## CHEMISTRY, COMMON SENSE AND INDIUM SCANNING AGENTS

The proliferation of methods for the preparation of various indium-based radiopharmaceuticals prompts me to make this plea for more chemistry and common sense in this field. I am concerned with

1. inappropriate additions of possibly pyrogenic materials, e.g. gelatin,
2. unnecessary additions of carrier iron and
3. unnecessary additions of other materials.

In general, gelatin is appropriate only when it functions as a protective colloid around colloidal-sized particles or as a binder of carrier-free indium (e.g. Ref. *1*). Gelatin-free agents have been proposed (*2*) and have been used routinely in our department for the last 18 months.

Carrier iron is necessary only for certain particulate preparations. In the presence of a chelating agent, iron competes with indium for the ligands and can have no useful function.

The addition of acetic acid to the brain scanning agent reported recently (*3*) is based on a number of misconceptions. Acetate was said to "stop(s) the indium hydroxide from precipitating." This is surely incorrect. The first three acid dissociation constants of DTPA are $10^{-1.5}$, $10^{-2.64}$ and $10^{-4.27}$ (*4*) whereas that of acetic acid is $1.76 \times 10^{-5}$ (*5*). Therefore, at pH less than 3, DTPA exists largely as an effective chelating agent (at least bidentate) before acetic acid is significantly ionized. The concentration weighting in the authors' system of 4:1 in favor of acetic acid does not affect this conclusion, particularly as carrier-free quantities of indium are concerned. Obviously, the chelating agent must be present before the pH is raised because indium complexes with phosphate and/or hydroxyl ion.

Not wishing my comments to be entirely destructive I give below in summary our preparations for liver/spleen scanning agent and a brain scanning agent. We use a tin column supplied by the Radiochemical Centre, Amersham, England.

**Liver/Spleen.** Column eluted with 5 ml 0.05 *N* HCl. About 10 $\mu$g of citric acid added in 1–2-ml solution. Mixture titrated to pH 6–7 with constant stirring and autoclaved 15 min at 15 psi. The use of a low concentration of citric acid (plus a low concentration of iron, now eliminated) was proposed by the Radiochemical Centre, Amersham, England (*6*). This agent is clearly not particulate.

**Brain.** Column eluted with 5 ml 0.05 *N* HCl. Two drops of DTPA solution (50 mg/ml) added. Three milliliters buffer solution syringed in while the vial is swirled. Final pH about 7. Autoclaved 15 min at 15 psi.

Buffer: 7.8 gm $NaH_2PO_4\ 2H_2O$
9.0 gm $Na_2H\ PO_4$

Sterile distilled water 1 liter. Two volumes of this buffer solution are mixed with 1 volume of 0.2 *N* sodium hydroxide to give the working buffer solution.

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REFERENCES

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*2.* GARNETT, E. S., BAYLY, R. J. AND MARLOW, C. G.: Pyrogen-free $^{113m}$In scanning agents. *Brit. J. Radiol.* **42**:709, 1969.

*3.* HILL, T. *et al:* A simplified method for the preparation of indium-DTPA brain scanning agent. *J. Nucl. Med.* **11**:28, 1970.

*4.* CATSCH, A.: *Radioactive Metal Mobilization in Medicine,* C. C. Thomas, Springfield, Illinois, 1964, p. 30.

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*6.* BAYLY, R. J.: Private communication.

## THE AUTHORS' REPLY

In reference to Mr. Mardell's comments regarding our paper "A Simplified Method for the Preparation of Indium-DTPA Brain Scanning Agent" (*1*), I feel that he has completely missed our reasoning for adding acetic acid to the reagent.

We admit that below pH 3, DTPA complexes with indium, this being obvious from our Fig. 1. However, above pH 3 the indium complexes with hydroxide or phosphate before complexing with DTPA. Chemically, one might explain this phenomenon by saying that above pH 3 *the rate* of reaction of indium with hydroxide or phosphate is greater than that with DTPA. Chemists (*2–4*) have added acetate or tartrate to aid in the formation of indium-EDTA chelates at higher pH. After searching the chemical literature we used this analytical chemistry technique of adding acetate to alter the rate determining step above pH 3 from the formation of hydroxide or phosphate to the formation of an organic complex. The dissociation constants Mr. Mardell