Control of radiopharmaceutical purity of ^{99m}Tc DMSA radiopharmaceutical

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RAD.24

TWELFTH INTERNATIONAL CONFERENCE, JUNE 17-21, 2024

INTRODUCTION

- Radiochemical purity is the fraction of total radioactivity in the desired chemical form present in the radiopharmaceutical. In the radiopharmacy, it is the presence of the undesired radiochemical impurities that is checked. These impurities include the presence of free and hydrolyzed technetium.
- Radiochemical purity can be determined by liquid chromatography, either planar or column chromatography. In this study it is used planar chromatography (as routinely used in radiopharmacy) to determine radiochemical purity of 99mTc-DMSA (Di Mercapto Succinic Acid) commonly used for static imaging renal scintigraphy.
- In planar chromatography, the stationary phase can be a paper strip or a thin layer of adsorbent on a plate. The separated fractions appear as spots behind the solvent front on the stationary phase.

INTRODUCTION

- The content of kit vials (1.25mg 2,3-dimercaptosuccinic acid, 0.5mg tin chloride, 0.4mg ascorbic acid, 25mg calcium gluconate) are labelled with technetium eluate from ^{99}Mo-^{99m}Tc generator and are analyzed for radiochemical control on these different systems: ITLC-SG/Acetone, NaCl 0.9%, Whatman No.31 ET Chr, Whatman S&S 2698c and Whatman S&S 2598a/Acetone, NaCl 0.9%, Acetonitrile 50%, MEK, Absolute Alcohol, Ethyl Acetate : MEK 3:2, Sodium Acetate 13.6%.
- A drop (1-10 µl) of the vials is spotted on a miniaturized instant thin layer chromatography (ITLC) or Paper Chromatographic (PC) strip and developed in different solvents ascending method under atmospheric conditions. The developed strips are dried and scanned or cut in pieces.

RADIOPHARMACEUTICAL DMSA

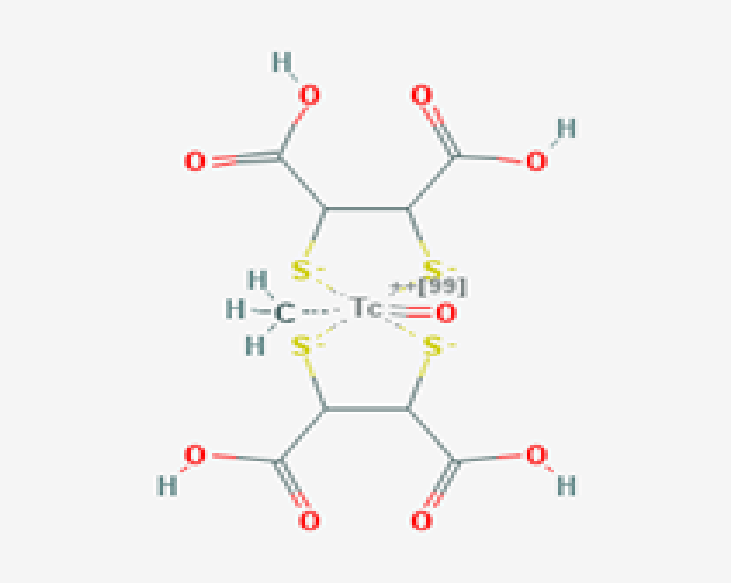
SUMARY DATA

- CHEMICAL NAME:

2,3 meso Di Mercapto Succinic Acid (DMSA), Technetium 99m.

- ^{99m}Tc-DMSA is a radiopharmaceutical widely used in nuclear medicine for the renal scan, renal function of two kidneys, renal ectopic infarction, hypertension, multicystic kidneys, etc.

STRUCTURAL FORMULA



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.
- More than 90% purity of the desired radiochemical form is recommended.

RADIOCHEMICAL PURITY

Radiochemical purity can be determined by different methods. More important are:

- paper chromatography (PC)
- thin-layer chromatography (TLC)
- instant thin layer chromatography(ITLC)
- electrophoresis
- size-exclusion chromatography
- gaz chromatography
- liquid chromatography (HPLC)

We chose:

ITLC PC

MATERIALS AND METHOD

The procedure is performed following these steps:

- Eluation of ^{99}Mo-^{99m}Tc generator
- Labeling of the “cold” kit
- Developing of radiochromatograms
- Scanning or cutting the radiochromatograms
- Analyzing of the radiochromatograms

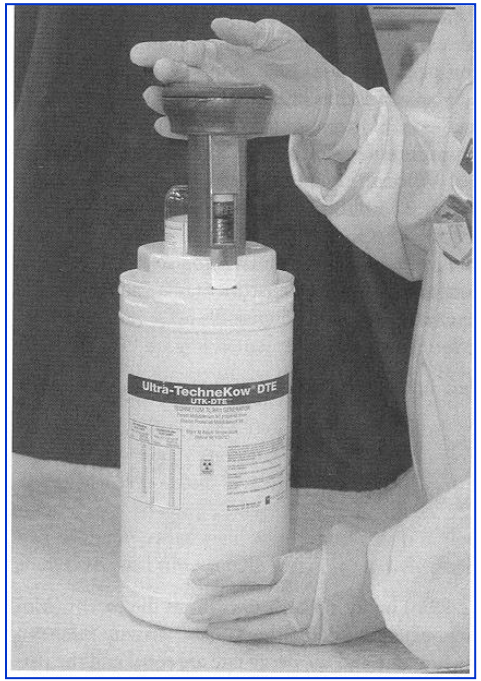
MATERIALS AND METHOD

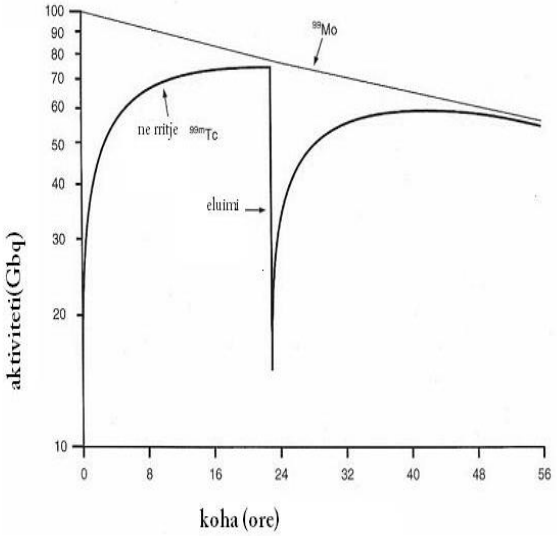
^{99}Mo-^{99m}Tc Generator Elution

- 99m-Tc eluate is milked from Elumatic III (IBA Molecular Company) Generator. Based on the elution curve and transient equilibrium between ^{99}Mo and ^{99m}Tc, after 24 hours the fresh eluate can be milked from the ^{99}Mo-^{99m}Tc generator.

- Elution process is performed with saline solution (NaCl 0.9%).

^{99}Mo-^{99m}Tc GENERATOR ELUATION





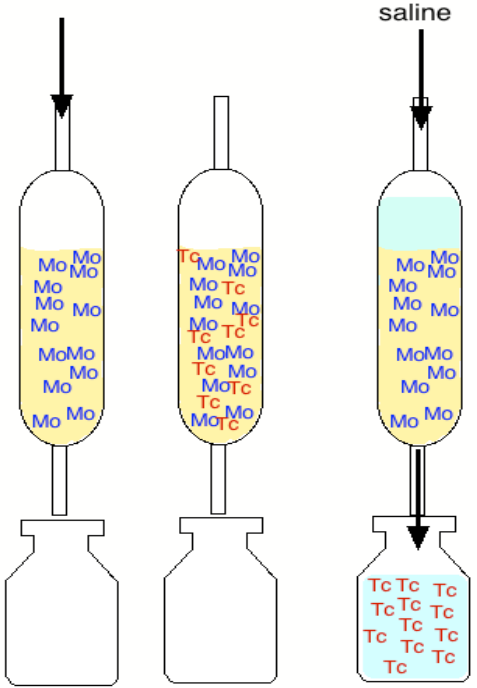
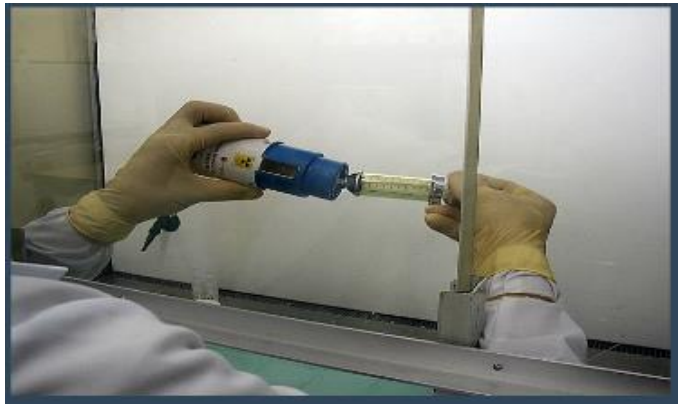


Fig.1

LABELLING OF DMSA COLD KIT



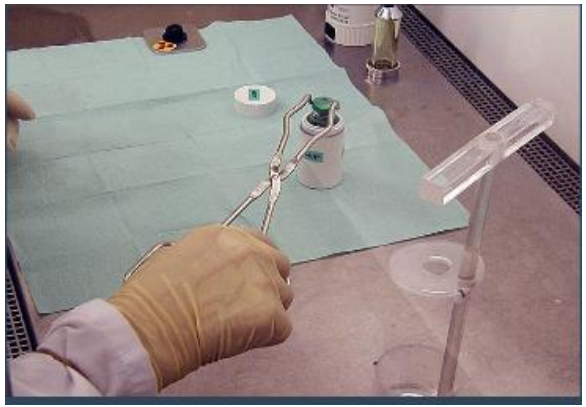
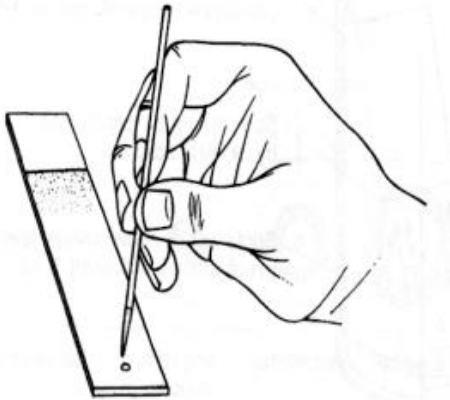


Fig.2

CHROMATOGRAPHY DEVELOPMENT

- Gelman Silica Gel media (stationary phase) and MEK, NaCl 0.9%, as mobile phases are used in ITLC method. The solvents like Acetone, NaCl 0.9%, Acetonitrile 50%, MEK, Alcohol absolute, Ethyl acetate: MEK 3:2, Sodium acetate 13.6% are used to perform paper PC method in Whatmman S&S 2698C, Whatmman S&S 2598a, Whatmman No. 31 ET Chr, as stationary phases.
- These chromatographic papers are cut in strips 1x10cm and are developed in chromatographic tanks with above mentioned solvents, so they did not touch the walls. After the chromatography run, the strips are dried in air and cut in 1cm pieces. The activities are determined using dedektor NaI (Tl) or the chromatograms are scanned in Berthold Automatic Linear Analysator Scanner.

CHROMATOGRAPHY DEVELOPMENT



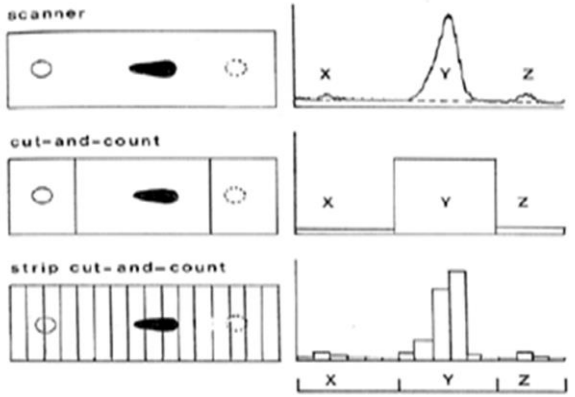


Fig. 3

SKANING OF CHROMATOGRAMS

Fig.4

RESULTS AND DISCUSSIONS

^{99m}Tc-DMSA

ITLC METHOD

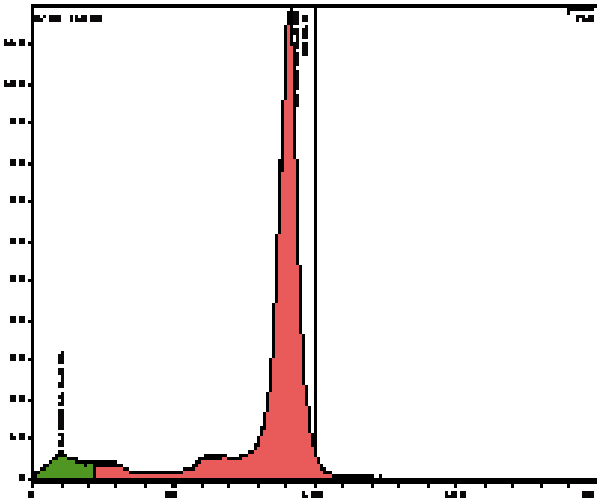


Figure 5. ITLC-SG/NaCl
(very good separation)

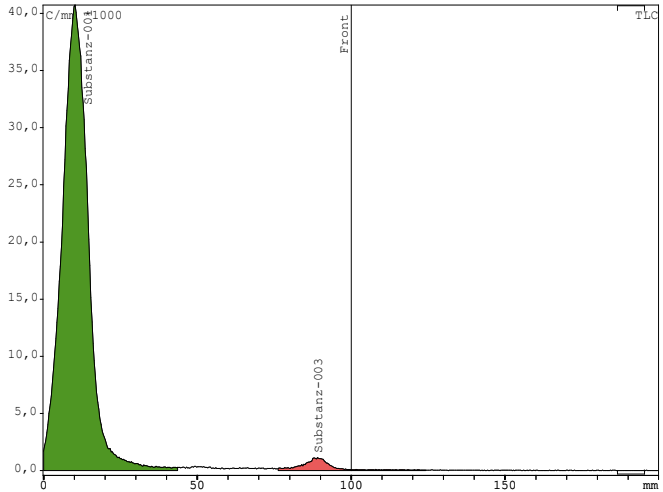


Figure 6. ITLC-SG/MEK
(very good separation)

RESULTS AND DISCUSSIONS

^{99m}Tc-DMSA

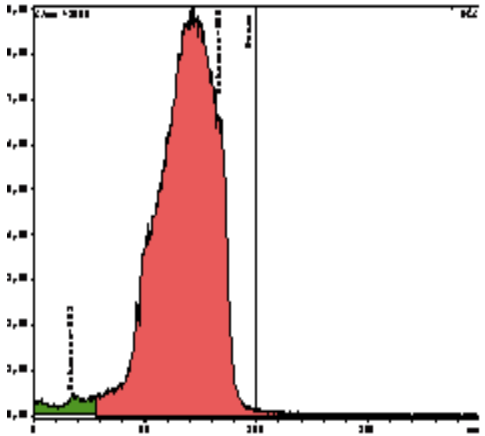


Figure 7. What.31ETChr/ Na acet. 13.6%
(bad separation and tail)

PC METHOD

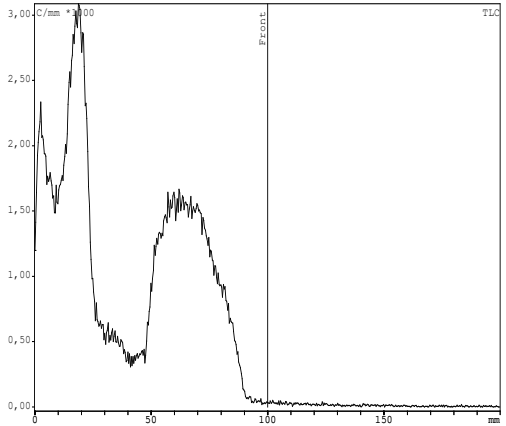


Figure 8. What. 31ET Chr/NaCl
(two maximum and tail)

RESULTS AND DISCUSSIONS

^{99m}Tc-DMSA

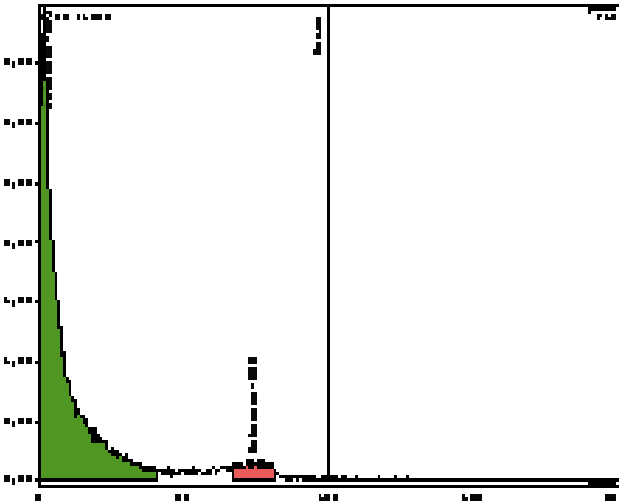


Figure 9. What.31ETChr/MEK (relatively good separation)

PC METHOD

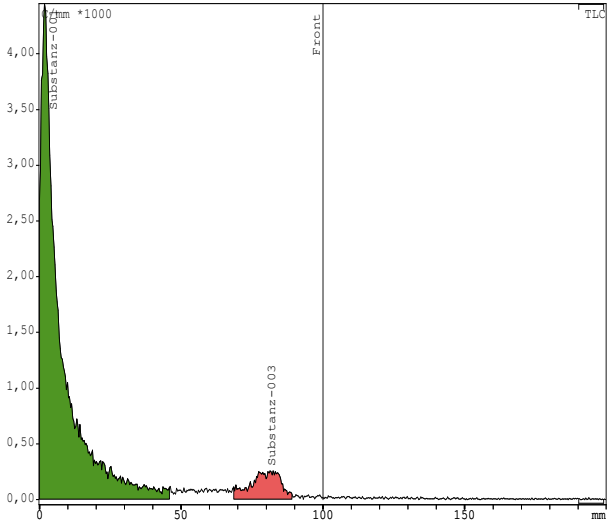


Figure 10. What. 31ET Chr/Aceton (very good separation)

RESULTS AND DISCUSSIONS

^{99m}Tc-DMSA

PC METHOD

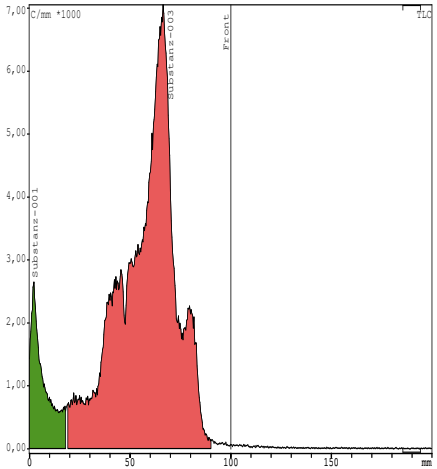


Figure 11. What.31ETChr/Ac.nitrile 50% (bad separation)

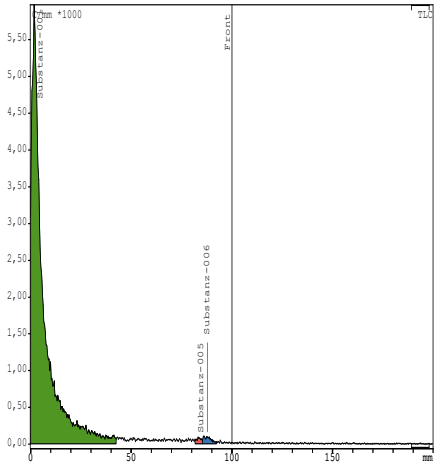


Figure 12. What. 31ET Chr/Ethyl acet: MEK (good separation for 1 component)

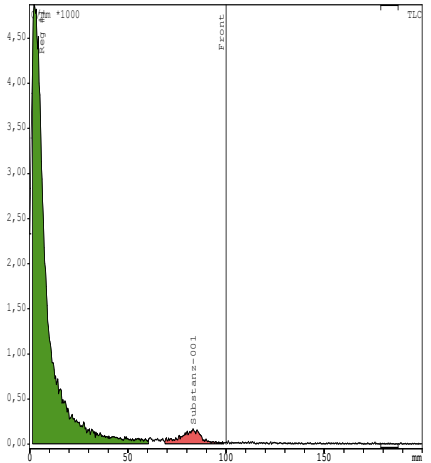


Figure 13. What.31ETChr/Alchool abs. (good separation)

RESULTS AND DISCUSSIONS

^{99m}Tc-DMSA

PC METHOD

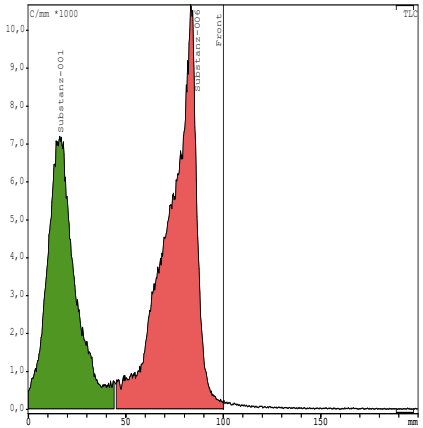


Figure 14. What. S$S 2598c/Na acet. 13.6% (bad separation, 2 maximum)

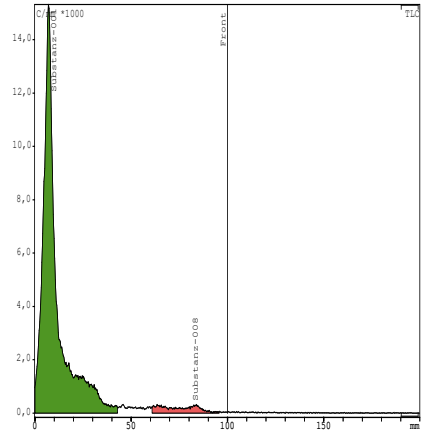


Figure 15. What. S$S 2598c/NaCl (good separation)

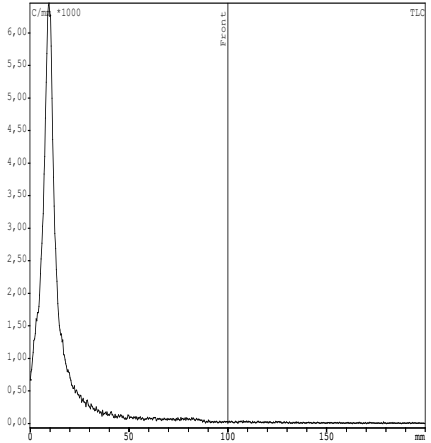


Figure 16. What. S$S 2598c/MEK (good separation for 1 component)

RESULTS AND DISCUSSIONS

^{99m}Tc-DMSA

PC METHOD

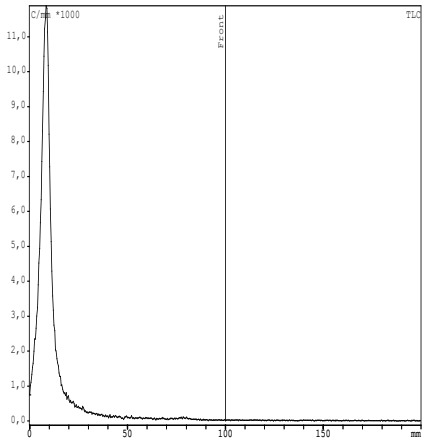


Figure 17. What. S$S 2598c/Acetone (good separation for 1 component)

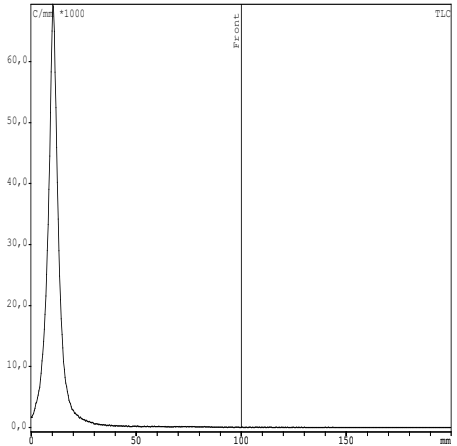


Figure 18.What. S$S 2598c/Acetonitrile 50% (good separation for 1 component)

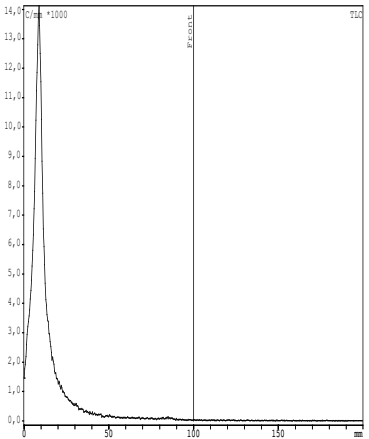


Figure 19. What. S$S 2598c/Ethyl ac:MEK (good separation for 1 component)

RESULTS AND DISCUSSIONS

^{99m}Tc-DMSA

PC METHOD

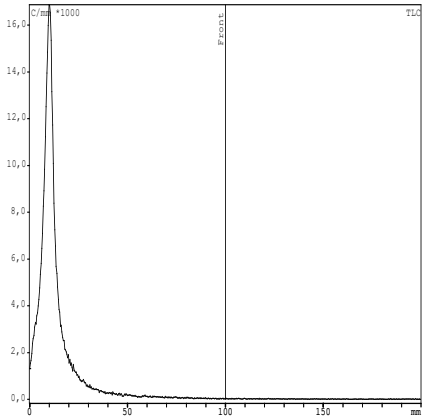


Figure 20. What. S$S 2598c/Alchool absolute (good separation for 1 component)

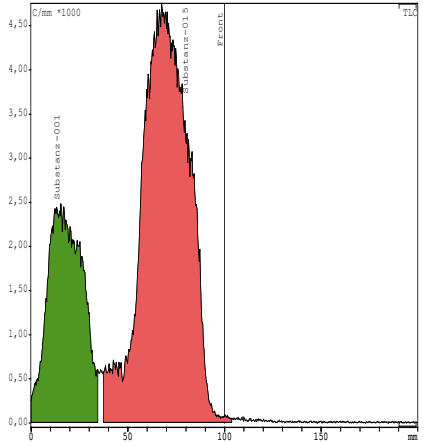


Figure 21. What.S$S 2598a/ Na ac. 13.6% (bad separation, 2 maximum)

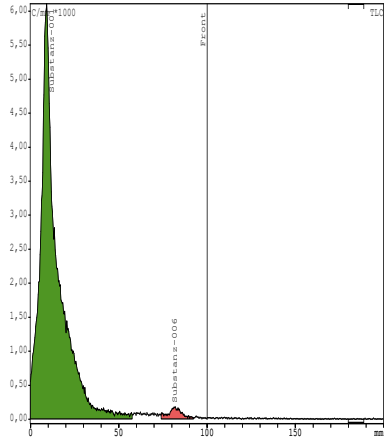


Figure 22. What. S$S 2598a/NaCl (good separation)

RESULTS AND DISCUSSIONS

^{99m}Tc-DMSA

PC METHOD

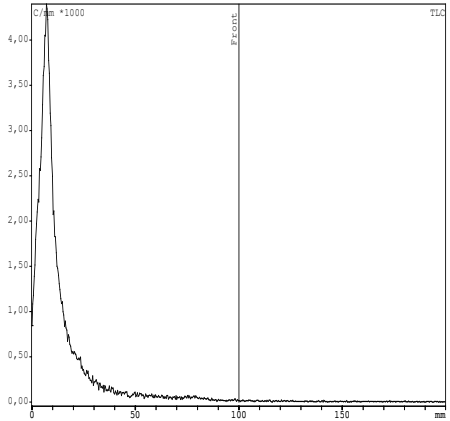


Figure 23. What. S$S 2598a/Acetonitrile 50% (good separation for 1 component)

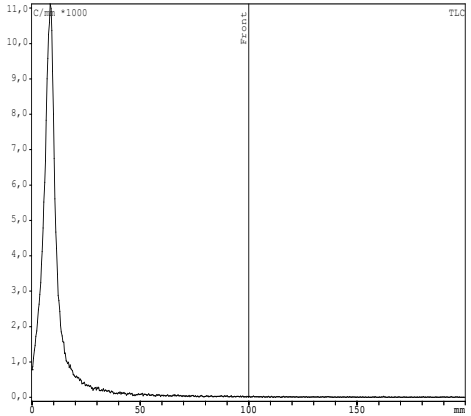


Figure 24. What.S$S 2598a/Ethyl ac.:MEK/3:2 (good separation for 1 component)

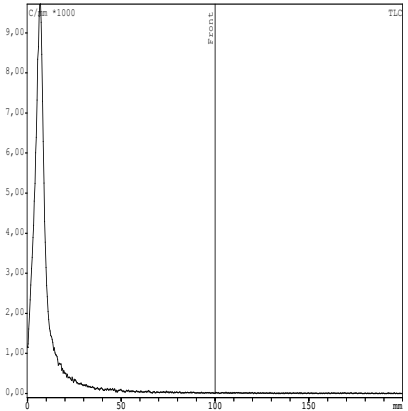


Figure 25. What. S$S 2598a/alc. Abs. (good separation for 1 component)

CONCLUSIONS

- According to our results the different systems assayed were not equivalent, some being more suitable than others to get clear picks and good separation of the patterns.
- Despite the relative difficulty of handling the silica gel sheets, which are brittle and need to be stored in a desiccator this stationary phase has been shown to be the best chromatographic support, considering spot diameter, ascending velocity and lack of artifacts.
- The system ITLC-SG (Acetone), ITLC-SG (NaCl 0.9%) can perfectly separate impurities fractions.
- The results for PC Method are shown in the Table.

CONCLUSIONS

	Whatmman S&S 2698c	Whatmman S&S 2598a	Whatmman No. 31 ET Chr
Acetone	**	-	***
NaCl 0.9%	***	***	*
Acetonitrile 50%	**	**	*
MEK	**	-	**
Alcohol absolute	**	**	***
Ethyl acetate: MEK 3:2	**	**	**
Sodium acetate 13.6%	*	*	*

Legend

* very bad separation

** good separation

*** very good separation

THANK YOU FOR YOUR ATTENTION