

STUDY 1

FORMULATION-00-ACTIVE INGREDIENT

Priestley, D. B., and J. P. Leahey. 1988. PP321: Aqueous photolysis at pH 5. Report No.: RJ 0605B. Unpublished study performed and submitted by ZENECA Agrochemicals, Bracknell Berkshire, UK.

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CONCLUSIONS

Degradation - Photodegradation in Water

1. This study is not scientifically valid and does not provide useful information on the photodegradation of lambda-cyhalothrin in pH 5 aqueous buffer solution. The test substance was not in solution at all sampling intervals.
2. This study does not meet Subdivision N Guidelines for the fulfillment of EPA data requirements on photodegradation in water for the following reasons:
 - (i) the experimental method was inadequate; and
 - (ii) the total light intensity of the artificial light source was not reported.
3. Cyclopropane ring-labeled [3-¹⁴C]lambda-cyhalothrin, at a nominal concentration of 4 µg/L, was studied in sterilized pH 5 aqueous buffer solution which was continuously irradiated with a xenon arc lamp and maintained at 25 ± 1.0°C for up to 282 hours (31 equivalent natural sunlight days). A half-life of the parent compound in the irradiated solution could not be accurately calculated because the radiolabeled test substance did not remain in solution throughout the incubation period. The parent compound was stable in the dark control samples. All data, reported as percentages of the applied radioactivity, represent percentages of the nominal application. All data are reported as reviewer-calculated means of two replicates (unless otherwise noted). Data are reported in hours of continuous irradiation; intervals were equivalent to 7, 15, 23, and 31 days of natural sunlight. In the irradiated solutions, the parent was initially 98.1% of the applied radioactivity, decreased to 82.1% by 82 hours, was 59.3-61.0% at 169-229 hours, and was 37.9% at 282 hours posttreatment. The major degradate Compound Ia varied from 5.9 to 8.8% of the applied radioactivity from 169 to 229 hours and was a maximum of 13.7% at 282 hours posttreatment. The minor degradate Compound Ib was 4.9-5.6% of the applied radioactivity at 169-229 hours and was a maximum of 7.1% at 282 hours posttreatment. Total [¹⁴C]volatiles initially (82 hours) accounted for 2.3% of the applied radioactivity, increased to 8.6% by 169 hours and 16.7% by 229 hours, and were a maximum of 18.2% at 282 hours posttreatment; evolved ¹⁴CO₂ accounted for the majority of the total [¹⁴C]volatiles.

Uniformly phenyl ring-labeled [¹⁴C]lambda-cyhalothrin, at a nominal concentration of 4 µg/L, was studied in sterilized pH 5 aqueous buffer solution which was continuously irradiated with a xenon arc lamp and maintained at 25 ± 1.0°C for up to 247 hours (31 equivalent natural sunlight days). A half-life of the parent compound in the irradiated solution could not be accurately calculated because the radiolabeled test substance did not remain in solution throughout the incubation period. All data, reported as percentages of the applied radioactivity, represent percentages of the nominal application. All data are

reported as reviewer-calculated means of two replicates (unless otherwise noted). Data are reported in hours of continuous irradiation; intervals were equivalent to 7, 15, 23, and 31 days of natural sunlight. In the irradiated solutions, the parent was initially 97.6% of the applied radioactivity, decreased to 78.6% by 72 hours, was 65.0% at 152 hours, and was 43.6-46.6% at 198-247 hours posttreatment. The major degradate Compound V was initially (72 hours) 6.4% of the applied radioactivity, increased to 11.7% by 152 hours, and was a maximum of 25.0% at 247 hours posttreatment. The minor degradate Compound IV was initially (72 hours) 2.7% of the applied radioactivity and was a maximum of 5.5% by 247 hours posttreatment. Total [^{14}C]volatiles initially (72 hours) accounted for 0.9% of the applied radioactivity, were 1.5-2.6% at 152-198 hours, and were 3.9% at 247 hours posttreatment; evolved $^{14}\text{CO}_2$ accounted for the majority of the total [^{14}C]volatiles.

METHODOLOGY

Cyclopropane ring-labeled [3- ^{14}C]lambda-cyhalothrin {PP321; 1:1 mixture of the enantiomers (*S*)- α -cyano-3-phenoxy-benzyl (1*R*)-*cis*-3-(*Z*-2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylate AND (*R*)- α -cyano-3-phenoxybenzyl (1*S*)-*cis*-3-(*Z*-2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethyl-cyclopropanecarboxylate; radiochemical purity >95%; specific activity 2.19 Gbq/mmol; pp. 9, 10, 14} OR uniformly phenyl ring-labeled [^{14}C]lambda-cyhalothrin (radiochemical purity >95%; specific activity 2.49 Gbq/mmol), dissolved in acetonitrile, was added at a nominal concentration of 4 $\mu\text{g/L}$ to sterilized pH 5.1 (acetate:acetic acid; 70:30, v:v) 0.01 M aqueous buffer solutions (pp. 8, 16). The test solutions were prepared in sterilized glass vessels with Teflon[®]-lined quartz lids and placed in a photolysis unit maintained at $25 \pm 1.0^\circ\text{C}$ using a recirculating water bath in a photolysis unit (Figures 4, 5, pp. 17, 18). Four additional samples were prepared as previously described in order to monitor temperature, pH, and radioactivity in solution (p. 18); temperature and pH data were reported in Appendix 5 (p. 49). Samples were continuously irradiated for up to 296 hours (cyclopropane label) or 257 hours (phenyl label) with a xenon arc lamp equipped with a filter to remove wavelengths of <300 nm (Appendix 3, Figure 5, p. 33; Tables 7a, 7b, pp. 45, 46). The mean light intensity (297-700 nm) of the artificial light source was measured using a spectroradiometer at the initiation and termination of the study (Appendix 3, p. 36; data were reported in Appendix 3, Tables 7a, 7b, pp. 45, 46); total light intensity was not reported (see Comment #2). A comparison graph of artificial and natural light (unspecified location) was provided in Appendix 3 (Figure 2, p. 34). Dark control samples were treated with the parent (both labels) and maintained in darkness under otherwise similar conditions (p. 16). To capture volatiles, filter-sterilized air was drawn (peristaltic pump) through the sample flasks and into the following series of traps: polyurethane foam, 1 M HCl, 2-methoxyethanol, and two ethanolamine traps (Figure 6, p. 19). Duplicate samples were removed for analysis at approximately 82, 169, 229, and 282 hours posttreatment (cyclopropane label; reviewer-calculated means from data in

Appendix 3, Table 7b, p. 46) or at 72, 152, 198, and 247 hours posttreatment (phenyl label; reviewer-calculated means from data in Appendix 3, Table 7a, p. 45); respective sampling intervals were equivalent to 7, 15, 23, and 31 days of natural sunlight (autumn in FL) for both label studies (p. 20). Dark control samples were removed for analysis at 0 and 31 equivalent natural sunlight days posttreatment (Table 2, p. 22). Volatile traps were collected for analysis and replaced with fresh traps at each sampling interval (p. 20).

At each sampling interval, samples were analyzed for total radioactivity by LSC (p. 20). Samples were acidified (6 M HCl) and passed through a reverse-phase bond-elut column (Analytichem International C18) preconditioned with methanol and distilled water, and the eluent was collected. The sample vessels were washed twice by ultrasonication with acetonitrile followed by a single wash with dichloromethane (see Comment #1); the solvents were collected after each wash and used to elute the bond-elut column. The eluents were collected and combined, and the aqueous and organic phases were each analyzed by LSC. To characterize radioactivity, the combined organic eluents (cyclopropane label) were concentrated under a stream of air and analyzed by one-dimensional TLC on silica gel plates developed with cyclohexane (saturated with formic acid:diethyl ether, 60:40, v:v) and with hexane:ethyl acetate:methanol:acetonitrile (70:20:5:5, v:v:v:v; pp. 13, 21). The combined organic eluents (phenyl label) were concentrated and analyzed by reverse-phase TLC on silica gel plates developed with acetonitrile:ammonium formate (70:30, v:v) and with methanol:ammonium formate (90:10, v:v). Dark control samples were analyzed by normal-phase TLC on silica gel plates developed with cyclohexane (saturated with formic acid:diethyl ether, 60:40, v:v). Samples were co-chromatographed with nonradiolabeled reference standards of the parent and the following potential degradates: Compounds Ia, Ib, IV, and V (Figure 2, pp. 11-12) which were visualized by UV (254 nm) light (parent and Compounds IV, V) or by spraying with bromophenol blue or distilled water (Compounds Ia, Ib). Areas of radioactivity were quantitated using X-ray film and radioimage scanning.

To determine the isomeric composition of the parent, the organic phase from selected irradiated and dark control samples (times 0 and 31 equivalent natural sunlight days) was evaporated to dryness and reconstituted with a stock solution of the parent compound and its eight isomers (p. 21; Table 6, p. 26). Duplicate aliquots of each sample solution were analyzed by HPLC (Hichrom S5W column) using an isocratic mobile phase of hexane:diethyl ether (97:3, v:v) with UV (230 nm) detection (p. 14). Eluate fractions were collected at one-minute intervals and analyzed by LSC (p. 13). Samples were co-chromatographed with nonradiolabeled reference standards of the parent and its isomers.

At each sampling interval, aliquots of the volatile trap solutions were analyzed for total radioactivity by LSC (p. 20). The method (if any) used to confirm the presence of $^{14}\text{CO}_2$ in the volatile traps was not reported. The polyurethane foam traps were extracted by refluxing with acetonitrile, and the extracts were analyzed for total radioactivity by LSC (p. 21). The silicon tubing which connected the sample vessels was removed and

extracted by soaking with methanol; the extract was analyzed by LSC (pp. 20, 21).

DATA SUMMARY

Cyclopropane ring-labeled [3-¹⁴C]lambda-cyhalothrin

Cyclopropane ring-labeled [3-¹⁴C]lambda-cyhalothrin (radiochemical purity >95%), at a nominal concentration of 4 µg/L, was studied in sterilized pH 5 aqueous buffer solution which was continuously irradiated with a xenon arc lamp and maintained at 25 ± 1.0°C for up to 282 hours (31 equivalent natural sunlight days). A half-life of the parent compound in the irradiated solution could not be accurately calculated because the radiolabeled test substance did not remain in solution throughout the incubation period (p. 29; see Comment #1). The parent compound was stable in the dark control samples. All data, reported as percentages of the applied radioactivity, represent percentages of the nominal application. All data are reported as reviewer-calculated means of two replicates (unless otherwise noted). Data are reported in hours of continuous irradiation; intervals were equivalent to 7, 15, 23, and 31 days of natural sunlight (p. 20). In the irradiated solutions, the parent compound was initially present at 98.1% of the applied radioactivity, decreased to 82.1% of the applied by 82 hours posttreatment, was 59.3-61.0% of the applied at 169-229 hours posttreatment, and was 37.9% of the applied at 282 hours posttreatment (Tables 5, 7, pp. 25, 27). The major degradate

(1*RS*)-cis-3-(*ZE*-2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylic acid (Compound Ia)

varied from 5.9 to 8.8% of the applied radioactivity from 169 to 229 hours posttreatment and was a maximum of 13.7% of the applied at 282 hours posttreatment (Table 7, p. 27; see Comment #5). The minor degradate (1*RS*)-trans-3-(*ZE*-2-chloro-3,3,3-trifluoroprop-1-enyl)-2,2-dimethylcyclopropanecarboxylic acid (Compound Ib) was 4.9-5.6% of the applied radioactivity at 169-229 hours posttreatment and was a maximum of 7.1% of the applied at 282 hours posttreatment. Uncharacterized radioactivity comprised of many components (designated as “unknowns”) was ≤4.5% of the applied radioactivity throughout the incubation period. Uncharacterized radioactivity (designated as “remainder on TLC”) was initially (82 hours) 6.8% of the applied radioactivity, increased to a maximum of 8.7% of the applied by 229 hours posttreatment, and was 3.4% of the applied at 282 hours posttreatment. Unidentified radioactivity (designated as “not analysed”) was 3.0-4.0% of the applied radioactivity at 82-229 hours posttreatment and was a maximum of 4.4% of the applied at 282 hours posttreatment. Total [¹⁴C]volatiles initially (82 hours) accounted for 2.3% of the applied radioactivity, increased to 8.6% by 169 hours and 16.7% by 229 hours, and were a maximum of 18.2% of the applied at 282 hours posttreatment; evolved ¹⁴CO₂ accounted for the majority of the total [¹⁴C]volatiles (Footnote “c” in Table 7, p. 27). Radioactivity in the polyurethane foam traps was ≤7.2% of the applied radioactivity throughout the incubation period. Radioactivity in the tubing

extract was $\leq 0.8\%$ (one of two replicates) of the applied radioactivity throughout the incubation period.

Material balances (based on LSC analysis of individual replicates) for the irradiated solutions were 93.4-117.3% of the applied radioactivity, with no observed pattern of decline (Table 3, p. 23). For the dark control solutions, the material balances were 99.0-101.0% of the applied radioactivity.

Uniformly phenyl ring-labeled [^{14}C]lambda-cyhalothrin

Uniformly phenyl ring-labeled [^{14}C]lambda-cyhalothrin (radiochemical purity $>95\%$), at a nominal concentration of $4\ \mu\text{g/L}$, was studied in sterilized pH 5 aqueous buffer solution which was continuously irradiated with a xenon arc lamp and maintained at $25 \pm 1.0^\circ\text{C}$ for up to 247 hours (31 equivalent natural sunlight days). A half-life of the parent compound in the irradiated solution could not be accurately calculated because the radiolabeled test substance did not remain in solution throughout the incubation period (p. 29; see Comment #1). The parent compound was stable in the dark control samples. All data, reported as percentages of the applied radioactivity, represent percentages of the nominal application. All data are reported as reviewer-calculated means of two replicates (unless otherwise noted). Data are reported in hours of continuous irradiation; intervals were equivalent to 7, 15, 23, and 31 days of natural sunlight (p. 20). In the irradiated solutions, the parent compound was initially present at 97.6% of the applied radioactivity, decreased to 78.6% of the applied by 72 hours posttreatment, was 65.0% of the applied at 152 hours posttreatment, and was 43.6-46.6% of the applied at 198-247 hours posttreatment (Tables 4, 8, pp. 24, 28). The major degradate

3-phenoxybenzoic acid (Compound V)

was initially (72 hours) present at 6.4% of the applied radioactivity, increased to 11.7% of the applied by 152 hours posttreatment, and was a maximum of 25.0% of the applied radioactivity at 247 hours posttreatment (Table 8, p. 28). The minor degradate 3-phenoxybenzaldehyde (Compound IV) was initially (72 hours) 2.7% of the applied radioactivity and increased to a maximum of 5.5% of the applied by 247 hours posttreatment. Uncharacterized radioactivity comprised of many components (designated as "unknowns") was $\leq 6.0\%$ of the applied radioactivity throughout the incubation period. Uncharacterized radioactivity (designated as "remainder on TLC") was initially (72 hours) 1.7% of the applied radioactivity, increased to a maximum of 8.8% of the applied by 198 hours posttreatment, and was 6.4% of the applied at 247 hours posttreatment. Uncharacterized [^{14}C]residues (designated as "not analysed") were 1.9-3.5% of the applied radioactivity throughout the incubation period. Total [^{14}C]volatiles initially (72 hours) accounted for 0.9% of the applied radioactivity, were 1.5-2.6% of the applied at 152-198 hours posttreatment, and were 3.9% of the applied at 247 hours posttreatment; evolved $^{14}\text{CO}_2$ accounted for the majority of the total [^{14}C]volatiles (Footnote "b" in Table

8, p. 28). Radioactivity in the polyurethane foam traps was $\leq 5.2\%$ of the applied radioactivity throughout the incubation period. Radioactivity in the tubing extract was $\leq 1.3\%$ (one of two replicates) of the applied radioactivity throughout the incubation period.

Material balances (based on LSC analysis of individual replicates) in the irradiated solutions were 91.3-100.7% of the applied radioactivity (Table 3, p. 23). In the dark control solutions, the material balances were 96.0-99.4% of the applied radioactivity.

COMMENTS

1. The experimental method, specifically the dissolution of the parent compound in the buffer solution, was inadequate. The half-life of the parent compound could not be accurately determined because the test substance was not in solution at all sampling intervals (p. 29). The reviewer notes that the test concentration of $4 \mu\text{g/L}$ was the reported solubility limit of the test compound at pH 5 (p. 8; Appendix 4, p. 48). Acceptable material balances (90-110%) were only achieved after the sample vessels were washed with acetonitrile (p. 29); therefore, the study authors stated that "an exact kinetic analysis to measure half-life is impossible." The study authors stated that, based on the data in Tables 7 and 8 (pp. 27, 28), the parent degraded with an observed half-life of 20 days. In addition, the study authors stated that LSC analysis of control samples treated with the parent indicated that radioactivity in solution varied from 15 to 85% of the applied over 31 equivalent natural sunlight days (p. 20; tabular data were not reported).
2. The total light intensity of the artificial light was not reported. Subdivision N Guidelines require the determination of the average light intensity of the artificial light source at the beginning and end of the study, and total light intensity over the course of the study.
3. A comparison graph of artificial and natural light was provided in Appendix 3 (Figure 2, p. 34); however, the location, date, and time of day when the sunlight was measured was not reported. Complete information is needed in order to accurately compare an artificial light source with natural light.
4. Although sterilized equipment was used in the experiment and the initial buffered solution was autoclaved, sterility was not confirmed throughout the incubation period.
5. In the cyclopropane label study, Compounds Ia and Ib were present at a combined amount of 3.6% of the applied radioactivity (reviewer-calculate mean) at 82 hours posttreatment (Table 7, p. 27); the study authors stated that the analytical method could not resolve the two compounds at this sampling interval.

6. The limits of quantitation and detection were not reported for LSC, TLC or HPLC analyses. Both limits of detection and quantitation should be reported for each method utilized in order to allow the reviewer to evaluate the adequacy of the method for the determination of the test compound and its degradates.
7. The study authors stated that the parent compound consisted of 72.9% and 83.6% of the enantiomeric pair B, and 19.2% and 11.6% of the enantiomeric pair A in the cyclopropane and phenyl label studies, respectively, at the initiation of the study (p. 10; Table 1, p. 14). The remainder of the test material was comprised of six isomers, each $\leq 2.1\%$ of the applied radioactivity.

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Pages 9 through 22 are not included in this copy.

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