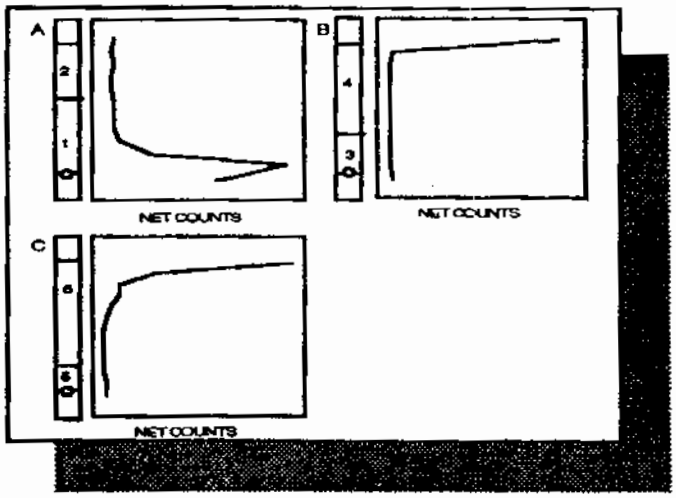
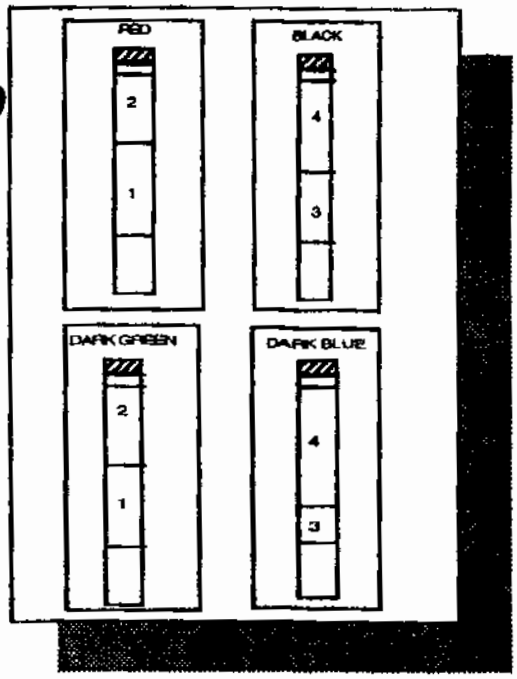
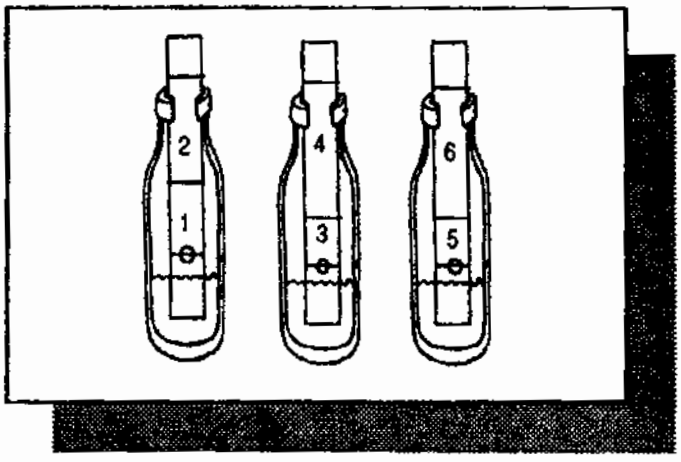
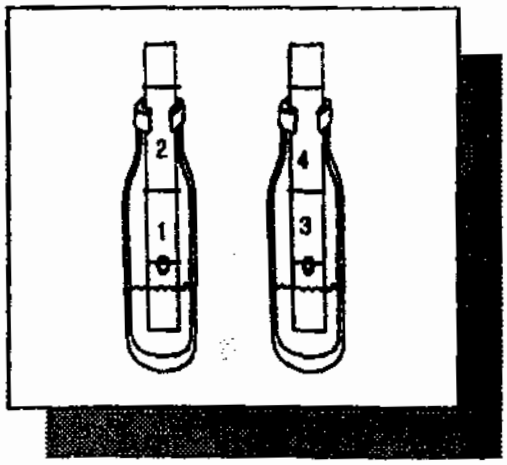
MINIATURIZED CHROMATOGRAPHY PROCEDURES FOR RADIOPHARMACEUTICALS: 1998 UPDATE

BY
A. MICHAEL ZIMMER PhD









MINIATURIZED CHROMATOGRAPHY PROCEDURES FOR RADIOPHARMACEUTICALS: 1998 UPDATE

A. MICHAEL ZIMMER, Ph.D.

Professor of Radiology
Northwestern University Medical Center
Head, Radiopharmacy
Nuclear Medicine Section
Northwestern Memorial Hospital
Chicago, Illinois 60611

Made in the United States of America.

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PREFACE

This manual provides miniaturized chromatography procedures for evaluating the radiochemical purity of currently used radiopharmaceuticals. Most of the chromatography procedures have been taken from the literature and all procedures listed are currently utilized in clinical nuclear medicine. The emphasis of this manual is in providing chromatography methods which are rapid and easy to use. The simplicity of the chromatographic procedures should expedite their incorporation into an existing nuclear medicine quality control program.

This manual is divided into four sections. The first section (Section 1) introduces miniaturized chromatography systems. Section 2 deals with the technical aspects and common errors associated with miniaturized chromatography systems. Section 3 deals with the solvents, chromatography support media and specific chromatography procedures. Section 4 discusses specific radiopharmaceuticals including common names, radiochemical impurities, quality control methods, chromatography strip activity distributions and appropriate references. The Appendix section contains information regarding chromatography systems of specific radiopharmaceuticals.

When using this manual, the individual should initially consult the specific radiopharmaceutical of interest, which is found in Section 4. After reviewing the chromatography system associated with the specific radiopharmaceutical, more information on the chromatography solvents, chromatography strips and specific chromatography procedures can be found in Section 3.

1

INTRODUCTION

Because radiopharmaceuticals are intended for human administration, quality control procedures are essential in ensuring the efficacy of these preparations. Although many extensive quality control procedures are performed by the manufacturer, many radiopharmaceutical preparations are prepared in nuclear medicine departments using kits and short-lived radionuclides including ^{99m}Tc and ^{111}In. As a result, the ultimate responsibility for quality assurance of radiopharmaceuticals lies with the nuclear medicine department, usually with the radiopharmacist or the nuclear medicine technologist responsible for the nuclear pharmacy.

Radiopharmaceuticals, whether commercial or in-house preparations, must be subjected to physicochemical and biological testing. Physicochemical testing includes the examination and determination of the physical state, osmolality, pH, chemical purity, radionuclidic purity and radiochemical purity. Biological testing of radiopharmaceutical preparations include sterility and pyrogenicity testing.

Radiochemical purity is defined as the proportion of the total activity that is present in the specified chemical form (1). Numerous methodologies can be employed to assess the radiochemical purity of radiopharmaceuticals including thin layer chromatography, paper chromatography, gel permeation chromatography, high performance liquid chromatography (HPLC), and gel electrophoresis. Because time is critical in a nuclear medicine department, the emphasis of radiochemical quality control procedures must be on rapid, yet relatively easy

procedures, in order to gain the maximum amount of information in the minimum amount of time.

Miniaturized chromatography procedures have been utilized to assess the radiochemical purity of radiopharmaceuticals because they are rapid and relativley easy to use. Most of these miniaturized chromatography systems are designed to separate specific radiochemical impurities and this limitation must be kept in mind. For stannous-reduced Tc-99m radiopharmaceuticals, the radiochemical impurities include free Tc-99m pertechnetate, Tc-99m tin colloid and Tc-99m dioxide (2).

This updated manual was written to review miniaturized chromatography systems and procedures for existing and also newer radiopharmaceuticals, with an emphasis on rapid and reliable systems. For several radiopharmaceuticals, more than one chromatography system is listed. All chromatography systems cited in this review have been or are currently utilized in a clinical nuclear medicine department.

2

TECHNICAL PARAMETERS ASSOCIATED WITH MINIATURIZED CHROMATOGRAPHY

Miniaturized chromatography systems and procedures are designed to be rapid and easy to use. However, problems can and do occur (3-5). Some of the errors and problems associated with using miniaturized chromatography systems are found in Table 2-1. In our experiences with miniaturized chromatography over the last 10 years, two major errors appear to predominate; incorrect strip elution techniques and inaccurate strip counting after solvent elution.

The most common error made by individuals first attempting to use miniaturized chromatography systems involves radiopharmaceutical spotting. After placing the radiopharmaceutical at the origin of the chromatography strip, the strip can be incorrectly positioned in the solvent so that the origin is in direct contact or below the initial solvent level. An example of this is shown in Figure 2-1. If the origin makes contact or is below the initial solvent level, the radiopharmaceutical will distribute throughout the chromatography strip resulting in inaccurate radiochemical purity assessment.

Another common error made by individuals when using miniaturized chromatography systems involves counting the strip segments. This is especially the case if one uses a sodium iodide detector counting system. When spotting radiopharmaceuticals, it is conceivable that several hundred microcuries may be spotted. If this activity is placed too close to a sodium iodide detector, significant counting loss ensues, resulting in gross counting errors. An example of counting losses as a function of detector distance for various Tc-99m activities is found in

Figure 2-2. If a sodium iodide detector is used for counting, it is recommended that the chromatography segments be placed at least 10 cm from the detector to minimize counting loss.

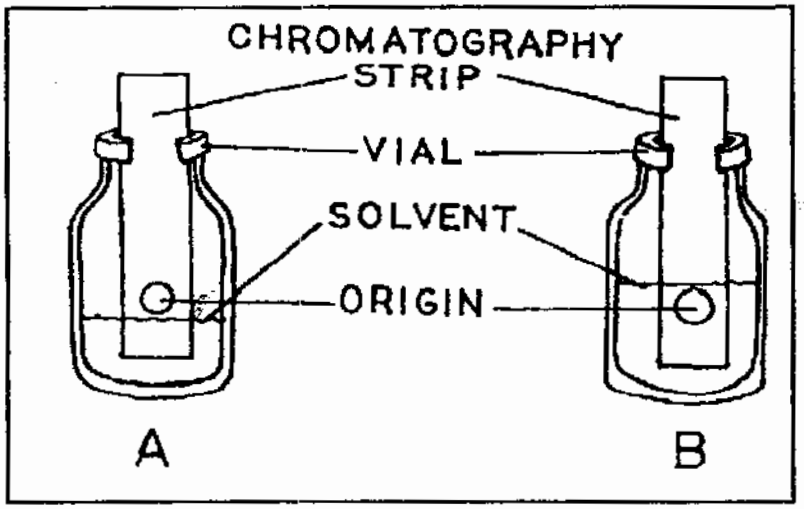


Figure 2-1. Eluting chromatography strips in which the origin is (A) above the initial solvent level (correct placement) and (B) below the initial solvent level (incorrect placement).

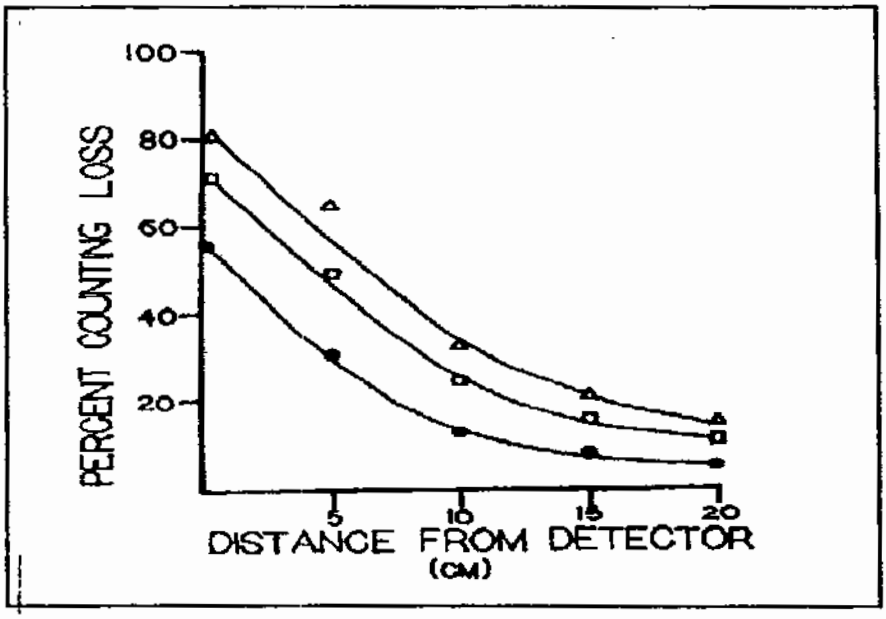


Figure 2-2. Counting loss from sodium iodide detector as a function of sample distance from detector. Sample included (0) 200 uCi, (') 300 uCi and (Δ) 400 uCi of Tc-99m pertechnetate.

Another error made by individuals using miniaturized chromatography systems involves drying the radiopharmaceutical spot prior to solvent elution. Spot drying Tc-99m radiopharmaceuticals may cause oxidation, thus overestimating the extent of radiopharmaceutical impurities. In addition, spot drying may enhance the binding of the radiopharmaceutical to the support media, also resulting in inaccurate asssessment of radiochemical purity.

When utilizing chromatography systems, the distance traveled by the radiochemical moity of interest is expressed by a relative front (Rf) value. Rf value is defined as the relative distance moved by the radiochemical species in relation to the distance that the solvent front moves. The distances moved are measured from the origin to the solvent front and the distance from the origin to the center of the radiochemical species:

$$Rf = \left(\frac{\text{DISTANCE FROM ORIGIN TO RADIOCHEMICAL SPECIES}}{\text{DISTANCE FROM ORIGIN TO SOLVENT FRONT}} \right)$$

An example of determining Rf values on a chromatography strip is illustrated in Figure 2-3. By carefully controlling the conditions of the chromatography procedures, the Rf values should remain constant for a specific chromatography system.

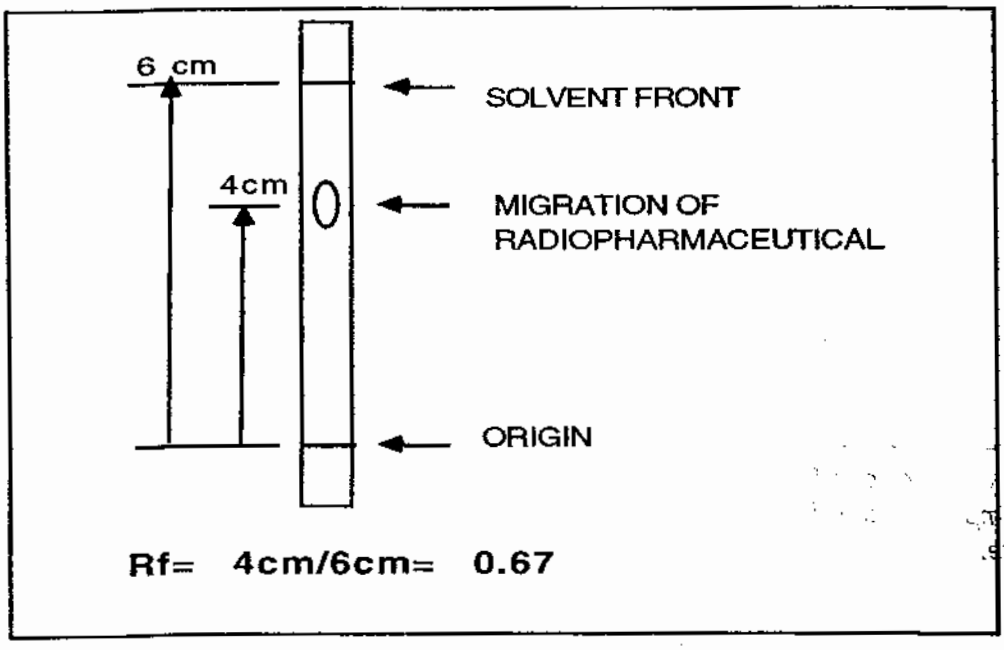


Figure 2-3. Rf measurement on a chromatography strip following elution.

Table 2-1
Common Errors or Pitfalls Associated with Miniaturized Chromatography Systems

Source of Error	Result
Origin, where strip spotted, is below the initial solvent level in the developing vial.	Activity will distribute throughout the entire chromatgraphy strip resulting in inaccurate results. Spot new strip correctly.
Strips are counted too close to the NaI(Tl) well detector.	Dead time of crystal may be excessive resulting in gross overestimation of percent activity associated with the lower activity section of the strip. Increase distance of strips to detector, thus reducing dead time.
Strips are counted in dose calibrator	Insensitivity of dose calibrator may result in large errors when counting low activity strips. If possible spot more radiopharmaceutical activity on strip prior to developing
Chromatography strips and solvents are too old.	Migration pattern of radiopharmaceutical may be changed. Also streaking of activity may occur. These can lead to erroneous results. Use new solvents and dry strips prior to use.
Strips and/or solvents reversed.	Total inaccurate results may be obtained. Repeat entire QC procedure.
Radiopharmaceutical spot is dried prior to solvent development.	Oxidation of radiopharmaceutical may occur. Also binding of radiopharmaceutical with support media may result. Results in inaccurate assessment of radiochemical purity. Repeat entire QC procedure.
Strip is eluted past solvent front line.	If strip is eluted significantly past the solvent front line, the cut line must be changed to maintain the same Rf value.

3

MATERIALS AND METHODS

This chapter is divided into three sections. The first section describes chromatography solvents (mobile phases) used in this manual. The second section describes various chromatography support media (stationary phases) and the last section describes specific chromatography procedures used.

CHROMATOGRAPHY SOLVENTS

High grade solvents, usually reagent grade, should be used for the various chromatography procedures. If solvents are mixed, this should be performed just prior to use. The various solvents used in specific chromatography systems are listed below, in alphabetical order.

ACETONE: Use reagent grade. Store in tight container.

50% AQUEOUS ACETONITRILE: Add equal volumes of HPLC grade acetonitrile and distilled water (sterile water for injection). Must be prepared fresh prior to use.

n-BUTANOL, SATURATED WITH 0.3N HCL: Shake n-butanol and 0.3N hydrochloric acid in equal volumes in separatory funnel for 1-2 minutes. Discard lower aqueous phase and use upper organic phase. Must be prepared fresh prior to use.

CHLOROFORM:ACETONE:TETRAHYDROFURAN (1:1:2): Use reagent grade only. Mix one volume of chloroform, one volume of acetone and two volumes of tetrahydrofuran. Must be prepared fresh prior to use.

CHLOROFORM:GLACIAL ACETIC ACID (1.00:0.05): Mix 1.0 ml of chloroform with 0.05 ml of glacial acetic acid. Must be prepared fresh prior to use.

CHLOROFORM:TETRAHYDROFURAN (1:1): Use reagent grade only. Mix equal volumes of each. Must be prepared fresh prior to use.

DISTILLED WATER: Can use Water for Injection USP. Must be non-preservative type.

0.05M DTPA: Dissolve 150 mg of DTPA in 10 ml of distilled water Adjust pH to 6.

ETHYL ACETATE: Use reagent grade. Store in tight container.

5% HSA: Add four volumes of distilled water to one volume of 25% Human Serum Albumin USP.

METHANOL: Use reagent grade. Store in tight container.

METHYL ETHYL KETONE (2-BUTANONE): Use reagent grade. Store in tight container.

METHYLENE CHLORIDE:ACETONE (65:35 v/v): Mix 0.65 ml methylene chloride with 0.35 ml of acetone. Must be prepared fresh prior to use.

METHYLENE CHLORIDE:ACETONE (1:1): Mix 0.50 ml methylene chloride with 0.50 ml of acetone. Must be prepared fresh prior to use.

NORMAL SALINE (0.9% SODIUM CHLORIDE): Dissolve 0.9 gm of sodium chloride in 100 ml of distilled water or use non-preservative type normal saline.

NORMAL SALINE:ACETONE (1:1): Mix equal volumes of normal saline and acetone. Must be prepared fresh prior to use.

10% SODIUM CHLORIDE: Dissolve 10.0 gm of sodium chloride in 100 ml of distilled water.

20% SODIUM CHLORIDE: Dissolve 20.0 gm of sodium chloride in 100 ml of distilled water. The resultant solution is 20% NaCl w/v.

CHROMATOGRAPHY STRIPS

Miniaturized chromatography procedures for determining the radiochemical purity of radiopharmaceuticals have been described in the literature. Chromatography strips used in this manual consist of different types of support media, which are listed in Table 3-1.

TABLE 3-1
SUPPORT MEDIA FOR MINIATURIZED CHROMATOGRAPHY STRIPS

SUPPORT MEDIA	MANUFACTURER
GELMAN ITLC-SG	GELMAN SCIENCES, ANN ARBOR, MI
GELMAN ITLC-SA	GELMAN SCIENCES, ANN ARBOR, MI
GELMAN SOLVENT SATURATION PADS	GELMAN SCIENCES, ANN ARBOR, MI
WHATMAN 31ET	WHATMAN CHROM PRODUCTS, CLIFTON, NJ
WHATMAN 17	WHATMAN CHROM PRODUCTS, CLIFTON, NJ
WHATMAN 1	WHATMAN CHROM PRODUCTS, CLIFTON, NJ

For the majority of chromatography procedures, two sizes of chromatography strips, which are shown in Figure 3-1, are utilized for radiochemical quality control assessment; 0.7 cm x 6 cm size strips and 0.7 cm x 7 cm size strips. For one specific chromatography procedure, longer chromatography strips are utilized (0.8 cm x 9 cm). Lines denoting the origin, cut line and solvent front line are drawn on each strip. The origin line is drawn 1cm from the bottom of

the strip and the solvent front line is drawn approximately 1 cm (for the shorter strip) and 0.5 cm (for the longer strip) from the top of the strip. The location of the cut line is dependent on the migration of the specific radiopharmaceutical. In addition, depending on the chromatography system, each section of the strip is appropriately numbered and the strip color-coded. Whenever appropriate, in order to assist in visualizing the solvent front, strips are marked with solvent-compatable colored markers. The colored markers, which are drawn on the back of the strip, migrate with the solvent front.

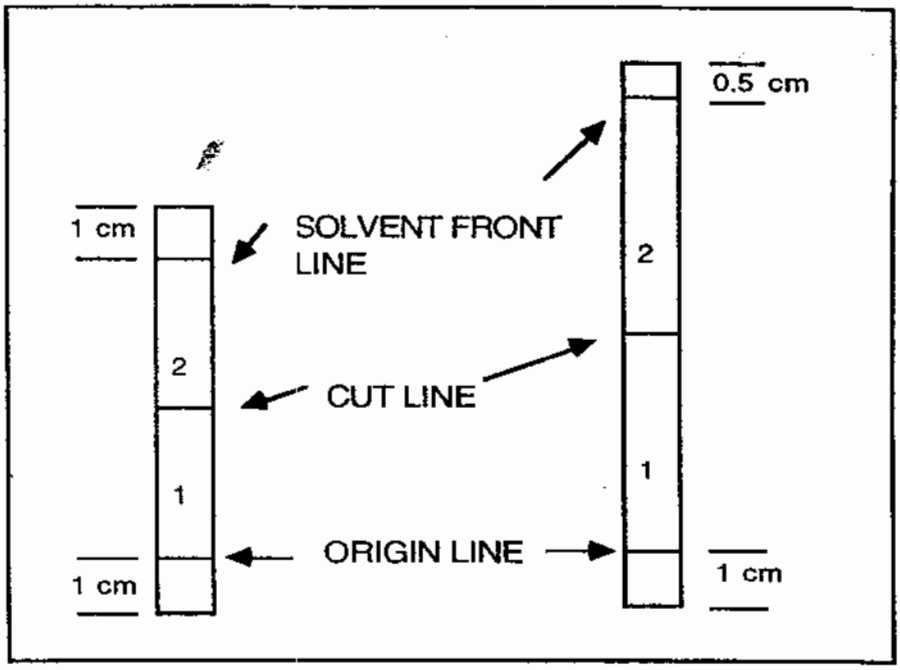
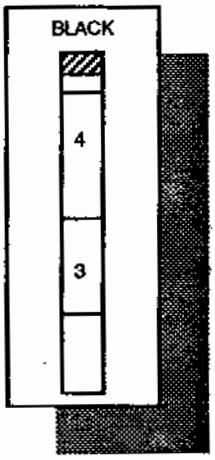


Figure 3-1. Typical miniaturized chromatography strips: 0.7 cm x 6 cm (left); 0.7 cm x 7 cm (right).

SPECIFIC COLOR-CODED CHROMATOGRAPHY STRIPS

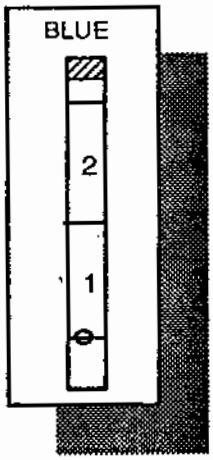
Chromatography strips are appropriately marked (origin, cut and solvent front lines) and numbered. Strips are the then color-coded for easy identification. Colored marker lines are drawn on the back of each strip in order to aid in identifying the solvent front. Chromatography strips are listed, alphabetically, according to the color-code identifier.

BLACK CHROMATOGRAPHY STRIPS:



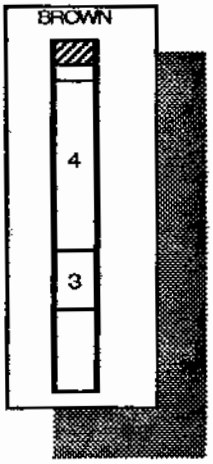
ITLC-SG black color-coded strips with 0.7 cm x 6 cm dimension. Origin and solvent front line located 1.0 cm and 5.0 cm from bottom of strip. Cut line located 2.7 cm from bottom of strip. An appropriate colored marker line, which will migrate with distilled water and normal saline, is drawn on the back of the strip. Chromatography sections are labeled 3 and 4.

BLUE CHROMATOGRAPHY STRIPS:



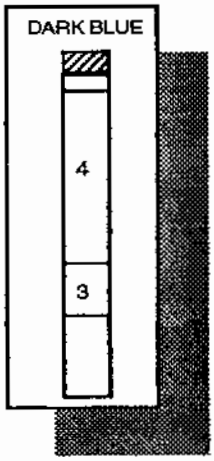
Whatman 1 blue color-coded strips with 0.7 cm x 6 cm dimension. Origin and solvent front line located 1.0 cm and 5.0 cm from bottom of strip. Cut line located 3.0 cm from bottom of strip. An appropriate colored marker line, which will migrate with methylene chloride:acetone (1:1), is drawn on the back of the strip. Chromatography sections are labeled 1 and 2.

BROWN CHROMATOGRAPHY STRIPS:



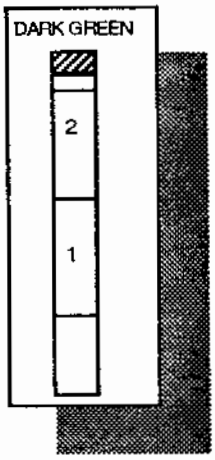
ITLC-SG brown color-coded strips with 0.7 cm x 6 cm dimension. Origin and solvent front line located 1.0 cm and 5.0 cm from bottom of strip. Cut line located 2.0 cm from bottom of strip. An appropriate colored marker line, which will migrate with methyl ethyl ketone, is drawn on the back of the strip. Chromatography sections are labeled 3 and 4.

DARK BLUE CHROMATOGRAPHY STRIPS:



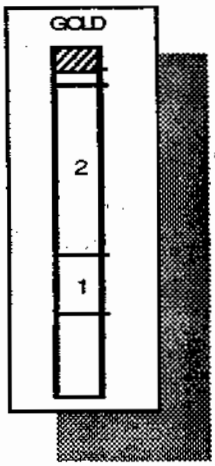
Whatman 31ET dark blue color-coded strips with 0.7 cm x 6 cm dimension. Origin and solvent front line located 1.0 cm and 5.0 cm from bottom of strip. Cut line located 2.0 cm from bottom of strip. An appropriate colored marker line, which will migrate with distilled water and normal saline, is drawn on the back of the strip. Chromatography sections are labeled 3 and 4.

DARK GREEN CHROMATOGRAPHY STRIPS:



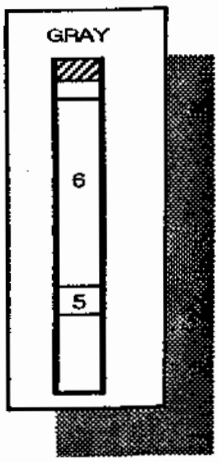
ITLC-SG dark green color-coded strips with 0.7 cm x 6 cm dimension. Origin and solvent front line located 1.0 cm and 5.0 cm from bottom of strip. Cut line located 3.0 cm from bottom of strip. An appropriate colored marker line, which will migrate with distilled water and normal saline, is drawn on the back of the strip. Chromatography sections are labeled 1 and 2.

GOLD CHROMATOGRAPHY STRIPS:



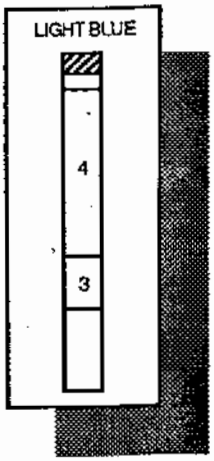
Whatman 17 gold color-coded strips with 0.7 cm x 7 cm dimension. Origin and solvent front line located 1.0 cm and 6.5 cm from bottom of strip. Cut line located 2.3 cm from bottom of strip. An appropriate colored marker line, which will migrate with ethyl acetate, is drawn on the back of the strip. Chromatography sections are labeled 1 and 2.

GRAY CHROMATOGRAPHY STRIPS:



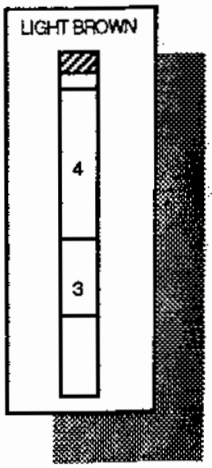
Whatman 31ET gray color-coded strips with 0.7 cm x 6 cm dimension. Origin and solvent front line located 1.0 cm and 5.0 cm from bottom of strip. Cut line located 1.8 cm from bottom of strip. An appropriate colored marker line, which will migrate with aqueous acetonitrile, is drawn on the back of the strip. Chromatography sections are labeled 5 and 6.

LIGHT BLUE CHROMATOGRAPHY STRIPS:



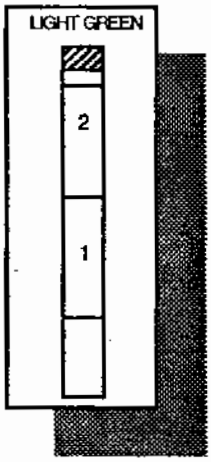
ITLC-SG light blue color-coded strips with 0.7 cm x 6 cm dimension. Origin and solvent front line located 1.0 cm and 5.0 cm from bottom of strip. Cut line located 2.0 cm from bottom of strip. An appropriate colored marker line, which will migrate with distilled water, is drawn on the back of the strip. Chromatography sections are labeled 3 and 4.

LIGHT BROWN CHROMATOGRAPHY STRIPS:



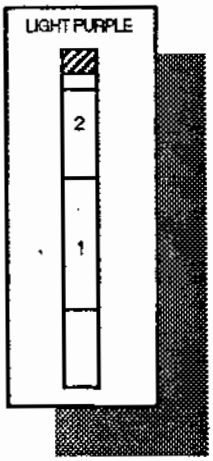
Whatman 31ET light brown color-coded strips with 0.7 cm x 7 cm dimension. Origin and solvent front line located 1.0 cm and 6.5 cm from bottom of strip. Cut line located 2.5 cm from bottom of strip. Origin, cut and solvent front lines are drawn in pencil. No colored marker line is drawn on the strip. Chromatography sections are labeled 3 and 4.

LIGHT GREEN CHROMATOGRAPHY STRIPS:



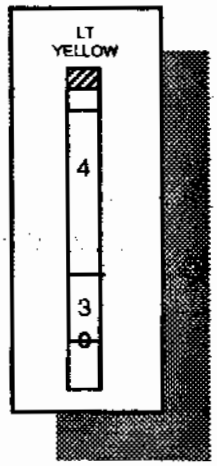
ITLC-SG light green color-coded strips with 0.7 cm x 6 cm dimension. Origin and solvent front line located 1.0 cm and 5.0 cm from bottom of strip. Cut line located 3.0 cm from bottom of strip. An appropriate colored marker line, which will migrate with acetone, is drawn on the back of the strip. Chromatography sections are labeled 1 and 2.

LIGHT PURPLE CHROMATOGRAPHY STRIPS:



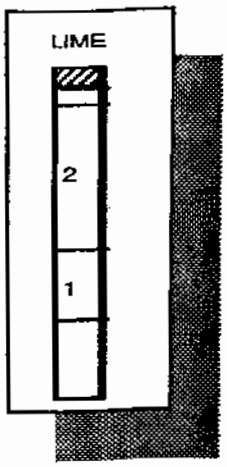
Whatman 31ET light purple color-coded strips with 0.7 cm x 7 cm dimension. Origin and solvent front line located 1.0 cm and 6.5 cm from bottom of strip. Cut line located 4.3 cm from bottom of strip. Origin, cut and solvent front lines are drawn in pencil. No colored marker line is drawn on the strip. Chromatography sections are labeled 1 and 2.

LIGHT YELLOW CHROMATOGRAPHY STRIPS:



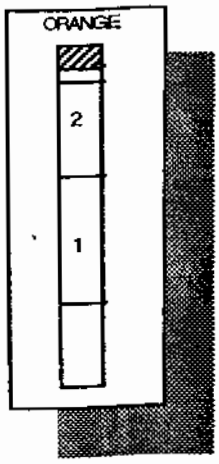
ITLC-SG light yellow color-coded strips with 0.7 cm x 6 cm dimension. Origin and solvent front line located 1.0 cm and 5.0 cm from bottom of strip. Cut line located 2.0 cm from bottom of strip. An appropriate colored marker line, which will migrate with distilled water, is drawn on the back of the strip. Chromatography sections are labeled 3 and 4.

LIME CHROMATOGRAPHY STRIPS



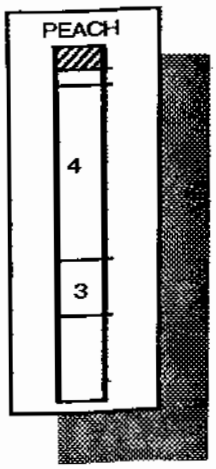
Gelman solvent saturation pads lime color-coded strips with 0.7 cm x 7 cm dimension. Origin and solvent front line located 1.0 cm and 6.5 cm from bottom of strip. Cut line located 3.0 cm from bottom of strip. An appropriate colored marker line, which will migrate with acetone:chloroform:tetrahydrofuran, is drawn on the back of the strip. Chromatography sections are labeled 1 and 2.

ORANGE CHROMATOGRAPHY STRIPS:



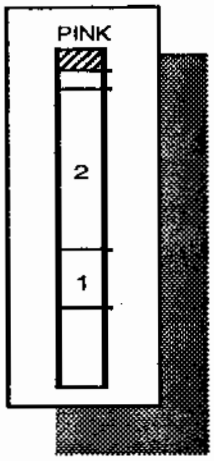
ITLC-SA orange color-coded strips with 0.7 cm x 6 cm dimension. Origin and solvent front line located 1.0 cm and 5.0 cm from bottom of strip. Cut line located 3.5 cm from bottom of strip. An appropriate colored marker line, which will migrate with 20% sodium chloride, is drawn on the back of the strip. Chromatography sections are labeled 1 and 2.

PEACH CHROMATOGRAPHY STRIPS:



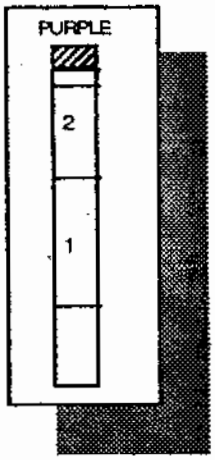
Gelman solvent saturation pads peach color-coded strips with 0.7 cm x 7 cm dimension. Origin and solvent front line located 1.0 cm and 6.5 cm from bottom of strip. Cut line located 2.5 cm from bottom of strip. An appropriate colored marker line, which will migrate with normal saline, is drawn on the back of the strip. Chromatography sections are labeled 3 and 4.

PINK CHROMATOGRAPHY STRIPS:



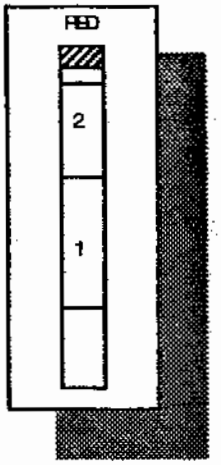
Whatman 31ET pink color-coded strips with 0.7 cm x 7 cm dimension. Origin and solvent front line located 1.0 cm and 6.5 cm from bottom of strip. Cut line located 2.5 cm from bottom of strip. An appropriate colored marker line, which will migrate with ethyl acetate, is drawn on the back of the strip. Chromatography sections are labeled 1 and 2.

PURPLE CHROMATOGRAPHY STRIPS:



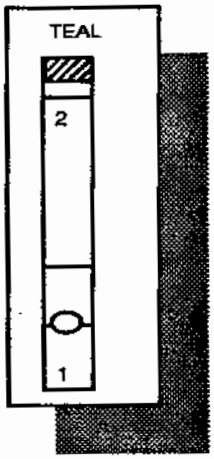
ITLC-SG purple color-coded strips with 0.7 cm x 6 cm dimension. Origin and solvent front line located 1.0 cm and 5.0 cm from bottom of strip. Cut line located 3.5 cm from bottom of strip. An appropriate colored marker line, which will migrate with normal saline, is drawn on the back of the strip. Chromatography sections are labeled 1 and 2.

RED CHROMATOGRAPHY STRIPS:



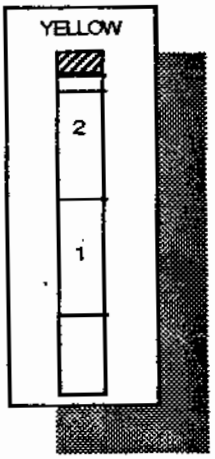
Whatman 31ET red color-coded strips with 0.7 cm x 6 cm dimension. Origin and solvent front line located 1.0 cm and 5.0 cm from bottom of strip. Cut line located 3.4 cm from bottom of strip. An appropriate colored marker line, which will migrate with acetone, is drawn on the back of the strip. Chromatography sections are labeled 1 and 2.

TEAL CHROMATOGRAPHY STRIPS:



Whatman 1 teal color-coded strips with 0.7 cm x 6 cm dimension. Origin and solvent front line located 1.0 cm and 5.0 cm from bottom of strip. Cut line located 2.0 cm from bottom of strip. Origin, cut and solvent front lines are drawn in pencil. An appropriate colored marker line is drawn on the back of the strip. Chromatography sections are labeled 1 and 2.

YELLOW CHROMATOGRAPHY STRIPS:



ITLC-SA yellow color-coded strips with 0.7 cm x 6 cm dimension. Origin and solvent front line located 1.0 cm and 5.0 cm from bottom of strip. Cut line located 3.0 cm from bottom of strip. An appropriate colored marker line, which will migrate with acetone, is drawn on the back of the strip. Chromatography sections are labeled 1 and 2.

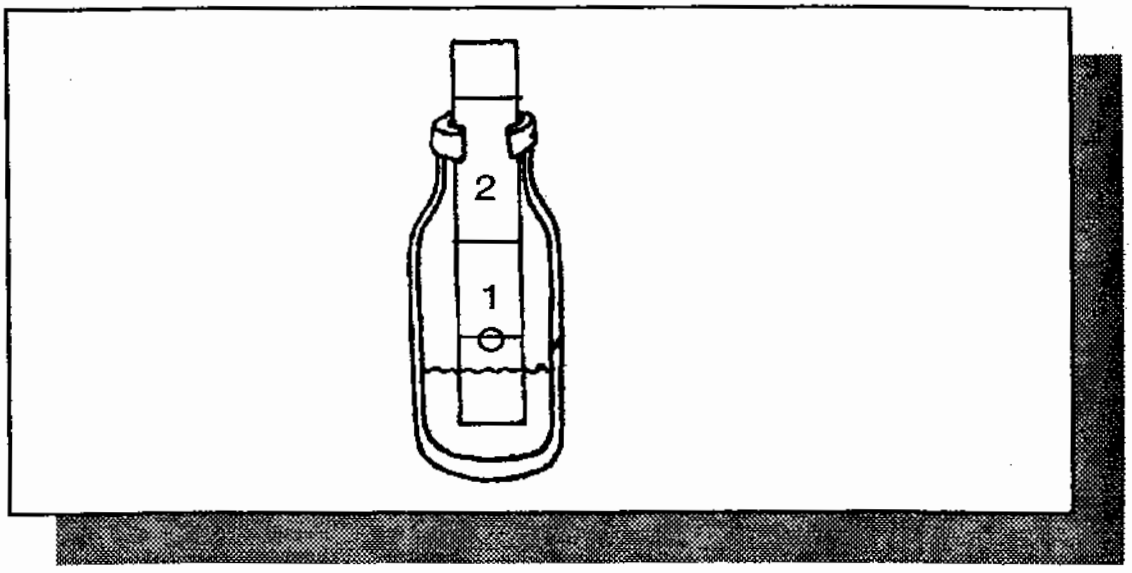
CHROMATOGRAPHY PROCEDURES

Chromatographic procedures include spotting the specific radiopharmaceutical on the origin line of the respective strips and eluting the strips in the appropriate solvent system. For ease of use, the strips are color-coded. Following solvent migration to the solvent front line, the strips are removed, cut at the cut line(s), and counted for activity using appropriate counting systems such as a well counter or dose calibrator.

Spotting the radiopharmaceutical on the chromatography strip is performed using a syringe with an appropriate sized needle. Better chromatographic separation, with minimal streaking, is obtained when small volumes of radiopharmaceutical are spotted. In order to achieve this, a small gauge needle size, such as a 25G or 27G, must be used. Approximately 4 and 6 ul of the radiopharmaceutical is delivered in each drop of a 25 gauge or a 27 gauge needle, respectively (6). Following spotting, the strip should be immediately placed in the solvent. Spot drying should be avoided.

Chromatographic procedures are divided into specific groups according to the the number of strips involved, namely single strip, two strip and three strip procedures. Within each specific group, variations in the procedures are also outlined.

SINGLE-STRIP PROCEDURES:



SINGLE-STRIP PROCEDURE 1A:

1. Place approximately 0.8 to 1.0 ml of the appropriate solvent in a clean empty 10-ml serum vial.
2. Spot the radiopharmaceutical at the origin line using a one-ml syringe with a 25G or 27G needle.
3. Immediately place the strip in the appropriate solvent and allow the solvent to migrate to the solvent front line. This will take approximately 30 to 60 seconds.
4. Remove the strip and cut at the cut line into sections 1 and 2.
5. Count each section using an appropriate counting system.

6. CALCULATIONS:

% FREE Tc-99m PERTECHNETATE, INDIUM, OR IODIDE

$$= \left[\frac{\text{(NET CTS SECTION 2)}}{\text{(NET CTS SECTION 1) + (NET CTS SECTION 2)}} \right] \text{X } 100$$

% BOUND RADIOPHARMACEUTICAL

$$= \left[\frac{\text{(NET CTS SECTION 1)}}{\text{(NET CTS SECTION 1) + (NET CTS SECTION 2)}} \right] \text{X } 100$$

SINGLE-STRIP PROCEDURE 1B:

1. Place approximately 0.8 to 1.0 ml of the appropriate solvent in a clean empty 10-ml serum vial.
2. Spot the radiopharmaceutical at the origin line using a one-ml syringe with a 25G or 27G needle.
3. Immediately place the strip in the appropriate solvent and allow the solvent to migrate to the solvent front line. This will take approximately 30 to 60 seconds.
4. Remove the strip and cut at the cut line into sections 1 and 2.
5. Count each section using an appropriate counting system.

6. CALCULATIONS:

% FREE Tc-99m PERTECHNETATE, INDIUM, OR IODIDE

$$= \left[\frac{\text{(NET CTS SECTION 1)}}{\text{(NET CTS SECTION 1) + (NET CTS SECTION 2)}} \right] \text{X } 100$$

% BOUND RADIOPHARMACEUTICAL

$$= \left[\frac{\text{(NET CTS SECTION 2)}}{\text{(NET CTS SECTION 1) + (NET CTS SECTION 2)}} \right] \text{X } 100$$

SINGLE-STRIP PROCEDURE 1C:

1. Place approximately 0.8 to 1.0 ml of the appropriate solvent in a clean empty 10-ml serum vial.
2. Add 0.05 ml of antibody radiopharmaceutical to 0.05 ml of 0.05M DTPA. Incubate for 60 seconds.
3. Spot the radiopharmaceutical-DTPA mixture at the origin line using a one-ml syringe with a 25G or 27G needle.
4. Immediately place the strip in the appropriate solvent and allow the solvent to migrate to the solvent front line. This will take approximately 30 to 60 seconds.
5. Remove the strip and cut at the cut line into sections 1 and 2.
6. Count each section using an appropriate counting system.

7. CALCULATIONS:

% FREE Tc-99m PERTECHNETATE, INDIUM, OR IODIDE

$$= \left[\frac{\text{(NET CTS SECTION 2)}}{\text{(NET CTS SECTION 1)} + \text{(NET CTS SECTION 2)}} \right] \text{X } 100$$

% BOUND RADIOPHARMACEUTICAL

$$= \left[\frac{\text{(NET CTS SECTION 1)}}{\text{(NET CTS SECTION 1)} + \text{(NET CTS SECTION 2)}} \right] \text{X } 100$$

SINGLE-STRIP PROCEDURE 1D:

1. Place approximately 0.8 to 1.0 ml of the appropriate solvent mixture in a clean empty 10-ml serum vial.
2. Spot the radiopharmaceutical at the origin line using a one-ml syringe with a 25G or 27G needle.
3. Immediately place the strip in the appropriate solvent and allow the solvent to migrate to the solvent front line. This will take approximately 60 to 120 seconds.
4. Remove the strip and cut at the cut lines into sections 1, 2 and 3.
5. Count each section using an appropriate counting system.
6. CALCULATIONS:

% FREE Tc-99m PERTECHNETATE

$$= \left[\frac{\text{(NET CTS SECTION 3)}}{\text{(NET COUNTS OFALL SECTIONS)}} \right] \text{X } 100$$

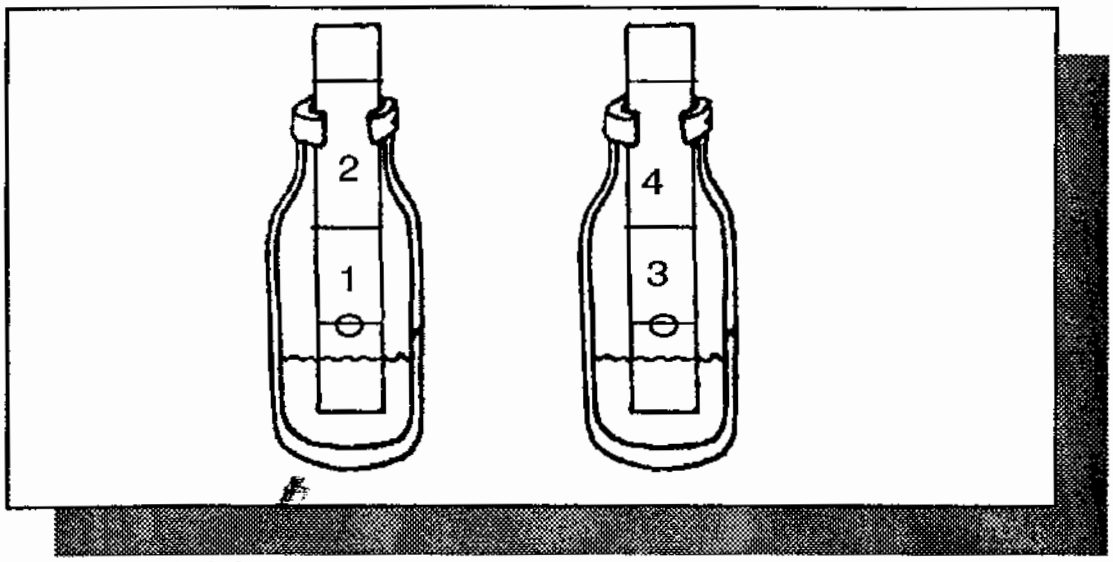
% HYROLYZED REDUCED Tc-99m

$$= \left[\frac{\text{(NET CTS SECTION 1)}}{\text{(NET COUNTS OFALL SECTIONS)}} \right] \text{X } 100$$

% BOUND RADIOPHARMACEUTICAL

$$= \left[\frac{\text{(NET CTS SECTION 2)}}{\text{(NET COUNTS OF ALL SECTIONS)}} \right] \text{X } 100$$

TWO-STRIP PROCEDURE:



TWO-STRIP PROCEDURE 2A:

1. Place approximately 0.8 to 1.0 ml of the appropriate solvents into two clean empty 10-ml serum vials.
2. Spot the radiopharmaceutical at the origin line on each of two strips using a one-ml syringe with a 25G or 27G needle.
3. Immediately place the strips in the appropriate solvents and allow the solvent to migrate to the solvent front line of each strip. This will take approximately 30 to 60 seconds.
4. Remove the strip and cut at the cut line into sections 1, 2, 3 and 4.
5. Count each section using an appropriate counting system.
6. CALCULATIONS:

% Tc-99m SOLUBLE IMPURITIES (Tc-99m PERTECHNETATE)

$$= \left[\frac{\text{(NET CTS SECTION 2)}}{\text{(NET CTS SECTION 1) + (NET CTS SECTION 2)}} \right] \times 100$$

% HYROLYZED REDUCED Tc-99m

$$= \left[\frac{\text{(NET CTS SECTION 3)}}{\text{(NET CTS SECTION 3) + (NET CTS SECTION 4)}} \right] \times 100$$

% BOUND RADIOPHARMACEUTICAL

= 100 - (Tc-99m SOLUBLE IMPURITIES) - (HYDROLYZED REDUCED Tc-99m)

TWO-STRIP PROCEDURE 2B:

1. Place approximately 0.8 to 1.0 ml of the appropriate solvents into two clean empty 10-ml serum vials.
2. Spot one drop of 5% HSA onto the dark blue chromatography strip using a one-ml syringe with a 22G needle.
3. Spot the radiopharmaceutical at the origin line on each of two strips using a one-ml syringe with a 25G or 27G needle.
4. Immediately place the strips in the appropriate solvents and allow the solvent to migrate to the solvent front line of each strip. This will take approximately 30 to 60 seconds.
5. Remove the strip and cut at the cut line into sections 1,2, 3 and 4.
6. Count each section using an appropriate counting system.
7. CALCULATIONS:

% Tc-99m SOLUBLE IMPURITIES (Tc-99m PERTECHNETATE)

$$= \left[\frac{\text{(NET CTS SECTION 2)}}{\text{(NET CTS SECTION 1) + (NET CTS SECTION 2)}} \right] \text{X } 100$$

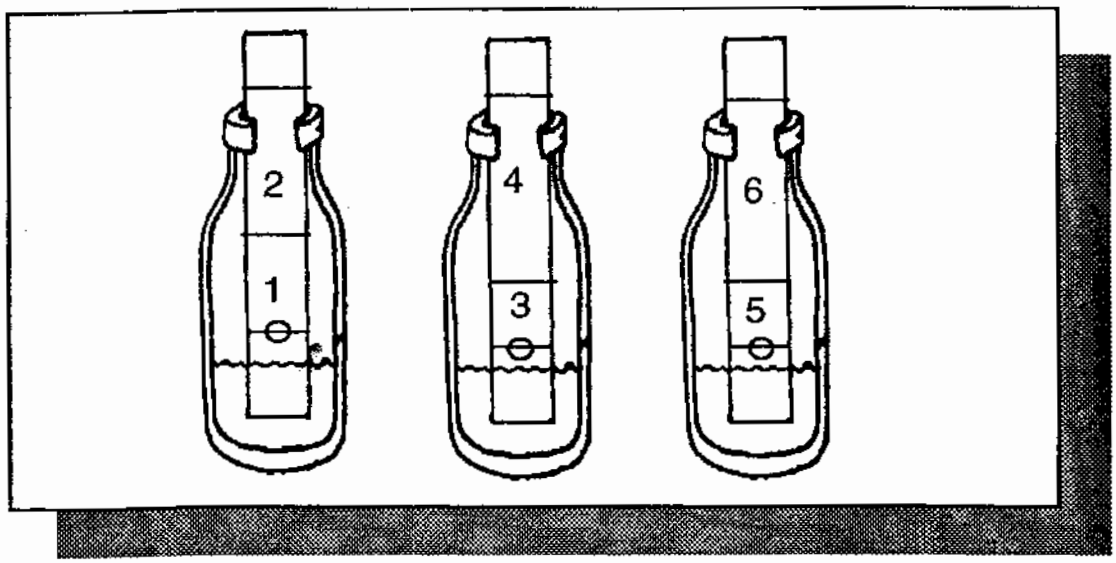
% HYROLYZED REDUCED Tc-99m

$$= \left[\frac{\text{(NET CTS SECTION 3)}}{\text{(NET CTS SECTION 3) + (NET CTS SECTION 4)}} \right] \text{X } 100$$

% BOUND RADIOPHARMACEUTICAL

= 100 - (Tc-99m SOLUBLE IMPURITIES) - (HYDROLYZED REDUCED Tc-99m)

THREE-STRIP PROCEDURE:



THREE-STRIP PROCEDURE 3:

1. Place approximately 0.8 to 1.0 ml of the appropriate solvents into three clean empty 10-ml serum vials.
2. Spot the radiopharmaceutical at the origin line on each of three strips using a one-ml syringe with a 25G or 27G needle.
3. Immediately place the strips in the appropriate solvents and allow the solvent to migrate to the solvent front line of each strip. This will take approximately 30 to 60 seconds.
4. Remove the strip and cut at the cut line into sections 1,2, 3, 4, 5 and 6.
5. Count each section using an appropriate counting system.

6. CALCULATIONS:

% Tc-99m PERTECHNETATE

$$= \left[\frac{\text{(NET CTS SECTION 2)}}{\text{(NET CTS SECTION 1) + (NET CTS SECTION 2)}} \right] \text{ X 100}$$

% HYROLYZED REDUCED Tc-99m

$$= \left[\frac{\text{(NET CTS SECTION 5)}}{\text{(NET CTS SECTION 5) + (NET CTS SECTION 6)}} \right] \text{ X 100}$$

% LIPOPHILIC EXAMETAZINE COMPLEX

$$= \left[\left[\frac{\text{(NET CTS SECTION 1)}}{\text{(NET CTS SECTION 1) + (NET CTS SECTION 2)}} \right] - \left[\frac{\text{(NET CTS SECTION 3)}}{\text{(NET CTS SECTION 3) + (NET CTS SECTION 4)}} \right] \right] \text{ X 100}$$

4

QUALITY CONTROL PROCEDURES FOR RADIOPHARMACEUTICALS

This section provides a list of the more commonly used radiopharmaceuticals including common names, radiochemical impurities, quality control methods, chromatography strip activity distributions and all applicable references. A summary of the chromatography systems used for specific radiopharmaceuticals is found in Appendix A. Because the emphasis is on currently used radiopharmaceuticals, some agents will not be listed in this section. A summary of chromatography systems for radiopharmaceuticals not listed in this section may be found in Appendix B.

TECHNETIUM Tc-99m SODIUM PERTECHNETATE

(Sodium pertechnetate, Tc-99m pertechnetate, TcO_4^-)

RADIOCHEMICAL IMPURITIES:

Reduced Technetium-99m, including hydrolyzed reduced Tc-99m.

QUALITY CONTROL METHOD:

CHROMATOGRAPHY SYSTEM:

Whatman 31ET (0.7 x 6 cm) with Acetone. Red color-coded chromatography strip. Technetium-99m pertechnetate migrates with the solvent front (Rf=1.0), other reduced Tc-99m radiochemical impurities remain at the origin (Rf=0.0). The cut line is located at Rf=0.6.

CHROMATOGRAPHY PROCEDURE:

Use Single-Strip Procedure (PROCEDURE 1A). Add acetone (0.8 to 1.0 ml) to serum vial. Following radiopharmaceutical spotting, immediately place the red strip in acetone and allow solvent to migrate to solvent front line. Remove strip, cut at cut line into sections 1 and 2 and count for activity. Calculations are performed as outlined in PROCEDURE 1A.

CHROMATOGRAPHY STRIP ACTIVITY DISTRIBUTION:

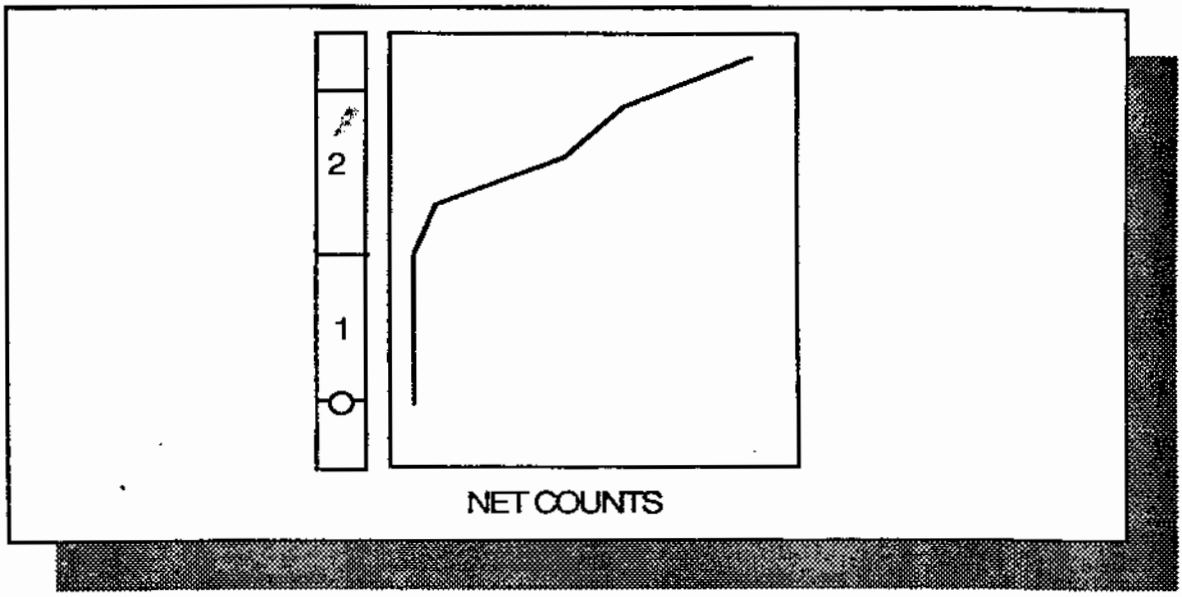


Figure 4-1. Strip activity distribution of Tc-99m pertechnetate on Whatman 31ET paper eluted with acetone.

ALTERNATE QUALITY CONTROL METHOD:

CHROMATOGRAPHY SYSTEM:

ITLC-SG (0.7 x 6 cm) with distilled water. Dark green color-coded chromatography strip. Technetium-99m pertechnetate migrates with the solvent front (Rf=1.0), other reduced Tc-99m radiochemical impurities remain at the origin (Rf=0.0). The cut line is located at Rf=0.5

CHROMATOGRAPHY PROCEDURE:

Use Single-Strip Procedure (PROCEDURE 1A). Add distilled water (0.8 to 1.0 ml) to serum vial. Following radiopharmaceutical spotting, immediately place the dark green strip in

distilled water and allow solvent to migrate to solvent front line. Remove strip, cut at cut line into sections 1 and 2 and count for activity. Calculations are performed as outlined in PROCEDURE 1A.

REFERENCES: (7)

TECHNETIUM Tc-99m SULFUR COLLOID

(TECHNECOLL™, TESULOID™, Tc-99m TSC™)

RADIOCHEMICAL IMPURITIES:

Technetium-99m pertechnetate

QUALITY CONTROL METHOD:

CHROMATOGRAPHY SYSTEM:

Whatman 31ET (0.7 x 6 cm) with Acetone. Red color-coded chromatography strip. Technetium-99m sulfur colloid remains at the origin whereas free technetium-99m pertechnetate migrates with the solvent front (Rf=1.0). The cut line is located at Rf=0.6.

CHROMATOGRAPHY PROCEDURE:

Use Single-Strip Procedure (PROCEDURE 1A). Add acetone (0.8 to 1.0 ml) to serum vial. Following radiopharmaceutical spotting, immediately place the red strip in acetone and allow solvent to migrate to solvent front line. Remove strip, cut at cut line into sections 1 and 2 and count for activity. Calculations are performed as outlined in PROCEDURE 1A.

CHROMATOGRAPHY STRIP ACTIVITY DISTRIBUTION:

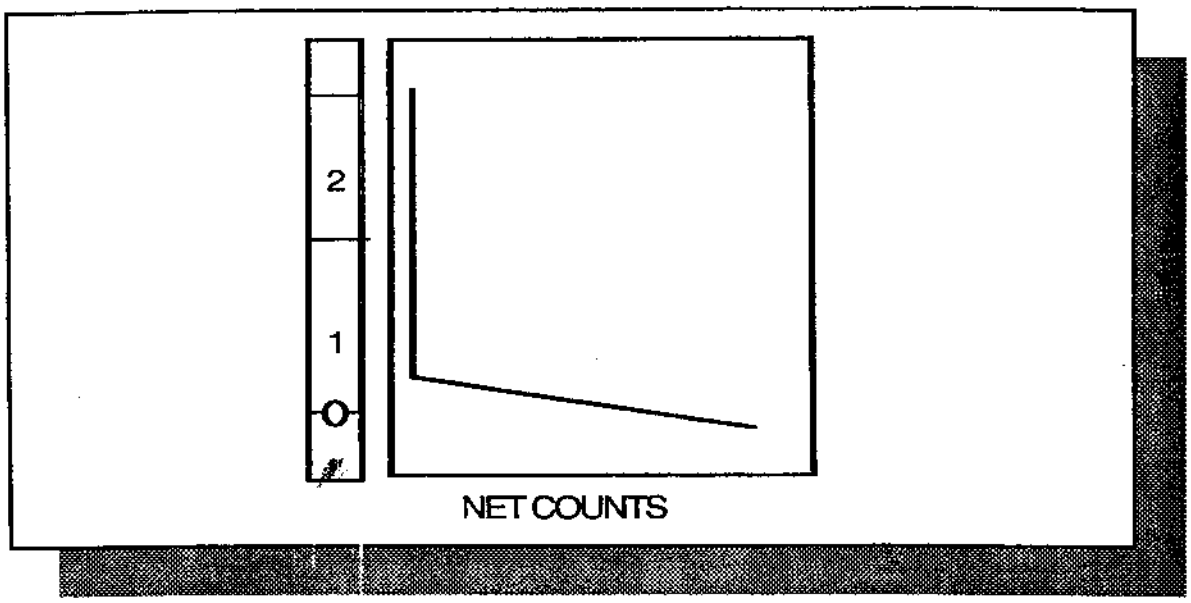


Figure 4-2. Strip activity distribution of Tc-99m sulfur colloid on Whatman 31ET paper chromatography eluted with acetone.

REFERENCES: (7)

TECHNETIUM Tc-99m ALBUMIN COLLOID
(MICROLITE™)

RADIOCHEMICAL IMPURITIES:

Technetium-99m pertechnetate

QUALITY CONTROL METHOD:

CHROMATOGRAPHY SYSTEM:

Whatman 31ET (0.7 x 6 cm) with Acetone. Red color-coded chromatography strip. Technetium-99m albumin colloid remains at the origin whereas free technetium-99m pertechnetate migrates with the solvent front (Rf=1.0). The cut line is located at Rf=0.6.

CHROMATOGRAPHY PROCEDURE:

Use Single-Strip Procedure (PROCEDURE 1A). Add acetone (0.8 to 1.0 ml) to serum vial. Following radiopharmaceutical spotting, immediately place the red strip in acetone and allow solvent to migrate to solvent front line. Remove strip, cut at cut line into sections 1 and 2 and count for activity. Calculations are performed as outlined in PROCEDURE 1A.

CHROMATOGRAPHY STRIP ACTIVITY DISTRIBUTION :

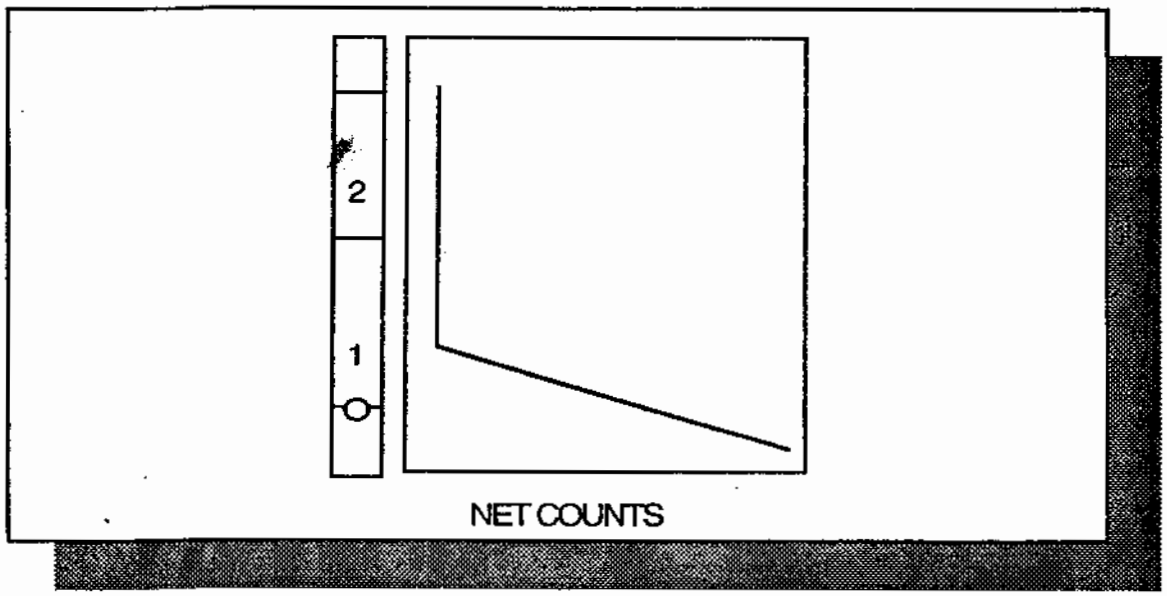


Figure 4-3. Strip activity distribution of Tc-99m albumin colloid on Whatman 31ET paper chromatography eluted with acetone.

TECHNETIUM Tc-99m ANTIMONY TRISULFIDE COLLOID
(Tc-99m SbS COLLOID)

RADIOCHEMICAL IMPURITIES:

Technetium-99m pertechnetate

QUALITY CONTROL METHOD:

CHROMATOGRAPHY SYSTEM:

ITLC-SG (0.7 x 6 cm) with 0.9% sodium chloride. Dark-green color coded chromatography strip. Technetium-99m pertechnetate migrates with the solvent front (Rf=1.0), other reduced

Tc-99m radiochemical impurities remain at the origin (Rf=0.0). The cut line is located at Rf=0.5.

CHROMATOGRAPHY PROCEDURE:

Use Single-Strip Procedure (PROCEDURE 1A). Add 0.9% sodium chloride (0.8 to 1.0 ml) to serum vial. Following radiopharmaceutical spotting, immediately place the dark green strip in normal saline and allow solvent to migrate to solvent front line. Remove strip, cut at cut line into sections 1 and 2 and count for activity. Calculations are performed as outlined in PROCEDURE 1A.

REFERENCES: (6)

TECHNETIUM Tc-99m ALBUMIN AGGREGATED

(Tc-99m MAA, Tc-99m MACROAGGREGATED ALBUMIN, PULMOLITE™, MACROTEC™, AN-MAA™)

RADIOCHEMICAL IMPURITIES:

Technetium-99m pertechnetate, Tc-99m soluble proteins, Tc-99m hyrolyzed reduced technetium.

QUALITY CONTROL METHOD:

CHROMATOGRAPHY SYSTEM:

Whatman 31ET (0.7 x 6 cm) with Acetone. Red color-coded chromatography strip. Technetium-99m MAA remains at the origin whereas free technetium-99m pertechnetate migrates with the solvent front (Rf=1.0). The cut line is located at Rf=0.6. Other radiochemical impurities, namely hydrolyzed reduced Tc-99m and Tc-99m soluble proteins also remain at the origin (Rf=0.0) and as a result, these impurities cannot be identified with the chromatography system outlined above.

CHROMATOGRAPHY PROCEDURE:

Use Single-Strip Procedure (PROCEDURE 1A). Add acetone (0.8 to 1.0 ml) to serum vial. Following radiopharmaceutical spotting, immediately place the red strip in acetone and allow

solvent to migrate to solvent front line. Remove strip, cut at cut line into sections 1 and 2 and count for activity. Calculations are performed as outlined in PROCEDURE 1A.

CHROMATOGRAPHY STRIP ACTIVITY DISTRIBUTION:

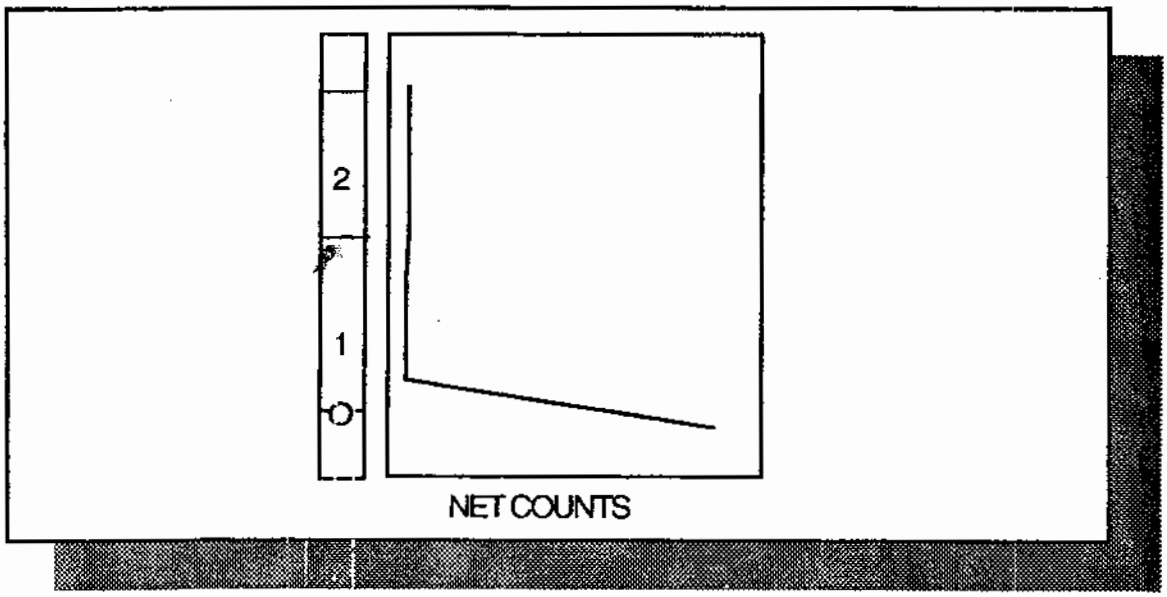


Figure 4-4. Strip activity distribution of Tc-99m MAA on Whatman 31ET paper chromatography eluted with acetone.

REFERENCES: (7)

TECHNETIUM Tc-99m PENTETATE

(Tc-99m DTPA, AN-DTPA™, TECHNEPLEX™)

RADIOCHEMICAL IMPURITIES:

Technetium-99m pertechnetate and Tc-99m hyrolyzed reduced technetium.

QUALITY CONTROL METHOD:

CHROMATOGRAPHY SYSTEM:

Two separate chromatography systems are utilized to assess radiochemical purity.

System 1

Whatman 31ET (0.7 x 6 cm) with Acetone. Red color-coded chromatography strip. Free Tc-99m pertechnetate migrates with the solvent front (Rf=1.0) whereas Tc-99m DTPA and hydrolyzed reduced Tc-99m remain at the origin (Rf=0.0). The cut line is located at Rf=0.6.

System 2

ITLC-SG (0.7 x 6 cm) with Distilled Water. Black color-coded chromatography strip. Free Tc-99m pertechnetate and Tc-99m DTPA migrate with the solvent front (Rf=1.0) whereas hyrolyzed reduced Tc-99m remains at the origin (Rf=0.0). The cut line is located at Rf=0.4.

CHROMATOGRAPHY PROCEDURE:

Use Two-Strip Procedure (PROCEDURE 2A). Add acetone (0.8 to 1.0 ml) and distilled water (0.8 to 1.0 ml) to separate serum vials. Following radiopharmaceutical spotting, immediately place the red strip in acetone and the black strip in distilled water and allow solvent to migrate to solvent front line. Remove strips, cut at cut lines into sections 1, 2, 3 and 4 and count for activity. Calculations are performed as outlined in PROCEDURE 2A.

CHROMATOGRAPHY STRIP ACTIVITY DISTRIBUTION :

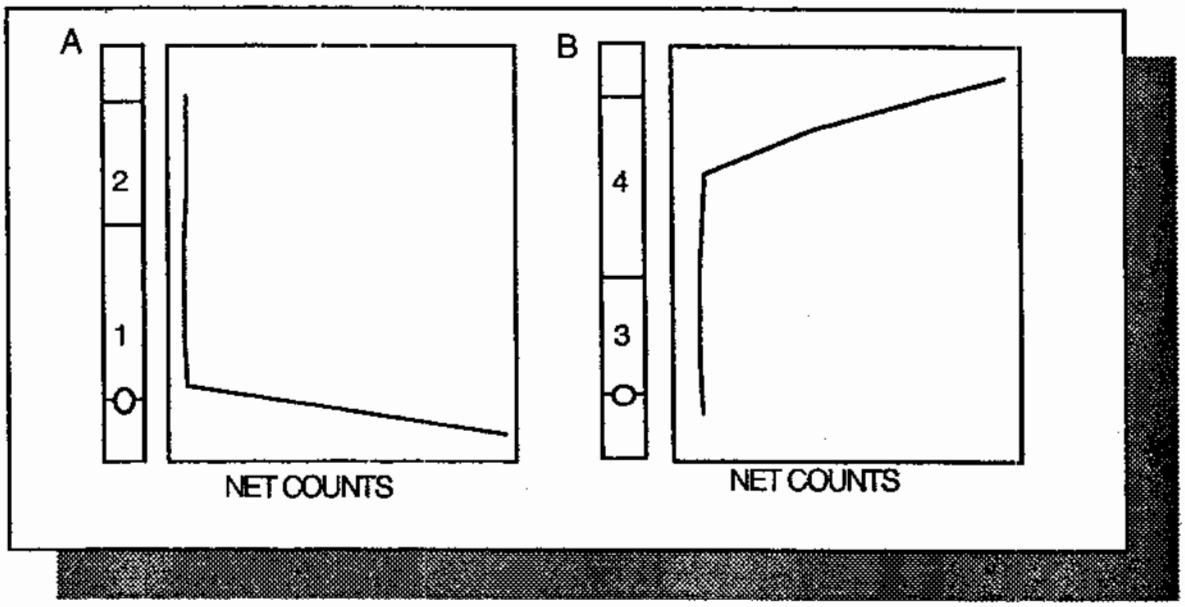


Figure 4-5. Strip activity distribution of Tc-99m DTPA on (A) Whatman 31ET paper, acetone solvent and (B) ITLC-SG paper, distilled water solvent.

REFERENCES: (7)

TECHNETIUM Tc-99m PYROPHOSPHATE

(Tc-99m PYP, TECHNESCAN PYP™, PHOSPHOTEC™)

RADIOCHEMICAL IMPURITIES:

Technetium-99m pertechnetate and Tc-99m hyrolyzed reduced technetium.

QUALITY CONTROL METHOD:

CHROMATOGRAPHY SYSTEM:

Two separate chromatography systems are utilized to assess radiochemical purity.

System 1

Whatman 31ET (0.7 x 6 cm) with Acetone. Red color-coded strip. Free Tc-99m pertechnetate migrates with the solvent front (Rf=1.0) whereas Tc-99m pyrophosphate and hydrolyzed reduced Tc-99m remain at the origin (Rf=0.0). The cut line is located at Rf=0.6.

System 2

ITLC-SG (0.7 x 6 cm) with Distilled Water. Black color-coded chromatography strip. Free Tc-99m pertechnetate and Tc-99m pyrophosphate migrate with the solvent front (Rf=1.0) whereas hyrolyzed reduced Tc-99m remains at the origin (Rf=0.0). The cut line is located at Rf=0.4.

CHROMATOGRAPHY PROCEDURE:

Use Two-Strip Procedure (PROCEDURE 2A). Add acetone (0.8 to 1.0 ml) and distilled water (0.8 to 1.0 ml) to separate serum vials. Following radiopharmaceutical spotting, immediately place the red strip in acetone and the black strip in distilled water and allow solvent to migrate to solvent front line. Remove strips, cut at cut lines into sections 1, 2, 3 and 4 and count for activity. Calculations are performed as outlined in PROCEDURE 2A.

CHROMATOGRAPHY STRIP ACTIVITY DISTRIBUTION :

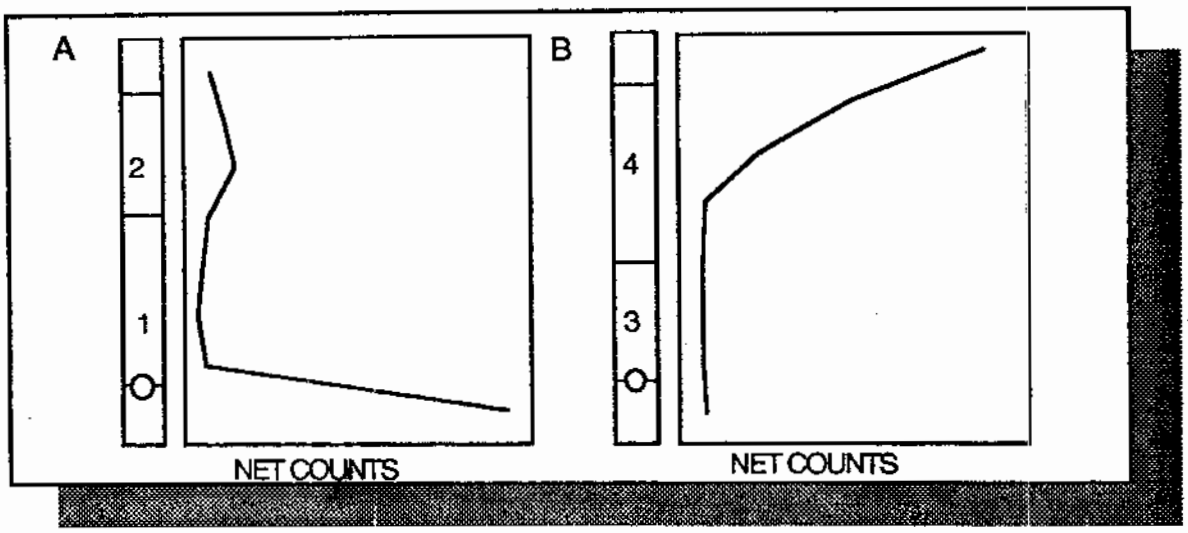


Figure 4-6. Strip activity distribution of Tc-99m Pyrophosphate on (A) Whatman 31ET paper, acetone solvent and (B) ITLC-SG paper, distilled water solvent.

REFERENCES: (7)

TECHNETIUM Tc-99m MEDRONATE

(Tc-99m MDP, Tc-99m METHYLENEDIPHOSPHONATE, AN-MDP™, OSTEOLITE™, TECHNESCAN MDP™,)

RADIOCHEMICAL IMPURITIES:

Technetium-99m pertechnetate and Tc-99m hyrolyzed reduced technetium.

QUALITY CONTROL METHOD:

CHROMATOGRAPHY SYSTEM:

Two separate chromatography systems are utilized to assess radiochemical purity.

System 1

Whatman 31ET (0.7 x 6 cm) with Acetone. Red color-coded chromatography strip. Free Tc-99m pertechnetate migrates with the solvent front (Rf=1.0) whereas Tc-99m MDP and hydrolyzed reduced Tc-99m remain at the origin (Rf=0.0). The cut line is located at Rf=0.6.

System 2

ITLC-SG (0.7 x 6 cm) with Distilled Water. Black color-coded chromatography strip. Free Tc-99m pertechnetate and Tc-99m MDP migrate with the solvent front (Rf=1.0) whereas

hyrolyzed reduced Tc-99m remains at the origin (Rf=0.0). The cut line is located at Rf=0.4.

CHROMATOGRAPHY PROCEDURE:

Use Two-Strip Procedure (PROCEDURE 2A). Add acetone (0.8 to 1.0 ml) and distilled water (0.8 to 1.0 ml) to separate serum vials. Following radiopharmaceutical spotting, immediately place the red strip in acetone and the black strip in distilled water and allow solvent to migrate to solvent front line. Remove strips, cut at cut lines into sections 1, 2, 3 and 4 and count for activity. Calculations are performed as outlined in PROCEDURE 2A.

CHROMATOGRAPHY STRIP ACTIVITY DISTRIBUTION:

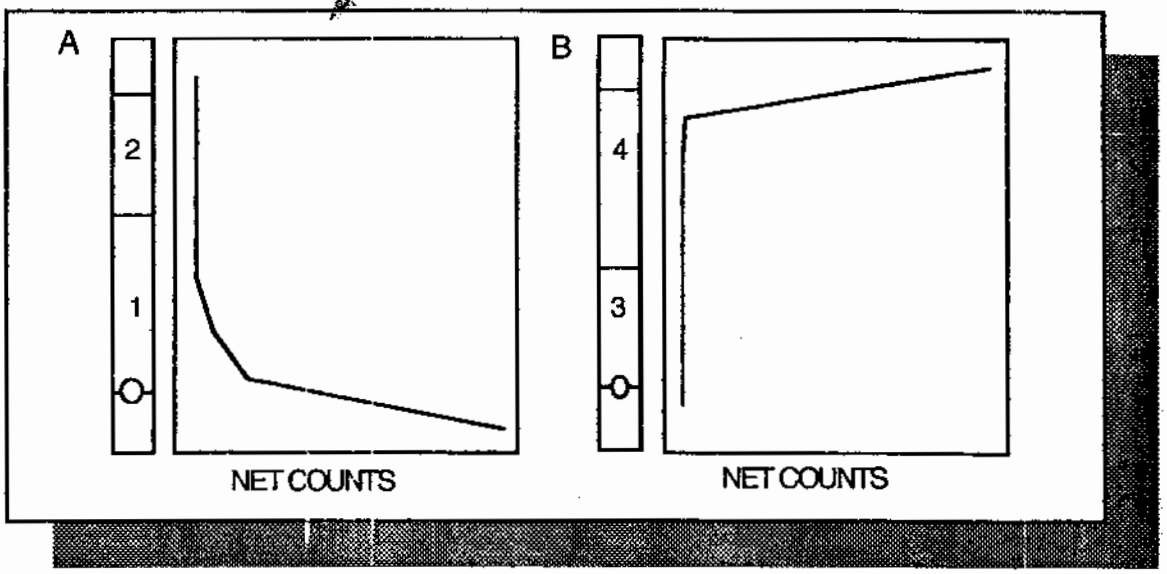


Figure 4-7. Strip activity distribution of Tc-99m MDP on (A) Whatman 31ET paper, acetone solvent and (B) ITLC-SG paper, distilled water solvent.

REFERENCES: (7)

TECHNETIUM Tc-99m OXIDRONATE

(Tc-99m HMDP, Tc-99m HDP, Tc-99m HYDROXYMETHYLENEDIPHOSPHONATE, OSTEOSCAN HDP™)

RADIOCHEMICAL IMPURITIES:

Technetium-99m pertechnetate and Tc-99m hyrolyzed reduced technetium.

QUALITY CONTROL METHOD:

CHROMATOGRAPHY SYSTEM:

Two separate chromatography systems are utilized to assess radiochemical purity.

System 1

Whatman 31ET (0.7 x 6 cm) with Acetone. Red color-coded chromatography strip. Free Tc-99m pertechnetate migrates with the solvent front (Rf=1.0) whereas Tc-99m HMDP and hydrolyzed reduced Tc-99m remain at the origin (Rf=0.0). The cut line is located at Rf=0.6.

System 2

ITLC-SG (0.7 x 6 cm) with Distilled Water. Black color-coded chromatography strip. Free Tc-99m pertechnetate and Tc-99m HMDP migrate with the solvent front (Rf=1.0) whereas hyrolyzed reduced Tc-99m remains at the origin (Rf=0.0). The cut line is located at Rf=0.4.

CHROMATOGRAPHY PROCEDURE:

Use Two-Strip Procedure (PROCEDURE 2A). Add acetone (0.8 to 1.0 ml) and distilled water (0.8 to 1.0 ml) to separate serum vials. Following radiopharmaceutical spotting, immediately place the red strip in acetone and the black strip in distilled water and allow solvent to migrate to solvent front line. Remove strips, cut at cut lines into sections 1, 2, 3 and 4 and count for activity. Calculations are performed as outlined in PROCEDURE 2A.

CHROMATOGRAPHY STRIP ACTIVITY DISTRIBUTION:

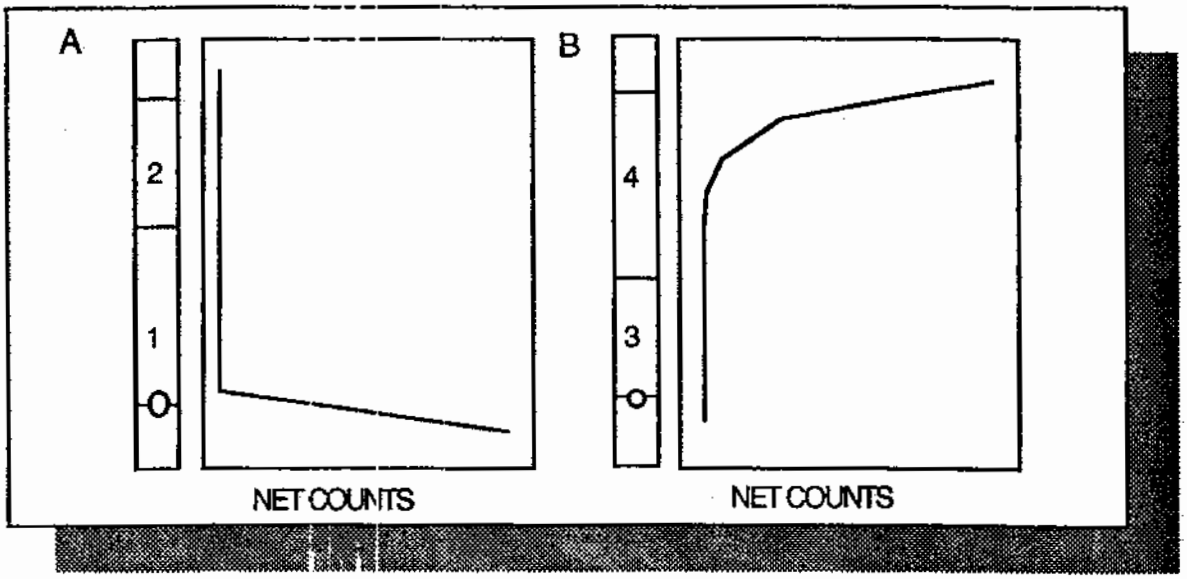


Figure 4-8. Strip activity distribution of Tc-99m HMDP on (A) Whatman 31ET paper, acetone solvent and (B) ITLC-SG paper, distilled water solvent.

REFERENCES: (8)

TECHNETIUM Tc-99m GLUCEPTATE

(Tc-99m GH, Tc-99m GLUCOHEPTONATE, GLUCOSCAN™, TECHNESCAN GLUCEPTATE™)

RADIOCHEMICAL IMPURITIES:

Technetium-99m pertechnetate and Tc-99m hyrolyzed reduced technetium.

QUALITY CONTROL METHOD:

CHROMATOGRAPHY SYSTEM:

Two separate chromatography systems are utilized to assess radiochemical purity.

System 1

Whatman 31ET (0.7 x 6 cm) with Acetone. Red color-coded strip. Free Tc-99m pertechnetate migrates with the solvent front (Rf=1.0) whereas Tc-99m Glucoheptonate and hydrolyzed reduced Tc-99m remain at the origin (Rf=0.0). The cut line is located at Rf=0.6.

System 2

ITLC-SG (0.7 x 6 cm) with Distilled Water. Black color-coded chromatography strip. Free Tc-99m pertechnetate and Tc-99m Glucoheptonate migrate with the solvent front (Rf=1.0) whereas hyrolyzed reduced Tc-99m remains at the origin (Rf=0.0). The cut line is located at Rf=0.4.

CHROMATOGRAPHY PROCEDURE:

Use Two-Strip Procedure (PROCEDURE 2A). Add acetone (0.8 to 1.0 ml) and distilled water (0.8 to 1.0 ml) to separate serum vials. Following radiopharmaceutical spotting, immediately place the red strip in acetone and the black strip in distilled water and allow solvent to migrate to solvent front line. Remove strips, cut at cut lines into sections 1, 2, 3 and 4 and count for activity. Calculations are performed as outlined in PROCEDURE 2A.

CHROMATOGRAPHY STRIP ACTIVITY DISTRIBUTION:

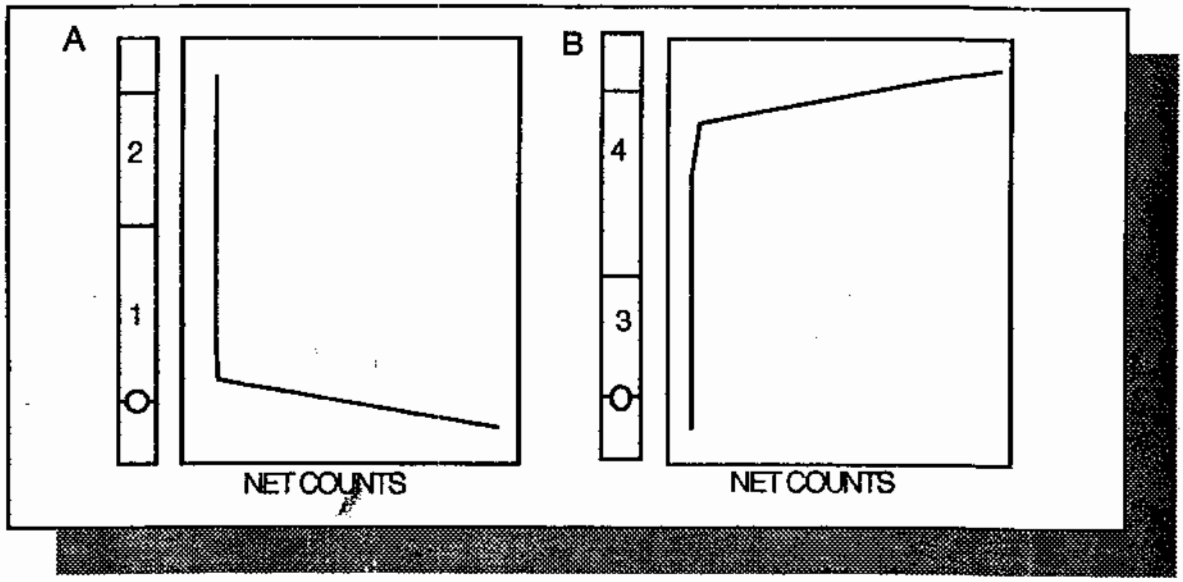


Figure 4-9. Strip activity distribution of Tc-99m Glucoheptonate on (A) Whatman 31ET paper, acetone solvent and (B) ITLC-SG paper, distilled water solvent.

REFERENCES: (7)

TECHNETIUM Tc-99m ALBUMIN

(Tc-99m HSA, Tc-99m HUMAN SERUM ALBUMIN)

RADIOCHEMICAL IMPURITIES:

Technetium-99m pertechnetate and Tc-99m hyrolyzed reduced technetium.

QUALITY CONTROL METHOD:

CHROMATOGRAPHY SYSTEM:

Two separate chromatography systems are utilized to assess radiochemical purity.

System 1

ITLC-SG (0.7 x 6 cm) with Acetone. Light green color-coded chromatography strip. Free Tc-99m pertechnetate migrates with the solvent front (Rf=1.0) whereas Tc-99m HSA and hydrolyzed reduced Tc-99m remain at the origin (Rf=0.0). The cut line is located at Rf=0.5.

System 2

Whatman 31ET strips (0.7 x 6 cm) with Distilled Water. Dark blue color-coded chromatography strip. Free Tc-99m pertechnetate and Tc-99m HSA migrate with the solvent front (Rf=1.0) whereas hyrolyzed reduced Tc-99m remains at the origin (Rf=0.0). The cut

line is located at Rf=0.25.

CHROMATOGRAPHY PROCEDURE:

Use Two-Strip Procedure (PROCEDURE 2B). Add acetone (0.8 to 1.0 ml) and distilled water (0.8 to 1.0 ml) to separate serum vials. Spot one drop of 5% HSA onto the dark blue strip and then spot radiopharmaceutical on both strips. Immediately place the light green strip in acetone and the dark blue strip in distilled water and allow solvent to migrate to solvent front line. Remove strips, cut at cut lines into sections 1, 2, 3 and 4 and count for activity. Calculations are performed as outlined in PROCEDURE 2B.

CHROMATOGRAPHY STRIP ACTIVITY DISTRIBUTION :

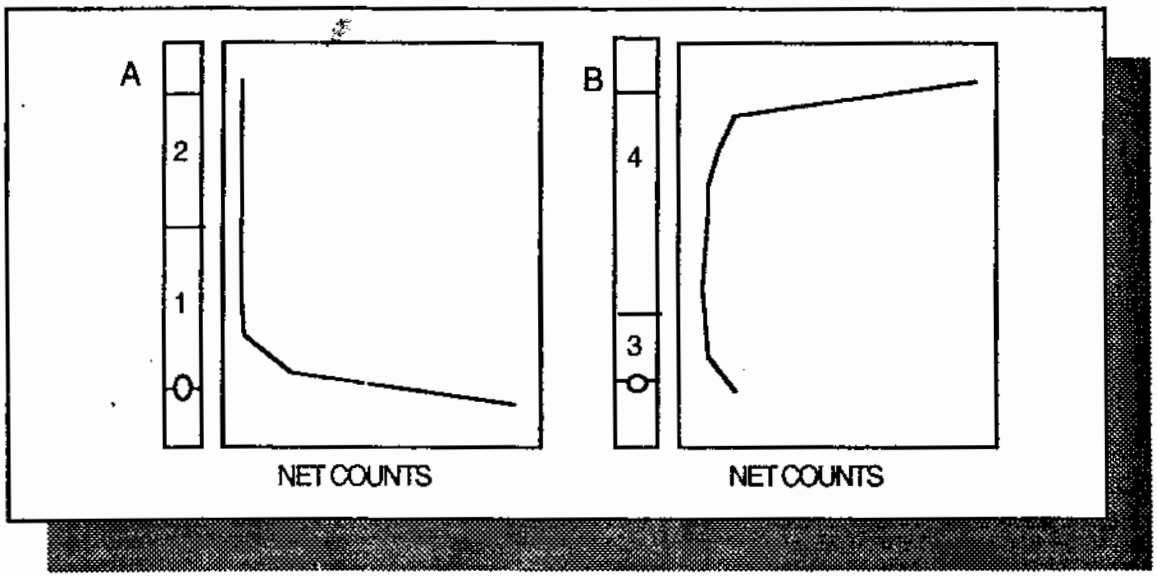


Figure 4-10. Strip activity distribution of Tc-99m HSA on (A) ITLC-SG paper, acetone solvent and (B) Whatman 31ET paper, distilled water solvent.

TECHNETIUM Tc-99m SUCCIMER

(Tc-99m DMSA, Tc-99m DIMERCAPTOSUCCINIC ACID)

RADIOCHEMICAL IMPURITIES:

Technetium-99m pertechnetate and Tc-99m hyrolyzed reduced technetium.

pertechnetate migrates with the solvent front (Rf=1.0) whereas Tc-99m DMSA remains at the origin (Rf=0.0). The cut line is located at Rf=0.5.

NOTE: With this chromatography system, one cannot distinguish between Tc-99m DMSA and hydrolyzed reduced Tc-99m.

CHROMATOGRAPHY PROCEDURE:

Use Single-Strip Procedure (PROCEDURE 1A). Add acetone (0.8 to 1.0 ml) to serum vial. Following radiopharmaceutical spotting, immediately place the yellow strip in acetone and allow solvent to migrate to solvent front line. Remove strip, cut at cut line into sections 1 and 2 and count for activity. Calculations are performed as outlined in PROCEDURE 1A.

CHROMATOGRAPHY STRIP ACTIVITY DISTRIBUTION :

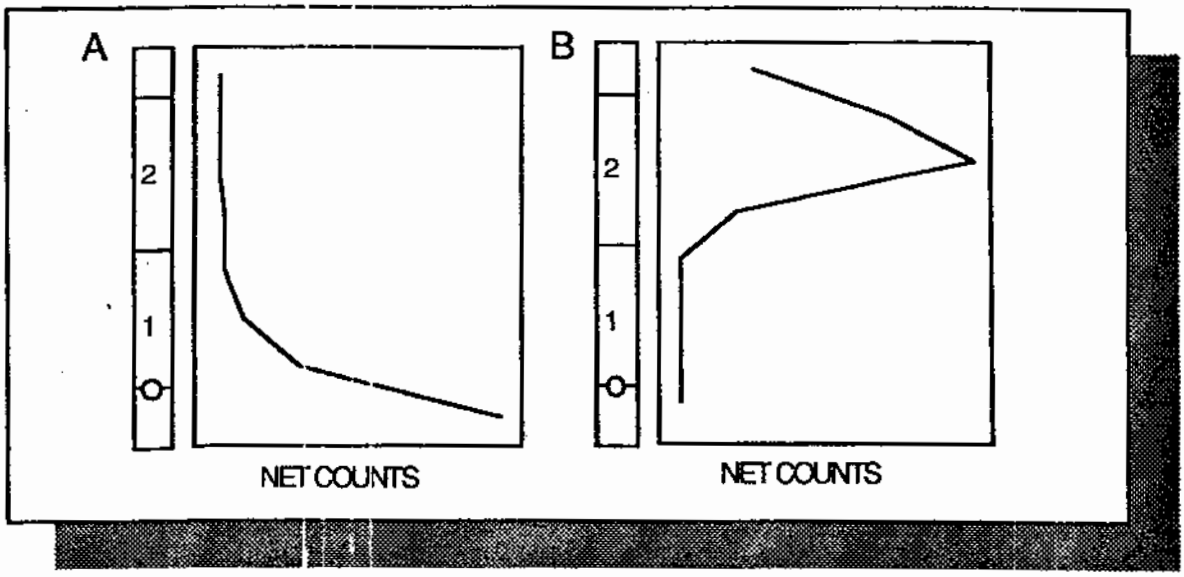


Figure 4-11. Strip activity distribution of (A) Tc-99m DMSA on ITLC-SA paper eluted with acetone and (B) Tc-99m pertechnetate on ITLC-SA paper eluted with acetone.

REFERENCES: (7)

ALTERNATE QUALITY CONTROL METHOD:

Use Single-Strip Procedure Method with Seprachrom (Gelman Sciences, Ann Arbor, MI) chromatography system.

CHROMATOGRAPHY SYSTEM

Large ITLC-SA strips (1 x 9.5 cm) with n-butanol saturated with 0.3N HCl as the solvent system. Tc-99m pertechnetate migrates with the solvent front (Rf=1.0), Tc-99m DMSA

migrates with an Rf=0.4-0.7 and hydrolyzed reduced Tc-99m remains at the origin (Rf=0.0). NOTE: The migration time of the solvent is slow, taking about 15-20 minutes. When counting, one should cut the strip into 0.5 cm sections. After counting each section, a histogram graph of counts vs Rf value must be plotted and areas under peaks measured for each specific radiochemical component. Alternately, a radiochromatogram scanner can be used to assess the various radiochemical components

REFERENCE: (6)

TECHNETIUM Tc-99m DISOFENIN
(Tc-99m DISIDA, Tc-99m HEPATOLITE™)

RADIOCHEMICAL IMPURITIES:

Technetium-99m pertechnetate and Tc-99m hyrolyzed reduced technetium.

QUALITY CONTROL METHOD:

CHROMATOGRAPHY SYSTEM:

Two separate chromatography systems are utilized to assess radiochemical purity.

System 1

ITLC-SA (0.7 x 6 cm) with 20% NaCl. Orange color-coded chromatography strip. Free Tc-99m pertechnetate migrates with the solvent front (Rf=1.0) whereas hyrolyzed reduced Tc-99m and Tc-99m Disofenin remain at the origin (Rf=0.0). The cut line is located at Rf=0.6.

System 2

ITLC-SG (0.7 x 6 cm) with Distilled Water. Light Blue color-coded chromatography strip. Free Tc-99m pertechnetate and Tc-99m Disofenin migrate with the solvent front (Rf=1.0) whereas hyrolyzed reduced Tc-99m remains at the origin (Rf=0.0). The cut line is located at Rf=0.25.

CHROMATOGRAPHY PROCEDURE:

Use Two-Strip Procedure (PROCEDURE 2A). Add 20% NaCl (0.8 to 1.0 ml) and distilled water (0.8 to 1.0 ml) to separate serum vials. Following radiopharmaceutical spotting, immediately place the orange strip in 20% NaCl and the light blue strip in distilled water and allow solvent to migrate to solvent front line. Remove strips, cut at cut lines into sections 1, 2, 3 and 4 and count for activity. Calculations are performed as outlined in PROCEDURE 2A.

CHROMATOGRAPHY STRIP ACTIVITY DISTRIBUTION :

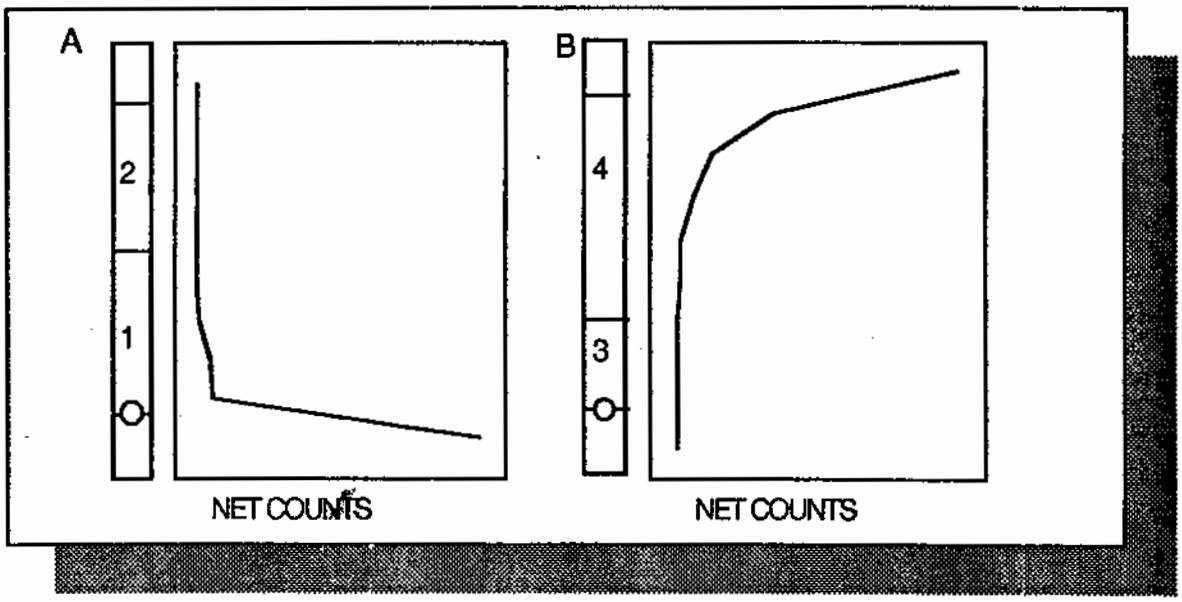


Figure 4-12. Strip activity distribution of Tc-99m Disofenin on (A) ITLC-SA paper eluted with 20% NaCl and (B) ITLC-SG paper eluted with distilled water.

REFERENCES: (9)

TECHNETIUM Tc-99m MEBROFENIN
(Tc-99m CHOLETEC™)

RADIOCHEMICAL IMPURITIES:

Technetium-99m pertechnetate and Tc-99m hyrolyzed reduced technetium.

QUALITY CONTROL METHOD:

CHROMATOGRAPHY SYSTEM:

Two separate chromatography systems are utilized to assess radiochemical purity.

System 1

ITLC-SA (0.7 x 6 cm) with 20% NaCl. Orange color-coded chromatography strip. Free Tc-99m pertechnetate migrates with the solvent front (Rf=1.0) whereas hyrolyzed reduced Tc-99m and Tc-99m Mebrofenin remain at the origin (Rf=0.0). The cut line is located at Rf=0.6.

System 2

ITLC-SG (0.7 x 6 cm) with Distilled Water. Light Blue color-coded chromatography strip. Free

Tc-99m pertechnetate and Tc-99m Mebrofenin migrate with the solvent front (Rf=1.0) whereas hyrolyzed reduced Tc-99m remains at the origin (Rf=0.0). The cut line is located at Rf=0.25.

CHROMATOGRAPHY PROCEDURE:

Use Two-Strip Procedure (PROCEDURE 2A). Add 20% NaCl (0.8 to 1.0 ml) and distilled water (0.8 to 1.0 ml) to separate serum vials. Following radiopharmaceutical spotting, immediately place the orange strip in 20% NaCl and the light blue strip in distilled water and allow solvent to migrate to solvent front line. Remove strips, cut at cut lines into sections 1, 2, 3 and 4 and count for activity. Calculations are performed as outlined in PROCEDURE 2A.

CHROMATOGRAPHY STRIP ACTIVITY DISTRIBUTION :

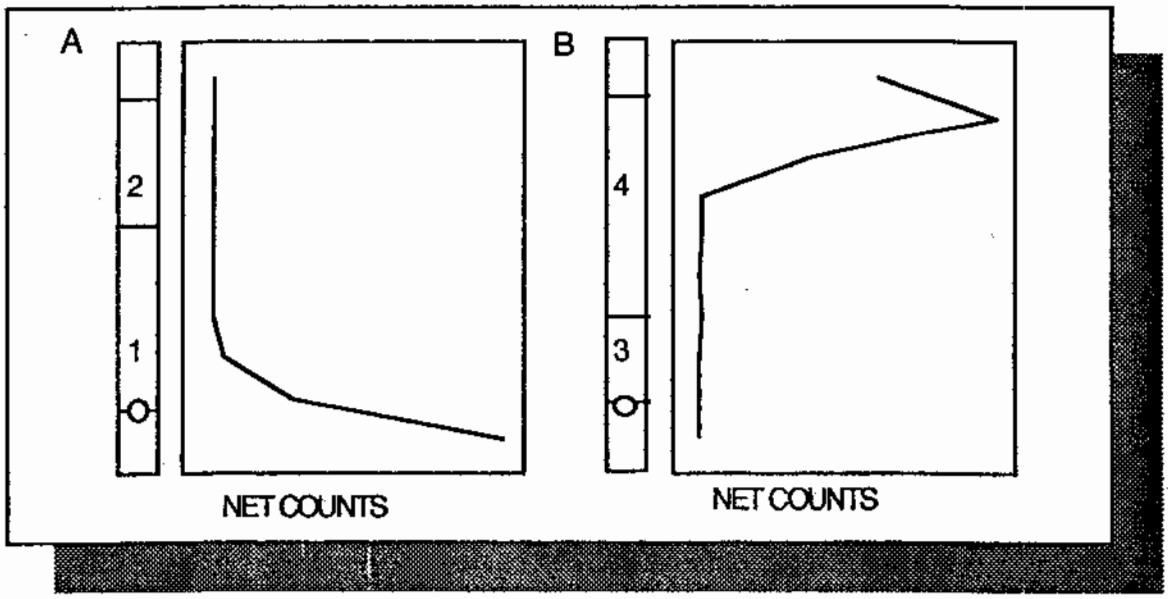


Figure 4-13. Strip activity distribution of Tc-99m Mebrofenin on (A) ITLC-SA paper eluted with 20% NaCl and (B) ITLC-SG paper eluted with distilled water.

TECHNETIUM Tc-99m EXAMETAZIME

(Tc-99m CERETEC™)

RADIOCHEMICAL IMPURITIES:

Technetium-99m pertechnetate, Tc-99m hyrolyzed reduced technetium and secondary less lipophilic Tc-99m complexes.

QUALITY CONTROL METHOD:

CHROMATOGRAPHY SYSTEM:

Three separate chromatography systems are utilized to assess radiochemical purity.

System 1

ITLC-SG (0.7 x 6 cm) with Normal Saline (0.9% NaCl). Purple color-coded chromatography strip. Free Tc-99m pertechnetate migrates with the solvent front (Rf=1.0) whereas other Tc-99m radiochemical components remain at the origin. The cut line is located at Rf=0.6.

System 2

ITLC-SG (0.7 x 6 cm) with Methy Ethyl Ketone (2-Butanone). Brown color-coded strip. With this system, the Tc-99m lipophilic component and free Tc-99m pertechnetate migrate with the solvent front (Rf=1.0) while hydrolyzed reduced Tc-99m and secondary less lipophilic Tc-99m components remain at the origin (Rf=0.0). The cut line is located at Rf=0.25

System 3

Whatman 31ET (0.7 x 6 cm) with 50% Aqueous Acetonitrile. Gray color-coded strip. With this system, hydrolyzed reduced Tc-99m remains at the origin (Rf=0.0) while other radiochemical components migrate with the solvent front (Rf=1.0). The cut line is located at Rf=0.2.

CHROMATOGRAPHY PROCEDURE:

Use Three-Strip Procedure (PROCEDURE 3). Add normal saline (0.8 to 1.0 ml), methyl ethyl ketone (0.8 to 1.0 ml) and 50% aqueous acetonitrile (0.8 to 1.0 ml) to separate serum vials. Following radiopharmaceutical spotting, immediately place the purple strip in normal saline, the brown strip in methyl ethyl ketone and the gray strip in 50% aqueous acetonitrile. Allow respective solvents to migrate to solvent front line of each specific strip. Remove strips, cut at cut lines into sections 1, 2, 3, 4, 5 and 6 and count each strip section for activity. Calculations are performed as outlined in PROCEDURE 3.

CHROMATOGRAPHY STRIP ACTIVITY DISTRIBUTION:

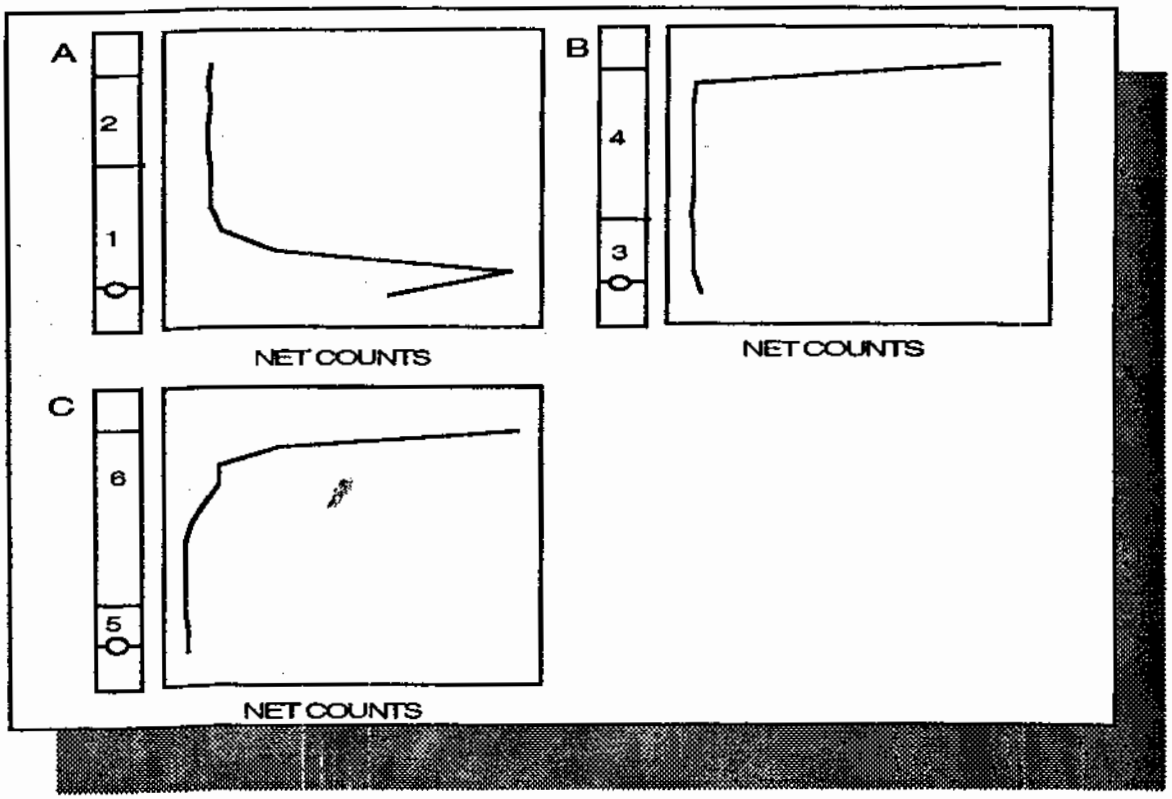


Figure 4-14. Strip activity distribution of TC-99m Exametazime on (A) ITLC-SG paper eluted with normal saline, (B) ITLC-SG paper eluted with methyl ethyl ketone and (C) Whatman 31ET paper eluted with 50% aqueous acetonitrile.

REFERENCES: (10) and (11)

ALTERNATE QUALITY CONTROL METHOD:

CHROMATOGRAPHY SYSTEM:

Whatman 17 paper (0.7 x 7 cm) with Ethyl Acetate. Gold color-coded chromatography strip. With this system, the Tc-99m lipophilic component migrates with the solvent front (Rf=1.0) while hydrolyzed reduced Tc-99m, free Tc-99m pertechnetate and secondary less lipophilic radiochemical components remain at the origin (Rf=0.0). The cut line is located at Rf=0.25.

CHROMATOGRAPHY PROCEDURE:

Use Single-Strip Procedure (PROCEDURE 1B). Add ethyl acetate (0.8 to 1.0 ml) to serum vial. Following radiopharmaceutical spotting, immediately place the gold strip in ethyl acetate and allow solvent to migrate to solvent front line. Remove strip, cut at cut line into sections 1 and 2

and count for activity. Calculations are performed as outlined in PROCEDURE 1B.

CHROMATOGRAPHY STRIP ACTIVITY DISTRIBUTION :

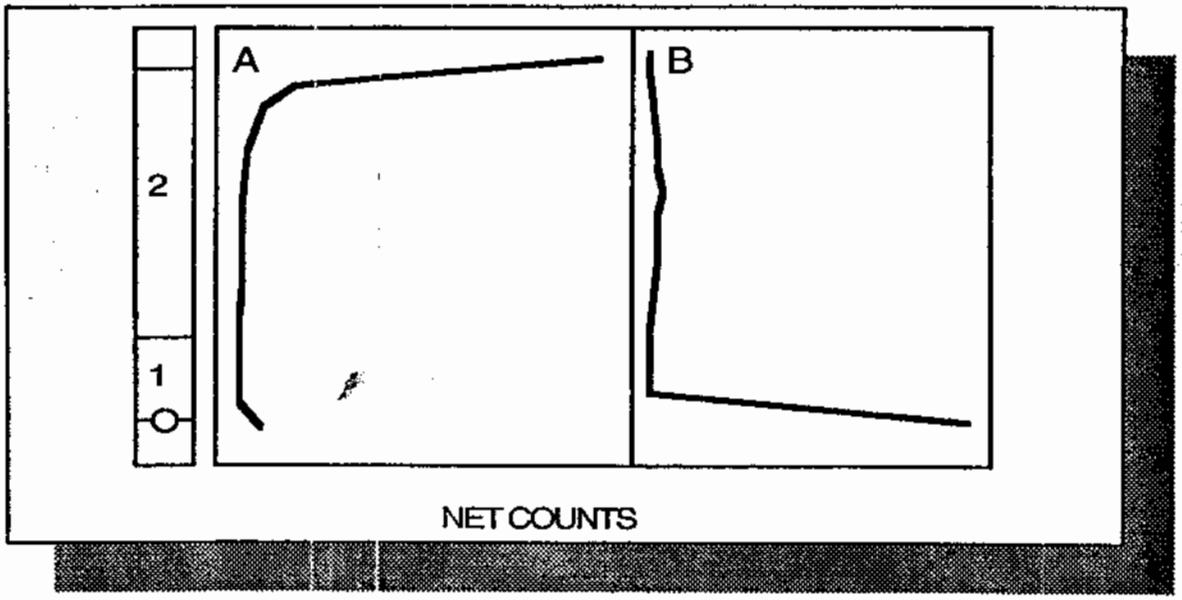


Figure 4-15. Strip activity distribution of (A) Tc-99m Exametazime on Whatman 17 paper eluted with ethyl acetate and (B) Tc-99m pertechnetate on Whatman 17 paper eluted with ethyl acetate.

REFERENCE: (12) and (13)

TECHNETIUM Tc-99m TEBOROXIME

(Tc-99m CARDIOTEC™)

RADIOCHEMICAL IMPURITIES:

Soluble technetium-99m contaminants, including Tc-99m pertechnetate, and Tc-99m hyrolyzed reduced technetium.

QUALITY CONTROL METHOD:

CHROMATOGRAPHY SYSTEM:

Two separate chromatography systems are utilized to assess radiochemical purity.

System 1

Whatman 31ET (0.7 x 7 cm) with normal saline (0.9% NaCl). Light purple color-coded

chromatography strip. Free Tc-99m pertechnetate and soluble Tc-99m contaminants migrate with the solvent front (Rf=1.0) whereas hyrolyzed reduced Tc-99m and Tc-99m Teboroxime remain at the origin (Rf=0.0). The cut line is located at Rf=0.6.

System 2

Whatman 31ET (0.7 x 7 cm) with normal saline/acetone (1:1). Light brown color-coded chromatography strip. Hyrolyzed reduced Tc-99m remains at the origin (Rf=0.0) while other Tc-99m radiochemical components, including Tc-99m pertechnetate and Tc-99m Teboroxime migrate with the solvent front (Rf=1.0). The cut line is located at Rf=0.3.

CHROMATOGRAPHY PROCEDURE:

Use Two-Strip Procedure (PROCEDURE 2A). Add normal saline (0.8 to 1.0 ml) and normal saline:acetone, in a 1:1 mixture (0.8 to 1.0 ml), to separate serum vials. Following radiopharmaceutical spotting, immediately place the light purple strip in normal saline and the light brown strip in normal saline:acetone and allow solvent to migrate to solvent front line. Remove strips, cut at cut lines into sections 1, 2, 3 and 4 and count for activity. Calculations are performed as outlined in PROCEDURE 2A.

CHROMATOGRAPHY STRIP ACTIVITY DISTRIBUTION :

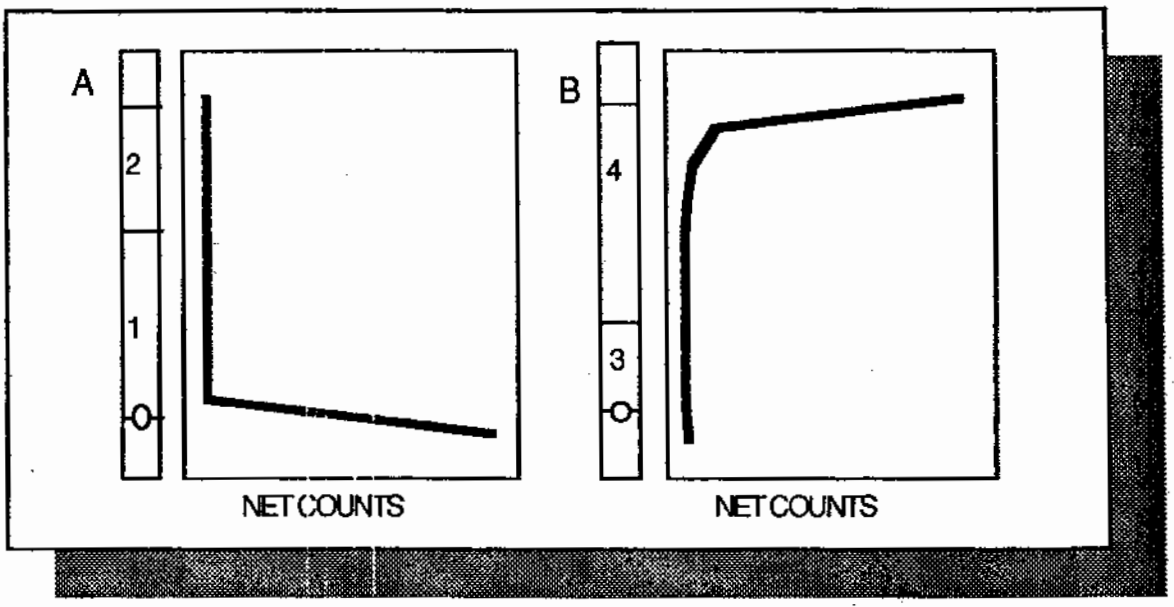


Figure 4-16. Strip activity distribution of Tc-99m Teboroxime on (A) Whatman 31ET paper eluted with Normal Saline and on (B) Whatman 31ET paper eluted with Normal Saline/Acetone (1:1).

REFERENCES: (13) and (14)

TECHNETIUM Tc-99m SESTAMIBI

(Tc-99m CARDIOLITE™, Tc-99m MIRALUMA™)

RADIOCHEMICAL IMPURITIES:

Soluble technetium-99m contaminants, including Tc-99m pertechnetate, and Tc-99m hyrolyzed reduced technetium.

QUALITY CONTROL METHOD:

CHROMATOGRAPHY SYSTEM

Whatman 31 paper (0.7 x 7 cm) with Ethyl Acetate. Pink color-coded chromatography strip. With this system, Tc-99m Sestamibi migrates from the origin (Rf=0.6-1.0) while hydrolyzed reduced Tc-99m and free Tc-99m pertechnetate remain at the origin (Rf=0.0). The cut line is located at Rf=0.25.

CHROMATOGRAPHY PROCEDURE:

Use Single-Strip Procedure (PROCEDURE 1B). Add ethyl acetate (0.8 to 1.0 ml) to serum vial. Following radiopharmaceutical spotting, immediately place the pink strip in ethyl acetate and allow solvent to migrate to solvent front line. Remove strip, cut at cut line into sections 1 and 2 and count for activity. Calculations are performed as outlined in PROCEDURE 1B.

CHROMATOGRAPHY STRIP ACTIVITY DISTRIBUTION:

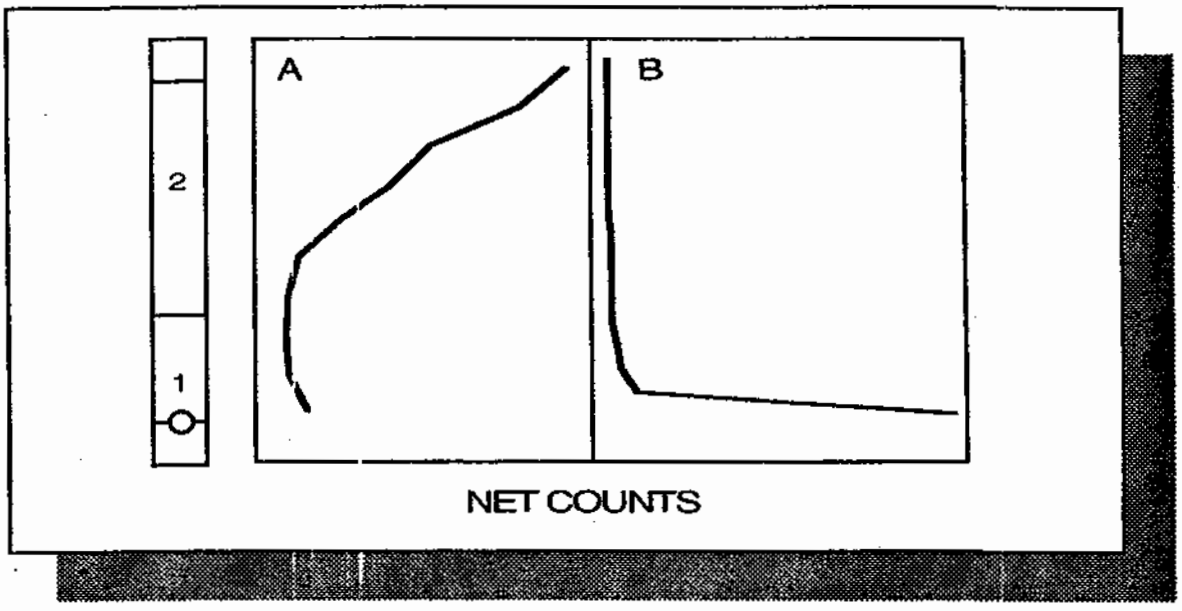


Figure 4-17. Strip activity distribution of (A) Tc-99m Sestamibi on Whatman 31ET paper eluted with ethyl acetate and (B) Tc-99m pertechnetate on Whatman 31ET paper eluted with ethyl acetate.

REFERENCE: (13)

ALTERNATE QUALITY CONTROL METHOD:

Use Single-Strip Chromatography Procedure Method 1B.

CHROMATOGRAPHY SYSTEM

Gelman Solvent Saturation Pads (0.7 x 8 cm) with chloroform/tetrahydrofuran (1:1). With this system, Tc-99m Sestamibi moves with the solvent to the upper half of the strip (Rf=0.5-1.0) whereas hydrophilic Tc-99m components and hyrolyzed reduced Tc-99m remains at the origin (Rf=0.0).

REFERENCE: (15)

TECHNETIUM Tc-99m MERTIATIDE

(Tc-99m MAG3, TECHESCAN MAG3™)

RADIOCHEMICAL IMPURITIES:

Soluble technetium-99m impurities, including Tc-99m pertechnetate, and Tc-99m hyrolyzed reduced technetium.

QUALITY CONTROL METHOD:

CHROMATOGRAPHY SYSTEM:

Two separate chromatography systems are utilized to assess radiochemical purity.

System 1

Gelman Solvent Saturation Pads (0.7 x 7 cm) with chloroform/acetone/tetrahydrofuran (1:1:2). Lime color-coded chromatography strip. Free Tc-99m pertechnetate and soluble Tc-99m impurities move with the solvent to the upper half of the strip (Rf=0.5-1.0) whereas hyrolyzed reduced Tc-99m and Tc-99m MAG3 remain at the origin (Rf=0.0). The cut line is located at Rf=0.33.

System 2

Gelman Solvent Saturation Pads (0.7 x 7 cm) with normal saline (0.9% NaCl). Peach color-coded chromatography strip. Hyrolyzed reduced Tc-99m remains at the origin (Rf=0.0) while other radiochemical components migrate with the solvent front (Rf=1.0). The cut line is located at Rf=0.25.

CHROMATOGRAPHY PROCEDURE:

Use Two-Strip Procedure (PROCEDURE 2A). Add chloroform:acetone:tetrahydrofuran mixture

(0.8 to 1.0 ml) and normal saline (0.8 to 1.0 ml), to separate serum vials. Following radiopharmaceutical spotting, immediately place the lime strip in chloroform: acetone:tetrahydrofuran and the peach strip in normal saline and allow solvent to migrate to solvent front line. Remove strips, cut at cut lines into sections 1, 2, 3 and 4 and count for activity. Calculations are performed as outlined in PROCEDURE 2A.

CHROMATOGRAPHY STRIP ACTIVITY DISTRIBUTION :

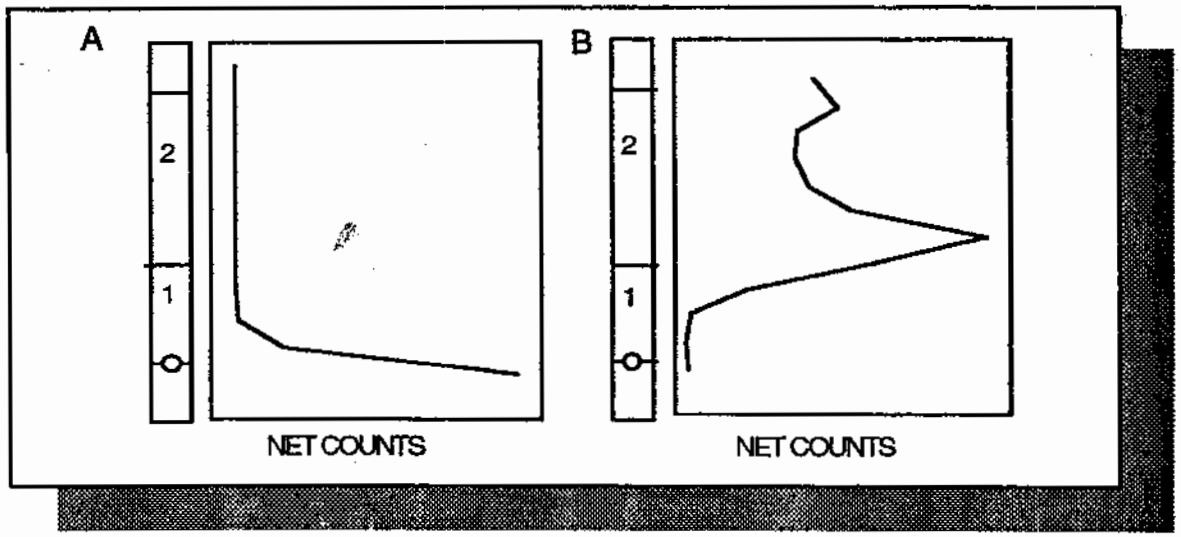


Figure 4-18. Strip activity distribution of (A) Tc-99m MAG3 on Solvent Saturation Pad eluted with chloroform/acetone/tetrahyfrofuran (1:1:2) and (B) Tc-99m pertechnetate on Solvent Saturation Pad eluted with chloroform/acetone/tetrahyfrofuran (1:1:2).

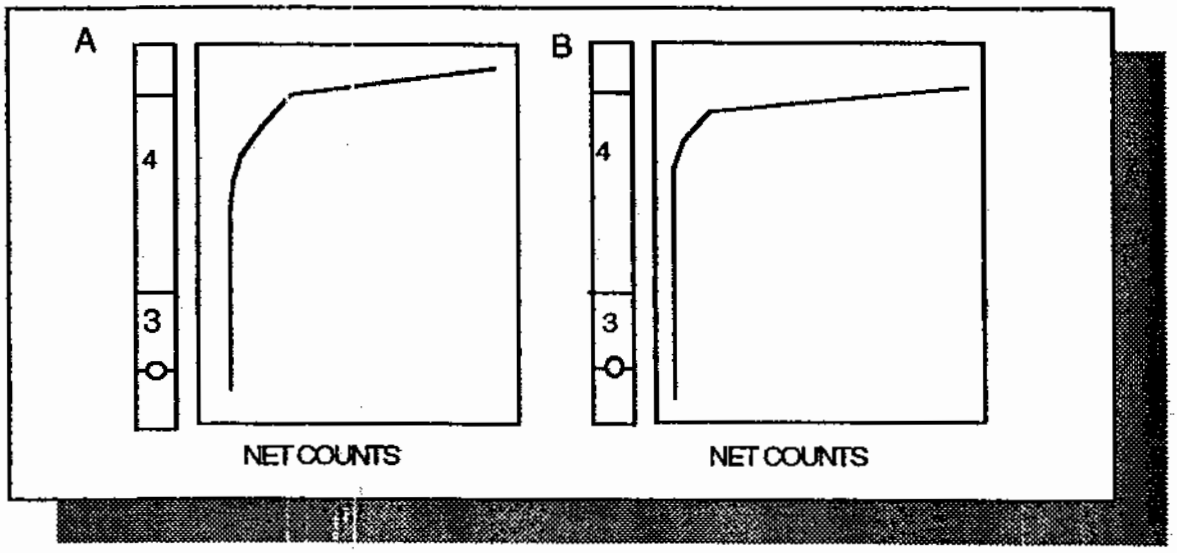


Figure 4-19. Strip activity distribution of (A) Tc-99m MAG3 on Solvent Saturation Pad eluted with normal saline and (B) Tc-99m pertechnetate on Solvent Saturation Pad eluted with normal saline.

REFERENCES: (16)

ALTERNATE PROCEDURE

RADIOCHEMICAL IMPURITIES:

Soluble technetium-99m impurities, including Tc-99m pertechnetate, and Tc-99m hyrolyzed reduced technetium.

QUALITY CONTROL METHOD:

CHROMATOGRAPHY SYSTEM:

Two separate chromatography systems are utilized to assess radiochemical purity.

System 1

Whatman 1 paper (0.7 x 6 cm) with methylene chloride:acetone (1:1). Blue color-coded chromatography strip. Free Tc-99m pertechnetate and soluble Tc-99m impurities move with the solvent front (Rf= 1.0) whereas hyrolyzed reduced Tc-99m and Tc-99m MAG3 remain at the origin (Rf=0.0). The cut line is located at Rf=0.5.

System 2

Gelman ITLC-SG (0.7 x 6 cm) with distilled water. Light yellow color-coded chromatography strip. Hyrolyzed reduced Tc-99m remains at the origin (Rf=0.0) while other radiochemical components migrate with the solvent front (Rf=1.0). The cut line is located at Rf=0.25.

CHROMATOGRAPHY PROCEDURE:

Use Two-Strip Procedure (PROCEDURE 2A). Add methylene chloride:acetone (1:1) mixture (0.8 to 1.0 ml) and distilled water (0.8 to 1.0 ml), to separate serum vials. Following radiopharmaceutical spotting, immediately place the blue strip in methylene chloride:acetone and the light yellow strip in distilled water and allow solvent to migrate to solvent front line. Remove strips, cut at cut lines into sections 1, 2, 3 and 4 and count for activity. Calculations are performed as outlined in PROCEDURE 2A.

CHROMATOGRAPHY STRIP ACTIVITY DISTRIBUTION :

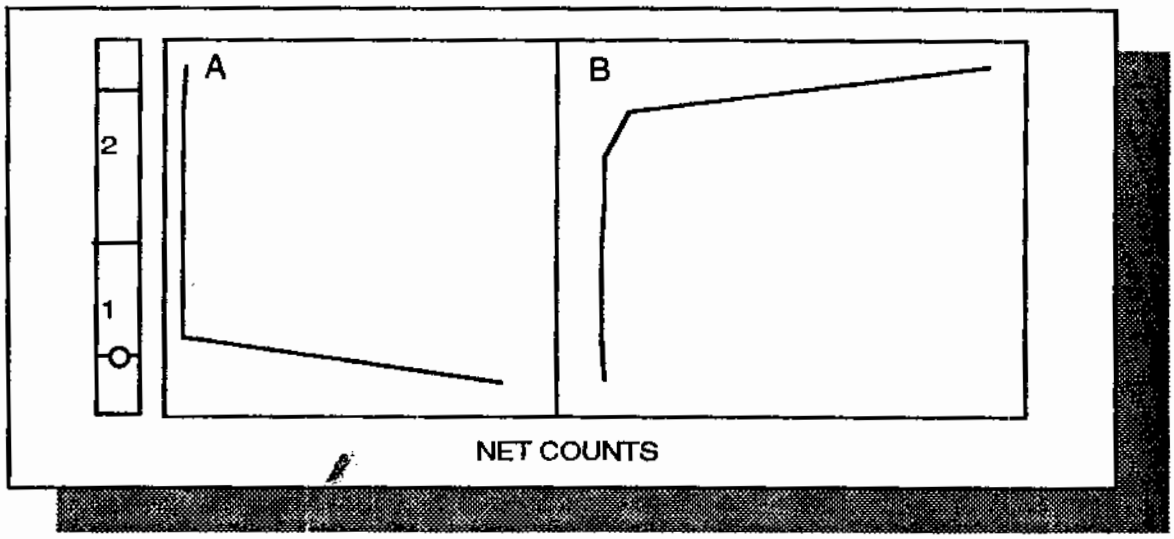


Figure 4-20. Strip activity distribution of (A) Tc-99m MAG3 on Whatman 1 paper eluted with methylene chloride:acetone (1:1) and (B) Tc-99m pertechnetate on Gelman ITLC-SG eluted with methylene chloride:acetone (1:1) .

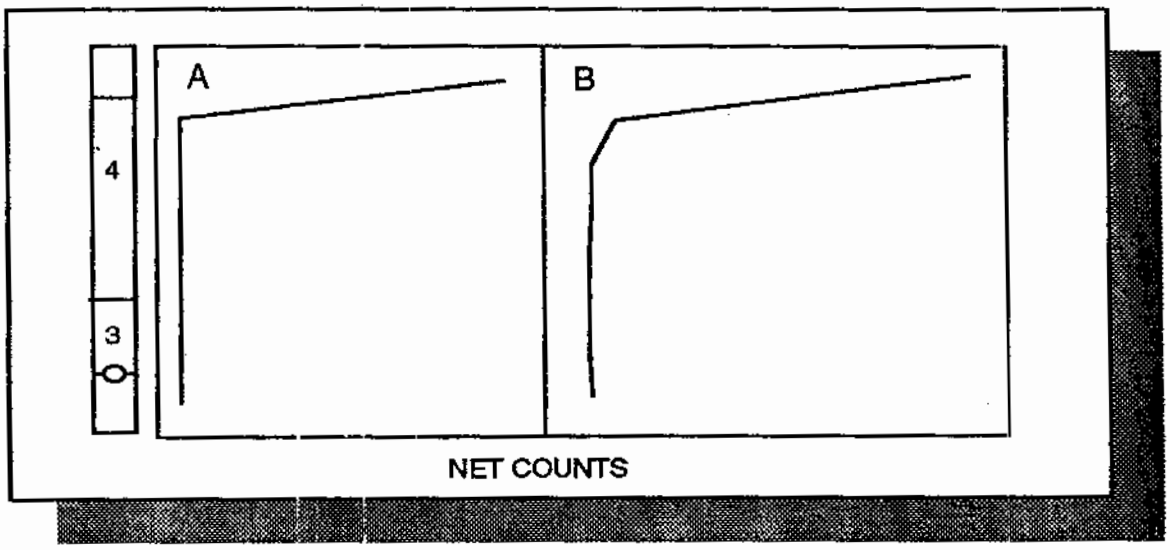


Figure 4-21. Strip activity distribution of (A) Tc-99m MAG3 on Gelman ITLC-SG eluted with distilled water and (B) Tc-99m pertechnetate on Gelman ITLC-SG eluted with distilled water .

REFERENCES: (25)

TECHNETIUM Tc-99m MONOCLONAL ANTIBODIES AND FRAGMENTS

(CEA-SCAN™, VERLUMA™)

RADIOCHEMICAL IMPURITIES:

Technetium-99m pertechnetate.

QUALITY CONTROL METHOD:

CHROMATOGRAPHY SYSTEM:

ITLC-SG chromatography strip (0.7 x 6 cm) with Normal Saline. Dark green color-coded chromatography strip. Technetium-99m monoclonal antibodies remain at the origin while free technetium-99m pertechnetate migrates with the solvent front (Rf=1.0). The cut line is located at Rf=0.5.

CHROMATOGRAPHY PROCEDURE:

Use Single-Strip Procedure (PROCEDURE 1A). Add normal saline (0.8 to 1.0 ml) to serum vial. Following radiopharmaceutical spotting, immediately place the dark green strip in normal saline and allow solvent to migrate to solvent front line. Remove strip, cut at cut line into sections 1 and 2 and count for activity. Calculations are performed as outlined in PROCEDURE 1A.

CHROMATOGRAPHY STRIP ACTIVITY DISTRIBUTION :

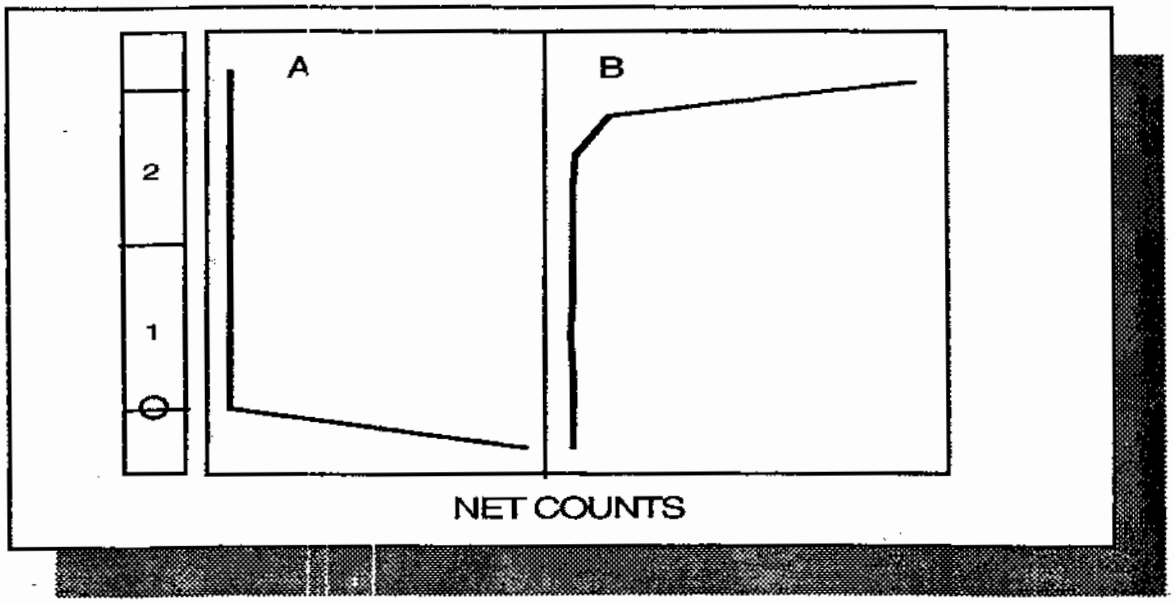


Figure 4-22. Strip activity distribution of (A) Tc-99m monoclonal antibody and (B) Tc-99m pertechnetate on ITLC-SG with 0.9% NaCl.

REFERENCES: (17)

TECHNETIUM-99m BICISATE
(NEUROLITE™)

RADIOCHEMICAL IMPURITIES:

Free Tc-99m pertechnetate and Tc-99m hyrolyzed reduced technetium.

QUALITY CONTROL METHOD:

CHROMATOGRAPHY SYSTEM:

Whatman 17 paper (0.7 x 7 cm) with Ethyl Acetate. Gold color-coded chromatography strip. With this system, Tc-99m Bicisate migrates close to the solvent front (Rf=0.8-1.0) while hydrolyzed reduced Tc-99m and free Tc-99m pertechnetate remain at the origin (Rf=0.0). The cut line is located at Rf=0.25.

CHROMATOGRAPHY PROCEDURE:

Use Single-Strip Procedure (PROCEDURE 1B). Add ethyl acetate (0.8 to 1.0 ml) to serum vial. Following radiopharmaceutical spotting, immediately place the gold strip in ethyl acetate and allow solvent to migrate to solvent front line. Remove strip, cut at cut line into sections 1 and 2 and count for activity. Calculations are performed as outlined in PROCEDURE 1B.

CHROMATOGRAPHY STRIP ACTIVITY DISTRIBUTION :

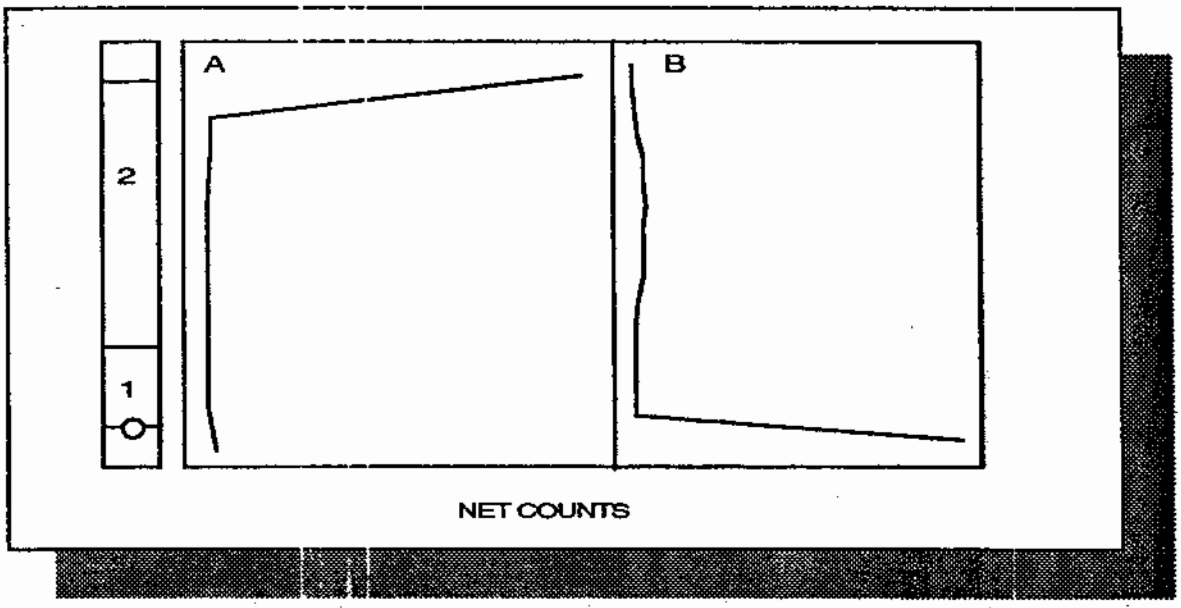


Figure 4-23. Strip activity distribution of (A) Tc-99m Bicisate on Whatman 17 paper eluted with ethyl acetate and (B) Tc-99m pertechnetate on Whatman 17 paper eluted with ethyl acetate.

REFERENCES: (18)

TECHNETIUM-99m TETROFOSMIN
(MYOVIEW™)

RADIOCHEMICAL IMPURITIES:

Free Tc-99m pertechnetate and Tc-99m hyrolyzed reduced technetium.

QUALITY CONTROL METHOD:

CHROMATOGRAPHY SYSTEM:

Whatman 1 chromatography strip (0.7 x 6 cm) with ethyl acetate. Teal color-coded chromatography strip. With this system, Tc-99m Tetrofosmin migrates with an Rf value of approximately 0.8-1.0 while free Tc-99m pertechnetate and hydrolyzed reduced Tc-99m remain at the origin (Rf=0.0). The cut line is located at Rf=0.25.

CHROMATOGRAPHY PROCEDURE:

Use Single-Strip Procedure (PROCEDURE 1B). Add ethyl acetate (0.8 to 1.0 ml) to serum vial. Following radiopharmaceutical spotting, immediately place the teal strip in solvent until solvent migrates to solvent front line. Remove strip, cut at cut line into sections 1 and 2 and count for activity. Calculations are performed as outlined in PROCEDURE 1B.

CHROMATOGRAPHY STRIP ACTIVITY DISTRIBUTION:

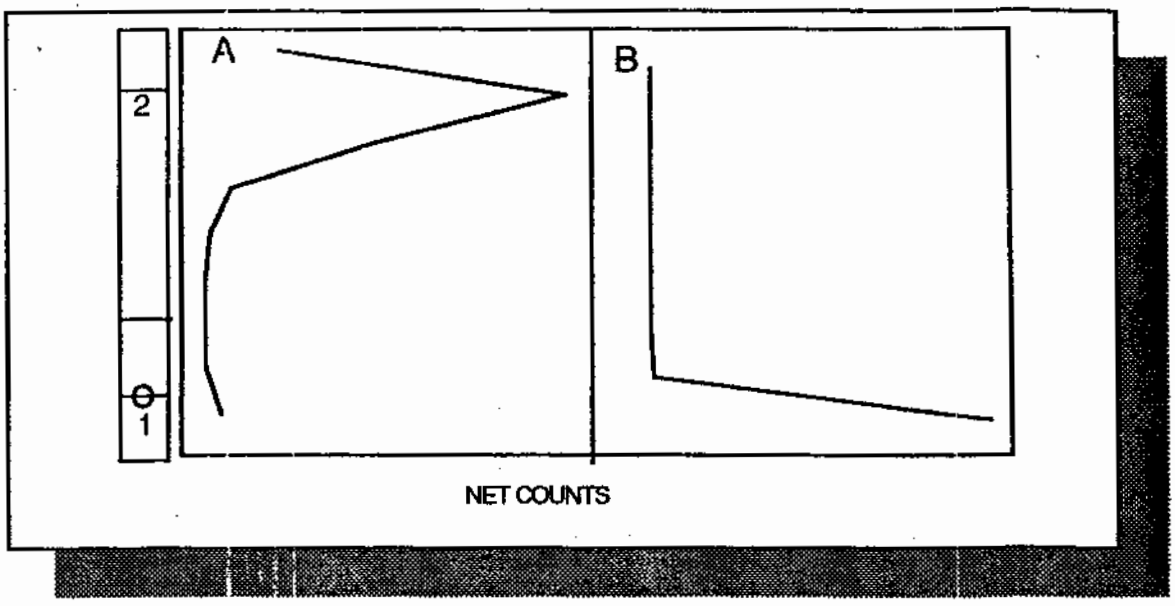


Figure 4-24. Strip activity distribution of (A) Tc-99m Tetrofosmin on Whatman 1paper eluted with ethyl acetate and (B) Tc-99m pertechnetate on Whatman 1paper eluted with ethyl acetate.

REFERENCES: (26)

INDIUM In-111 MONOCLONAL ANTIBODIES
(ONCOSCINT™, PROSTASCINT™)

RADIOCHEMICAL IMPURITIES:

Unbound and non-specific bound In-111

QUALITY CONTROL METHOD:

CHROMATOGRAPHY SYSTEM:

ITLC-SG chromatography strip (0.7 x 6 cm) with Normal Saline. Dark green color-coded chromatography strip. In-111 monoclonal antibodies remain at the origin while unbound or non-specific bound In-111, as the DTPA complex, migrates with the solvent front (Rf=1.0). The cut line is located at Rf=0.5. Prior to spotting, the In-111 antibody preparation is challenged with DTPA (0.05M) in order to complex unbound In-111.

CHROMATOGRAPHY PROCEDURE:

Use Single-Strip Procedure (PROCEDURE 1C). Add normal saline (0.8 to 1.0 ml) to serum vial. Add one drop of 0.05 M DTPA solution to one drop of radiopharmaceutical. Spot the radiopharmaceutical-DTPA mixture at the origin line and immediately place the dark green strip in normal saline and allow solvent to migrate to solvent front line. Remove strip, cut at cut line into sections 1 and 2 and count for activity. Calculations are performed as outlined in PROCEDURE 1C.

CHROMATOGRAPHY STRIP ACTIVITY DISTRIBUTION:

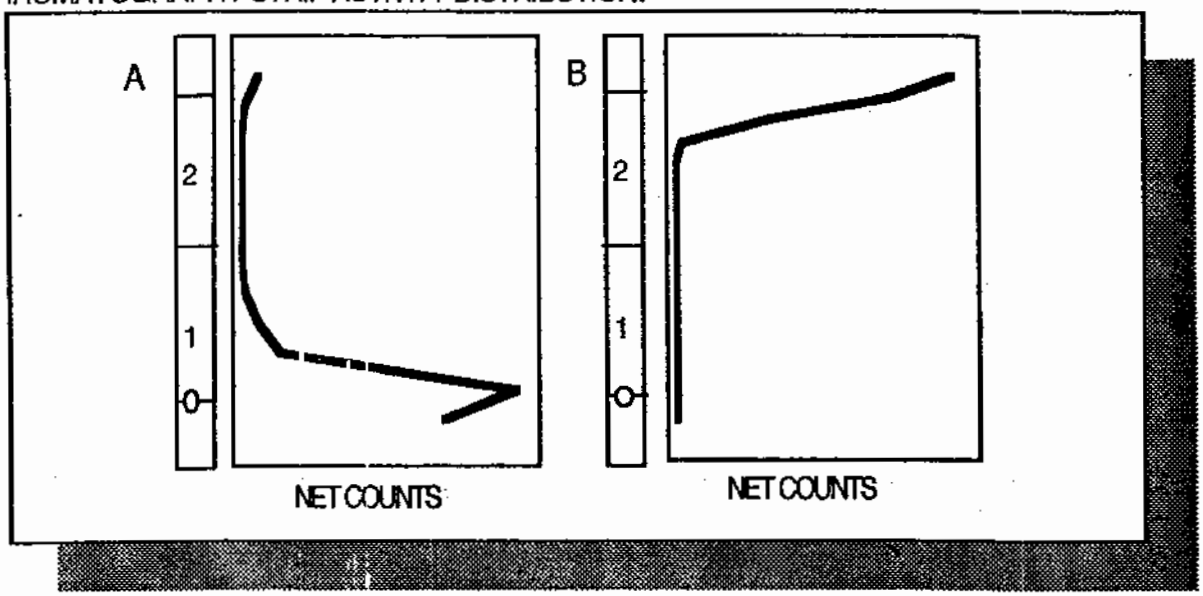


Figure 4-25. Strip activity distribution of (A) In-111 monoclonal antibody on ITLC-SG paper eluted with normal saline and (B) In-111 complexed to DTPA on ITLC-SG eluted with normal saline.

REFERENCES: (20)

INDIUM In-111 OCTREOTIDE
(OCTREOSCAN™)

RADIOCHEMICAL IMPURITIES:

Unbound and non-specific bound In-111

QUALITY CONTROL METHOD:

CHROMATOGRAPHY SYSTEM:

ITLC-SG chromatography strip (0.7 x 6 cm) with Normal Saline. Dark green color-coded chromatography strip. In-111 Octreotide remains at the origin while unbound or non-specific bound In-111, as the DTPA complex, migrates with the solvent front (Rf=1.0). The cut line is located at Rf=0.5. Prior to spotting, the In-111 octreotide preparation is challenged with DTPA (0.05M) in order to complex unbound In-111.

CHROMATOGRAPHY PROCEDURE:

Use Single-Strip Procedure (PROCEDURE 1C). Add normal saline (0.8 to 1.0 ml) to serum vial. Add one drop of 0.05 M DTPA solution to one drop of radiopharmaceutical. Spot the radiopharmaceutical-DTPA mixture at the origin line and immediately place the dark green strip in normal saline and allow solvent to migrate to solvent front line. Remove strip, cut at cut line into sections 1 and 2 and count for activity. Calculations are performed as outlined in PROCEDURE 1C.

CHROMATOGRAPHY STRIP ACTIVITY DISTRIBUTION:

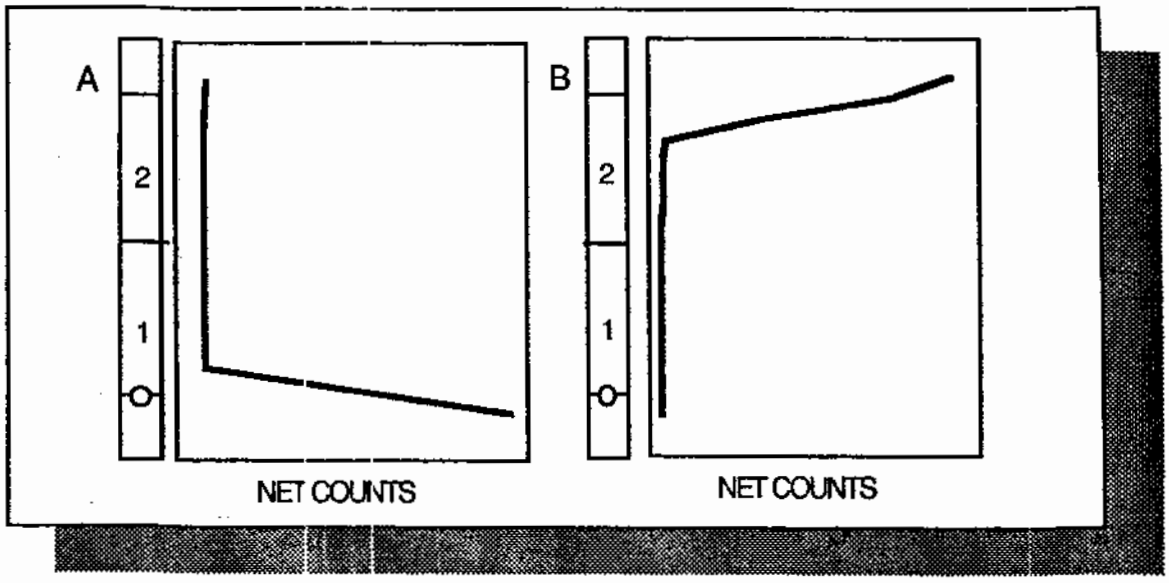


Figure 4-26. Strip activity distribution of (A) In-111 Octreotide and (B) In-111 complexed to DTPA on chromatography system consisting of ITLC-SG paper eluted with normal saline.

REFERENCES: (21)

IODINE I-131 MONOCLONAL ANTIBODIES

RADIOCHEMICAL IMPURITIES:

Free I-131 sodium iodide.

QUALITY CONTROL METHOD:

CHROMATOGRAPHY SYSTEM:

ITLC-SG chromatography strip (0.7 x 6 cm) with Normal Saline. Dark green color-coded chromatography strip. I-131 monoclonal antibodies remain at the origin while unbound I-131 sodium iodide migrates with the solvent front (Rf=1.0). The cut line is located at Rf=0.5.

CHROMATOGRAPHY PROCEDURE:

Use Single-Strip Procedure (PROCEDURE 1A). Add normal saline (0.8 to 1.0 ml) to serum vial. Following radiopharmaceutical spotting, immediately place the dark green strip in normal saline and allow solvent to migrate to solvent front line. Remove strip, cut at cut line into sections 1 and 2 and count for activity. Calculations are performed as outlined in PROCEDURE 1A.

CHROMATOGRAPHY STRIP ACTIVITY DISTRIBUTION:

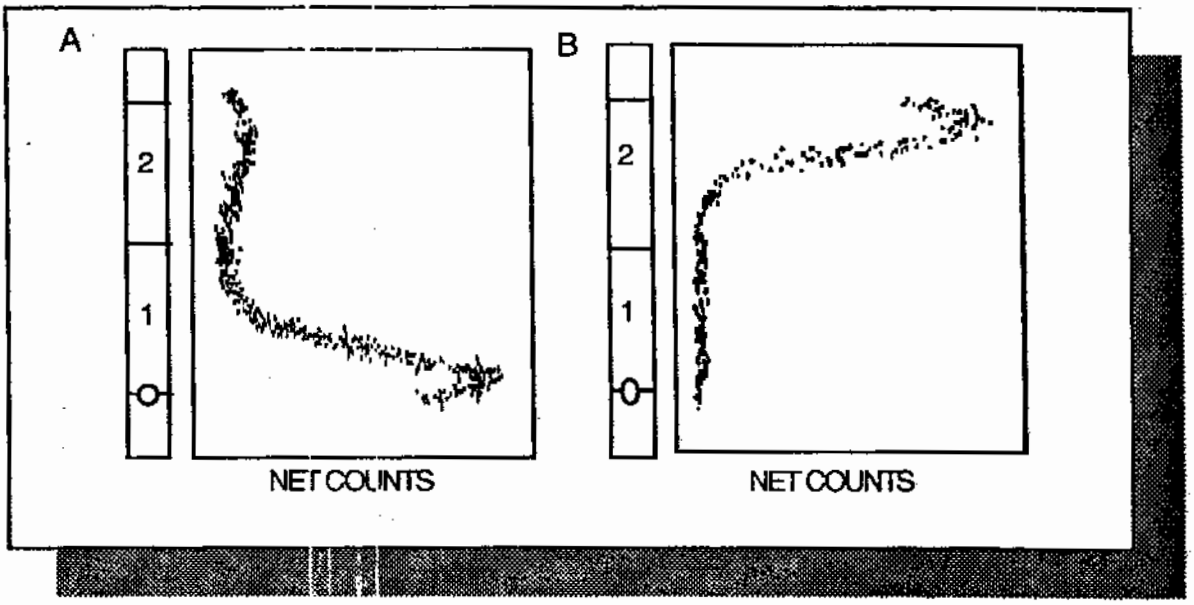


Figure 4-27. Strip activity distribution of (A) I-131 monoclonal antibody on ITLC-SG paper eluted with normal saline and (B) I-131 sodium iodide on ITLC-SG eluted with normal saline.

REFERENCES: (22)

IODOHIPPURATE SODIUM I-131 INJECTION

(IODOHIPPURATE™, HIPPURAN™, HIPPUTOPE™)

RADIOCHEMICAL IMPURITIES:

Free I-131 sodium iodide.

QUALITY CONTROL METHOD:

CHROMATOGRAPHY SYSTEM:

ITLC-SA chromatography strip (0.7 x 6 cm) with chloroform/glacial acetic acid (1.00:0.05 v/v). Orange color-coded chromatography strip. I-131 Iodohippurate migrates with or close to the solvent front (Rf=0.8-1.0) while free I-131 sodium iodide remains at the origin (Rf=0.0). The chromatography strip should be cut at Rf=0.2.

CHROMATOGRAPHY PROCEDURE:

Use Single-Strip Procedure (PROCEDURE 1B). Add chloroform:glacial acetic acid mixture (0.8 to 1.0 ml) to serum vial. Following radiopharmaceutical spotting, immediately place the orange strip in mixture and allow solvent to migrate to solvent front line. Remove strip, cut at cut line into sections 1 and 2 and count for activity. Calculations are performed as outlined in PROCEDURE 1B.

CHROMATOGRAPHY STRIP ACTIVITY DISTRIBUTION:

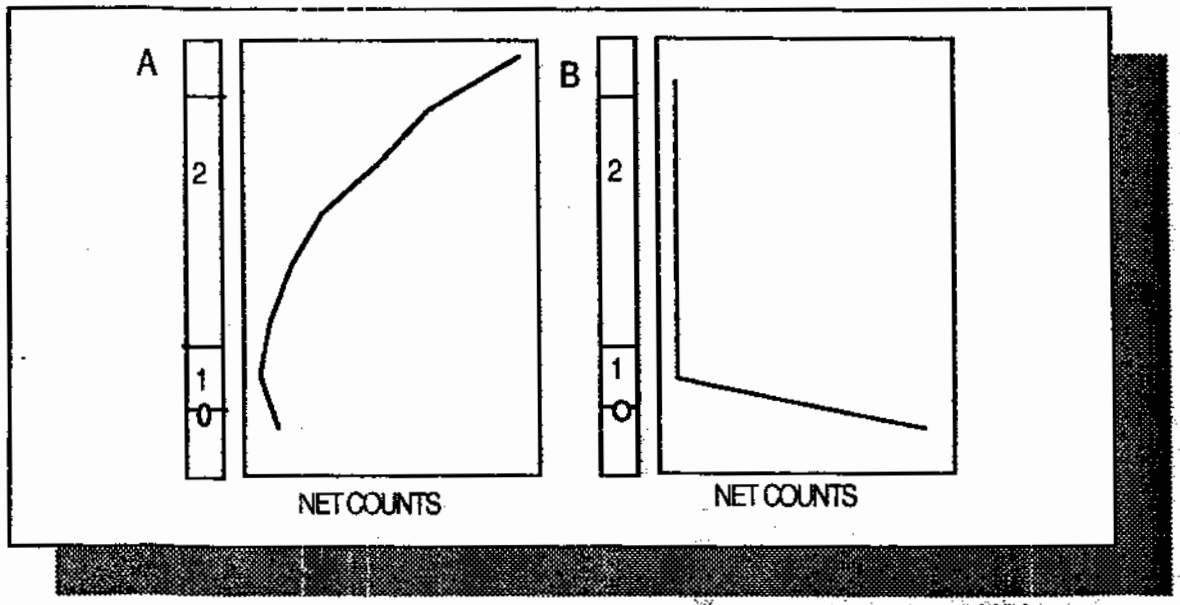


Figure 4-28. Strip activity distribution of (A) I-131 iodohippurate on ITLC-SA paper eluted with chloroform/glacial acetic acid (1.00:0.05) and (B) I-131 sodium iodide on ITLC-SA paper eluted with chloroform/glacial acetic acid (1.00:0.05).

REFERENCES: (23)

IODINATED I-125 ALBUMIN INJECTION
(I-125 RISA, I-125 RADIOIODINATED SERUM ALBUMIN)

RADIOCHEMICAL IMPURITIES:

Free I-125 sodium iodide.

QUALITY CONTROL METHOD:

CHROMATOGRAPHY SYSTEM:

ITLC-SG chromatography strip (0.7 x 6 cm) with methanol. Light green color-coded chromatography strip. Unbound I-125 sodium iodide migrates with the solvent front (Rf=1.0) while I-125 RISA remains at the origin (Rf=0.0). The cut line is located at Rf=0.5.

CHROMATOGRAPHY PROCEDURE:

Use Single-Strip Procedure (PROCEDURE 1A). Add methanol (0.8 to 1.0 ml) to serum vial. Following radiopharmaceutical spotting, immediately place the light green strip in methanol and allow solvent to migrate to solvent front line. Remove strip, cut at cut line into sections 1 and 2 and count for activity. Ca'culations are performed as outlined in PROCEDURE 1A.

CHROMATOGRAPHY STRIP ACTIVITY DISTRIBUTION:

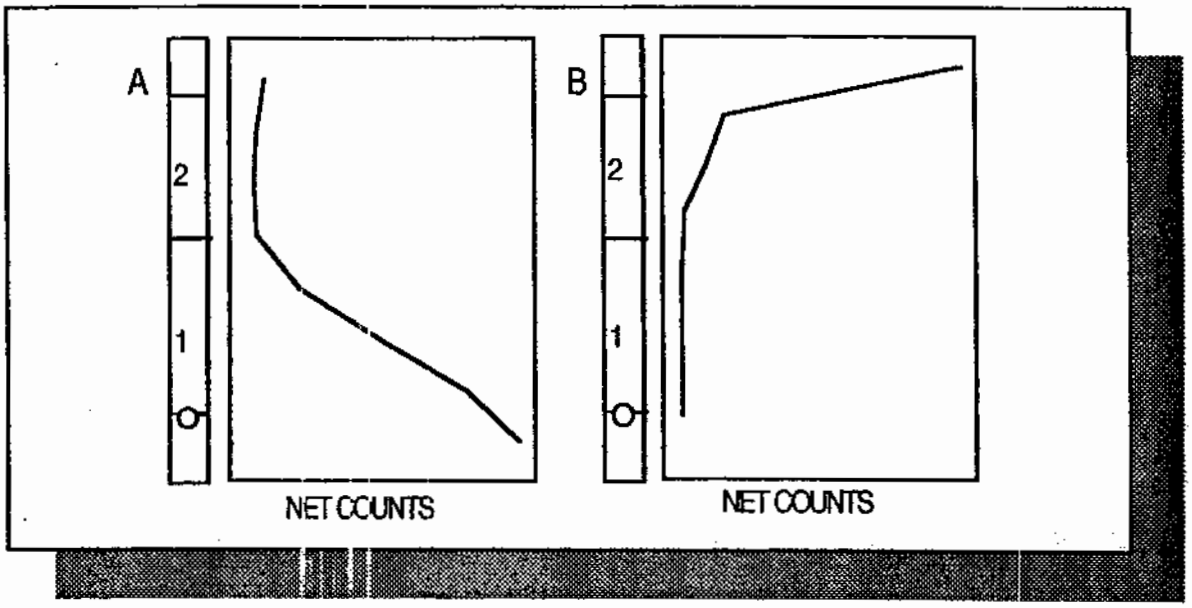


Figure 4-29. Strip activity distribution of (A) I-125 RISA on ITLC-SG paper eluted with methanol and (B) I-125 sodium iodide on ITLC-SG paper eluted with methanol.

REFERENCES: (23)

IOFETAMINE HCL I-123 INJECTION

(I-123 IMP, I-123 IODOAMPHETAMINE, SPECTAMINE™)

RADIOCHEMICAL IMPURITIES:

Free I-123 sodium iodide.

QUALITY CONTROL METHOD:

CHROMATOGRAPHY SYSTEM:

ITLC-SA chromatography strip (0.7 x 6 cm) with 10% Sodium Chloride. Orange color-coded chromatography strip. Unbound I-123 sodium iodide migrates with the solvent front (Rf=1.0) while I-123 Iodoamphetamine remains at the origin (Rf=0.0). The cut line is located at Rf=0.6.

CHROMATOGRAPHY PROCEDURE:

Use Single-Strip Procedure (PROCEDURE 1A). Add 10% NaCl (0.8 to 1.0 ml) to serum vial. Following radiopharmaceutical spotting, immediately place the orange strip in 10% NaCl and allow solvent to migrate to solvent front line. Remove strip, cut at cut line into sections 1 and 2 and count for activity. Calculations are performed as outlined in PROCEDURE 1A.

CHROMATOGRAPHY STRIP ACTIVITY DISTRIBUTION:

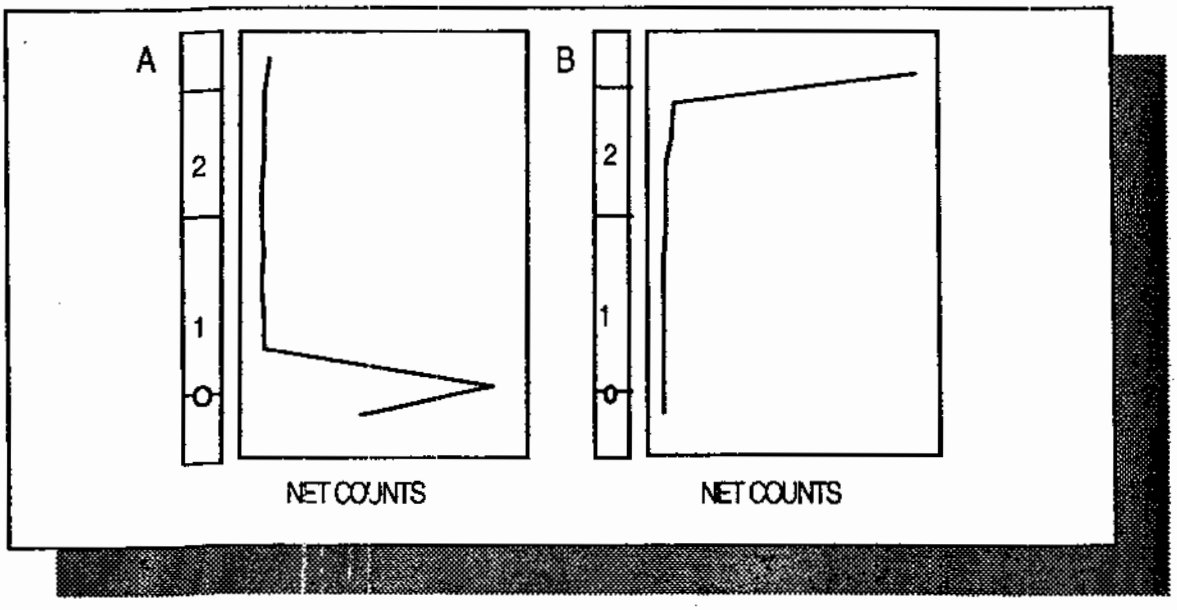


Figure 4-30. Strip activity distribution of (A) I-123 Iodoamphetamine on ITLC-SA paper eluted with 10% NaCl and (B) I-123 sodium iodide on ITLC-SA paper eluted with 10% NaCl.

REFERENCES: (24)

APPENDIX A

SUMMARY OF CHROMATOGRAPHY SYSTEMS

SUMMARY CHART OF CHROMATOGRAPHY SYSTEMS FOR RADIOPHARMACEUTICALS

AGENT	MEDIA	SOLVENT	STRIP SIZE	RF CUT LINE
Tc-99m Pertechnetate	Whatman 31ET	Acetone	0.7 x 6 cm	0.6
Tc-99m Pertechnetate	ITLC-SG	DI Water	0.7 x 6 cm	0.5
Tc-99m Sulfur Colloid	Whatman 31ET	Acetone	0.7 x 6 cm	0.6
Tc-99m Albumin Colloid	Whatman 31ET	Acetone	0.7 x 6 cm	0.6
Tc-99m Antimony Trisulfide Colloid	ITLC-SG	0.9%NaCl	0.7 x 6 cm	0.5
Tc-99m MAA	Whatman 31ET	Acetone	0.7 x 6 cm	0.6
Tc-99m DTPA	Whatman 31ET	Acetone	0.7 x 6 cm	0.6
	ITLC-SG	DI Water	0.7 x 6 cm	0.4
Tc-99m Pyrophosphate	Whatman 31ET	Acetone	0.7 x 6 cm	0.6
	ITLC-SG	DI Water	0.7 x 6 cm	0.4
Tc-99m MDP	Whatman 31ET	Acetone	0.7 x 6 cm	0.6
	ITLC-SG	DI Water	0.7 x 6 cm	0.4
Tc-99m HMDP	Whatman 31ET	Acetone	0.7 x 6 cm	0.6
	ITLC-SG	DI Water	0.7 x 6 cm	0.4

AGENT	MEDIA	SOLVENT	STRIP SIZE	RF CUT LINE
Tc-99m Gluco	Whatman 31ET	Acetone	0.7 x 6 cm	0.6
	ITLC-SG	DI Water	0.7 x 6 cm	0.4
Tc-99m HSA	ITLC-SG	Acetone	0.7 x 6 cm	0.5
	Whatman 31ET	DI Water	0.7 x 6 cm	0.25
Tc-99m DMSA	ITLC-SA	Acetone	0.7 x 6 cm	0.5
Tc-99m Disofenin	ITLC-SA	20% NaCl	0.7 x 6 cm	0.6
	ITLC-SG	DI Water	0.7 x 6 cm	0.25
Tc-99m Mebrofenin	ITLC-SA	20% NaCl	0.7 x 6 cm	0.6
	ITLC-SG	DI Water	0.7 x 6 cm	0.25
Tc-99m Exametazime	ITLC-SG	0.9% NaCl	0.7 x 6 cm	0.6
	ITLC-SG	MEK	0.7 x 6 cm	0.25
	Whatman 31ET	50% Aque Acetonitrile	0.7 x 6 cm	0.2
Tc-99m Exametazime	Whatman 17	Ethyl Acetate	0.7 x 7 cm	0.25
Tc-99m Teboroxime	Whatman 31ET	0.9% NaCl	0.7 x 7 cm	0.6
	Whatman 31ET	0.9% NaCl/ Acetone	0.7 x 7 cm	0.3
Tc-99m Sestamibi	Whatman 31ET	Ethyl Acetate	0.7 x 7 cm	0.25
Tc-99m Sestamibi	Solvent Sat Pads	Chloroform: Tetrahyrofuran (1:1)	0.7 x 7 cm	0.25

AGENT	MEDIA	SOLVENT	STRIP SIZE	RF CUT LINE
Tc-99m MAG3	Solvent Sat Pads	Chloroform: Acet: Tetra-hydrofuran (1:1:2)	0.7 x 7 cm	0.33
	Solvent Sat Pads	0.9% NaCl	0.7 x 7 cm	0.25
Tc-99m MAG3	Whatman 1	Methylene Chloride: Acetone (1:1)	0.7 x 6 cm	0.50
	ITLC-SG	DI Water	0.7 x 6 cm	0.25
Tc-99m Monoclonal Antibodies	ITLC-SG	0.9% NaCl	0.7 x 6 cm	0.5
Tc-99m Bicisate	Whatman 17	Ethyl Acetate	0.7 x 7 cm	0.25
Tc-99m Tetrofosmin	Whatman 1	Ethyl Acetate	0.7 x 6 cm	0.25
In-111 Monoclonal Antibodies	ITLC-SG	0.9% NaCl (DTPA chall)	0.7 x 6 cm	0.5
In-111 Octreotide	ITLC-SG	0.9% NaCl (DTPA chall)	0.7 x 6 cm	0.5
I-131 Monoclonal Antibodies	ITLC-SG	0.9% NaCl	0.7 x 6 cm	0.5
I-131 Hippuran	ITLC-SA	chloroform/ gl acetic acid (1.00:0.05)	0.7 x 6 cm	0.2
I-125 RISA	ITLC-SG	methanol	0.7 x 6 cm	0.5
I-123 IMP	ITLC-SA	10% NaCl	0.7 x 6 cm	0.6

APPENDIX B

MINIATURIZED CHROMATOGRAPHY SYSTEMS FOR INFREQUENTLY USED AGENTS

SUMMARY CHART OF CHROMATOGRAPHY SYSTEMS FOR RADIOPHARMACEUTICALS

AGENT	MEDIA	SOLVENT	REFERENCE
Tc-99m Phytate	Whatman 31ET	Acetone	(7)
Tc-99m Sn Chloride	Whatman 31ET	Acetone	(7)
Tc-99m Diphosphonate	Whatman 31ET ITLC-SG	Acetone DI Water	(7)
Tc-99m HIDA	ITLC-SA ITLC-SG	20%NaCl DI Water	(9)
Tc-99m PIPIDA	ITLC-SA ITLC-SG	20%NaCl DI Water	(9)
I-131 Rose Bengal	ITLC-SA	Chloroform Gl acetic acid (1.00:0.05)	(23)
I-131 Iodocholesterol	ITLC-SG	0.9% NaCl	(23)

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