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DATA EVALUATION RECORD

STUDY 3

CHEM 109801

Iprodione

\$162-4

FORMULATION--00--ACTIVE INGREDIENT

STUDY ID 41927601

Spare, W.C. 1991. Aerobic Aquatic Metabolism of Iprodione. Laboratory Project ID: Agrisearch Project No. 1514. Unpublished study performed by Agrisearch Inc., Frederick, MD, and submitted by Rhône-Poulenc AG Company, Research Triangle Park, NC.

DIRECT REVIEW TIME = 4

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December 2, 1991.

CONCLUSIONS:

Metabolism - Aerobic Aquatic:

1. The submitted study cannot be used to fulfill the Aerobic Aquatic Metabolism (162-4) data requirement at this time.
2. Iprodione degraded with an observed half-life of 3-7 days (registrant-calculated half-life of 9 days) in a flooded silt loam sediment system that was incubated in the dark at 25 °C. The major non-volatile degradate was 3-(1-methylethyl)-N-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide (RP-30228); other non-volatile degradates were 3-(3,5-dichlorophenyl)-2,4-(dioxo-1-imidazol)idinecarboxamide (RP-32490), and 3-(1-methylethyl)-N-(3,5-dichlorophenyl)-1-ureylenecarboxamide (RP-36221).
3. The study is scientifically sound, but does not meet Subdivision N guidelines because not all degradates detected at >0.01 ppm were identified; three unidentified [¹⁴C]compounds comprised up to 1.8% (0.15 ppm), 11.5% (0.93 ppm), and 1.7% (0.14 ppm) of the applied radioactivity.
4. In order for this study to fulfill the Aerobic Aquatic Metabolism data requirement, the registrant should make an earnest attempt to identify degradates present at a concentration of >0.01 ppm.

METHODOLOGY:

Water (pH 8.5, total hardness 6.8 mg cations/L, total alkalinity 348 mg CaCO₃/L, total suspended solids 2.0 mg/L) collected from a rice paddy was treated with phenyl ring-labeled [¹⁴C]iprodione (uniformly labeled, radiochemical purity 98.9%, specific activity 10.5 uCi/mg, Rhône-Poulenc), dissolved in acetone, at 8.12 ppm. Samples (25 g dry weight equivalent) of silt loam sediment (6.64% sand, 68.96% silt, 24.4% clay, 1.53% organic matter, pH 6.3, CEC 7.67 meq/100 g) collected from the same paddy were placed in flasks and flooded with 50 mL of the [¹⁴C]iprodione-treated water; twelve soil:water systems were prepared. The flasks were wrapped in foil, stoppered with polyurethane foam plugs, and incubated in darkness at 25 ± 1 °C. Two of the flasks were attached to a gas collection system; humidified air was drawn (40-60 mL/minute) through the flasks for 1 hour each weekday, then sequentially through one tube each of ethylene glycol and 1 N potassium hydroxide trapping solutions (Figure 2). Duplicate soil:water systems were collected and trapping solutions were changed at 1, 2, 3, 7, 14, and 30 days posttreatment; the [¹⁴C]iprodione-treated water was analyzed as the time 0 sample.

At each sampling interval, the water fraction was decanted from the sediment and centrifuged; the pelleted sediment was combined with the remaining sediment fraction. Aliquots of each water sample were analyzed for total radioactivity using LSC. Additional aliquots of the water samples were acidified with 0.05 M potassium phosphate buffer (pH 2) and partitioned twice with methylene chloride:ethyl acetate (9:1, v:v). The aqueous phase was neutralized with 1 N sodium hydroxide and repartitioned twice with methylene chloride:ethyl acetate. All organic phases were combined, concentrated by rotary evaporation, and analyzed by two-dimensional TLC on silica gel plates developed in toluene:ethyl acetate (9:1, v:v) followed by methylene chloride:ethyl acetate:formic acid (80:15:5, v:v:v). Radioactive areas were visualized and quantified using a radioanalytical imaging system; identification was made by comparison with unlabeled reference standards

cochromatographed with the samples and visualized by UV absorbance (254 nm). Selected samples were also analyzed using GC with electron capture detection. The limits of detection for TLC analyses of the water and soil samples were 0.014 ppm.

Sediment fractions were extracted three times with acetone:methanol:water:hydrochloric acid (50:40:10:0.2, v:v:v:v) for 20 minutes using sonication; the slurries were centrifuged, and the extracts were combined and analyzed for radioactivity using LSC. The 14- and 30-day sediment samples were further extracted with a 2-hour reflux using the extraction sequence described above; the extracts were analyzed by LSC. The 30-day sediment was further extracted three times with acetone:water:phosphoric acid (66:33:1, v:v:v) for 20 minutes using sonication followed by 2- and 16-hour refluxes in fresh solvent; extracts were analyzed by LSC. Organic solvents were removed from the various sonication and reflux extracts by rotary evaporation; the remaining aqueous solutions were acidified, partitioned, and analyzed as previously described for the water samples. Unextracted [^{14}C]residues remaining in the extracted sediment were quantified by LSC following combustion.

Aliquots of the trapping solutions were analyzed for total radioactivity using LSC. The presence of $^{14}\text{CO}_2$ in the potassium hydroxide trapping solutions was confirmed using barium chloride precipitation.

Two additional flasks of silt loam sediment were autoclaved at 15 psi and 121 °C for 1 hour prior to treatment. The rice paddy water was autoclaved (under the same conditions) separately from the sediment, and was treated with [^{14}C]iprodione at 15.46 ppm. Aliquots (50 mL) of the treated sterile water were added to the sterilized sediment, and the flasks were stoppered and incubated as previously described. The two sterile soil:water systems were sampled at 30 days posttreatment and analyzed as previously described.

DATA SUMMARY:

Phenyl ring-labeled [^{14}C]iprodione (uniformly labeled, radiochemical purity 98.9%), at 8.12 ppm, degraded with an observed half-life of 3-7 days in a flooded silt loam sediment system that was incubated in the dark at 25 ± 1 °C for 1 month; the registrant-calculated half-life was 9 days ($r^2 = 0.987$). Iprodione decreased from an average of 98.7% of the applied radioactivity at time 0 to 36.5-40.3% at 7 days, and 7.1-8.5% at 30 days (Tables VII and VIII). The major non-volatile degradate was the isomer 3-(1-methylethyl)-N-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide (RP-30228). RP-30228 increased to 64.0-64.6% of the applied at 14 days posttreatment and was 52.0-59.7% at 30 days (Tables VII and VIII). Other nonvolatile degradates identified during the study were 3-(3,5-dichlorophenyl)-2,4-(dioxo-1-imidazol)idinecarboxamide (RP-32490; maximum concentration 11.9-14.6% of the applied at 2 days posttreatment) and 3-(1-methylethyl)-N-(3,5-dichlorophenyl)-1-ureylenecarboxamide (RP-36221; 1.2% at 30 days).

Three unidentified [^{14}C]compounds were isolated and detected at maximums of 1.7% (Unknown 10), 1.8% (Unknown 6), and 11.5% (Unknown 9) of the applied. [^{14}C]Residues remaining at the origin of the TLC plates increased to 5.0-8.9% of the applied by 30 days posttreatment. At 30 days posttreatment, evolved $^{14}\text{CO}_2$ totaled 2.2-2.6% of the applied radioactivity, organic volatiles totaled 0.2-0.5%, and unextracted [^{14}C]residues accounted for 6.1-8.3% (Table VI). [^{14}C]Residues associated with the water fraction of the sediment:water systems decreased from 57.9-67.8% of the applied at 1 day posttreatment to 7.4-8.4% at 30 days. Material balances ranged from 97.2% to 111.1% of the applied (Table VI).

In sterilized sediment:water systems, iprodione comprised 5.4-15.9% of the applied by 30 days posttreatment. At 30 days posttreatment, RP-30228 was

the major degradate comprising 77.2-87.0% of the applied; RP-32490 and RP-36221 were also detected at $\leq 2.3\%$ of the applied.

CONCERNS:

1. Not all degradates detected at >0.01 ppm (0.12% of the applied) were identified. Three unidentified [^{14}C] compounds were isolated; Unknown 6 comprised up to 1.8% (0.15 ppm) of the applied, Unknown 9 up to 11.5% (0.93 ppm), and Unknown 10 up to 1.7% (0.14 ppm). [^{14}C] Residues remaining at the origin of the TLC plates increased to $5.0-8.9\%$ of the applied by 30 days posttreatment.

2. The test water was not completely characterized; the dissolved oxygen content of the rice paddy water was not determined.

3. It was reported that "bulk" incubations were conducted to produce sufficient material for degradate identifications. Two samples (100 g equivalent dry weight) of silt loam sediment were flooded with 200 mL of [^{14}C] iprodione-treated (8.12 ppm) water and incubated as described above for the nonsterile soil:water systems. However, it was not reported at what sampling interval the bulk incubations were collected, and quantitative data concerning the bulk incubations were not reported.

4. In a hydrolysis study (MRID 41885401), the degradate 3-(isopropyl-carbamoyl)-5-(3,5-dichlorophenyl)hydantoin (RP-35606) was detected at a maximum $10.8-11.9\%$ of the applied at 30 days posttreatment in pH 5 solution and $9.8-10.4\%$ at 40.4 hours in pH 7 solution. Apparently, RP-35606 was not analyzed for in this study, since a reference standard was not received for TLC cochromatography.

5. A storage stability study was conducted by analyzing the time 0 water extracts for parent iprodione after 0, 11, 20, and 31 days of frozen storage. The data indicate that the extracted iprodione was stable under the storage conditions up to 31 days (Table III). It was not reported how long the study sample extracts were stored prior to analysis.