STABILITY TESTS FOR ^{99M}TC-DTPA RADIOPHARMACEUTICAL

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RAP.24 INTERNATIONAL CONFERENCE ON RADIATION APPLICATIONS

INTRODUCTION

- Applications for marketing authorization in respect of radiopharmaceuticals should be accompanied, as in case of all medicinal products, by the particulars and documents referred to in Directives 65/65EEC and 75/31/EEC as amended and in the Annex of Directive 75/318 EEC as amended.

- Most radiopharmaceuticals are used for the purpose of medical diagnosis. They contain only small amounts of active substances with a radionuclide attached to them to allow scintigraphic imaging or measurement of biodistribution.

INTRODUCTION

- Radiopharmaceuticals have changing composition with time, associated with radioactive decay. The physical half-life of the radionuclide is often so short (like ^{99m}Tc). In these cases, the final preparation must be done immediately before administration to the patients.
- For all radiopharmaceuticals, the shelf life of the product as supplied by the manufacturer should be specified and justified, as should a shelf life after reconstitution where applicable, considering radiochemical and radionuclide degradation products.

INTRODUCTION

- The aim of this study was determination of stability of ^{99m}Tc-DTPA (Diethylenetriaminepentaacetic acid) radiopharmaceuticals used for brain and kidney scanning.

- Stability is defined by analyzing radiochemical purity of the ^{99m}Tc-DTPA radiopharmaceuticals in different times after reconstitution (labelling of cold DTPA-kit with ^{99m}Tc-eluate) and production (shelf-life of cold DTPA-kit).

INTRODUCTION

- Chromatographic methods of assaying radiopharmaceuticals are used for determining the radiochemical purity of ^{99m}Tc-DTPA radiopharmaceuticals.

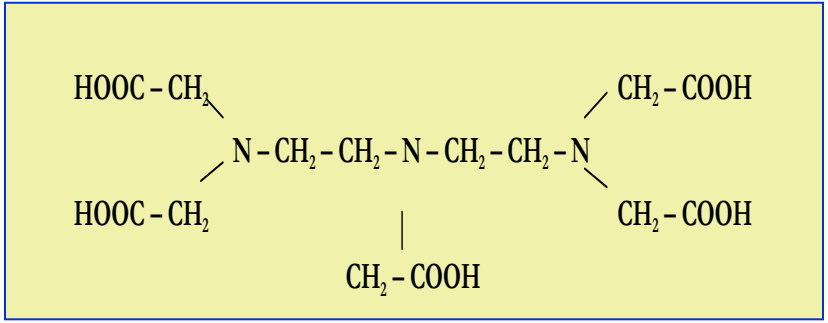
- The system used was ITLC-SG/Acetone and ITLC-SG/Saline to determine the sum of radiochemical impurities (free and hydrolyzed ^{99m}Tc). In conclusion of many experiments, the results show that ^{99m}Tc DTPA radiopharmaceutical was stable up to 2 hours after its reconstitution and 1 year after cold kit production.

DTPA - RADIOPHARMACEUTICAL

SUMARY DATA

- - Chemical Name:
  Diethylene Triamine Penta Aceticacid (DTPA)
- - Technetium tc-99m DTPA is a Radioactive Diagnostic Agent.
- - The mechanism of action of technetium tc-99m DTPA is as a Radiopharmaceutical Activity.
- - A technetium diagnostic aid used in renal function determination

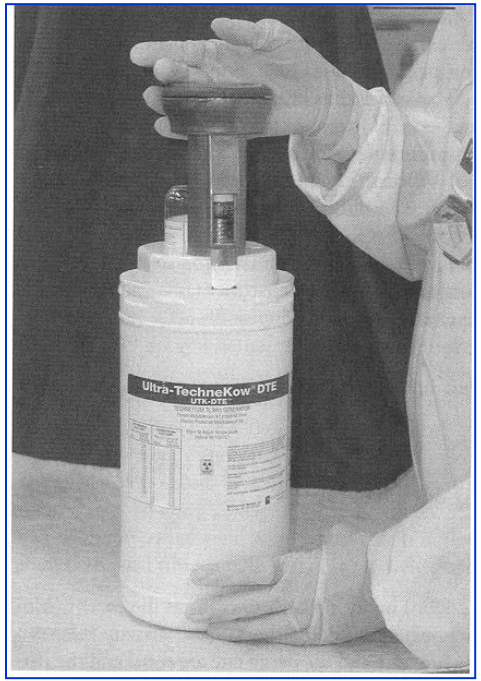
STRUCTURAL FORMULA

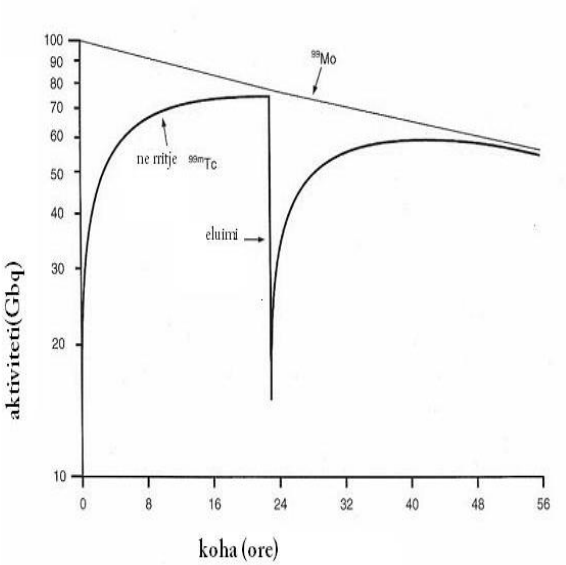


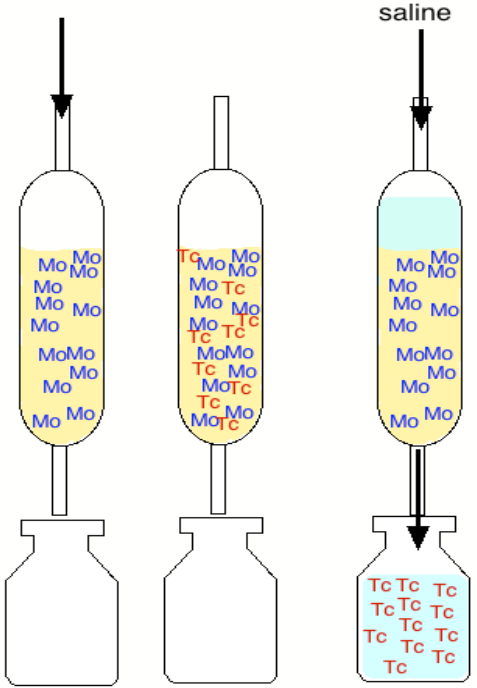
PROCEDURE

- Eluation of ^{99}Mo-^{99m}Tc Generator
- Labelling of cold kit
- Developing of chromatography in different time after labelling and production
- Scanning of the radiochromatograms
- Analyzing the results

ELUATION OF GENERATOR



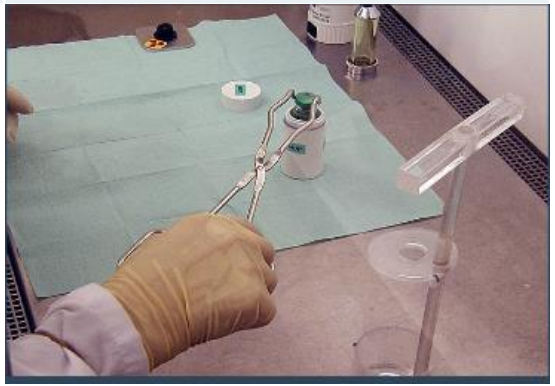




LABELLING OF COLD KIT

Content (%) of the compounds in cold kit

Compounds	Version A	Version B
DTPA	5.00 mg	9 mg
$SnCl_2x2H_2O$	0.25 mg	0.6 mg
Ascorbic acid	0.15 mg	0.5 mg
NaCl	-	20 mg



STABILITY OF LABELLED KIT

- Stability in-vitro means for how long the labelled kit is stable, which means that radiochemical purity more than 90%.
- Determination of radiochemical purity 15 min, 3 hours and 24 hours after labelling.
- The results ate presented in the table below

RADIOCHEMICAL PURITY

- Radiochemical purity is the fraction of total activity in the desired radiochemical form present in the radiopharmaceutical.
- In the radiopharmacy, it is the presence of the undesired radiochemical impurities that is checked.
- These impurities are due to decomposition of the radiopharmaceutical caused by solvent, temperature, light of radiolysis or labeling of a chemical impurity with the same radionuclide.

Radiochemical purity (% ^{99m}Tc-R/F)= 100 – (% $^{99m}TcO_4^-$ - % $^{99m}TcO_2$)

CHROMATOGRAPHIC SYSTEMS

INSTANT THIN LAYER CHROMATOGRAPHY METHOD

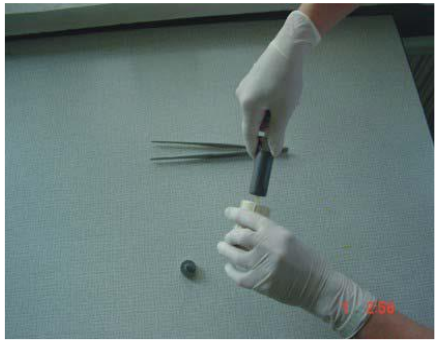
- **Stationary Phase:**

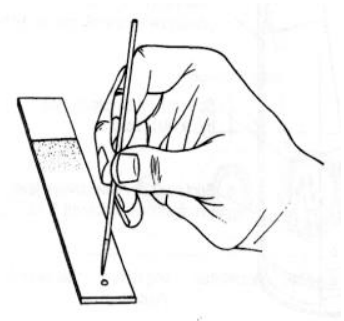
  ITLC-SG

- **Mobile Phase:**

  Acetone and NaCl

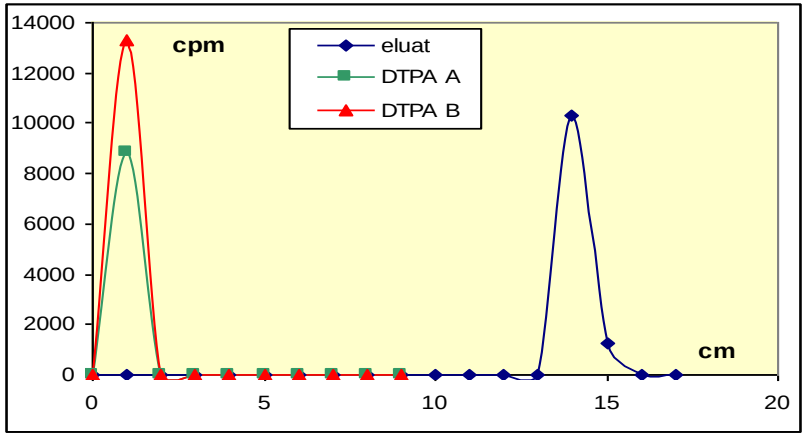
DEVELOPMENT OF CHROMATOGRAPHY



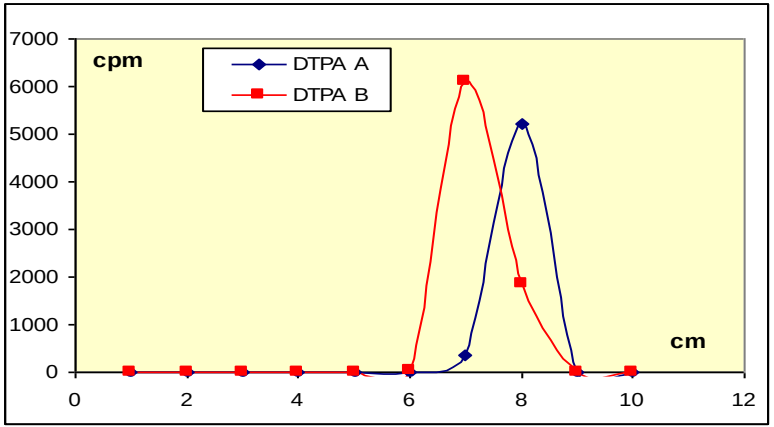


RADIOCHEMICAL PURITY

Activity curve (PC) Acetone 85%



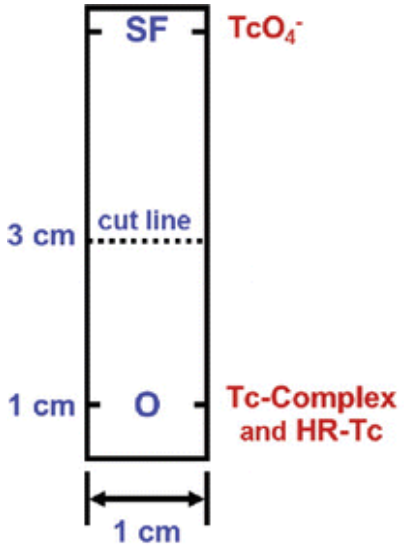
Activity curve (PC) 0.9%NaCl %



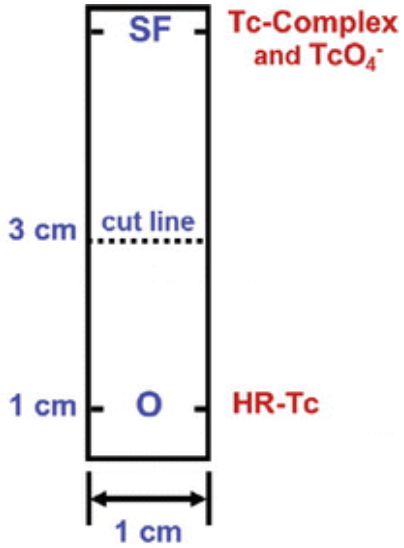
RADIOCHEMICAL PURITY

Activity (%) of cut parts

DTPA (Acetone)		DTPA (0.9%NaCl)	
Origin	97.00 (%)	Origin	2.61 (%)
Middle	1.92 (%)	Middle	1.81 (%)
Front	1.18 (%)	Front	95.58 (%)



Acetone



Normal Saline

STABILITY OF LABELLED KIT

In - Vitro Stability of kit prepared/labelled (two versions)

Time after labelling	^{99m}Tc – DTPA (*Version A*)			^{99m}Tc – DTPA (*Version B*)		
	^{99m}Tc free	*^{99m}Tc coloid*	*^{99m}Tc complex*	*^{99m}Tc free*	*^{99m}Tc coloid*	*^{99m}Tc complex*
15 min	0.12	0.35	99.53	0.22	0.43	99.35
1 hour	0.41	0.34	99.25	0.29	0.40	99.31
2 hours	0.50	0.40	**99.10**	0.43	0.41	**99.16**

SHELF-LIFE

Shelf-life of DTPA (3 months after production)

Time after labelling	^{99m}Tc – DTPA (Version A)			^{99m}Tc – DTPA (Version B)		
	^{99m}Tc coloid	^{99m}Tc free	^{99m}Tc complex	^{99m}Tc coloid	^{99m}Tc free	^{99m}Tc complex
30 min	3.10	2.80	94.10	1.79	0.09	98.12
2 hours	2.95	3.10	**93.95**	2.04	1.07	**96.89**

Shelf-life of DTPA (1 year after production)

Time after labelling	^{99m}Tc – DTPA (Version A)			^{99m}Tc – DTPA (Version B)		
	^{99m}Tc coloid	^{99m}Tc free	^{99m}Tc complex	^{99m}Tc coloid	^{99m}Tc free	^{99m}Tc complex
15 min	3.5	2.64	93.86	1.93	0.16	97.91
2 hours	1.90	4.12	**93.98**	1.30	0.27	**98.43**

CONCLUSIONS

. 99m TC - DTPA Radiopharmaceutical produced in sterile and freeze dried form fulfill all the requirements for stability

-` The results show that ^{99m}Tc DTPA radiopharmaceutical was stable

- up to 2 hours after its reconstitution and
- 1 year after cold kit production in freeze dried form

- ITLC method used to determine radiochemical purity is accurate, simple and fast

THANK YOU