onto vials, we prepared all radiopharmaceuticals using standard labeling techniques (*7–9*). The vial containing lyophilized material was reconstituted with 3 mL of freshly eluted $Na^{99m}TcO_4$. All preparations were stored at room temperature (~22°C). At 0.25, 0.5, 1, 3, and 5 h after reconstitution, the following procedure was adopted to measure the degree of radioactivity adhesion in vials. The vial was weighed, and the ^{99m}Tc activity was measured using a dose calibrator. A 1-mL sample of the solution in the vial was withdrawn into a syringe. The vial was reweighed, and the activity remaining in the vial was measured. The sample was reinjected into the vial. From the original weight and activity of the solution in the vial, the initial activity per gram was calculated. From the weight

and activity remaining in the vial after withdrawal of the sample, the activity per gram of sample was calculated. From the difference between the initial activity per gram and the activity per gram of sample, the percentage of ^{99m}Tc adsorbed onto the vial was calculated. All experiments were performed on 3 separate occasions.

To study the adsorption of ^{99m}Tc-radiopharmaceuticals onto the disposable plastic syringes, we kept all preparations in the syringe for 15 min and measured the activity before and after emptying the syringe. The needle and plunger of the syringe were separated, and activity in the needle and plunger was also measured. All experiments were performed on 3 separate occasions.

Radioactivity on the rubber stopper was determined just after reconstitution of the kit. The activity in the sealed vial was measured using a dose calibrator. The rubber stopper was then carefully removed and blotted dry, the activity on the stopper was measured, and the percentage of activity was calculated.

RESULTS

The ingredients of different freeze-dried kits are given in Table 1. Table 1 also gives the pH value at which labeling efficiency is maximal. The labeling efficiency of all radiopharmaceuticals used during these studies was more than 95%. Table 2 presents the percentage adhesion activity of ^{99m}Tc-radiopharmaceuticals on vials and rubber stoppers. The activity on rubber stoppers was measured just after reconstitution of the kit. In most cases, the activity of ^{99m}Tc on rubber stoppers was less than 1%. The maximum activity, approximately 1%, was found for sestamibi, mercaptoacetyltriglycine, and dimercaptosuccinic acid (DMSA) (V)—radiopharmaceuticals for which a boiling or shaking step was used for labeling.

The adsorption of ^{99m}Tc onto vials increased gradually with storage time. Adsorption was minimal at the initial stages, whereas retention was maximal after 5 h. After 15 min, retention was less than 1%, except in vials of sestamibi, mercaptoacetyltriglycine, dextran, ciprofloxacin, and DMSA (III and V). After 5 h of storage time, nearly 5% adsorption of activity was observed for vials of sestamibi, mercaptoacetyltriglycine, dextran, ciprofloxacin, and DMSA (III and V). These findings indicate that total retention of radioactivity on vials and stoppers is insignificant in our setting.

Mean values for the percentage of radioactivity remaining in the 3 types of syringes and their parts are presented in Table 3. The percentage of activity left on a syringe and parts was calculated using the following formula: residual activity (%) = (residual activity/initial activity) × 100. Retention of activity on needles ranged from 1% to 2% for all preparations studied. Plungers did not retain any significant radioactivity; in most cases, retention was less than 0.5%. The maximum retention of radioactivity on plastic syringe bodies was more than 3% for sestamibi, DMSA, dextran, pyrophosphate, and phytate. However, it cannot be concluded that one brand of syringe showed less retention of radioactivity than the others for all study radiopharmaceuticals.

DISCUSSION

For the last 2 decades, the Kit Production Group at PINSTECH has been manufacturing and supplying freeze-dried kits for the preparation of ^{99m}Tc-radiopharmaceuticals to more than 20 hospitals practicing nuclear medicine in different cities of Pakistan. During that time, no incidents of loss of activity on vials or syringes have been reported by the end users. In contrast, adsorption of ^{131}I (oral solution of sodium iodide [^{131}I] in carbonate buffer) on rubber stoppers has been reported a few times. Investigations of the adsorption of ^{131}I on rubber stoppers are in progress and may be the subject of another publication.

It would be reasonable to expect manufacturers of freeze-dried kits for ^{99m}Tc-radiopharmaceuticals to investigate the compatibility of their products with vials and rubber stoppers. It is also important that hospital radiopharmacies check for compatibility between syringes and radiopharmaceuticals. The use of an inappropriate syringe may reduce the administered radioactivity to a patient, leading to poor-quality images.

CONCLUSION

Freeze-dried kits produced at our institute show insignificant adhesion of radioactivity on the vial, rubber stopper, plastic syringe, needle, and plunger after labeling with ^{99m}Tc. Because the time of use after reconstitution affects adsorption of radioactivity onto syringes, needles, and vials, users should reconstitute the preparation soon before administration to the patient. Determining the compatibility of radiopharmaceuticals with these objects is an integral part of quality assurance programs.

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