Graduate College Journal – NU
Vol.15 -2020, No. (6)
ISSN: 1858-6228, http://www.neelain .edu.sd

مجلة الدراسات العليا - جامعة النيلين
المجلد (15) –2020، العدد (6)
الرقم الدولي الموحد للدوريات: 1858-6228

The Radiochemical purity of free Tc^{99m} Pertechnetate and Tc^{99m} Radiopharmaceuticals during In-use Shelf-life

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Abstract
Radiochemical purity determines the biodistribution of free Tc^{99m} pertechnetate and Tc^{99m} radiopharmaceuticals. The radiochemical impurities in free Tc^{99m} pertechnetate is the hydrolyzed Tc^{99m}, while the radiochemical impurities in Tc^{99m} labeled radiopharmaceuticals are free Tc^{99m} pertechnetate and hydrolyzed Tc^{99m}. The impact of these impurities includes poor image quality which leads to wrong diagnosis and also gives unnecessary radiation dose to the patient. The objective of this study was to find out the influence of storage temperature on radiochemical purity of Tc^{99m} pertechnetate and Tc^{99m} radiopharmaceuticals. 65 Samples of free Tc^{99m} pertechnetate and Tc^{99m} radiopharmaceuticals were utilized for radiochemical purity determination at storage temperature from 25 C^0- 29 C^0 by the chromatography method which is consist from mobile phase and ITLC strips as stationary phase. The mean radiochemical purity resulted was 98.2% with STD 0.7 for all samples. Radiochemical purity of free Tc^{99m} pertechnetate and Tc^{99m} radiopharmaceuticals remains stable in 95.4% of the samples and 4.6% of the samples were out of the internationally acceptable limit. This may be attributed neither to temperature nor to the designed storage period. It is recommended that, follow up of quality assurance protocol including double check should be implemented
Keywords: Radiochemical purity, Tc^{99m} pertechnetate, Tc^{99m} radiopharmaceuticals, radiopharmaceuticals compounding.

Introduction

Radiopharmacy also called nuclear pharmacy is a clinical service that procures, prepares or compounds, dispenses radiopharmaceuticals, and assures quality for diagnostic or therapeutic use in patients referred to the nuclear medicine service of a hospital.[5]

A radiopharmaceutical is a radioactive drug used for the diagnosis and therapeutic treatment of human diseases. A radiopharmaceutical has two components: a radionuclide and a pharmaceutical. The usefulness of a radiopharmaceutical is dictated by the characteristics of these two components. [9]

The nuclear pharmacy prepares the radiopharmaceutical product using the components of the kit and by adding radioactive material eluted from a radionuclide generator for eventual administration to a patient.[10]

More than 80% of radiopharmaceuticals used in nuclear medicine are Technetium 99m labeled compounds. The reason for such a preeminent position of Tc^{99m} in clinical use is its favorable physical and radiation characteristics.[9]

Tc^{99m} radiopharmaceuticals formulations must have high radiation safety standards as well as high pharmaceutical standards because radiation is harmful for both patients and staff.[9]

Most commonly used Tc^{99m} radiopharmaceuticals

Free Tc^{99m} Pertechnetate

Free Tc^{99m} pertechnetate is eluted from Moly generators as pertechnetate $^{99m}TcO^{4-}$ with 6 hours half-life, and a high yield of 140 keV Gamma γ rays, which is ideal for the current generation of imaging devices in nuclear medicine.[7]

Technetium 99m has the ability to readily bind to a wide variety of compounds under physiological conditions without causing physiological changes in the patient.[2]

Free Tc^{99m} eluate is primarily used for preparation of Tc^{99m} radiopharmaceuticals, but it is used as such for thyroid imaging and Meckel's diverticulum detection.[9]

Tc^{99m} Phosphonate and Phosphate Radiopharmaceuticals

Of several phosphonate compounds, methylene diphosphonate (MDP), and hydroxymethylene diphosphonate (HDP), are most commonly used in nuclear medicine. Tc^{99m} MDP and Tc^{99m} HDP are used for bone imaging, whereas Tc^{99m} PYP is used for myocardial infarct imaging.[9]

Tc^{99m} Colloid:

Tc^{99m} tin colloid is most useful in liver and spleen imaging and at times in imaging bone marrow. It is also used for gastrointestinal blood loss studies and for making Tc^{99m} labeled egg sandwich for gastric emptying studies. [9]

Tc^{99m} nanocolloid is useful for bone marrow imaging, inflammation scintigraphy and lymphoscintigraphy. [9]

Tc^{99m} Diethyllenetriamine pentaacetic acid (DTPA):

The primary use of Tc^{99m} DTPA is for renal flow study, glomerular filtration rate (GFR) measurement, and aerosol preparation in lung ventilation studies. [9]

Tc^{99m} Dimercaptosuccinic Acid (DMSA):

DMSA is used for renal cortical imaging.

Tc^{99m} Sestamibi (MIBI):

Tc^{99m} MIBI is used primarily for detection of myocardial perfusion abnormalities in patients, particularly for detection of myocardial ischemia and infarcts. It is also useful for the assessment of myocardial function using the first pass radionuclidic ventriculographic technique. Tc^{99m} sestamibi is also used for the detection of breast tumors (miraluma) and hyperparathyroidism.[9]

All Tc^{99m} radiopharmaceuticals are compounded in hospital radiopharmacy units, and most of them are administered intravenously and they have short shelf life therefore it should pass all quality assurance parameters before dispensing it for patient administrations, to ensure its safety, purity and efficiency.[2]

Radiochemical purity (RCP) of a radiopharmaceutical is defined as the percentage of the total radioactivity present in the desired chemical form in a radioactive pharmaceutical. Without acceptable RCP in a diagnostic radiopharmaceutical, image interpretation can be compromised which can result in a delay of an accurate diagnosis and unnecessary radiation exposure since the nuclear medicine study must be repeated. In clinical practice, the RCP analysis must be quick, accurate, and economical.[11]

Radiochemical purity is important in radiopharmacy because determines the biodistribution of the radiopharmaceuticals. Radiochemical impurities will have different patterns of biodistribution which may obscure the diagnostic image obtained and render the investigation meaningless.[6]

Radiochemical impurities arise from decomposition due to the action of solvent, change in temperature or pH, light, presence of oxidizing or reducing agents, incomplete reaction, and radiolysis. The radiochemical impurities are (hydrolyzed Tc^{99m} in free Tc^{99m} pertechnetate) and (free Tc^{99m} pertechnetate and hydrolyzed Tc^{99m} in Tc ^{99m} labeled complexes).[3]

In Tc ^{99m} radiopharmaceuticals preparations, the major fraction of radioactivity must be in the bound form. The free and hydrolyzed Tc^{99m} fractions (unbound form) are undesirable and must be reduced to a minimum level so that they do not interfere significantly with the diagnostic test.[2]

The most simple and widely performed procedure used to determine the radiochemical impurities is thin-layer chromatography (TLC) in which the various compounds may be separated because they are differentially distributed between a liquid (mobile) phase and a solid (stationary) phase.[3]

Radiochemical RCP testing plays a key role in assessing the impact of change and identify defective products, which can result in patient harm.[8]

The acceptance limits of total radiochemical impurities in Tc^{99m} pertechnetate and Tc^{99m} radiopharmaceuticals according to the International Atomic Energy Agency IAEA, European Pharmacopoeia EP, the United States Pharmacopeia USP and the manufacturer is that it should not be more than 5% and the complex form should not be less than 95%.[7] The storage temperature for Tc^{99m} pertechnetate andTc^{99m} radiopharmaceuticals after reconstitutions is below 25 C^0 and the storage period are generally designed by the manufacturer.

The main objective of this study is to find out the influence of storage temperature on radiochemical purity of Tc^{99m} pertechnetate and Tc^{99m} radiopharmaceuticals. That is because the temperature is high in summer, the presence of heating instruments and particularly the free Tc^{99m} eluate and Tc^{99m} radiopharmaceuticals which are stored in lead blocks shield and may be subjected to higher temperature.

Materials and Methods

Materials

Instant thin-layer chromatography (ITLC) strips as stationary phase; red, black, yellow, orange, and pink strips, from Biodex Medical Inc. New York, USA. Each (ITLC) chromatography strip has three distinct lines: an origin line, a cut line, and a solvent front line. The back of each strip is marked with a soluble dye.

Acetone, normal saline, distilled water, and ethyle acetate as mobile phase.

Dose calibrator as counting instruments, CAPENTEC Inc. CRC 25R, USA and Veenstra, VDC- 404, Netherlands. 10 ml serum vial as developing vial and 19-26G needle and syringe.0.01cc spots per sample from free Tc^{99m} pertechnetate. 0.01cc spots per sample from prepared Tc^{99m} radiopharmaceuticals. Scissor for cutting chromatography strips and empty serum vials for holding the strips for

measuring it in the dose calibrator. Room temperature thermometer VIRRA 18951.

Study Design:

Total 65 Samples (14 Tc^{99m} eluate, 14 Tc^{99m} MDP, 5 Tc^{99m} HDP, 8 Tc^{99m} DTPA, 11 Tc^{99m} DMSA, 5 Tc^{99m} MIBI and 8 Tc^{99m} Colloid) were taken for radiochemical purity after reconstitution at storage temperature $\geq 25\ C^0$ ($25\ C^0 – 29C^0$).

The samples were collected randomly from three hospital radiopharmacy units and the laboratory units in nuclear medicine department in Khartoum. The temperature and the storage period before injection were recorded.

Methods

Determination of free Tc^{99m} pertechnetate in Tc^{99m} labeled Colloid (IAEA guidelines, manufactures and Biodex instructions)[7,12]

1. 1cc of acetone solvent was added to a developing vial.

2. A red chromatography strip was used, 10 microliters of the test sample was spotted onto the bottom line (origin line) of the test strip.

3. Immediately the test strip was placed into the developing vial containing acetone, and developed until the solvent front migrates to top line (solvent front).

4. Strip was removed from the vial and allowed to dry.

5. Strip was cut at central line (cut line), producing sections 1 and 2.

6. A dose calibrator was used , count background and calculate the net counts by subtracting the background counts from the number of counts registered for each strip section.

% free pertechnetate = (counts cut 2) / (counts cut 1) + (counts cut 2) *100%

Determination of free pertechnetate, hydrolyzed Tc^{99} and labeling efficiency in Tc^{99m} labeled DTPA, HDP And MDP (IAEA guidelines, manufactures and Biodex instructions) [7,12]

Repeat the above six steps then proceed to the following steps.

7. 1cc of distilled H_2O was placed in a clean solvent developing vial.

8. A strip of the black chromatography paper was selected and 10 microliters of the test compound sample was spotted onto the bottom line (origin line).

9. The test strip was immediately placed into the developing vial containing distilled water and developed until the solvent front migrates to top line.

10. The strip was removed from the vial and allowed to dry.

11. Strip was cut at center line (cut line) into sections 3 and 4.

12. A dose calibrator was used, count background and calculate the net counts by subtracting the background counts from the number of counts registered for each strip section.

% hydrolyzed Tc^{99m} = (counts cut 3) / (counts cut 3) + (counts cut 4) *100%

% of labeling efficiency =100 - % of free pertechnetate - % of hydrolyzed Tc ^{99m}.

Determination of free pertechnetate in Tc^{99m} labeled DMSA (IAEA guidelines, manufactures and Biodex instructions) [7,12]

The same method as above but using yellow chromatography strip was used, 10 microliters of the DMSA sample was spotted onto the bottom line (origin line) of the test strip.

2.3.4 Determination of free pertechnetate in Tc^{99m} labeled Sestamibi (IAEA guidelines, manufactures and Biodex instructions) [7,12]

1.1cc of ethylacetate solvent was added to a developing vial.

2. A pink chromatography strip was used, 10 microliters of MIBI sample was spotted onto the bottom line (origin line) of the test strip and proceed as above.

Results

The hydrolyzed Tc^{99m} in free Tc^{99m} pertechnetate.

Table 1. Radiochemical purity for Tc^{99m} pertechnetate

Radio-pharmaceutical	Temp.C^0 (Guidelines storage temp. < 25 C^0)	Storage period (labeled shelf life is 12 hrs)	Impurities (% hydrolzed Tc^{99m}) Cut1 reading in mCi	Purity(% ($freeTc^{99m}$) Cut 2 reading in mCi	% $freeTc^{99m}$ = Cut2 / (Cut1+cut2)
Free Tc^{99m} perechnetate	27 C^0	5,25 hours	0.003 mCi	0.509 mCi	99.4%
Free Tc^{99m} perechnetate	27 C^0	5,75 hours	0.004 mCi	0.611 mCi	99.3%
Free Tc^{99m} perechnetate	28 C^0	5 hours	0.000 mCi	0.341 mCi	100%
Free Tc^{99m} perechnetate	28 C^0	6 hours	0.0001 mCi	0.068 mCi	99.9%
Free Tc^{99m} perechnetate	26 C^0	5 hours	0.003 mCi	0.480 mCi	99.3%
Free Tc^{99m} perechnetate	26 C^0	4,75 hours	0.000 mCi	0.037 mCi	100%
Free Tc^{99m} perechnetate	27 C^0	5,5 hours	0.004 mCi	0.506 mCi	99.2%
Free Tc^{99m} perechnetate	28 C^0	3,5 hours	0.0005 mCi	0.078 mCi	99.3%
Free Tc^{99m} perechnetate	26 C^0	4,5 hours	0.008 mCi	0.418 mCi	98.1%
Free Tc^{99m} perechnetate	26 C^0	4 hours	0.102 mCi	0.800 mCi	88.7%*
Free Tc^{99m} perechnetate	26 C^0	4,5 hours	0.001 mCi	0.508 mCi	99.8%
Free Tc^{99m} perechnetate	26 C^0	4,25 hours	0.000 mCi	0.130 mCi	100%
Free Tc^{99m} perechnetate	25 C^0	6 hours	0.001 mCi	0.601 mCi	99.8%
Free Tc^{99m} perechnetate	26 C^0	5,25 hours	0.003 mCi	0.781 mCi	99.6%

Mean 98.7%

All the results at the ambient temperature and use within the designed in-use shelf life were within the international limits. According to these results impurity would be attributed neither to high temperature nor to the storage period.

Determination of free Tc^{99m} pertechnetate and hydrolyzed Tc^{99m} in Tc^{99m} labeled MDP

Table 2. Radiochemical purity for Tc^{99m} MDP (methylene diphosphonate)

Radio-pharmaceutical	Temp.C^0 Guidelinesst orage temp. < 25 C^0	storage period (labeled shelf life 8 hrs)	Impurities %		Purity %
			% free Tc^{99m}	% hydrolzed Tc^{99m}	% Bound= (100 - Free - Hydrolzed)
Tc^{99m} MDP	26 C^0	5 hours	0.00%	0.7%	99.3%
Tc^{99m} MDP	26 C^0	3,5 hours	0.00%	0.6%	99.4%
Tc^{99m} MDP	29 C^0	3,25 hours	0.8%	1.5%	97.7%
Tc^{99m} MDP	26 C^0	3,75 hours	0.00%	0.00%	100%
Tc^{99m} MDP	27 C^0	6 hours	0.01%	1%	98.9%
Tc^{99m} MDP	27 C^0	5,5 hours	1%	0.2%	98.8%
Tc^{99m} MDP	27 C^0	6 hours	0.8%	1.1%	98.1%
Tc^{99m} MDP	28 C^0	4,75 hours	0.00%	0.00%	100%
Tc^{99m} MDP	28 C^0	5,25 hours	0.005	0.3%	99.7%
Tc^{99m} MDP	28 C^0	6 hours	0.1%	0.4%	99.5%
Tc^{99m} MDP	27 C^0	5,25 hours	1.8%	0.6%	97.6%
Tc^{99m} MDP	27 C^0	6 hours	1%	0.9%	98.1%
Tc^{99m} MDP	26 C^0	5,5 hours	0.9%	0.8%	98.3%
Tc^{99m} MDP	27 C^0	5,5 hours	0.1%	0.8%	99.1%

Mean 98.8%

All the samples showed acceptable results and the purity was within the limits.

Determination of free Tc^{99m} pertechnetate and hydrolyzed Tc^{99m} in Tc^{99m} labeled HDP

Table 3. Radiochemical purity for Tc^{99m} HDP (hydroxy methylene diphosphonate)

Radio-pharmaceutical	Test Temp.C^0 Ideal storage temp. < 25 C^0	Test storage period (shelf life 8 hrs)	Impurities %		Purity %
			% free Tc^{99m}	% hydrolzed Tc^{99m}	% Bound = (100-F-H)
Tc^{99m} HDP	25 C^0	4,5 hours	0.00%	0.7%	99.3%
Tc^{99m} HDP	26 C^0	5,5 hours	0.1%	0.1%	99.8%
Tc^{99m} HDP	25 C^0	6,5 hours	0.0%	11%	89%*
Tc^{99m} HDP	26 C^0	4 hours	0.3%	2%	97.7%
Tc^{99m} HDP	25 C^0	3.5 hours	0.00%	2.6%	97.4%

Mean 96.6%

All the results at the ambient temperature and use within the designed in-use shelf life was within the international limits. According to these results impurity would be attributed neither to high temperature nor to the storage period.

Determination of free pertechnetate in Tc^{99m} labeled Sestamibi

Table 4. Radiochemical purity for Tc^{99m} MIBI

Radiopharma-ceutical	Temp.C^0 Ideal storage temp. < 25 C^0	storage period (shelf life 8 hrs)	Impurities	Purity	%Bound Cut2/(Cut1 +Cut2)
			Cut1 reading in mci (%freeTc^{99m})	Cut 2 reading in mci (BoundTc^{99m})	
Tc^{99m} Sestamibi	26 C^0	6 hours	0.0009 mCi	0.047 mCi	98.1%
Tc^{99m} Sestamibi	26 C^0	6.5 hours	0.0002 mCi	0.044 mCi	99.5%
Tc^{99m} Sestamibi	25 C^0	5	0.0036 mCi	0.092 mCi	96.2%
Tc^{99m} Sestamibi	26 C^0	4,5 hours	0.0024 mCi	0.091 mCi	97.4%
Tc^{99m} Sestamibi	25 C^0	3,5 hours	0.0014 mCi	0.046 mCi	97%

Mean 97.6%

All the samples showed acceptable results and the purity is within the limits.

Determination of free Tc^{99m} pertechnetate, and hydrolyzed Tc^{99m} in Tc^{99m} DTPA

Table 5. Radiochemical purity for Tc^{99m} DTPA (diethyllenetriamine pentaacetic acid)

Name of Radio-pharmaceutical	Temp.C^0 Ideal storage temp. < 25 C^0	storage period (shelf life 8 hrs)	Impurities %		Purity %
			% free Tc^{99m}	% Tc^{99m} hydrolzed	% Bound= (100 –Free - Hydrlozed)
Tc^{99m} DTPA	26 C^0	5 hours	0.1%	0.3%	99.6%
Tc^{99m} DTPA	29 C^0	5,5 hours	0.1%	0.4%	99.5
Tc^{99m} DTPA	26 C^0	3 hours	0.8%	1.5%	97.7%
Tc^{99m} DTPA	26 C^0	5,5 hours	0.00%	0.00%	100%
Tc^{99m} DTPA	27 C^0	5,5 hours	0.8%	1.1%	98.1%
Tc^{99m} DTPA	27 C^0	4,5 hours	0.0%	0.0%	100%
Tc^{99m} DTPA	28 C^0	5,5 hours	0.9%	1.1%	98%
Tc^{99m} DTPA	25 C^0	5 hours	0.6%	1.4%	98%

Mean 98.8%

All the samples showed acceptable results and the purity is within the limits.

Determination of free Tc^{99m} pertechnetate in Tc^{99m} labeled DMSA

Table 6. Radiochemical purity for Tc^{99m} DMSA (dimercaptosuccinic acid)

Radio- pharmaceutical	Temp.C^0 Ideal storage temp. < 25C^0	storage period (shelf life 4 hrs)	Purity	Impurites	%Bound = cut1 / (cut1+cut2)
			Cut1 reading in mci (BoundTc^{99m})	Cut 2 reading in mci (% freeTc^{99m})	
Tc^{99m} DMSA	25 C^0	2,5 hours	0.068 mCi	0.0001 mCi	99.9%
Tc^{99m} DMSA	25 C^0	4,25 hours	0.031 mCi	0.002 mCi	93.9%*
Tc^{99m} DMSA	28 C^0	4 hours	0.048 mCi	0.001 mCi	97.9%
Tc^{99m} DMSA	26 C^0	2 hours	0.015 mCi	0.0002 mCi	98.6%
Tc^{99m} DMSA	27 C^0	2 hours	0.022 mCi	0.0002 mCi	99.1%
Tc^{99m} DMSA	26 C^0	2,5 hours	0.02 mCi	0.0005 mCi	97.5%
Tc^{99m} DMSA	26 C^0	2 hours	0.0099 mCi	0.0001 mCi	99%
Tc^{99m} DMSA	25 C^0	2,5 hours	0.000 mCi	0.014 mCi	100%
Tc^{99m} DMSA	25 C^0	3 hours	0.0083 mCi	0.0003 mCi	96.5%
Tc^{99m} DMSA	25 C^0	2,5 hours	0.0079 mCi	0.000 mCi	100%
Tc^{99m} DMSA	25 C^0	3 hours	0.011 mCi	0.000 mCi	100%

Mean 98.4%.

All the results at the ambient temperature and use within the designed in-use shelf life were within the international limits. According to these results impurity would be attributed neither to high temperature nor to the storage period.

Determination of free Tc^{99m} pertechnetate in Tc^{99m} labeled Colloid

Table 7. Radiochemical purity for Tc^{99m} Colloid (Tin & Nano)

Radio- pharmaceutical	Temp.C^0 Ideal storage temp. < 25 C^0	storage period (shelf life 6 hrs)	Purity	Impurities	%Bound Cut1/(cut1+Cut2)
			Cut1 reading in mci (BoundTc^{99m})	Cut 2 reading in mci (% freeTc^{99m})	
Tc^{99m} Colloid	27 C^0	5,5 hours	0.047 mCi	0.0015 mCi	96.9%
Tc^{99m} Colloid	25 C^0	5,5 hours	0.051 mCi	0.0008mCi	98.4%
Tc^{99m} Colloid	25 C^0	5,5 hours	0.062 mCi	0.001 mCi	98.4%
Tc^{99m} Colloid	25 C^0	3 hours	0.012 mCi	0.0001 mCi	99.9%
Tc^{99m} Colloid	26 C^0	4 hours	0.021 mCi	0.00 mCi	100%
Tc^{99m} Colloid	25 C^0	5 hours	0.046 mCi	0.00 mCi	100%
Tc^{99m} Colloid	25 C^0	5 hours	0.029 mCi	0.001 mCi	99.6%
Tc^{99m} Colloid	26 C^0	3,5 hours	0.155 mCi	0.0019 mCi	98.7%

Mean 98.9 %

All the results were within the specified limits.

The results showed that the mean radiochemical purity for free Tc^{99m} pertechnetate and Tc^{99m} radiopharmaceuticals at ambient temperature between 25 C^0-29 C^0 were: Tc^{99m} eluate 98.7% STD 2.8, Tc^{99m} MDP 98.8% STD 0.7, Tc^{99m} HDP 96.6% STD 3.9, Tc^{99m} DTPA 98.8% STD 0.9, Tc^{99m} DMSA 98.4% STD 1.8, Tc^{99m} Colloid 98.9% STD 1.02 and Tc^{99m} Sestamibi 97.6% STD 1.11. The mean radiochemical purity result for the all samples of free Tc^{99m} eluate and Tc^{99m} radiopharmaceuticals was 98.2% STD 0.7.Radiochemical purity of free Tc^{99m} pertechnetate and Tc^{99m} radiopharmaceuticals remain stable in 95.4% of samples and there is radiochemical impurities in three samples out of 65 samples constituting 4.6% of samples.

Figures illustrating Radiochemical Purity of free Tc^{99m} pertechnetate and Tc^{99m} radiopharmaceuticals at Temperature (25 C^0-29 C^0)

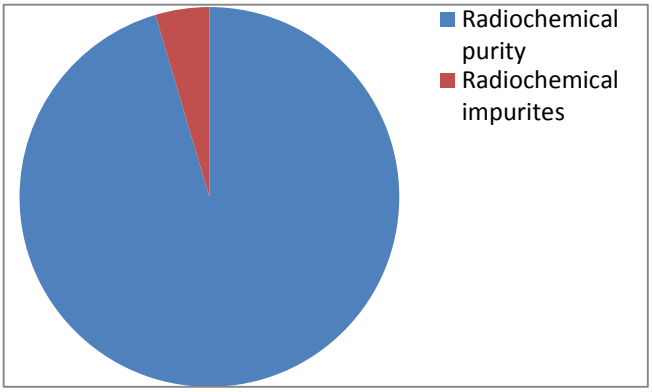


Figure 1. Radiochemical purity and impurities for Tc^{99m} eluate and Tc^{99m} radiopharmaceuticals

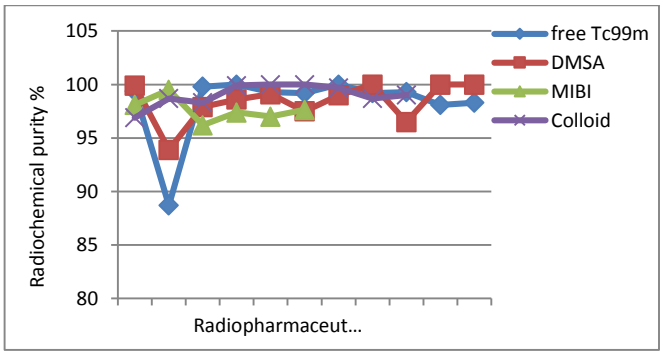
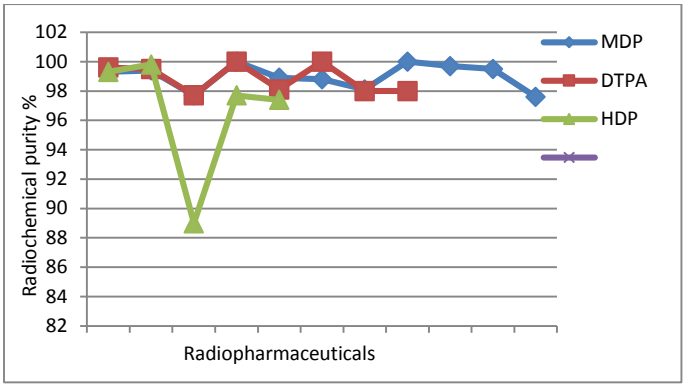


Figure 2. Radiochemical purity for Tc^{99m} and Tc^{99m}-(DMSA, MIBI, and Colloid)

Figure 3. Radiochemical purity for Tc^{99m} radiopharmaceuticals (MDP. HDP. DTPA)



Discussion

The number of samples being tested was 65 samples. The specific test had been done according to the medical request and every specific kit can only be used to test the specific impurity leading to inconsistency of the number of samples for every test. The Tc^{99m} elution and kit reconstitution were performed according to the methods described in the package insert and all the samples were collected during shelf life when ambient storage temperature is 25 C^0-29 C^0.

The acceptance limit for total radiochemical impurities % Tc^{99m} pertechnetate and Tc^{99m} radiopharmaceuticals, should not be more than 5% and the complex form should not be less than 95%. The suitable storage temperature after reconstitutions is below 25 C^0 according to the manufacturer instructions, the International Atomic Energy Agency IAEA, the European Pharmacopoeia EP and the United States Pharmacopeia USP.[7]

The mean radiochemical purity in free Tc^{99m} pertechnetate, was 98.7% STD 2.8. The samples were collected during the shelf life of 12 hours, at storage temperature 25 C^0-29 C^0. The radiochemical purity of all the samples remained stable (≥ 95%) except only one sample which gave radiochemical purity 88.7% -which is less than 95%- this sample was taken at storage temperature 26 C^0 and after 4 hours from elution time. According to the other results, impurity cannot be attributed neither to high temperature nor to the storage period. That is because the storage period after reconstitution was within the designed limits and the when temperature is 28 C^0 and 26 C^0, the purity is 100% and 99.99%.

The mean radiochemical purity for Tc^{99m} MDP (methylene diphosphonate) was 98.8%STD 0.7. The samples were collected during the shelf life of 8hours, at storage temperature 25 C^0-29 C^0. The radiochemical purity of all the samples remained stable (≥ 95%). The mean radiochemical

purity for Tc^{99m} HDP (hydroxy methylene diphosphonate) was 96.6. The samples were collected during the shelf life of 8 hours, at storage temperature 25 C^0-29 C^0. The radiochemical purity of all the samples remained stable (≥ 95%) except only one sample which gave radiochemical purity 89% -which is less than 95%- The only sample which is out of the limits, the storage temperature after reconstitution is 25 C^0 and the storage period is within the designed period. This result cannot be attributed to temperature, neither to the storage period.

The mean radiochemical purity for Tc^{99m} DMSA (dimercaptosuccinic acid) was 98.4% STD 1.8. The samples were collected during the shelf life of 4 hours, at storage temperature 25 C^0-29 C^0. The radiochemical purity of all samples remained stable (≥ 95%) except only one sample which showed radiochemical purity 89.9% -which is less than 95%- but it had been tested within the specified storage period and being subjected to the specified storage 25 C^0 temperature, however it failed the test by showing 93.9% radiochemical purity. So, this failure cannot be attributed to the in-use storage temperature nor to the storage period.

The mean radiochemical purity for Tc^{99m} DTPA (diethyllenetriamine pentaacetic acid) was 98.8% STD 0.9. The samples were collected during the shelf life of 8hours, at storage temperature 25 C^0-29 C^0. The radiochemical purity of all samples remained within the specified limit (≥ 95%).

The mean radiochemical purity for Tc^{99m} Colloid (tin an nano) was 98.9% STD 1.02. The samples were collected during the shelf life of 6 hours, at storage temperature 25 C^0-29 C^0. The radiochemical purity of all samples remained within the specified limit (≥ 95%).

The mean radiochemical purity for Tc^{99m} Sestamibi was 97.6% STD 1.11. The samples were collected during the shelf life of 8hours, at storage temperature 25 C^0-29 C^0. The radiochemical purity of all samples remained within the specified limit (≥ 95%).

It had been found that the radiochemical purity of free Tc^{99m} eluate and Tc^{99m} radiopharmaceuticals remained stable in 95.4% of samples and there were radiochemical impurities in 4.6% of samples. This 4.6% change in radiochemical was proved not to be attributed to the storage temperature or to the storage period.

Poor diagnostic image quality and high patient radiation dose are the main impact of radiochemical impurities in free Tc^{99m} and Tc^{99m} radiopharmaceuticals. These results are in conformance with the study done in Italy by Licia Uccelli, fixing the temperature ≥ 25 C^0, testing the radiochemical impurity at three intervals and concluded that the temperature variability, measured inside the isolator, does not have any effect on the radiochemical purity of Tc^{99m} radiopharmaceutical products until the shelf life.[14]

The significance of the 3 samples which showed impurities out of the limits is that improper diagnostic image may result or/and the patient may be subjected to untoward radiations.

This makes it highly necessary to implement a quality assurance program with double check testing to avoid experimental errors, mankind errors and ensures the quality of the kits.

Conclusion

Radiochemical purity determines the biodistribution of the free pertechentate Tc^{99m} and Tc^{99m} radiopharmaceuticals and the specified limits of radiochemical purity guarantee the interpretation of image, leading perfect diagnosis and eliminate the incidence of unnecessary exposure to radiation. The specified international storage temperature for Tc^{99m} pertechentate and most of Tc^{99m} radiopharmaceutical compounds after reconstitution is below 25 C^0 and the storage period is generally specified by the manufacturer. Following the manufacturer instructions will guarantee the stability of free Tc^{99m} eluate and Tc^{99m} radiopharmaceutical compounds during the shelf life.

Recommendations

The radiochemical purity tests for free Tc^{99m} pertechentate and Tc^{99m} radiopharmaceuticals should be performed on all prepared radiopharmaceutical kits before administered intravenously to patients.

The radiochemical purity for free Tc^{99m} and Tc^{99m} radiopharmaceuticals should follow the manufacturer instructions, International Atomic Energy Agency IAEA, European Pharmacopoeia and the United States Pharmacopeia USP.

The storage temperature for free Tc^{99m} and Tc^{99m} radiopharmaceuticals should be monitored before and after the reconstitutions. It is recommended that, the preparation of Tc^{99m} radiopharmaceuticals from kits and generators to be carried out in the specified conditions.

It is also being recommended to implement a quality assurance program with double check testing to avoid experimental errors, mankind errors and ensures the quality of the kits and to keep records for Tc^{99m} and Tc^{99m} radiopharmaceuticals preparation and radiochemical purity test.

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