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RADIOCHROMATOGRAPHIC QUALITY CONTROL: A SIMPLIFIED SYSTEM

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A simple means of graphically displaying the degree of radiocompound binding purity using a shielded G-M tube integrated with a rate meter and strip chart recorder is described. The instrument produces a permanent quality-control record and eliminates time-consuming radiochromatographic segment counting.

Many departments of nuclear medicine now prepare sterile and pyrogren-free radiopharmaceuticals from commercial kits or from reagents prepared in their own laboratories. As part of the quality-control program, an accurate, rapid, and simple chromatography system is required to assess the radiopurity of these products.

We have developed a rapid, simple, chromatographic method for measuring purity of radiopharmaceuticals that uses instrumentation commonly available in most radioisotope laboratories and costs less than $1,000 if purchased new.

EQUIPMENT AND METHODS

The distribution of radioactivity along the chromatographic paper strip is determined by means of a Geiger-Muller (G-M) tube and a rate meter [Picker, Model No. 624081 (10K range increased to 100K)] and the results are recorded on a strip chart recorder (Picker, Model No. PRR-600-090) (Fig. 1). The G-M detector is shielded externally by a lead sleeve with a narrow slit opening (3 × 11 mm) located over the front and center of the G-M detector (Fig. 2A), which is mounted with lead shield on a ring stand 4 in. above the front of the strip chart recorder. A small stainless steel rod is connected to the ring stand 9 in. above the G-M tube to support the chromatography paper. In order to maintain the position of the chromatography strip as it passes over the slit window, a Lucite strip guide is placed on the front of the lead sleeve (Fig. 2B). The lower end of the chromatographic strip is attached to the chart paper which pulls the strip across the front of the G-M tube at a constant speed. Output from the G-M tube is measured by the rate meter and its output recorded on the paper chart, proportional to the counting rate meter level.

PROCEDURE

Whatman No. 1 chromatography paper is cut in lengths 1 × 45 cm and a fold made 1 cm from one

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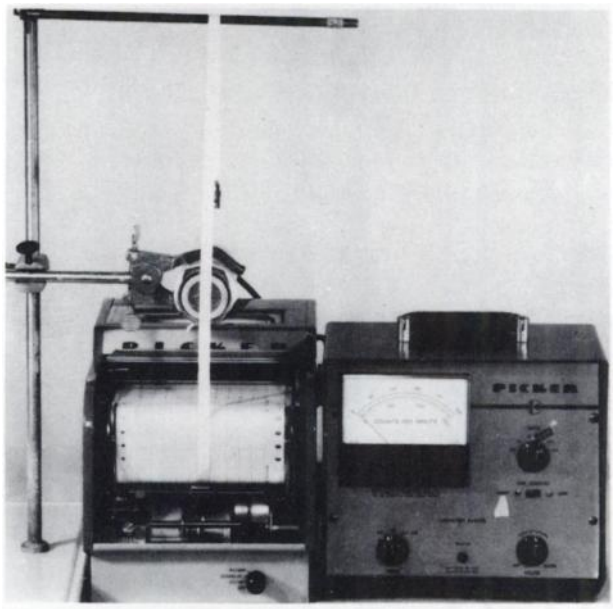

FIG. 1. Radiochromatography system.

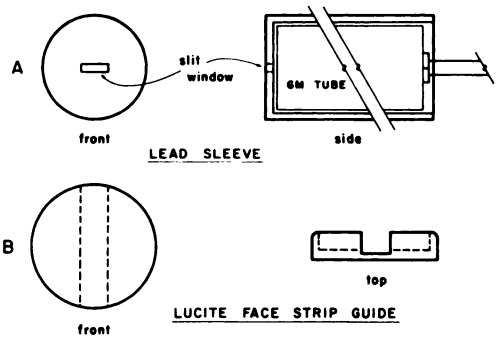

FIG. 2. (A) Lead sleeve cover for G-M tube. (B) Lucite face strip guide attached to front of lead sleeve.

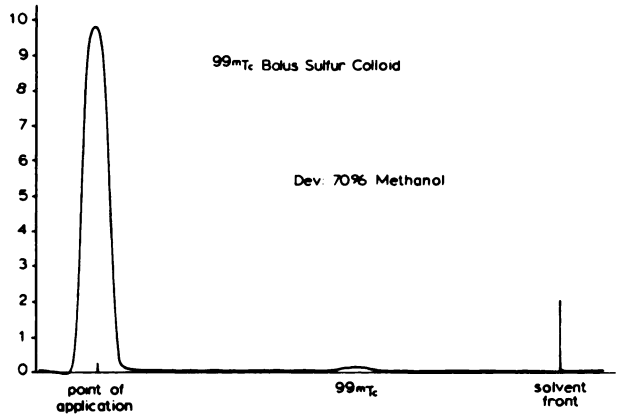

FIG. 3. Radiochromatogram of bolus ^{99m}Tc-sulfur colloid.

end of the strip in order to anchor the strip into the slit side of a Teflon tube. A mark is placed on the paper strip approximately 4 cm from the Teflon tube end and one drop of the ^{99m}Tc compound is spotted on this mark and dried with a small warm air dryer. If more than one drop is required in order to obtain adequate counting levels, each drop is dried separately. The paper strip is placed in a 500-ml graduated cylinder containing 50 ml solvent with the Teflon tube end slightly immersed under the surface of the solvent. A 70% methanol in water solvent is employed rather than the more common 85% methanol solvent because the higher concentration of water retards the ascending speed of the solvent and produces sharper details on the recording of ^{99m}Tc compounds (Fig. 3). When the glass stopper is inserted into place, approximately 7 cm of the paper strip extends outside the graduate.

After the ascending chromatogram has hung for 2 hr, the stopper is removed, the strip is quickly removed from the graduate and placed on clean napkins, and the solvent front is marked. After the paper strip has been dried with a small warm air dryer, the Teflon weight is removed and the strip is placed in the Lucite guide track over the face of the G-M tube. The solvent end of the chromatography strip is attached to the Picker recorder chart paper with Scotch tape. The chromatography paper progresses over the face of the G-M tube at the speed of the recorder. When the solvent front (SF) is directly over the narrow slit of the G-M tube, the recorder is momentarily stopped and the paper chart marked with the recording pen at the corresponding level. After the chromatography strip has traversed the G-M tube, the recording paper is removed from the instrument with the chromatogram still attached. The application point (AP) is then marked on the graph. The recording time for the graph is less than 2 min.

For most preparations the most suitable setting range on the rate meter is 100K/min. To obtain accurate separation of peaks and detect multipeaks, a chart speed of 6 in./min has been found satisfactory. However, the baseline is constant and reproducible at any speed of the strip chart recorder.

In order to determine that there were no count losses from the primary peak due to the relatively slow recovery time of the G-M tube, several chromatography strips were fractionally counted in a scintillation well counter up to 48 hr later and the results obtained were directly proportional within 1.0% of the respective displacement on the strip chart recording.

With this integrated chromatographic system we have processed over 250 ^{99m}Tc-bolus sulfur colloid chromatograms (*1*). The relative counts for the bound ^{99m}Tc-bolus sulfur colloid and the unbound ^{99m}Tc were about 98,000 and 2,000, respectively, and the R_f value for the unbound ^{99m}Tc was 0.57 (Fig. 3).

DISCUSSION AND CONCLUSIONS

Haney, et al (*2*) described a method for measuring the radiopurity of ^{99m}Tc-sulfur colloid preparations by means of ascending chromatography in 85% methanol. The chromatographic strip was divided between the application point and the solvent front and the radioactivity in each half determined. The radiochemical purity of the ^{99m}Tc-sulfur colloid was expressed as the ratio of the net counts on the spotted half of the strip divided by the total net counts of the entire strip. The R_f values for the ^{99m}Tc-sulfur colloid and the unreacted ^{99m}Tc were found to be 0.00 and 1.00, respectively.

Gutkowski and Dworkin (*3*) designed a chromatography system that used a lead-lined tray with a 1-cm slit centered over an open scintillation well. The chromatography strip was placed in the tray with the application point directly over the slit and the crystal and a 0.5-min count was recorded. The chromatography strip was advanced at 1-cm intervals and the radioactivity counts recorded. After all of the 1-cm segments of the strip had been counted, the radiopurity of the compound was expressed as the

percentage of radioactivity of the application point to the total counts of the strip.

Lewis and Bramlet (*4*) described a dialysis procedure that compared the predialysis and the postdialysis radioactivity of the dialysis membrane and saline solution.

The radiochromatography method described in this communication enables the radiochemical purity of labeled pharmaceuticals to be determined simply and rapidly.

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