

# Method of Preparation of Soluble Radiophosphate

Sir:

The radiopharmaceutical, sodium radiophosphate solution,<sup>1</sup> obtained from commercial sources by this laboratory, showed, on many occasions, a loss of activity on filtration through Whatman No. 1 filter paper or on transferring to a different container owing to surface adsorption, even at the recommended pH range from 5.0 to 6.0 (1). These adsorbable radiophosphate preparations exhibited a different tissue distribution from that of a soluble radiophosphate when injected intramuscularly into the rat (2). Inasmuch as the radiological and therapeutic efficacy of this radiopharmaceutical depends upon its ready diffusibility and ionizability in solution near pH 7.0 (3), a method for the conversion of the adsorbable preparations into soluble radiophosphate would appear to be desirable.

Radiophosphorus ( $P^{32}$ ) is prepared from sulfur by an (n,p) reaction. Following oxidation of the elemental radiophosphorus to radiophosphate, two methods are in current use for the isolation of the radiophosphate: (a) distillation of the bulk of the sulfur in a nitrogen atmosphere at 500° (4) and (b) addition of a nonisotopic carrier to transfer the radioactivity as a metal phosphate, followed by removal of the metal ions with resin column (5). The former method of preparation is used at the Chalk River Plant of Atomic Energy of Canada Ltd., and in our experience yields a soluble phosphate; the latter method is employed by the Oak Ridge National Laboratory and may give preparations unsatisfactory for reasons stated above.<sup>2</sup>

It has been suggested that the precipitate formed on neutralization of the solution of the unsatisfactory preparations is organic in nature (6). However, we have calcined the precipitate at 500° and digested it with aqua regia and were still unable to effect solution at pH 7.0. We have found, however, that a soluble radiophosphate can always be prepared from the unsatisfactory preparations by passing a 0.1*N* hydrochloric acid solution of the phosphate through a Dowex 50-X8, 100–200 mesh resin column (hydrogen form, 1 cm. × 15 cm.) at a flow rate of approximately 2 ml./min. After the effluent is evaporated to dryness on a water bath, the residue is present as phosphoric acid in trace amounts. It is taken up in isotonic saline and the solution filtered to give the soluble radiophosphate.

Extensive conditioning of the cation exchange resin is essential for the success of the above procedure; this can be done with alternate 1 *N* hydrochloric acid and 1 *N* sodium hydroxide washes, followed by exhaustive extraction with 95% ethanol to remove any organic impurities. In order to minimize radiation damage to the resin, the carrier-free radiophosphate solution is diluted to give an activity of approximately 1 mc. per ml. for passage through the column. The resin column is washed with 0.1 *N* hydrochloric acid after use and stored. The overall loss of radioactivity due to manipulation is negligible.

(1) Peng, C. T., *THIS JOURNAL*, 50, 88(1961).

(2) Peng, C. T., and Scott, K. G., see (1), unpublished data.

(3) Beierwaltes, W. H., Johnson, P. C., and Solari, A. J., "Clinical Use of Radioisotopes," W. B. Saunders Co., Philadelphia, Pa., 1957, p. 240; Quimby, E. H., Feitelberg, S., and Silver, S., "Radioactive Isotopes in Clinical Practice," Lea & Febiger, Philadelphia, Pa., 1958, p. 350.

(4) Evans, C. C., and Stevenson, J., British pat. 765,489, January 9, 1957.

(5) Rupp, A. F., *Proc. Intern. Conf. Peaceful Uses Atomic Energy Geneva*, 14, 77(1955).

(6) Private communication, Mr. Blauer, Isotope Division, Oak Ridge National Laboratory, Oak Ridge, Tenn.

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<sup>1</sup> These commercial preparations were marketed as sodium radiophosphate solution U.S.P. and presumably conformed to all the U.S.P. specifications and cautions.

<sup>2</sup> This statement should not be interpreted to be a criticism of the quality of the product since the Oak Ridge National Laboratory has specifically indicated that "the product is not pharmaceutically refined" on form X-375 accompanying each radioisotope shipment.