Dextrose Solutions Yield Radiochemical Impurities: The "Sweet" Scans

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Objective: If additional chemicals are inadvertently introduced in the preparation of radiopharmaceutical kits, radiochemical impurities may be formed. We report our experience with erroneously diluting ^{99m}Tc-pertechnetate eluate with 5% dextrose solution rather than normal saline during the preparation of ^{99m}Tc-tetrofosmin, ^{99m}Tc-methylene diphosphonate (MDP), ^{99m}Tc-stannous colloid, and ^{99m}Tc-mebrofenin.

Methods: Scintigrams for 3 of the 4 radiochemicals unintentionally prepared with 5% dextrose were found to have an altered biodistribution. Therefore, radiopharmacy procedures for the day were reviewed, and instant thin-layer chromatography (ITLC) was performed.

Results: Scintigrams showed an altered biodistribution consistent with an impurity. Review of procedures that day uncovered the error of using 5% dextrose to dilute the ^{99m}Tc eluate. The altered biodistribution on ^{99m}Tc-stannous colloid, ^{99m}Tc-MDP, and ^{99m}Tc-mebrofenin scintigrams consisted of cardiac blood-pool activity (possibly as a result of slow clearance of ^{99m}Tc-dextrose), soft-tissue background activity (possibly as a result of interstitial distribution of ^{99m}Tc-dextrose), renal and bladder activity (possibly as a result of renal elimination of ^{99m}Tc-dextrose), and gallbladder activity (possibly as a result of hepatobiliary excretion of ^{99m}Tc-dextrose). Both scintigrams and ITLC showed no evidence of impurities for the ^{99m}Tc-tetrofosmin prepared using 5% dextrose.

Conclusion: Unintended preparation of radiochemicals with 5% dextrose rather than normal saline often results in the production of impurities, possibly ^{99m}Tc-dextrose. Because some but not all commercial radiochemical kits prepared with 5% dextrose will suffer this fate, nuclear medicine physicians reviewing the day's images will be confronted with a confusing combination of expected and grossly abnormal findings.

Key Words: radiochemicals; radiopharmaceuticals; ^{99m}Tc; dextrose

J Nucl Med Technol 2003; 31:33–36

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When preparing most ^{99m}Tc radiochemicals, normal saline without preservative is used to dilute the ^{99m}Tc-pertechnetate eluate previously obtained from a generator. For example, when ^{99m}Tc-methylene disphosphonate is prepared (MDP), a suitable activity of eluate from a ^{99m}Tc sterile generator is first diluted with sterile 0.9% sodium chloride to a volume of 2–8 mL and then added to a shielded MDP reaction vial (*1,2*). When such radiochemicals are prepared, strict adherence to protocol should be enforced. However, practitioners also should be aware of the impurities that will be encountered with various unintended deviations from protocol. With this in mind, we report our experience with erroneously diluting ^{99m}Tc-pertechnetate eluate with 5% dextrose solution rather than normal saline.

MATERIALS AND METHODS

In our laboratory, 0.9% normal saline (without preservatives) and 5% dextrose solution were stored on adjacent shelves. This potentially dangerous situation arose when new supplies were delivered and unpacked without adequate supervision. Shortly thereafter, a technologist unknowingly used 5% dextrose to dilute the ^{99m}Tc-pertechnetate eluate. The dextrose solution was used in preparing ^{99m}Tc-tetrofosmin, ^{99m}Tc-MDP, ^{99m}Tc-stannous colloid, and ^{99m}Tc-mebrofenin. In our laboratory, instant thin-layer chromatography (ITLC) is not routinely performed before clinical use of radiochemicals.

During the working day, patients were injected with each of these radiochemicals and images were obtained. ^{99m}Tc-tetrofosmin myocardial perfusion studies, the first images reviewed by nuclear medicine physicians that day, were unremarkable. Later in the day, altered biodistribution was noted on liver/spleen, bone, and hepatobiliary scintigraphy. ITLC was then performed for each ^{99m}Tc radiochemical using previously described techniques (*3,4*). Briefly, solvent systems (acetone, ethyl alcohol, or saline) were used to separate and quantitate the presence of any $^{99m}TcO_4^-$ and reduced hydrolyzed ^{99m}Tc ($^{99m}TcO_2 \cdot xH_2O$) in the radiochemical preparations.

RESULTS

^{99m}Tc-tetrofosmin cardiac images viewed early during the working day showed the expected radiochemical biodistribution. Thereafter, ^{99m}Tc-stannous colloid imaging (Fig. 1) showed the unexpected finding of significant kidney, bladder, cardiac blood pool, and soft-tissue background activity in addition to liver/spleen uptake. Later, a similarly altered biodistribution for ^{99m}Tc-MDP (Fig. 2) and ^{99m}Tc-mebrofenin (Fig. 3) was encountered. When laboratory procedures for the day were reviewed, the error of using 5% dextrose to dilute the ^{99m}Tc eluate was discovered. Fresh radiochemicals were prepared using normal saline, as is our standard procedure.

ITLC was performed (Table 1; Fig. 4). For both ^{99m}Tc-tetrofosmin and ^{99m}Tc-mebrofenin, results of ITLC were not altered when the radiochemical was prepared using 5% dextrose solution. However, for ^{99m}Tc-stannous colloid and ^{99m}Tc-MDP, preparation using 5% dextrose rather than 0.9% sodium chloride yielded significantly different findings on ITLC. For these 2 radiochemical preparations, ITLC found a radiochemical impurity with limited solubility in saline, ethyl alcohol, or acetone, consistent with a probable ^{99m}Tc complex of dextrose.

After identification of the error in preparing radiochemicals, scans were repeated within 72 h for the 6 patients involved in this incident. Review of medical records and consultation with referring physicians uncovered no evidence that this delay had negative effects on patient care. Although all Kuwaiti citizens receive medical care at no charge, the issues of unnecessary radiation exposure and inconvenience for these 6 patients must be seriously considered.

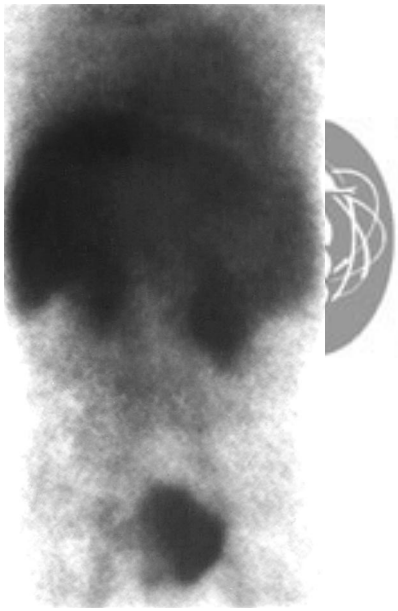

FIGURE 1. Anterior-view ^{99m}Tc-stannous colloid image shows unexpected findings of significant kidney, bladder, cardiac blood-pool, and soft-tissue background activity indicating altered biodistribution as well as uptake in liver and spleen.

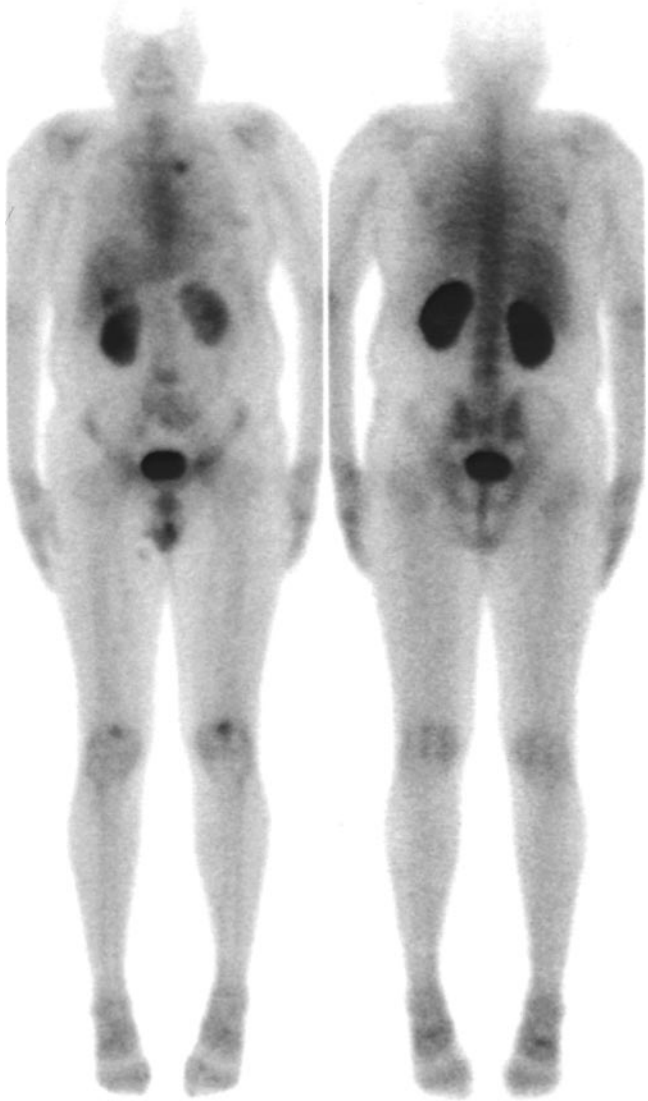

FIGURE 2. Whole-body anterior- and posterior-view ^{99m}Tc-MDP images show unexpected findings of significant kidney, bladder, cardiac blood-pool, gallbladder, and soft-tissue background activity.

DISCUSSION

When radiochemicals erroneously prepared with 5% dextrose solution were used, bone, liver/spleen, and hepatobiliary scintigrams all showed altered biodistribution (Figs. 1–3). Furthermore, ITLC for ^{99m}Tc-MDP and ^{99m}Tc-stannous colloid prepared with 5% dextrose showed an impurity attributed to ^{99m}Tc-dextrose. Although ITLC failed to identify an impurity for ^{99m}Tc-mebrofenin prepared with 5% dextrose, the abnormal scintigraphy strongly argued that some impurity was present. This ^{99m}Tc-dextrose impurity probably migrated much like ^{99m}Tc-mebrofenin during ITLC testing. Therefore, we concluded that during preparation of these 3 radiochemicals, a ^{99m}Tc-dextrose product may have been formed. It should be emphasized that the radiochemical impurity has not been proven to be ^{99m}Tc-dextrose; instead, the biodistribution and chromatography

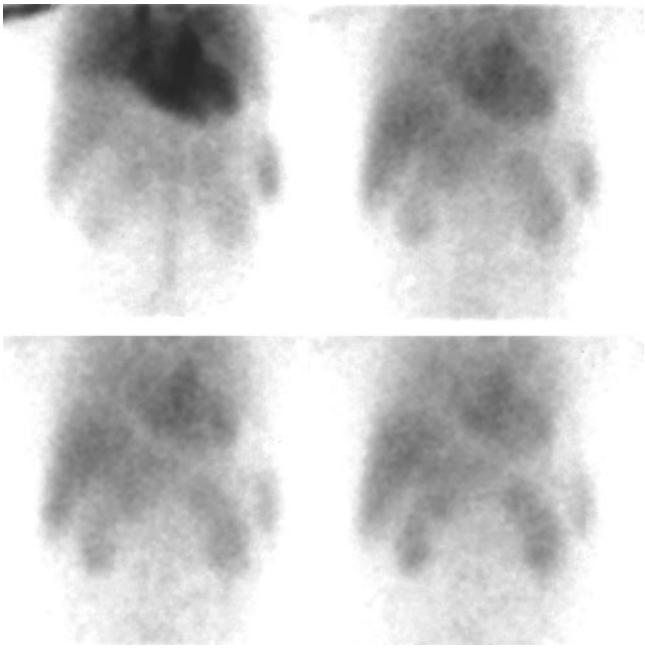

FIGURE 3. Series of 4 anterior-view images over first 10 min after injection of ^{99m}Tc-mebrofenin in patient with normal liver function. Images show reduced liver uptake with no excretion into bile ducts and significant kidney, cardiac blood-pool, and soft-tissue background activity.

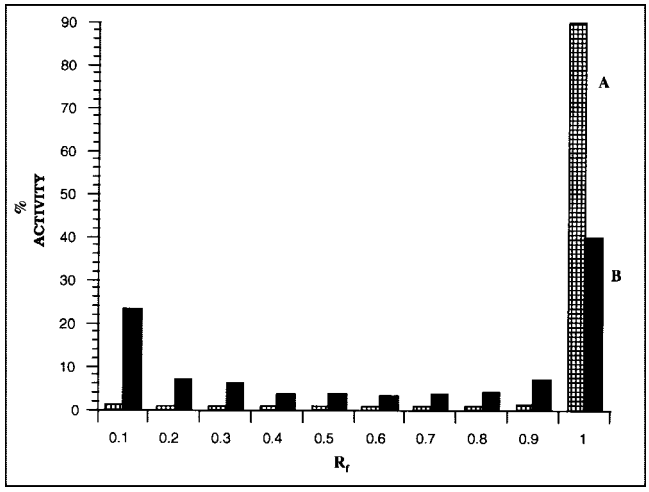

FIGURE 4. Saline chromatograms of ^{99m}Tc-MDP preparations for which ^{99m}Tc-pertechnetate was diluted with either normal saline (A) or 5% dextrose (B). Notice that preparation B contains radiopharmaceutical impurities that do not migrate with solvent front.

data are consistent with the hypothesis that the radiochemical impurity is ^{99m}Tc-dextrose.

If there are deviations from protocol so that other chemicals are present during radiochemical preparation, then impurities may be formed. For example, it is common practice not to use saline with preservative for dilution of ^{99m}Tc-pertechnetate eluate precisely because the preservative, generally benzyl alcohol, reacts with the reduced ^{99m}Tc (*5*). The normal procedure for preparation of any ^{99m}Tc radiochemical is to add the diluted ^{99m}Tc eluate to a vial containing the reducing agent and the chemical to be labeled (e.g., MDP). Because 5% dextrose was erroneously used to dilute the eluate, in the presence of both the reducing agent and MDP a competitive reaction probably occurred between the MDP and dextrose for the reduced ^{99m}Tc, leading to formation of both ^{99m}Tc-MDP and ^{99m}Tc-dextrose. In this case, ^{99m}Tc-dextrose is a radiochemical impurity.

However, when 5% dextrose was used in the preparation of ^{99m}Tc-tetrofosmin, an insignificant amount of ^{99m}Tc-dextrose or other impurity was obtained. For this radiochemical preparation, myocardial scintigrams were unremarkable and ITLC identified no impurity. This successful preparation with 5% dextrose of ^{99m}Tc-tetrofosmin stands out relative to the problems encountered with ^{99m}Tc-MDP and ^{99m}Tc-mebrofenin. We noted that for MDP and mebrofenin, pertechnetate is first reduced by the stannous ion and then immediately chelated by the desired ligand. For tetrofosmin, the stannous-reduced technetium is first chelated by gluconate. Gluconate serves as a transfer ligand and "holds" the ^{99m}Tc until it is eventually transchelated by tetrofosmin. Sulfosalicylate, also present in the commercial tetrofosmin kit, accelerates this otherwise slow ligand exchange. Thus, it may be presumed that if ^{99m}Tc-dextrose were formed it would, like ^{99m}Tc-gluconate, undergo ligand exchange to form ^{99m}Tc-tetrofosmin.

Because the ^{99m}Tc-tetrofosmin used for the first clinical studies of the day contained little or no impurities, a normal biodistribution was seen on the images. However, subsequently encountered ^{99m}Tc-stannous colloid (Fig. 1), ^{99m}Tc-MDP (Fig. 2), and ^{99m}Tc-mebrofenin (Fig. 3) images all showed a biodistribution consistent with a ^{99m}Tc-dextrose impurity. In particular, cardiac blood-pool activity (possibly resulting from slow clearance of ^{99m}Tc-dextrose), soft-tissue background activity (possibly resulting from interstitial distribution of ^{99m}Tc-dextrose), renal and bladder activity (possibly resulting from renal elimination of ^{99m}Tc-dextrose), and gallbladder activity (possibly resulting from hepatobiliary excretion of ^{99m}Tc-dextrose) are expected findings for such "sweet" scans (*6–11*).

Performing ITLC before clinical use of radiochemicals would have identified the presence of impurities and pre-

TABLE 1
Results of Thin-Layer Chromatography

Radiopharmaceutical (prepared with either dextrose or saline)	% Activity toward origin	% Activity toward solvent front	Solvent
MDP (saline)	5	95	Saline
MDP (dextrose)	47	53	Saline
Tin colloid (saline)	95	5	Acetone
Tin colloid (dextrose)	85	15	Acetone
Mebrofenin (saline)	98	2	Water
Mebrofenin (dextrose)	96	4	Water
Tetrofosmin (saline)	98	2	Ethyl alcohol
Tetrofosmin (dextrose)	98	2	Ethyl alcohol

MDP = methylene diphosphonate.

vented unnecessary patient exposure. Although ITLC before clinical use is the standard in commercial radiopharmacies, it is not a universal practice (*12*). Given the low yield of positive results and the limited consequences for patient care, private institutions preparing their own radiochemicals may choose not to perform such routine ITLC. In this instance, all examinations were repeated with no harm to the patients. For corrective action, we have removed 5% dextrose (and all other unnecessary reagents) from the radiochemical preparation area. In addition, strict adherence to protocols has been emphasized.

CONCLUSION

We conclude that unintended preparation of radiochemicals with 5% dextrose rather than 0.9% sodium chloride often results in the production of ^{99m}Tc-dextrose impurities. Because some but not all commercial radiochemical kits prepared with 5% dextrose will suffer this fate, nuclear medicine physicians reviewing the day's images will be confronted with a confusing combination of expected and grossly abnormal findings. Review of ITLC results will clarify this situation.

REFERENCES

1. Kit for preparation of Tc-99m medronate [product information]. Amersham, UK: Amersham International, PLC; 1999.
2. Kit for preparation of Tc-99m tetrofosmin [product information]. Amersham, UK: Amersham International, PLC; 2000.
3. Zimmer AM, Pavel DG. Rapid miniaturized chromatographic quality control procedure for Tc-99m radiopharmaceuticals. *J Nucl Med.* 1977;18: 1230–1237.
4. Owunwanne A, Patel M, Sadek S. *The Handbook of Radiopharmaceuticals.* London, UK: Chapman and Hall Medical; 1995:20–21.
5. Hung JC, Ponto JA, Hammes RJ. Radiopharmaceutical-related pitfalls and artifacts. *Semin Nucl Med.* 1996;26:208–255.
6. Russel CD, Speiser AG. Complexes of technetium with hydroxycarbonic acids: gluconic, glucoheptonic, tartaric, and citric. *J Nucl Med.* 1980;21: 1086–1090.
7. Shafiq YF, Al-Janabi MAA. Preparation, quality control and application of Tc99m-gluco-ene-diolate for renal scanning. *Nuklearmedizin.* 1985;24:93–95.
8. Ballinger JR, Proulx A, Ruddy TD. Stable kit formulation of technetium-99m glucarate. *Appl Radiat Isot.* 1991;42:405–406.
9. Gerson MC, McGoron AJ. Technetium-99m glucarate: what will be its clinical role? *J Nucl Cardiol.* 1997;4:336–340.
10. Ozker K, Collier BD, Linder DJ, et al. Biodistribution of technetium-99m labeled 5-thio-D-glucose. *Nucl Med Commun.* 1999;20:1055–1058.
11. Hladik WB, Nagg KK, Rhodes BA. Drug-induced changes in the biologic distribution of radiopharmaceuticals. *Semin Nucl Med.* 1982;12:184–218.
12. Callahan RJ, Chilton HM, Goodwin DA, et al. Society of Nuclear Medicine Procedure Guidelines for the Use of Radiopharmaceuticals. In: *Society of Nuclear Medicine Procedure Guidelines Manual 1999*. Reston, VA: Society of Nuclear Medicine; 1999:77–79.