

US EPA ARCHIVE DOCUMENT

CONCLUSIONS

Degradation - Photodegradation in Soil

1. The photodegradation in soil study is partially acceptable. This study can be upgraded if the following information is submitted:
 - (a) an explanation of why the dark control half-life (155 days) did not correlate well with the aerobic soil metabolism half-life (10 days) and why the data for the dark control study was highly variable.
 - (b) why was the analytical purity of the test substance 78% at 0 hour? The Agency prefers that the analytical purity be between 90 - 110% at 0 hour.
 - © additional information on the rate of degradation and metabolites for the phenyl-labeled study, both the irradiated study and dark control
 - (d) what were the method detection limits for these studies?
 - (e) an explanation for the differences in the degradates between the dark control and the aerobic soil metabolism study.
2. EFED notes the following:
 - (i) it could not be determined if the soil moisture was maintained at 75% of 0.33 bar throughout the study; and
 - (ii) individual test vessels were not utilized for each sampling interval, precluding the use of duplicate samples for analysis. Instead, only a single container of soil was treated (for each label), and a single soil sample was removed (with duplicate subsamples used for analysis) at each sampling interval.
 - (iii) the study was conducted at the least stable pH (5.5).
4. Pyridinyl ring-labeled [4,6-¹⁴C]diflufenzopyr (SAN 835 H)

Pyridinyl ring-labeled [4,6-¹⁴C]diflufenzopyr (SAN 835 H), at a nominal concentration of 0.4 ppm, degraded with an uncorrected half-life of 130 hours or 12.5 days in loam soil that was irradiated continuously with a xenon arc lamp while incubated at $22 \pm 1^\circ\text{C}$ for 328 hours. The dark-control corrected half-life was 336 hours (14 days), while the adjusted net photolysis rate (corrected for light intensity) was 436 hours (18.2 days). However, the registrant-calculated half-life may be questionable because of the variability in the dark control data which indicated that the parent compound increased by each of the next two

sampling intervals. All data (designated as percentages of the applied) represent percentages of the nominal application. In the irradiated soil, the parent compound decreased from an initial 78.10% of the applied radioactivity to 50.38% by 119 hours posttreatment and was 32.97% at 328 hours. In the dark control, the parent compound was present at 73.53-91.26% of the applied radioactivity from 0 to 328 hours posttreatment, and did not exhibit a clear degradation pattern. The major degradate M1 was present in the irradiated soil at 10.63% of the applied radioactivity at 47 hours posttreatment and was a maximum of 18.21% at 328 hours. The major degradate M6 was present in the irradiated soil at 10.35% of the applied at 23 hours posttreatment and was a maximum of 14.35% at 328 hours. The minor degradate M5 was detected in the irradiated soil at a maximum of 2.73% of the applied radioactivity. For the irradiated soil, radiolabeled [¹⁴C]volatiles were negligible. In contrast, M1 was present as a major degradate in the dark control soil, at 10.88% of the applied radioactivity at 328 hours posttreatment. In addition, M6 and M5 were present as minor degradates in the dark control at a maximum of 8.08% and 2.73% of the applied, respectively.

Uniformly phenyl ring-labeled [¹⁴C]diflufenzopyr (SAN 835 H)

Uniformly phenyl ring-labeled [¹⁴C]diflufenzopyr (SAN 835 H), at a nominal concentration of 0.4 ppm, degraded with an unspecified half-life in loam soil that was irradiated continuously with a xenon arc lamp while incubated at 22 ± 1 °C for 358 hours (14.9 days). The parent compound was also observed to degrade with an unspecified half-life in dark control soil incubated at 22 ± 1 °C for 358 hours. No half-life calculations were performed for this compound. All data (designated as percentages of the applied) represent percentages of the nominal application. In the irradiated soil, the parent compound decreased from an initial 90.16% of the applied radioactivity to 55.67% by 118 hours posttreatment and was 38.30% at 358 hours posttreatment. In contrast, 63.72% of the applied radioactivity remained as parent following 358 hours of incubation in the dark control soil. The minor degradate M5 was detected in the irradiated soil at a maximum of 9.43% of the applied radioactivity at 358 hours posttreatment. Radioactivity associated with the fulvic acid, humic acid and humin fractions in the irradiated soil was 1.53%, 7.86% and 2.91% of the applied, respectively, at 358 hours posttreatment. Radiolabeled ¹⁴CO₂ was 2.06% of the applied following 358 hours of incubation; [¹⁴C]organic volatiles were negligible. In the dark control soil, M5 was present as a major degradate at a maximum of 11.59% of the applied radioactivity at 358 hours posttreatment.

METHODOLOGY

Pyridinyl ring-labeled [4,6-¹⁴C]diflufenzopyr (SAN 835 H; 2-(methyl-(((3,5-difluorophenylamine)-carbonyl)-hydrazone-methyl)-3-pyridine carboxylic acid; radiochemical purity 98.1%, specific activity 53 mCi/mmol) or uniformly phenyl-ring labeled [¹⁴C]diflufenzopyr (radiochemical purity 98.0%, specific activity 77 mCi/mmol), dissolved in acetonitrile, was added at a nominal concentration of 0.4 ppm (equivalent to the highest field application rate of 0.2 lb a.i./acre) to a bulk sample (200 g) of loam soil (28% sand, 46% silt, 26% clay; 3.4% organic matter; pH 5.5; CEC 16.2 meq/100 g; p. 12). A subsample (100 g) of the treated soil was placed in an amber glass container which was wrapped with aluminum foil and maintained at 22 ± 1 °C to serve as a dark control. The remainder of the treated soil was transferred to a glass photolysis dish equipped with a water cooling jacket to maintain the temperature at 22 ± 1 °C. The test vessel had outlets which were connected to a series of volatile traps containing silica gel, ethylene glycol and sodium hydroxide; air was drawn through the traps by means of a vacuum pump (Figure 1, p. 37). The photolysis dish was covered with a borosilicate glass plate (to filter out light below 290 nm) and continuously irradiated for approximately 15 days with a 2500 watt xenon arc lamp. The light intensity between 300 nm and 800 nm was measured at the initiation and termination of the incubation period. A comparison of the irradiance for the artificial light used to natural light was presented in Figure 2 (p. 29). The average light intensity for the pyridinyl radiolabel was 7.55 × 10² W/m²; and for the phenyl radiolabel was 8.99 × 10² W/m² (p. 12). The reported natural sunlight intensity in spring at 40°N latitude was 5.83 × 10² W/m² (p. 12). Subsamples of the irradiated and dark control soils were removed for analysis at 0, 23, 47, 119, 191, 287 and 328 hours posttreatment (pyridinyl label); or 0, 22, 46, 118, 214, 286, and 358 hours posttreatment (phenyl label).

Subsamples of irradiated and dark control soils were extracted three times with 20 mL of acetonitrile:(1 *N*) sodium hydroxide (1:1, v:v). The combined extracts were partially evaporated to remove the acetonitrile. The remaining fraction was mixed with concentrated HCl and the acidified samples were partitioned three times with ethyl acetate; the organic and aqueous fractions were analyzed by LSC (p. 13). Extracts with greater than 10% of the applied radioactivity were analyzed by either one or two-dimensional TLC using silica gel plates (with fluorescent indicator) developed with numerous solvent systems (p. 13). Organic extracts were spotted alone or co-chromatographed with reference standards which were visualized by UV detection and then quantified using radioimage scanning. To confirm compound identities, additional analysis was performed using reverse-phase HPLC (Phenomenex C18 column) with a mobile phase of acetonitrile:water with 1% acetic acid (50:50, v:v) and radioactive flow detection; samples were co-chromatographed with reference standards detected by UV.

DATA SUMMARY

Pyridinyl ring-labeled [4,6-¹⁴C]diflufenzopyr (SAN 835 H)

Pyridinyl ring-labeled [4,6-¹⁴C]diflufenzopyr (SAN 835 H; radiochemical purity 98.1%), at a nominal concentration of 0.4 ppm, degraded with an uncorrected half-life of 130 hours (12.5 days) in loam soil that was irradiated continuously with a xenon arc lamp while incubated at 22 ± 1°C for 328 hours or 13.7 days ($r^2 = 0.96$, Figure 3, p. 30; Table 9, p. 27; see Comment #9). The dark-control corrected half-life was 336 hours (14 days), while the adjusted net photolysis rate was 436 hours (18.2 days). However, the corrected half-lives may be questionable because the dark control data was variable. The parent compound degraded with an extrapolated half-life of 2,772 hours or 115.5 days in the dark control soil incubated at 22 ± 1°C for 328 hours ($r^2 = 0.24$; Figure 3, p. 30; Table 9, p. 27). The time zero data, determined from the same soil sample for both the irradiated and dark control soils, were questionable because the dark control data indicated that the parent compound increased by each of the next two sampling intervals. All data (designated as percentages of the applied) represent percentages of the nominal application. In the irradiated soil, the parent compound decreased from an initial 78.10% of the applied radioactivity to 50.38% by 119 hours posttreatment and was 32.97% at 328 hours (Table 5, p. 23). In the dark control, the parent compound was present at 73.53-91.26% of the applied radioactivity from 0 to 328 hours posttreatment, and did not exhibit a clear degradation pattern (Table 6, p. 24). In irradiated samples, the major degradate

8-methyl-5(6H)-pyrido[2,3-d]pyridazinone (M1)

was initially present (0 hours) at 2.11% of applied radioactivity, increased to 10.63% by 47 hours posttreatment and was a maximum of 18.21% at 328 hours posttreatment. The major degradate

2-acetylnicotinic acid (M6)

was initially present (0 hours) at 4.51% of applied radioactivity, increased to 10.35% by 23 hours posttreatment and was a maximum of 14.35% at 328 hours posttreatment. The minor degradate 6-((3,5-difluorophenyl-carbamoyl)-8-methyl)-pyrido (2,3-d)-5-pyridazinone (M5) was present at a maximum of 2.73% of the applied radioactivity at 0 hours posttreatment. For the irradiated soil, radiolabeled ¹⁴CO₂ accounted for 0.87% of the applied radioactivity following 328 hours of incubation; [¹⁴C]organic volatiles were negligible. Nonextractable [¹⁴C]residues were a maximum of 5.22% of the applied radioactivity in the irradiated soil at 287 hours posttreatment. In the dark control, M1 was present as a major degradate, at 10.88% of the applied radioactivity at 328 hours posttreatment. The minor degradates M6 and M5 were present in the dark control at maximums of 8.08% (328 hours posttreatment) and 2.73% (0 hours posttreatment) of the applied radioactivity, respectively.

Material balances for the irradiated soil ranged from 92.93% to 98.96% of the applied radioactivity (Table 5, p. 23), and were 92.93-106.95% for the dark control (Table 6, p. 24).

Uniformly phenyl ring-labeled [¹⁴C]diflufenzopyr (SAN 835 H)

Uniformly phenyl ring-labeled [¹⁴C]diflufenzopyr (SAN 835 H; radiochemical purity 98.0%), at a nominal concentration of 0.4 ppm, degraded with an unspecified half-life in loam soil that was irradiated continuously with a xenon arc lamp at $22 \pm 1^\circ\text{C}$ for 358 hours (14.9 days). The parent compound was also observed to degrade with an unspecified half-life in dark control soil incubated at $22 \pm 1^\circ\text{C}$ for 358 hours. No half-life calculations were performed for this compound. All data (designated as percentages of the applied) represent percentages of the nominal application. In the irradiated soil, the parent compound decreased from an initial 90.16% of the applied radioactivity to 55.67% by 118 hours posttreatment and was 38.30% at 358 hours (Table 7, p. 25). In contrast, in the dark control soil the parent decreased from an initial 90.16% of the applied radioactivity to 80.84% by 22 hours posttreatment, increased to 83.85-84.10% by 46-118 hours, then decreased to 63.20- 63.72% of applied radioactivity by 286-358 hours posttreatment. In the irradiated soil, the minor degradate M5 was initially present (0 hours) at 4.32% of the applied radioactivity and generally increased to a maximum of 9.43% of the applied radioactivity by 358 hours posttreatment. Nonextractable [¹⁴C]residues were a maximum of 12.29% of the applied radioactivity in the irradiated soil at 358 hours posttreatment. Radioactivity associated with the fulvic acid, humic acid and humin fractions in the irradiated soil was 1.53%, 7.86% and 2.91% of the applied, respectively. Radiolabeled ¹⁴CO₂ accounted for 2.06% of the applied radioactivity following 358 hours of incubation; [¹⁴C]organic volatiles were negligible. Unidentified [¹⁴C]radioactivity in the irradiated soil was a maximum at 25.43% of the applied at 214 hours posttreatment, however, none of the unidentified compounds were present at $\geq 10\%$ of the applied. In the dark control soil, the major degradate M5 was present at a maximum of 11.59% of the applied radioactivity at 358 hours posttreatment. Nonextractable [¹⁴C]residues were a maximum of 5.68% of the applied in the dark control soil at 358 hours posttreatment.

Material balances for the treated irradiated soil ranged from 90.24% to 102.09% of the applied radioactivity (Table 7, p. 25), and were 89.62-102.54% for the dark control (Table 8, p. 26).

COMMENTS

1. The dark control half-life (155 days) did not correlate well with the aerobic soil metabolism half-life (10 days). In addition, the two studies showed different degradates. The author stated that the Elliot loam soil used in both studies were the same. The registrant needs to explain these discrepancies.
2. In the pyridinyl ring-labeled study, the corrected registrant-calculated half-life of the parent compound in the irradiated soil was reported as 336 hours (14 days). However, the data indicated that only 50.38% of the applied radioactivity remained as parent compound in the irradiated soil at 119 hours posttreatment. For both the dark control and irradiated soils, the parent compound was present at only 78.1% of the applied radioactivity immediately following treatment (0 hours posttreatment). In contrast, uniformly phenyl ring-labeled [¹⁴C]diflufenzopyr was initially present at 90.16% of the applied in irradiated and dark control soils. The low recovery of radioactivity as the parent compound (pyridinyl label) immediately after treatment is indicative of poor test preparation and/or analytical methods. Because the time zero data were determined from the same soil sample for both the irradiated and dark control soils, and dark control data indicated increased parent compound with time, the time zero data (and, thus, half-lives calculated using the data) are questionable for both the irradiated and dark control soils.
3. In the pyridinyl ring-labeled study, the data for the dark control were variable. The parent was initially present at 78.10% of the applied radioactivity at 0 hours posttreatment, increased to 91.26% by 47 hours, decreased to 78.27% by 191 hours, then increased to 82.55% by 287 hours and was 73.53% at 328 hours posttreatment (Table 6, p. 24). The coefficient of determination for the linear regression of this data was very poor ($r^2 = 0.24$, Figure 3, p. 30; Table 9, p. 27). The applied radioactivity present as parent compound in the dark control soil treated with uniformly phenyl ring-labeled [¹⁴C]diflufenzopyr was also variable with time. The parent was initially present at 90.16% of applied radioactivity at 0 hours posttreatment, decreased to 80.84% by 22 hours, then increased to 83.85%-84.10% by 46-118 hours (Table 8, p. 26).
4. The half-lives of the parent compound and degradates in the uniformly phenyl ring-labeled [¹⁴C]diflufenzopyr study were not calculated. The study was terminated before the formation and decline of these degradation products could be clearly established.
5. The soil moisture content was not reported for the irradiated or dark control soils. Therefore, the reviewer could not determine whether the test soils were maintained at the recommended 75% of 0.33 bar moisture content during the incubation period.
6. Method detection limits were not reported. Method detection limits (LSC and TLC) should be reported to assure the adequacy of the methods for determination of parent and metabolites in the test system.

7. The study author stated that the photointensity of the artificial light source was 1.30 to 1.54 times the light intensity for natural sunlight during spring at 40°N. The study author calculated an "adjusted net photolysis" based on the results of the dark control and the greater photointensity of the xenon light source; values are presented in Table 19 (p. 27).
8. Individual test vessels were not utilized for each sampling interval, precluding the use of duplicate samples for analysis. Instead, only a single container of soil was treated (for each label) and a single soil sample was removed (with duplicate subsamples used for analysis) at each sampling interval. The use of single samples is generally not considered to be good laboratory practice. At a minimum, duplicate sampling (removed from individual, duplicate test vessels at each sampling interval) should be used for determining a half-life.
9. The study was conducted at the least stable pH (5.5).

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