# Quick Preparation and Quality Control Methods for $^{99m}$Tc-Tin- Colloid: A Liverscintigraphic Agent

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**Summary:** $^{99m}$Tc-Tin- colloid is a radiopharmaceutical that can be useful in evaluation of the patients with liver cancer. The current method for preparation requires a lengthy boiling water bath procedure and the recommended quality control procedure is cumbersome and time consuming. Using a microwave oven, the heating time necessary to provide a maximum labeling efficiency has been reduced to 10 second. A new mini paper chromatography (MPC) system has been developed to analyze the radiochemical purity of the labeled preparation involving two different developing solvents. The recommended thin layer chromatography (TLC) system involving the use of an $Al_2O_3$ coated plate requires an average time for drying and development of 34.5 ± 0.44 min (n = 30) to complete, whereas the new MPC system has an average developing time of 2.1 ± 0.2 min (n= 20). For radiochemical purity values the MPC and TLC methods are correlated closely (r=0.94). The combined use of the microwave oven heating method and over quick quality control system will facilitate the rapid emergency use of $^{99m}$Tc-Tin- colloid.

## Introduction

Technetium-99m-Stannous Chloride colloid ($^{99m}$Tc-Tin- colloid) is a promising radio pharmaceutical for liver imaging. In patient with known lesions detected by computerized tomography (C.T) or by ultrasonography or by magnetic resonance imaging (MRI) (e,g. ; tumor, hematoma, cyst, abscess) liverscintigraphy may be used to assess further the nature of these lesions [1].

Liverscintigraphy can be utilized in-patients with palpable liver [2]. $^{99m}$Tc-Tin- colloid injection must therefore be rapidly available to permit administration without any delay just because of the 6.02 hours half-life of Technetium-99m ($^{99m}$Tc) [3]. The preparation (labeling) required 10-15 min to bring the water bath to boiling state and another 10 min to a boiling period for heating the vial contents.

It has been considered a part of the good radiopharmacy practice to determine the radio chemical purity (RCP) of a radiopharmaceutical prior to patient administration to ensure a dosage form of the highest safety, purity and efficacy [4]. The recommended radio chromatographic procedure for the determination of RCP of labeled colloid involves the use of an aluminum oxide ($Al_2O_3$) coated thin layer chromatography (TLC) plate with absolute ethanol as developing solvent [5-7]. In our experience the entire chromatographic procedure including the time to dry the sample spots and to run the TLC plates takes approximately 30-40 min. This time consuming labeling and quality control procedure needs to be significantly reduced in order to utilize the labeled preparation for the investigation purpose.

The purpose of this study is to find the feasibility of using microwave oven heating method for labeling and to develop a simple and rapid procedure for quality control.

## Results and Discussion.

### *Preparation of $^{99m}$Tc-Tin-colloid with Microwave Oven*

Five $^{99m}$Tc-Tin-colloid kits were prepared in the microwave oven with the addition of 3 mCi (111 MBq) $^{99m}$Tc activity. The labeling efficiency (Mean ± $S.D_{0.025t}$) determined by the TLC method at 0 hrs, 0.5 hrs, 1 hrs, 1.5 hrs, 3 hrs, 6 hrs, and 24 hrs was 99.795±0.0021%, 99.795±0.0021%, 99.671± 0.0017%, 99.671±0.0017%, 99.601±0.0015, 99.316± 0.003% and 99.232±0.0084%, respectively.

### *Comparison of TLC & MPC Methods*

The distribution of $^{99m}$Tc-Tin-colloid on the MPC strip was much broader in comparison with the

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$Al_2O_3$ TLC plate "Fig. (2), and Fig. (3)". However this considerable trailing pattern of the $^{99m}$Tc-Tin-colloid did not fall below the cut line at R$f$= 0.5 in either good $^{99m}$Tc-Tin- colloid preparations "Fig. (2)"or bad $^{99m}$Tc-Tin-colloid preparations "Fig. (3)".

The average time for drying and developing the $Al_2O_3$ TLC plate was 34.5±0.44 min (n=30), whereas the average time for developing the MPC strip was 2.1±0.2 min (n=20). There was no pre-drying time for the MPC strip to be considered since the strip was placed in the tube while the spot was still wet.

The results from using the MPC procedure and then reference TLC system were in good agreement (r = 0.94) "Fig. (1)". Intermediate RCP values i.e. 82-92% are listed in Table (1). The RCP values of the MPC system exceeded that measured by TLC system in only two cases (kit#9 and kit#11). Which suggests that the new MPC system slightly underestimate the RCP values determined by TLC system (Table 1) and thus a sample with acceptable RCP by MPC should also be acceptable by TLC.

$^{99m}$Tc-Tin-colloid must be available on demand to asses palpable Liver masses without rapid method of formulation and quality control it would be prepared every day due to 6.02 hrs half life of Technetium-99m. This costly and impractical procedure is necessitated by lengthy labeling procedures with a boiling water bath and the time-consuming quality control method using the recommended TLC procedure.

Table-1: Comparison between TLC and MPC system for Intermediate RCP values

| Sample | *TLC (%) | †MPC (%) | ‡ Difference (%) |
|---|---|---|---|
| 1 | 84.4 | 82.1 | -2.7 |
| 2 | 91.6 | 88.9 | -2.7 |
| 3 | 87.4 | 86.3 | -1.1 |
| 4 | 85.2 | 84.1 | -1.1 |
| 5 | 83.2 | 82.7 | -0.5 |
| 6 | 90.1 | 90.0 | -0.1 |
| 7 | 88.5 | 88.3 | -0.2 |
| 8 | 86.3 | 85.4 | -0.9 |
| 9 | 84.9 | 84.1 | 1.2↑ |
| 10 | 90.2 | 88.6 | -1.6 |
| 11 | 88.5 | 88.9 | 0.4↑ |
| 12 | 84.2 | 82.7 | -1.5 |
| 13 | 85.1 | 83.6 | -1.5 |
| 14 | 90.2 | 89.1 | -1.1 |
| 15 | 88.4 | 87.1 | -1.3 |
| 16 | 83.1 | 83.0 | -0.1 |
| 17 | 85.1 | 84.0 | -0.8 |
| 18 | 90.6 | 88.9 | -1.7 |
| 19 | 92.3 | 91.6 | -0.7 |
| 20 | 83.8 | 82.9 | -0.9 |

*TLC % = % labeling yield using thin layer chromatography
†MPC % = % labeling yield using mini paper chromatography
‡Difference % = MPC % TLC %

A microwave oven have been utilized to prepare $^{99m}$Tc-Tin-colloid injections and shown to reduce the heating period considerably. In this study we have confirmed that it only takes 10 second of heating in a microwave oven to label $^{99m}$Tc-Tin-colloid. The RCP values are maintained at an average of 99% with small variations throughout the entire 24

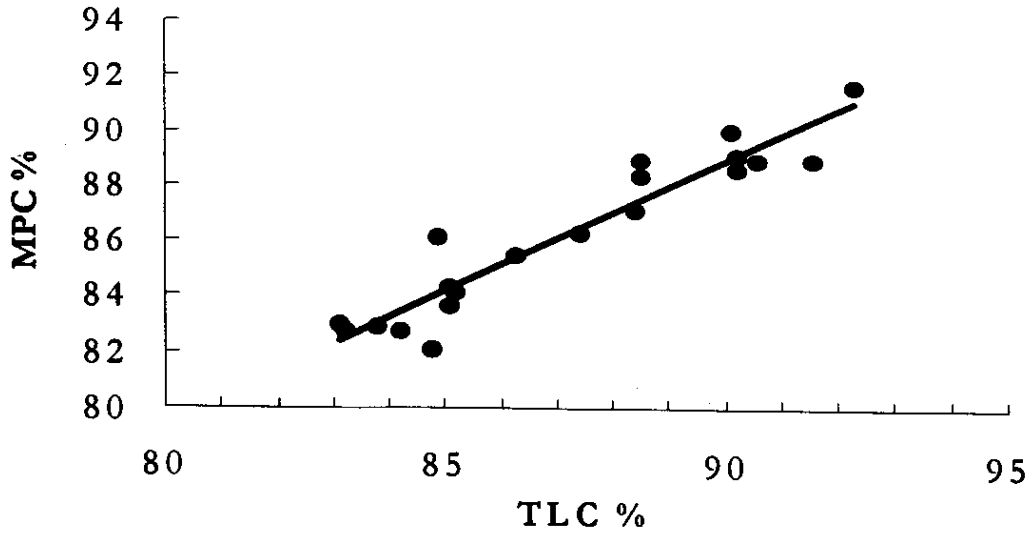


Fig. 1: Overall comparison between TLC and MPC methods in the measurement of RCP of $^{99m}$Tc-Tin-colloid.

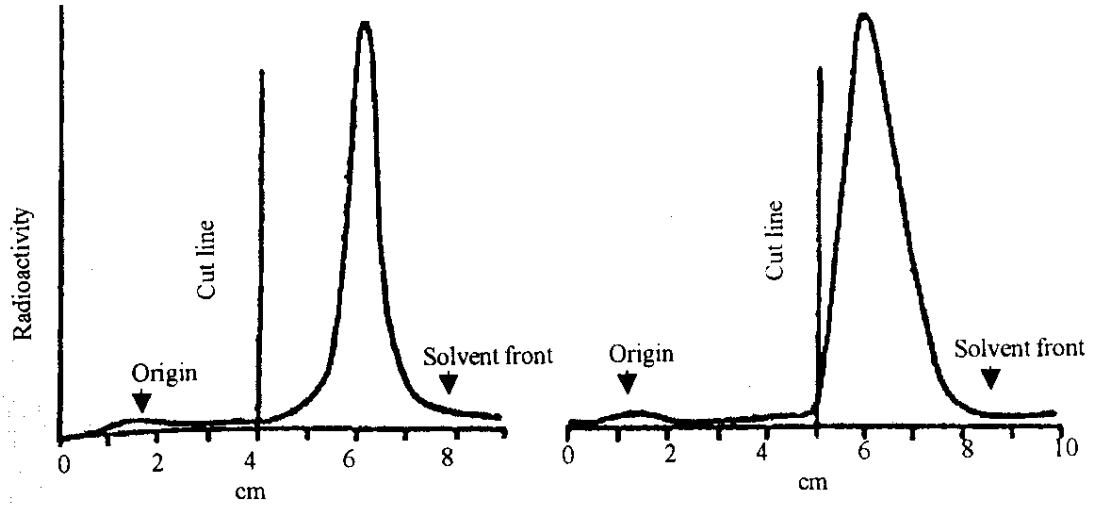


Fig. 2: Radiochromatogram scans for a good $^{99m}$Tc-Tin-colloid preparation (left)TLC method, (right) MPC method.

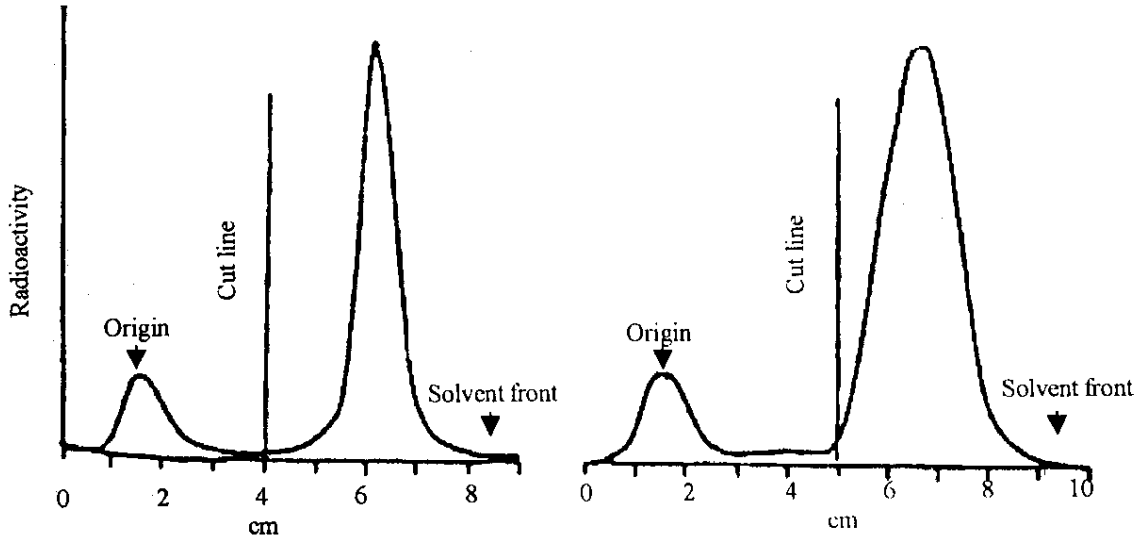


Fig. 3: Radiochromatogram scans for a bad $^{99m}$Tc-Tin-colloid preparation (left)TLC method, (right) MPC method.

hours evaluation period which indicates that microwave oven heating method is a useful technique to prepare $^{99m}$Tc-Tin-colloid injection.

There are four technical precautions that must be considered in using the microwave oven for the preparation of $^{99m}$Tc-Tin-colloid. First, the optimum heating time and wattage for successful labeling of $^{99m}$Tc-Tin-colloid with a particular microwave oven should be experimentally determined. Second, the metal cap of the vial needs to be covered with styrofoam to avoid electrical sparking. Third, a vacuum condition must be achieved before the labeled vial is heated with microwave oven. Any residual gas left in the head space of the vial could cause an ejection of the rubber stopper due to the excess steam pressure built up in the vial. Finally, microwave ovens with digital control panel are more suitable for setting short heating time (i.e. 10 sec) since they can be accurately set at the required heating period.

As stated earlier, the performance of RCP determination of $^{99m}$Tc-Tin-colloid has been regarded as part of good radiopharmacy practice [4]. There are several technical circumstances that would make it a necessity to verify the RCP of $^{99m}$Tc-Tin-colloid before the clinical use of this radiopharmaceutical in patients.

1. In this study, we only tested a 3 ml volume of $^{99m}$Tc-Tin-colloid in the vial. This volume is ideal for providing the desired specific concentration for liver imaging studies.

2. A more homogenous temperature of liquid in the vial can be expected when it is heated in a boiling water bath in comparison with microwave oven. Inconsistent power out put or variable microwave frequency may furthermore cause uneven heat distribution in the liquid solution. Although our results have indicated that the microwave oven heating method is quite reliable in preparing acceptable $^{99m}$Tc-Tin-colloid, the study is based upon only a relatively small scale of observations using a specific type of commercial microwave oven. In addition, the loss or variation of microwave power out put and the frequency related to the extended use of the microwave oven should be evaluated on a long term basis. Consequently, the verification of RCP of $^{99m}$Tc-Tin-colloid as part of the microwave oven preparation would be essential.

3. Any technical error in setting the microwave oven heating time below or beyond the predetermined time may result in the $^{99m}$Tc-Tin-colloid being rendered unsuitable for clinical use. RCP measurements must, therefore be performed before $^{99m}$Tc-Tin-colloid is accepted for administration to patients. The recommended TLC method used for the determination of RCP would take at least 30 min to complete. This time consuming procedure defeats the purpose of using a microwave oven to expedite the preparation of $^{99m}$Tc-Tin-colloid. It is not only impractical for routine use of the $^{99m}$Tc-Tin-colloid but is unacceptable for any emergency clinical application. Although, the MPC strip showed a relatively broader distribution of $^{99m}$Tc-Tin-colloid radioactivity compared with a clear separation of $^{99m}$Tc-Tin-colloid species on the TLC plate, our procedure dose provide a much simpler and more rapid procedure for routine and /or urgent quality control of $^{99m}$Tc-Tin-colloid.

Our proposed method for quality control provided radiochromatographic values that were closely correlated with recommended TLC method. More importantly, the measurements by the two techniques were very close to the intermediate range. Our proposed method consistently underestimated purity to a slight degree in the intermediate range; it gave a slightly higher value in only 2 of 20 kits in this range. Thus, if the > 90% standard was used for each technique, our method might result in the occasional rejection of a kit that would be acceptable by the TLC method, but would be very unlikely to accept a kit that was rejected by TLC method.

## Experimental

### *Equipments*

Heating parameters were measured on thermocouple 9800 K, digital thermometer probe. Quick heating was done with Kenmore 565.8962781, microwave oven. Radiochromatograms (TLC and MPC strips) were scanned with a Radiomatic VISTA 100, Radiochromatogram scanner.

### *Preparation of $^{99m}$Tc-Tin- Colloids with Microwave Oven.*

To determine the optimal heating parameters (e.g., heating time and out put power of the microwave oven) a digital thermometer probe was utilized to measure the temperature of 3 ml 0.9% NaCl injection (E.I du pont de Nemours & co., Billerica, MA) vial. After 10 min heating in a boiling water bath (96.2±1.5°C (n=15)) the temperature of solution in the vial was measured to be 98.3±0.1°C (n=11). It took 8 sec to reach the same temperature range using a microwave oven at a microwave output power of 452.5 watts. We arbitrarily added two more seconds of heating time to optimize the microwave oven heating method and final temperature of solution inside the vial after 10 second microwave heating was 105.6 ±2.9°C (n=21).

$^{99m}$Tc-Tin-colloid injection was prepared using microwave oven to heat five kits. Each $^{99m}$Tc-Tin colloid vial contained 1113.33 Nano-gram Stannous Chloride stoppered under nitrogen. The maximum activity (111MBq) of sodium pertechnetate ($Na^{99m}TcO_4$) was added to the kit and the total volume was adjusted to 3-ml using normal saline.

Before placing the kit in the microwave oven, approximately 10-15 ml of the nitrogen was withdrawn from the vial using a 20-ml syringe until a vacuum was created. A Styrofoam block was placed

$RCP_{hig}$ = measured RCP of vial prepared in step 1.$RCP_{Int}$ = desired RCP of intermediate solution (step 3).

$RCP_{low}$ = measured RCP of vial prepared in step 2+1 %

b = amount of $^{99m}$Tc- activity (mCi) added to vial in step 2.

c = amount of $^{99m}$Tc- activity (mCi) added to vial in step 1.

The volumes $Vol_{hig}$ and $Vol_{low}$ calculated above were combined to prepare solutions of intermediate RCP. Because of the gradual change in RCP in the low RCP kit, the actual RCP of the intermediate RCP solution was determined by reference TLC procedure and the newly proposed MPC procedure at the same time.

## Conclusion

We suggest that the combined use of the microwave oven heating method along with an expedient strip RCP testing system can be performed in any Nuclear Medicine department and provides a fast and reliable way to make $^{99m}$Tc-Tin-colloid for quick diagnostic purpose.

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