A SIMPLIFIED METHOD FOR THE PREPARATION OF INDIUM-DTPA BRAIN SCANNING AGENT

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Recently various articles have been published outlining the method of preparation of ^{113m}In radiopharmaceuticals for blood pool, liver, spleen, lung and brain scans (*1,2*). Indium-113m emits a monoenergetic 390-keV radiation and has a relatively short physical half-life (1.7 hr). It is obtained from a generator system using ^{113}Sn with a physical half-life of 118 days. These characteristics have placed ^{113m}In high on the list of desirable radiopharmaceuticals. To add to the desirability of ^{113m}In as a broad-spectrum scanning agent is its ease of preparation for various body organs.

Stern *et al* have presented methods for chelating

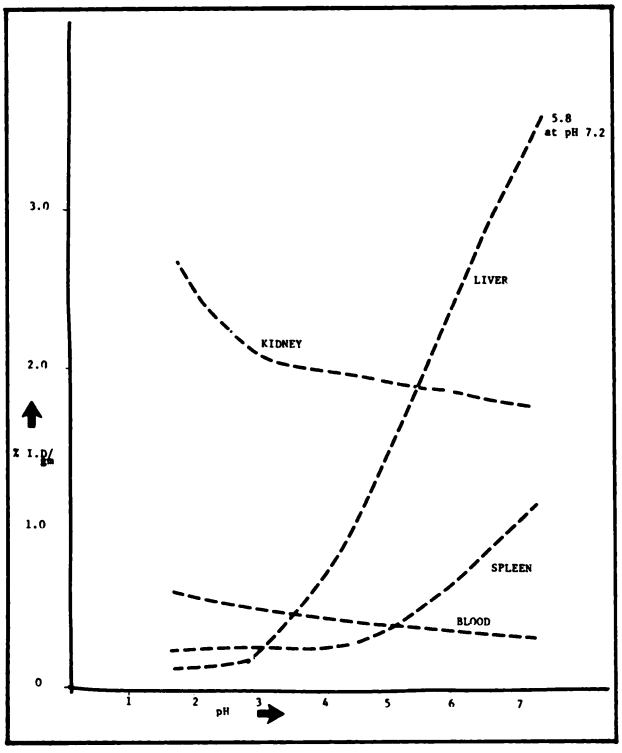

FIG. 1. Distribution of preparation at various pH's formed by omission of stepwise procedure (in 150-gm albino female rats at 10 min).

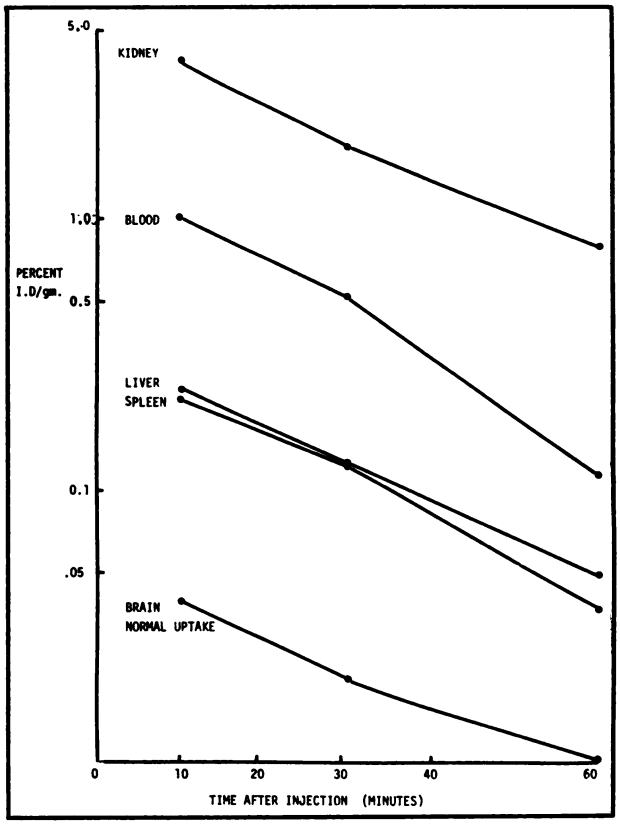

FIG. 2. Behavior of simplified chelate in 150-gm albino female rats.

^{113m}In with DTPA (diethyl triamine pantaacetic acid) for brain scanning (*3*). Presented here is another method for preparing ^{113m}In-chelate for brain scanning. This method eliminates the need for titration by the technician and enables the vials to be made up in advance as a preprepared system.

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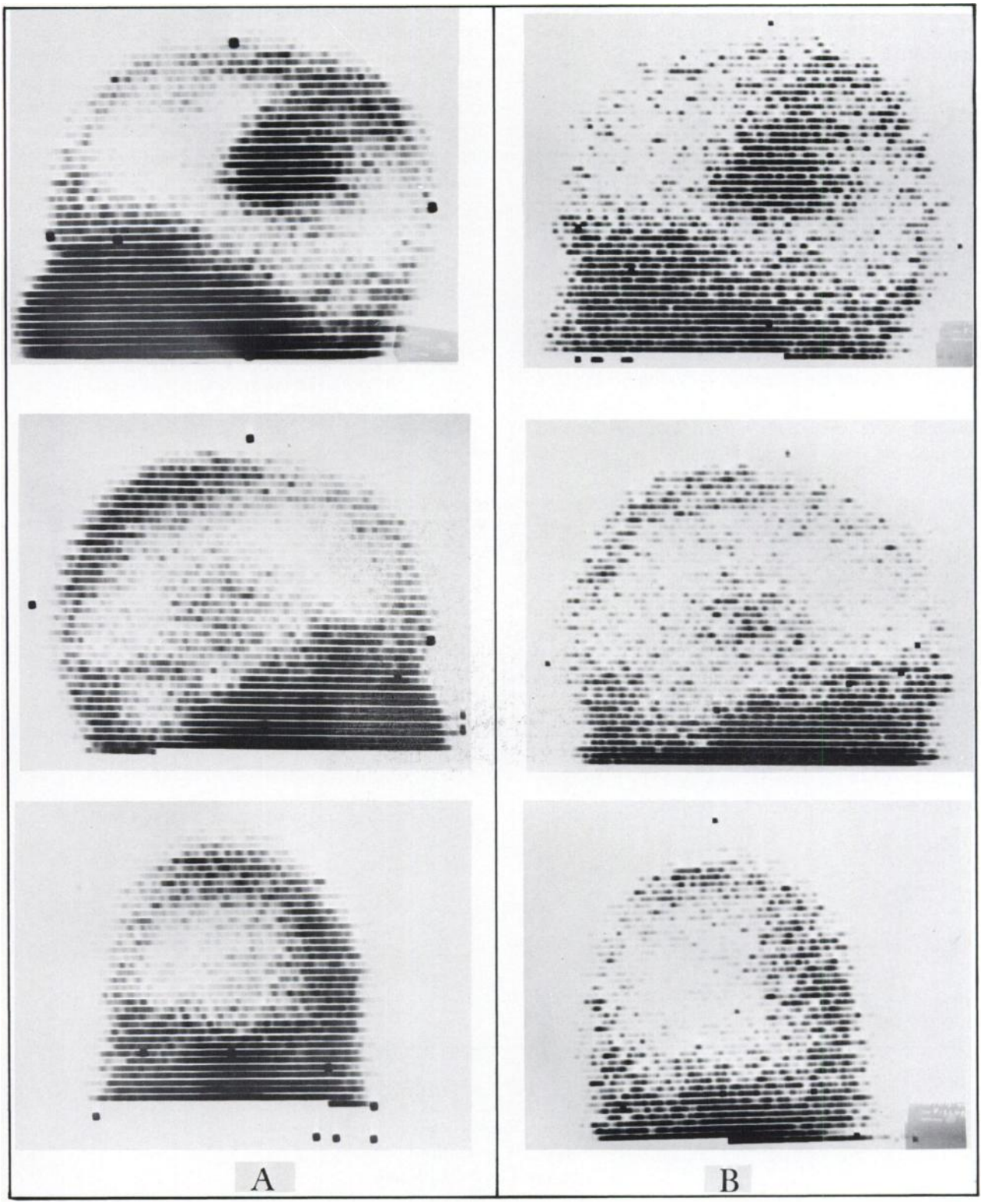

FIG. 3. Comparison of scan performed using (A) ^{99m}Tc-labeled pertechnetate and (B) new indium chelate preparation.

METHOD

A 25 or 50-mc ^{113}Sn-^{113m}In generator is eluated with 8 cc of 0.05 *N* hydrochloric acid (pH 1.4) into a vial containing the following: 1 ml of DTPA (1.6 mg/ml); 0.1 ml acetic acid (1/100 dilution of glacial acetic acid); and 1 ml sodium phosphate buffer (44.23 gm $Na_2HPO_4 \cdot 7H_2O$ and 15.99 gm $Na_3PO_4 \cdot 12H_2O$ in 250 ml of pyrogen-free water; pH 10.4). The final pH is in the range of 7.1–7.2. The solution

is shaken well. Tin leakage, as checked with hematoxylin, is less than 0.002%. Radioactivity dose is calibrated by standard assay techniques.

RESULTS AND DISCUSSION

The omission of stepwise addition in previous methods results in a scanning agent which does not behave in the desirable manner. In a series of experiments performed on 150-gm albino female rats, the blood activity is much lower than in the multistep preparation and does not diminish with time. There is also a significant liver uptake of approximately 6% injected dose/gm, which means that over 50% of the activity accumulates in the liver. These undesirable properties, due to the formation of insoluble colloids, are not observed if the indium is chelated at an acidic pH and then titrated to the desirable neutral level. The behavior of chelates formed at various pH's and titrated to neutral pH is shown in Fig. 1.

If this stepwise procedure is to be abandoned, a more effective chelate has to be made in the neutral pH range. It is known that indium acetate and tartrate remain soluble up to the neutral pH range whereas the indium hydroxide precipitates at a much lower pH. Thus, by adding acetate or tartrate, the indium can be chelated at a lower pH (*4,5*). Acetate stops the indium hydroxide from precipitating, but the equilibrium constant

$$\text{In-acetate complex} + \text{DTPA} \overset{K}{\rightleftharpoons} \text{Acetate} + \text{In-DTPA complex}$$

favors the formation of the DTPA complex. This eliminates the stepwise titration method of preparation. This system can be preprepared with the column eluate being added to the DTPA, buffer and acetic acid in a single step. The time-dependent behavior is shown in Fig. 2, and this behavior duplicates the more complicated method (*6*). An example of an indium scan and a technetium scan done on the same patient is shown in Fig. 3. With this system the possible errors in preparation are eliminated, and the time taken by the technician in preparing an effective indium radiopharmaceutical for brain scanning is reduced.

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