DATA EVALUATION RECORD

STUDY 1

CHEM 080808 Propazine §161-1

FORMULATION--00--ACTIVE INGREDIENT

STUDY ID 436898-02
Perdue, D. 1994. Hydrolysis of [^{14}C]Propazine in Aqueous Buffered Solutions at pH 5, 7 and 9. Project No. 850. Report No. 1640. Unpublished study performed by PTRL East, Inc., Richmond, KY, and submitted by Griffin Corporation, Valdosta, GA.

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CONCLUSIONS:

Degradation - Hydrolysis

1. This study is acceptable and fulfills EPA Data Requirements for Registering Pesticides by providing information on the hydrolysis of propazine in sterile aqueous solutions buffered to pH 5, 7, and 9 and incubated in the dark at 25°C for 30 days.

2. Propazine was hydrolytically stable, showing no significant degradation at concentrations of 5 ppm in sterile aqueous pH 5, 7 and 9 buffered solutions after 30 days. The plot of propazine concentration with time showed no evidence of decline over the study. The slope was not significantly >0.

3. No additional information on the hydrolysis of propazine is required at this time.

METHODOLOGY:

Ring-labeled [^{14}C]-propazine [6-chloro-N,N'-bis(1-methylethyl)-1,3,5-triazine-2,4-diamine; radiochemical purity 98.4%, specific activity 104.4 uCi/mg] was added to aqueous buffered solutions of pH 5 (0.1 M acetate), pH 7 (0.1 M phosphate), or pH 9 (0.01 M borate) at a concentration of 5 ppm (Comment 1). The [^{14}C]-propazine stock solutions were prepared in toluene and added to autoclaved buffered solutions (Comment 2). Acetonitrile was added as a co-solvent at a concentration of 1%. Aliquots of the solutions were radioassayed to confirm that the [^{14}C]-propazine was completely in solution. The sample flasks were incubated in the dark at 25 ± 0°C. Triplicate samples were removed for analysis after 0, 1, 3, 7, 14, 21, and 30 days of incubation. Aliquots of the 0- and 30-day samples were tested for sterility using trypticase soy and potato dextrose agar plates (Comment 3).

At each sampling interval, aliquots of the test solutions were analyzed for total radioactivity by LSC. Additional aliquots were analyzed for specific compounds by HPLC using an ODS reverse phase column, eluted with various ratios of 1% acetic acid/0.1% triethylamine in water and in acetonitrile. The column was equipped with UV (254 nm) and radioactivity detection. Day 30 samples were analyzed by two-dimensional TLC on silica gel plates developed with chloroform:methanol:formic acid:water (75:20:4:2) and ethyl acetate (100%). Radiolabeled areas were detected by image scanning. Nonradioactive reference standards were visualized under UV light. All radioactive zones were scraped from the plates and quantified by LSC. The pH of the solutions were measured at each sample interval (Comment 4).

DATA SUMMARY:

Total recovered radioactivity ranged from 97.8 - 107.5% (mean 100.7 ± 2.5%) for the pH 5 samples; 98.4 - 106.6% (mean 102.2 ± 2.5%) for the pH 7 samples; and 96.9 - 106.4% (mean 102.3 ± 2.7%) for the pH 9 samples. Propazine showed no evidence of decline in the pH 5, 7, or 9 buffer solutions (Tables V-VII). At the end of the 30-day incubation period, recovered propazine levels comprised approximately 103% of the initial radioactivity in all buffer solutions, with no degradates in excess of 1.5% of the applied. The plot of propazine concentration with time showed no evidence of decline over the study. The slope was not significantly >0.

While volatiles were not trapped, the material balances suggest that volatile losses were not significant. Results of the study indicate that hydrolysis is not a major avenue of environmental degradation for propazine (Comment 5).

REVIEWER COMMENTS:

1. Final concentrations of propazine in the test solutions, based on 0-day replicates, were 5.02 ppm for pH 5, 4.95 ppm for pH 7, and 4.95 ppm for pH 9.

2. The solubility of propazine is 8.6 mg/l in water at 20°C.

3. No microbial growth was observed in the Day 0 or Day 30 samples in either agar culture.

4. Mean pH values for the pH 5, 7, and 9 buffers were, respectively, 5.32, 7.08, and 8.98 at Day 0, and 5.32, 7.08, and 8.81 at Day 30. Except for the Day 21 pH 7 (measured range 6.83-6.87) and 9 (measured range 8.30-8.59) samples, the pH values remained steady throughout the study.

5. In a 1977 supplemental study (reference 001537-08), propazine was stable in non-sterile pH 7 and 9 buffered solutions and degraded with a calculated half-life of 38 days in a non-sterile pH 5 buffer solution. The results of the present study suggest that the degradation at pH 5 may have been at least partly influenced by the non-sterile conditions.

STUDY AUTHOR'S RESULTS AND CONCLUSIONS

INCLUDING PERTINENT TABLES AND FIGURES

Table V. Quantitative Characterization of Propazine in Hydrolysis Samples at pH 5 as Determined by HPLC.

	Percent of Applied Radiocarbon As:				
			Unknown Degradates		
Sample Description	Propazine (43.5-44.5 min.)(a)	Propazine-2-hydroxy (27.0 min.)(a)	A (39.0-40.0 min.)(a)	B (46.0-47.0 min.)(a)	C (49.0-50.0 min.)(a)
Day 0	97.7	ND(b)	ND	0.9	1.4
Day 1	98.3	ND	ND	0.7	0.3
Day 3	97.7	ND	0.4	0.9	0.2
Day 7	97.4	ND	0.7	0.7	0.1
Day 14	99.3	ND	1.0	0.7	0.1
Day 21	98.5	0.2	1.2	0.7	ND
Day 30	103.0	0.3	1.5	0.7	ND

(a) Approximate HPLC retention time range. Analytical reference standards co-injected with every sample resulting in accurate degradate identification by retention time.
(b) None detected greater than 2 x background.

Table VI. Quantitative Characterization of Propazine in Hydrolysis Samples at pH 7 as Determined by HPLC.

	Percent of Applied Radiocarbon As:				
			Unknown Degradates		
Sample Description	Propazine (43.5-44.5 min.)(a)	Propazine-2-hydroxy (27.0 min.)(a)	A (39.0-40.0 min.)(a)	B (46.0-47.0 min.)(a)	C (49.0-50.0 min.)(a)
Day 0	97.1	ND(b)	0.9	0.8	1.1
Day 1	101.8	ND	0.9	0.8	0.2
Day 3	98.3	ND	0.8	0.9	0.3
Day 7	98.0	ND	0.8	0.6	0.2
Day 14	101.5	ND	1.0	0.9	0.3
Day 21	99.9	ND	1.2	0.9	0.2
Day 30	102.7	ND	1.2	1.0	0.3

(a) Approximate HPLC retention time range. Analytical reference standards co-injected with every sample resulting in accurate degradate identification by retention time.

(b) None detected greater than 2 x background.

Table VII. Quantitative Characterization of Propazine in Hydrolysis Samples at pH 9 as Determined by HPLC.

	Percent of Applied Radiocarbon As:				
			Unknown Degradates		
Sample Description	Propazine (43.5-44.5 min.)(a)	Propazine-2-hydroxy (27.0 min.)(a)	A (39.0-40.0 min.)(a)	B (46.0-47.0 min.)(a)	C (49.0-50.0 min.)(a)
Day 0	96.4	ND(b)	1.0	1.0	1.4
Day 1	101.3	ND	1.1	1.0	0.3
Day 3	99.6	ND	1.0	0.9	0.3
Day 7	97.3	ND	1.1	0.9	0.2
Day 14	101.5	ND	1.0	1.0	0.2
Day 21	99.5	ND	1.0	1.0	0.3
Day 30	103.0	ND	1.0	0.8	0.3

(a) Approximate HPLC retention time range. Analytical reference standards co-injected with every sample resulting in accurate degradate identification by retention time.

(b) None detected greater than 2 x background.

RESULTS AND DISCUSSION

Radiochemical Purity of [^{14}C]Propazine

The radiochemical purity of [^{14}C]propazine was determined to be 98.40% (mean of two injections) by HPLC analysis prior to initiation of the incubation period. Radiochemical purity was also determined by HPLC following the last sampling interval (98.47%), thus demonstrating its stability at the test site. Radiochromatograms and peak integration summaries are presented in Figures 7 - 9. Non-radiolabeled reference standards, Figures 2 - 6 were analyzed qualitatively by HPLC prior to initiation and following the last sampling interval to establish their stability at the test site for the duration of the study.

Schedule of Sampling Events and Temperature Measurements

Sampling was performed following 0, 1, 3, 7, 14, 21 and 30 days of incubation. A schedule of sampling events is presented in Table II. Incubator temperatures during the 30-day period were 25.0 ± 0.0°C (mean ± standard deviation). Daily measurements are presented in Table II.

pH and Sterility of Hydrolysis Test Solutions

The pH of each pH 5, 7 and 9 hydrolysis test solution was measured at each sampling interval. Measured values are presented in Table III. The pH values were stable over the study period. The mean pH values (average of replicate solutions) at initiation (Day 0) in the pH 5, 7 and 9 solutions were 5.32, 7.08 and 8.98, respectively. The mean pH values following 30 days of incubation were 5.32, 7.08 and 8.81, respectively, for these solutions.

Sterility of the pH 5, 7 and 9 test solutions was determined at Day 0 and Day 30 of the study. No microbial growth was observed following culturing of Day 0 and Day 30 aliquots of these solutions on the potato dextrose agar and trypticase soy agar. It was concluded that the hydrolysis solutions were sterile throughout the 30-day incubation phase.

Material Balance of [^{14}C]Propazine Throughout Study Period

The total radiocarbon as a percent of the applied dose for pH 5, 7 and 9 was 100.7 ± 2.5, 102.2 ± 2.5 and 102.3 ± 2.7%, respectively (mean ± standard deviation for all sample intervals, Table IV). The overall recovery was 101.7 ± 0.5% (mean ± standard error). These data establish that [^{14}C]propazine did not degrade significantly to volatile products or $^{14}CO_2$ under the test conditions employed in this study.

Quantitative Characterization of [^{14}C]Propazine and Degradation Products

The quantitative characterization of radiocarbon present in pH 5, 7 and 9 hydrolysis solutions at each sample interval is presented in Tables V, VI and VII, respectively. Representative HPLC radiochromatograms for pH 5, 7 and 9 Day 30 samples are presented in Figures 10 - 12, respectively. After 30 days of incubation, 103.0, 102.7 and 103.0% of the applied radiocarbon remained as parent compound in the pH 5, 7 and 9 solutions, respectively. Three unidentified degradates individually accounted for no more than 1.5% of the applied radiocarbon in any one sample. Additional representative HPLC radiochromatograms for pH 5, 7 and 9, Day 0 and 14 samples are presented in Appendix 3.

TLC analysis was used to confirm HPLC characterizations in pH 5, 7 and 9 Day 30 samples. Representative thin layer radiochromatograms (Day 30, pH 5, 7 and 9) are presented in Figures 13 - 15. Integration summaries are presented in Tables VIII, IX and X. A comparison of radiocarbon characterization in Day 30 samples by HPLC and TLC is presented in Table XI. These data demonstrate that similar chemical identities and concentrations in the samples were obtained by these two analytical methodologies.

Hydrolysis Rate of Propazine

Hydrolysis half-lives determined from the 30-day incubation of propazine in pH 5, 7 and 9 buffer solutions were significantly greater than 30 days. Rate constant and half-life calculations are presented in Table XII. Degradation profiles of [^{14}C]propazine at pH 5, 7 and 9 in aqueous buffered solutions are presented in Figure 16.

Sample Storage Stability

Analyses were performed on all samples immediately after sample collection; therefore, no sample storage stability data are required to support the results presented.

CONCLUSIONS

Aqueous buffered sterile solutions of [^{14}C]propazine at pH 5, 7 and 9 were incubated in darkness for a period of 30 days at approximately 25°C. The nominal concentration of [^{14}C]propazine was 5.0 ppm. Propazine exhibited no significant degradation as a result of hydrolysis in acidic, neutral or basic buffered media. The hydrolysis half-life of propazine was significantly greater than 30 days. After 30 days of incubation, 103.0, 102.7 and 103.0% of the applied radiocarbon remained as parent compound in the pH 5, 7 and 9 samples, respectively. Three unidentified degradates individually accounted for no more than 1.5% of the applied radiocarbon in any one sample. Results of this study would not predict hydrolysis to be a significant environmental degradation mechanism of propazine.