DATA EVALUATION RECORD

STUDY 3

CHEM 129112 Trifloxystrobin §161-3
CAS No. 141517-21-7
FORMULATION--00-ACTIVE INGREDIENT

STUDY ID 44496728
Cohen, S. P. 1997. Photodegradation of [phenyl(A)-U-$^{14}$C]-CGA-279202 on a loamy sand under artificial sunlight irradiation. PERL Study No. ME 9400174. Novartis Study No. 367-94. Unpublished study performed by Pittsburgh Environmental Research Laboratory, Inc., Pittsburgh, PA; and submitted by Novartis Crop Protection, Inc., Greensboro, NC.

DIRECT REVIEW TIME = 41.5 Hours

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CONCLUSIONS

Degradation - Photodegradation on Soil

1. This study is scientifically valid and provides useful information on the photodegradation of trifloxystrobin on soil. However, a photolytic half-life could not be accurately determined because the parent compound degraded rapidly with similar half-lives in the irradiated and dark control soils. Photolytic degradation was indicated by the differences in the degradates and the levels of the degradates observed between the two systems. The major degradate CGA-321113 was observed to be relatively more stable in the dark control soils, indicating that photodegradation of this major degradate may have occurred in the irradiated soils.

2. This study meets Subdivision N Guidelines for the fulfillment of EPA data requirements on photodegradation on soil.

3. Uniformly phenyl ring-labeled [$^{14}$C]trifloxystrobin, at a nominal rate of 3.0 ppm, degraded rapidly with respective half-lives of 1.8 and 1.7 days (0-7 day data) in irradiated and dark control samples of loamy sand soil maintained at 75% of 0.33 bar moisture content and incubated at 25 ± 1 °C for up to 30 days. Biphasic degradation was observed in both systems, with the rapid phase occurring through 7 days posttreatment. However, due to similar and rapid rates of degradation observed in the irradiated and dark control soils, the registrant-calculated photolytic half-life of 25.7 days was of questionable worth. Photolytic degradation was indicated by the differences in the degradates and the levels of the degradates observed between the two systems. The major degradate CGA-321113 was observed to be relatively more stable in the dark control soils, indicating that photodegradation of this major degradate may have occurred in the irradiated soils. All data, designated as percentages of the applied radioactivity, represent percentages of the nominal application rate. In the irradiated soils, the parent compound was initially 99.0% of the applied radioactivity, decreased to 19.0% by 2 days and 4.3% by 7-14 days posttreatment, and was last detected at 1.1% at 21 days. In the dark controls, the parent compound was initially 98.6% of the applied radioactivity, decreased to 18.9% by 2 days and 5.1% by 7 days posttreatment, and was 2.9% at 30 days. In the irradiated soil, the major degradate CGA-321113 was first detected at a maximum of 50.7% of the applied radioactivity at 2 days posttreatment, decreased to 35.5% by 7 days, and was 21.2% at 30 days. In contrast, in the dark controls, the major degradate CGA-321113 was first detected at 75.4% of the applied radioactivity (2 days), was a maximum of 92.3% at 14 days, and was 80.4% of the applied at 30 days posttreatment. In the irradiated soils, the major degradate CGA-373466 was first detected at 23.9% of the applied (2 days), was a maximum of 41.1% at 7 days, and was 28.5% at 30 days. In contrast, in the dark controls, the minor degradate CGA-373466 was a maximum of 1.0% of the applied at 30 days posttreatment. Radiolabeled residues comprised of CGA-357261 and NOA-409480 were present in the irradiated soils at a maximum of 10.4% of the applied (30 days). In

contrast, CGA-357261 and NOA-409480 were detected in the dark controls only once, at 1.9% of the applied at 30 days posttreatment. The minor degradate CGA-357276 was present at respective maximums of 6.4% and 1.6% of the applied (30 days) in the irradiated and dark control soils. The minor degradate CGA-331409 was detected once at 1.4% (1 of 2 replicates; 2 days) of the applied in the irradiated soils and was not detected in the dark controls. In the irradiated samples, $^{14}CO_2$ was 1.6% of the applied radioactivity at 7 days posttreatment and increased to 4.9% by 14 days and 10.0% by 30 days. In the dark control samples, evolved $^{14}CO_2$ was a maximum of 0.5% of the applied at 30 days posttreatment.

## METHODOLOGY

This study was conducted using uniformly phenyl ring-labeled [$^{14}$C]trifloxystrobin labeled on the α-ring. An additional study (MRID 44496729) was conducted using the β-labeled parent compound.

Subsamples (8 g wet weight) of preincubated (2 weeks in darkness at 75% of 0.33 bar soil moisture content) loamy sand soil (collected from Franklin County, NC; 81% sand, 10% silt, 9% clay, 0.5% organic matter, pH 7.3, CEC 3.9 meq/100 g; Table II, p. 36) were sieved (2 mm) and weighed onto individual stainless steel plates to form a 2-mm thick layer (p. 18). The soil samples were treated by syringe with uniformly phenyl ring-labeled [$^{14}$C]trifloxystrobin {CGA-279202; (E,E)-α-(methoxyimino-2-[[[[1-[3-trifluoromethyl)phenyl]ethylidene]amino]oxy]methyl]acetic acid methyl ester; radiochemical purity 99.1%, specific activity 30.4 μCi/mg; p. 14}, dissolved in acetonitrile, at a nominal rate of 3.0 ppm (p. 18). The samples were placed in an incubation chamber covered with a quartz glass plate and equipped with a cooling jacket to maintain the temperature at 25 ± 1°C (p. 16; Figure 4, p. 61); temperature and moisture content was monitored using probes placed on a reference soil (Table VI, p. 49; Figure 9, p. 66). The soil moisture content in the irradiated samples was maintained at 75% of 0.33 bar by the addition of reagent water throughout the incubation period as necessary. Dark control samples were covered with a stainless steel cover and incubated in a similar manner, but without the addition of moisture during the incubation period. To capture volatiles, humidified air was drawn through the chamber and into two ethylene glycol traps, two 2 *N* KOH traps, polyurethane plugs, and activated charcoal in series (pp. 16, 19). Volatiles traps were collected for analysis and replaced with fresh traps at each sampling interval. Samples were irradiated for up to 30 days on a 12-hour light/dark cycle using a xenon arc lamp equipped with a filter to remove wavelengths of <290 nm (p. 17; Figure 4, p. 61). The light intensity of the artificial light source (measured only at 280 nm, 365 nm, and 440 nm at 0 and 30 days) was similar at the initiation and termination of the study and was a mean of 2.6-2.7 × $10^{-2}$ W/m$^2$ at each measured wavelength over the incubation period (Table III, p. 37). The nominal intensity of the artificial light source was 765 W/m$^2$. A comparison graph of the spectral distribution of

the artificial light source with natural sunlight (at noon in June in Phoenix, AZ) was presented in Figure 5 (p. 62); plotted data indicated similar total irradiance (across the visible light range) between the two light sources. Duplicate subsamples of irradiated and dark control soil were removed for analysis at 0, 2, 7, 14, 21, and 30 days posttreatment (p. 19).

At each sampling interval, soil samples were extracted three times by sonicating with acetonitrile:acidified water (glacial acetic acid, pH 4; 80:20, v:v) and centrifuged (p. 21). The supernatants were decanted and combined, and duplicate aliquots were analyzed for total radioactivity by LSC; the limit of detection was 75 dpm (p. 22). Soil samples collected after 2 days posttreatment were further extracted by sonicating with acetone:2 M acetic acid (80:20, v:v) and centrifuged. Duplicate aliquots of the supernatant were analyzed for total radioactivity by LSC. Aliquots of both extracts were filtered, concentrated by rotary evaporation, and analyzed by LSC. Aliquots of the concentrated extracts were analyzed by reverse-phase HPLC (Alltech Lichrosorb RP-18 column) using a mobile phase gradient of aqueous 1% formic acid:acetonitrile (100:0 to 35:65, v:v) with UV (250 nm) and radioactive flow detection; the limit of detection was 500 dpm (Table V, p. 39). Eluate fractions were collected at one-minute intervals and analyzed for total radioactivity by LSC; column recoveries were 97.9 ± 6.7% (p. 20). Samples were co-chromatographed with nonradiolabeled reference standards. The extracts were further analyzed by two-dimensional TLC on silica gel plates developed sequentially in toluene:chloroform:ethyl ether:formic acid (60:34:5:1, v:v:v:v) and toluene:ethyl acetate:acetic acid (70:30:1.5, v:v:v); radioactive areas on the TLC plates were quantified by radioimage scanning. Samples were co-chromatographed with nonradiolabeled reference standards which were visualized with UV (254 nm) light. The concentrated soil extracts were analyzed by TLC as previously described; radioactive areas were scraped from the plates, mixed with water, and analyzed by LSC. Post-extracted soil subsamples were analyzed for total radioactivity by LSC following combustion.

At each sampling interval, duplicate aliquots of the ethylene glycol and KOH volatile trapping solutions were analyzed for total radioactivity by LSC (p. 21). To confirm the presence of $^{14}CO_2$ in the KOH traps, selected aliquots (days 14 and 21) were precipitated with $BaCl_2$; data were provided in Table X (p. 44). The analytical methods for the analysis of the polyurethane plugs and activated charcoal were not specified.

To confirm the viability of the soil, selected irradiated (days 0 and 30) and dark control (day 30) soil subsamples were extracted by vortexing with sterile 0.1 M $CaCl_2$ solution (p. 18). The supernatants were decanted, serially diluted, and plated on agar for approximately 48 hours at 25°C. Viability was evaluated by enumerating total colony-forming units (CFU) of bacteria and actinomycetes; microbial data indicated that the soils were viable at the intiation and termination of the study (Table VII, p. 41).

DATA SUMMARY

Uniformly phenyl ring-labeled [$^{14}$C]trifloxystrobin (radiochemical purity 99.1%), at a nominal rate of 3.0 ppm, degraded rapidly with respective half-lives of 1.8 and 1.7 days (0-7 day data) in irradiated and dark control samples of loamy sand soil maintained at 75% of 0.33 bar moisture content and incubated at 25 ± 1 °C for up to 30 days (p. 29). Biphasic degradation was observed in both systems, with the rapid phase occurring through 7 days posttreatment. However, due to the similar and rapid rates of degradation observed in the irradiated and dark control soils, the registrant-calculated photolytic half-life of 25.7 days was of questionable worth. Photolytic degradation was indicated by the differences in the degradates and the levels of the degradates observed between the two systems. The major degradate CGA-321113 was observed to be relatively more stable in the dark control soils, indicating that photodegradation of this major degradate may have occurred in the irradiated soils. All data, designated as percentages of the applied radioactivity, represent percentages of the nominal application rate. In the irradiated soils, the parent compound was initially present at 99.0% of the applied radioactivity, decreased to 19.0% by 2 days and 4.3% by 7-14 days posttreatment, and was last detected at 1.1% of the applied at 21 days (Table XI, p. 45). Similarly, in the dark control soils, the parent compound was initially present at 98.6% of the applied radioactivity, decreased to 18.9% by 2 days and 5.1% by 7 days posttreatment, and was 2.9% of the applied at 30 days posttreatment (Table XIII, p. 47). In the irradiated soil samples, the major degradate

(E,E)-α-(methoxyimino-2-[[[[1-[3-trifluoromethyl)phenyl]ethylidene]amino] oxy]methyl]acetic acid methyl ester (CGA-321113)

was first detected at a maximum of 50.7% of the applied radioactivity at 2 days posttreatment, decreased to 35.5% of the applied by 7 days, and was 21.2% of the applied at 30 days posttreatment. The major degradate

(Z,E)-α-(methoxyimino-2-[[[[1-[3-trifluoromethyl)phenyl]ethylidene]amino] oxy]methyl]acetic acid methyl ester (CGA-373466)

was first detected in the irradiated soils at 23.9% of the applied radioactivity at 2 days posttreatment, increased to a maximum of 41.1% of the applied by 7 days, and then decreased to 28.5% of the applied by 30 days posttreatment. Radiolabeled residues comprised of (Z,E)-α-(methoxyimino-2-[[[[1-[3-trifluoromethyl)phenyl]ethylidene] amino]oxy]methyl] acetic acid methyl ester (CGA-357261) and NOA-409480 (Z isomer; chemical name not reported; structure presented in Figure 1, p. 56) were first detected at 2.5% of the applied radioactivity at 2 days posttreatment, were 9.6% and 7.2% of the applied at 14 and 21 days, respectively, and were a maximum of 10.4% of the applied at 30 days posttreatment. The minor degradate (E)-α-(methoxyimino-2-[[[[1-[3-trifluoromethyl)phenyl]ethylidene]amino]oxy]methyl] acetic acid methyl ester (CGA-357276) was initially 1.9% at 7 days posttreatment and was present at a maximum of

6.4% of the applied radioactivity at 30 days. The minor degradate (E,Z)-α-(methoxyimino-2-[[[[1-[3-trifluoromethyl)phenyl]ethylidene]amino]oxy]methyl]acetic acid methyl ester (CGA-331409) was detected once at 1.4% (1 of 2 replicates) of the applied radioactivity at 2 days posttreatment. Four unidentified degradates were each present at ≤4.2% of the applied radioactivity. Uncharacterized [$^{14}$C]residues (designated as others) were ≤1.3% of the applied radioactivity. Nonextractable [$^{14}$C]residues were 4.4% of the applied at 14 days posttreatment, and were a maximum of 13.2% of the applied at 30 days (Table VIII, p. 42). Evolved $^{14}CO_2$ was 1.6% at 7 days posttreatment and increased to 4.9% by 14 days and to a maximum of 10.0% of the applied radioactivity by 30 days posttreatment.

In the dark control soil samples, the major degradate

CGA-321113

was first detected at 75.4% of the applied radioactivity at 2 days posttreatment, increased to a maximum of 92.3% of the applied by 14 days, and was 80.4% of the applied at 30 days. The minor degradates CGA-373466 (detected as a major degradate in the irradiated soil samples) and CGA-357276 were present at respective maximums of 1.0% and 1.6% of the applied radioactivity at 30 days posttreatment. Radiolabeled residues comprised of CGA-357261 and NOA-409480 were detected once at 1.9% of the applied radioactivity at 30 days posttreatment. Three unidentified degradates were each present at ≤1.2% of the applied radioactivity. Uncharacterized [$^{14}$C]residues (designated as others) accounted for ≤2.3% of the applied radioactivity. Nonextractable [$^{14}$C]residues were 2.5% of the applied at 7 days, and were a maximum of 7.8% of the applied at 30 days (Table IX, p. 43). Evolved $^{14}CO_2$ increased throughout the incubation period and was a maximum of 0.5% of the applied radioactivity at 30 days posttreatment.

Material balances (for individual replicates) were 92.1%-101.3% and 94.0%-102.4% of the applied radioactivity for the irradiated and dark control samples, respectively (Tables VIII, IX, pp. 42, 43).

COMMENTS

1. It could not be determined whether photodegradation of the parent compound actually occurred because the parent degraded rapidly (≤19% remained as parent at 2 days posttreatment in both systems) and with similar half-lives in the irradiated and dark control soils. Therefore, the registrant-calculated photolytic half-life of 25.7 days was of questionable worth. Photolytic degradation was indicated by the differences in the degradates and the levels of the degradates observed between the two systems. The major degradate CGA-321113 was observed to be relatively more stable in the dark control soils, indicating that photodegradation of this major degradate may have occurred in the

irradiated soils.

2. The reviewer notes that the parent compound (labeled on the α-ring) degraded more rapidly in the current study than was observed in an additional photodegradation on soil study (MRID 44496729) which was conducted using the β-labeled parent compound; soil characterization data indicated that the same soil type was utilized in studies. In the current study (α-label), the parent compound was present in the irradiated and dark control soils at 19.0% and 18.9% of the applied, respectively, at 2 days posttreatment and decreased to 1.1% (21 days) and 2.9% (30 days), respectively, by the last sampling interval in which it was detected. In the β-label study, the parent compound was present in the irradiated and dark control soils at 49.5% and 53.1% of the applied, respectively, at 2 days posttreatment and decreased to 12.7% and 11.5%, respectively, by 30 days posttreatment. Additionally, the major degradate CGA-321113 (which was more stable in each dark control compared with the irradiated soils) was present in the dark control samples of the α-label study at a greater percentage (80.4%) of the applied radioactivity at 30 days posttreatment compared with the percentage (56.1%) observed in the β-label study at that sampling interval. It was unclear to the reviewer why the rate and pattern of degradation would be dissimilar between the two studies which utilized similar experimental methods and differed only in the location of the radiolabel on the parent compound. Clarification by the registrant is necessary.

3. The soil utilized in this study was a loamy sand soil collected from North Carolina. The reviewer notes that a loamy sand soil from North Carolina, with generally similar characteristics, was also utilized in an aerobic soil metabolism study (MRID 44496732). Since soil series names were not reported in either study, the reviewer could not confirm that they were the same type of soil. Clarification by the registrant is necessary.

4. The spectral distribution of the artificial light source was compared with that of representative natural sunlight (Figure 5, p. 62); however, the total light intensity of the artificial light source was not reported. It is necessary that the registrant provide this information in all photodegradation studies submitted to EPA.

5. The complete chemical name of the degradate NOA-409480 was not reported by the study author; the structure was presented in Figure 1 (p. 56). In future studies submitted to the EPA, chemical names of all confirmed degradates should be reported.

6. The proposed metabolic pathway for the degradation of trifloxystrobin is presented in Figure 27 (p. 84).

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Pages 8 through 31 are not included.

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