DATA EVALUATION RECORD

STUDY 1

CHEM 106701 Fosamine Ammonium §161-1

FORMULATION--00--ACTIVE INGREDIENT

STUDY ID 40133701

Koeppe, M. 1986a. Hydrolysis of [carbonyl-^{14}C]fosamine ammonium. Laboratory Project ID AMR-567-86. Unpublished study performed and submitted by E.I. du Pont de Nemours and Company, Inc., Wilmington, DE.

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CONCLUSIONS:

EFGWB concludes that the study submitted satisfies data requirements for hydrolysis.

Carbonyl-labeled [^{14}C]fosamine ammonium (radiochemical purity >99%), at 9.2 to 10.3 ppm, did not hydrolyze in sterile aqueous buffered solutions (pH 5, 7, 9) incubated in the dark at 25 ± 1 C for 30 days. [^{14}C]Fosamine ammonium, present in all solutions at ≥99%, was the sole compound identified in the buffer solutions at all sampling intervals. Recovery of [^{14}C]residues from all solutions was ≥99% of the initial [^{14}C]residue concentrations. No significant amounts of $^{14}CO_2$ were recovered in the sodium hydroxide traps (<0.001% of total dpm applied).

MATERIALS AND METHODS:

Carbonyl-labeled [^{14}C]fosamine ammonium (radiochemical purity >99%, specific activity 19.4 uCi/mg, du Pont) was added to sterile aqueous buffer solutions adjusted to pH 5 (0.1 M sodium acetate), 7 (0.1 M sodium phosphate), and 9 (0.01 M sodium borate) to produce test solutions at 10.3, 9.2, and 9.2 ppm, respectively. Samples were taken immediately after preparation of the test solutions (Day 0) and analyzed using LSC to determine the initial concentration of [^{14}C]fosamine ammonium in each solution (pH 5, 7, and 9). The apparatus for the study consisted of a Pyrex beaker, and a sterilized rubber stopper fitted with a rubber-stoppered centrifuge tube used to hold a caustic solution and a glass tubing bridge to allow for movement of $^{14}CO_2$ from the main beaker into the trap (Figure 2). Twenty mL of 1 N sodium hydroxide were added to each caustic trap and the sampling tubes for the caustic traps and the test solutions were sealed with sterilized medicine dropper bulbs. The beakers were wrapped in aluminum foil and incubated in the dark at 25 ± 1 C for 30 days. Samples of each test solution were aseptically removed for analysis at 0, 1, 2, 3, 4, 6, 8, 10, 12, 14, 17, 21, and 30 days posttreatment.

Duplicate aliquots of each sample were analyzed for total radioactivity using LSC. Duplicate aliquots of each sample were analyzed using TLC on silica gel plates developed in methanol:0.5 M ammonium carbonate (4:1). To confirm the results obtained using the silica TLC system, duplicate aliquots of each sample were analyzed using TLC on cellulose plates developed in 0.5 M ammonium carbonate:methanol:water (5:60:35) on days 0, 1, 2, 3, 4, and 30 only. Reference standards of [^{14}C]fosamine ammonium and possible degradation product [^{14}C]carbamoylphosphonic acid, dissolved in pH 7.4 buffer, were applied alongside the samples on each TLC plate. Radioactive areas on the TLC plates were located and quantitated using a Berthold TLC scanner; radioactive areas were also located using autoradiography. The 1 N sodium hydroxide solutions in the caustic traps were collected on days 14 and 30; the traps were replenished with 20 mL of fresh solution on Day 14. Duplicate aliquots of each sodium hydroxide solution were analyzed for total radioactivity using LSC.

REPORTED RESULTS:

Carbonyl-labeled [^{14}C]fosamine ammonium (radiochemical purity >99%), at 9.2 to 10.3 ppm, did not hydrolyze in sterile aqueous buffered solutions (pH 5, 7, 9) incubated in the dark at 25 ± 1 C for 30 days. [^{14}C]Fosamine ammonium, present in all solutions at ≥99%, was the sole compound identified in the buffer solutions at all sampling intervals (Tables 3, 4 and 5). Recovery of [^{14}C]residues from all solutions was ≥99% of the initial [^{14}C]residue concentrations (Table 1). No significant amounts of $^{14}CO_2$ were recovered in the sodium hydroxide traps (<0.001% of total dpm applied).

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