Aerobic Soil Metabolism of Pymetrozine

Report: Das, Y. T. 1996. Metabolism of [pyridinyl-5-14C]CGA-21 5944 under aerobic soil conditions. Ciba-Geigy Study No: 45-94. Unpublished study performed by Innovative Scientific Services, Inc., Piscataway, NJ; and submitted by Ciba-Geigy Corporation, Greensboro, NC.

Document No.: MRID 44024965

Guideline: OPPTS 835.4100

Classification: A study classification was not provided on the attached Data Evaluation Record, therefore, this study is now classified as Supplemental. This study is scientifically valid and provides useful information on the aerobic soil metabolism of pymetrozine. An adequate attempt was not made to extract and characterize degradates. The NaOH extractions were not characterized due to the harsh nature of the extraction and were >20% of the applied radioactivity in the 1.6 ppm and 9.6 ppm treated soils.

PC Code: 101103

Reviewer: Jessica L. O. Joyce, Fate Scientist
U.S. EPA Date: Date: 2018.02.08 08:00:02 -05'00'

Rochelle F.H. Bohaty, Senior Scientist
U.S. EPA Date: 2018.02.08 07:51:05 -05'00'

TEXT SEARCHABLE DOCUMENT 2011

DATA EVALUATION RECORD

STUDY 4a

CHEM 101103

Pymetrozine

§162-1

CAS No. 123312-89-0
FORMULATION--00--ACTIVE INGREDIENT

STUDY ID 44024965
Das, Y. T. 1996. Metabolism of [pyridinyl-5-^{14}C]CGA-215944 under aerobic soil conditions. Ciba-Geigy Study No: 45-94. Unpublished study performed by Innovative Scientific Services, Inc., Piscataway, NJ; and submitted by Ciba-Geigy Corporation, Greensboro, NC.

DIRECT REVIEW TIME = 43 hours

REVIEWED BY: D. E. Toland, M.S.
TITLE: Scientist
Signature:
Date:

EDITED BY: C. A. Little, Ph.D.
TITLE: Sr. Scientist/ Asst. Project Manager
Signature:
Date:

APPROVED BY: P. H. Howard, Ph.D.
TITLE: Project Manager
Signature:
Date:

ORG: Syracuse Research Corp.
Arlington, VA 22202

TEL: 703/413-9369

APPROVED and REVISED by: Thuy L. Nguyen, MS
TITLE: Chemist
ORG: ERB III/EFED/OPP
TEL: 703/605-0562

SIGNATURE: EFED Share drive Copy

2087119

TEXT SEARCHABLE DOCUMENT 2011

CONCLUSIONS

Metabolism - Aerobic Soil

1. This study is scientifically valid and provides useful information on the aerobic soil metabolism of pymetrozine.

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

3. Pyridinyl ring-labeled [5-^{14}C] CGA-215944, at nominal applications of 1.6 ppm (low dose) and 9.7 ppm (high dose), degraded with half lives ranging from 8.1 and 45.5 days, respectively, in sandy loam soil adjusted to 75% of 0.33 bar moisture content and incubated in darkness at 25 ± 1 °C for 357 days. These half-lives were based on a monophasic degradation behavior. A biphasic linear regression characterized by rapid metabolism of the available pymetrozine from day 0 to day 30, followed by a slower degradation until the study termination (day 120 for low dose application and day 357 for high dose) was also studied: the low dose half-lives were 3.2 and 299 days, for the primary and secondary phases, respectively; the high dose half-lives were 4.1 days and 405 days. These biphasic half-lives closely represent the degradation rate of pymetrozine during the studies.

   Reported concentrations were calculated by the reviewer based on the nominal application rate; degradate concentrations were corrected for the molecular weight of the compounds. Based on HPLC analysis of the acetonitrile:water extracts, the parent compound in the 1.6 ppm treated soil was initially 94.0% (1.5 ppm) of the applied radioactivity, decreased to 47.0% (0.75 ppm) by 120 days and was 32.4% (0.52 ppm) at 357 days posttreatment. In the 9.6 ppm treated soil, the parent compound was initially 95.1% (9.1 ppm) of the applied radioactivity, decreased to 54.4% (5.2 ppm) by 120 days, and was 36.2% (3.5 ppm) at 357 days posttreatment. The major degradate CGA-180777 was detected in the 1.6 ppm treated soil at a maximum of 16.5% (0.15 ppm) at 58 days posttreatment and was 0.5% (0.005 ppm; one replicate) at 238 days. In the 9.6 ppm treated soil, CGA-180777 was a maximum of 13.9% (0.76 ppm) of the applied at 14 days posttreatment and was 0.1-2.2% (0.005-0.12 ppm) from 92 to 357 days. The minor degradate CGA-359009 (2U) was detected in the 1.6 ppm and 9.6 ppm treated soils at maximums of 4.6% (0.079 ppm) of the applied radioactivity (238 days) and 7.7% (0.79 ppm) of the applied (182 days), respectively. The minor degradate CGA-319251 was detected in the 1.6 ppm treated soil at 0.1% (0.001 ppm) of the applied (one replicate; 92 days posttreatment) and in the 9.6 ppm treated soil at 0.2% (0.012 ppm) at 58 (one replicate) and 182 days posttreatment. In the 1.6 and 9.6 ppm treated soils, 7 (≤4.6% of the applied) and 8 (≤5.6% of the applied) unknown minor degradates were detected, respectively. Radiolabeled $^{14}CO_2$ was 1.6% and 3.8% of the applied radioactivity at 58 days posttreatment for respective soils treated at 1.6 ppm and 9.6 ppm, and accounted for maximums of 29.1% and 30.7% at 357 days posttreatment, respectively. Uncharacterized radioactivity in NaOH extracts was 21.4-27.5% of the applied in the 1.6 ppm treated soil and 16.4-24.2% in the 9.6 ppm treated

TEXT SEARCHABLE DOCUMENT 2011

soil at 30-357 days posttreatment; nonextractable [^{14}C]residues were maximums of 4.9% and 3.6% of the applied (day 0), respectively.

METHODOLOGY

Subsamples (5 g) of sieved (2 mm) Hanford sandy loam soil (collected from Sanger, CA; 71% sand, 20% silt, 9% clay, 0.3% organic matter, pH 7.4, CEC 4.6 meq/100 g; Table II, p. 41) were adjusted to 75% of the soil moisture content at 0.33 bar, weighed into glass bottles and preincubated in darkness at 25 °C for 23 days (p. 21). Following preincubation, the soils were treated with pyridinyl ring-labeled [5-^{14}C]pymetrozine (CGA-215944; 6-methyl-4-(pyridin-3-yl-methylenamino)-4,5-dihydro-1,2,4-triazin-3(2H)-one; radiochemical purity 98.0%, specific activity 55.4 µCi/mg; p. 20), dissolved in acetonitrile, at nominal concentrations of 1.6 (low dose) and 9.6 (high dose) ppm which were 1 and 6 times the recommended seasonal application rate (pp. 22, 36). The treated soil samples were incubated in darkness at 25 ± 1 °C for up to one year; the soil moisture level was monitored and adjusted as necessary throughout the incubation period (p. 25). Volatile traps containing KOH were suspended in the test vessels (p. 24). To maintain aerobic conditions, approximately once a week and prior to sample removal, the headspace was flushed with air and analyzed for total radioactivity by LSC following combustion. Duplicate samples were removed for analysis at 0, 1, 3, 7, 14, 30, 58, 92, 120, 182 (high dose only), 238 (low dose only), 273 (high dose only) and 357 days posttreatment (p. 23). Additional samples were removed at 0, 30, 58, 92, 120, 182 (high dose), 238 (low dose), 273 (high dose), and 357 days posttreatment to measure the soil oxygen concentration; and at 0, 30, 58, 92, 238 (low dose), 273 (high dose), and 357 days posttreatment to determine microbial populations. Soil oxygen concentrations were a mean of 8.4 ± 0.2 ppm for both the 1.6 and 9.6 ppm treated soils (Table IX, p. 50). Microbial analysis results are presented in Table VIII (p. 49); data indicated soils were viable.

Immediately following collection at each sampling interval, soil samples were extracted three times by shaking and sonicating with acetonitrile:water (8:2, v:v). Following each extraction, the samples were centrifuged and the combined supernatants were analyzed for total radioactivity by LSC (p. 25); the limit of detection was 0.2 ng of the parent material (p. 23). Soil samples were then re-extracted twice by shaking and sonicating at 80 °C with 1*N* NaOH followed by centrifugation. The combined supernatants were analyzed by LSC. The acetonitrile:water extracts were filtered (0.45 and 0.2 µm) and concentrated prior to HPLC analysis (Zorbax SB-C18 column) using a mobile phase gradient of 0.05% trifluoroacetic acid in water:methanol (100:0 to 95:5 to 0:100) with radioactive flow detection; the limit of detection was 0.01% of the injected radioactivity. Samples were co-chromatographed with non-radiolabeled reference standards which were visualized by UV (220 nm) light (p. 27). Eluent fractions were collected and analyzed by LSC; mean column recoveries were greater than 99%. To confirm compound identities, selected samples were analyzed by two-dimensional TLC on silica gel plates developed perpendicularly with chloroform:methanol:ammonium hydroxide:water (80:30:2:4, v:v:v:v) followed by either ethyl acetate:methanol:water (75:15:10, v:v:v) or chloroform:methanol:formic acid:water (75:25:4:2, v:v:v:v) with UV (254 nm) and

TEXT SEARCHABLE DOCUMENT 2011

radioactive scanning detection (pp. 27, 28). *Samples were co-chromatographed with nonradiolabeled reference standards.* Compound identities were further confirmed by HPLC/MS (p. 28).

Post-extraction soil samples were analyzed for total radioactivity by LSC following combustion. Radioactivity in the KOH traps was determined by LSC; $^{14}CO_2$ was confirmed by precipitation with $BaCl_2$ (pp. 24, 31).

DATA SUMMARY

Pyridinyl ring-labeled [5-^{14}C]pymetrozine, at application rates of 1.6 and 9.6 ppm, degraded with registrant-calculated half-lives of 101 days (r^2 = 0.96) and 142 days (r^2 = 0.96), respectively, in sandy loam soil adjusted to 75% of 0.33 bar moisture content and incubated in darkness at 25 ± 1 °C for 357 days (p. 38; Figures on pp. 478, 479). Reported half-lives were based on the linear regression of log transformed concentration data *vs.* cube-root transformed time data. Biphasic degradation was observed (using a first-order model; see Comment #2). All data, designated as percentages of the applied, are percentages of the nominal application. Reported concentrations were calculated by the reviewer based on the nominal application rate; degradate concentrations were corrected for the molecular weight of the compounds. Based on HPLC analysis of the acetonitrile:water extracts, the parent compound in the 1.6 ppm treated soil was initially present at 94.0% (1.5 ppm) of the applied radioactivity, decreased to 63.6% (1.0 ppm) of the applied by 30 days posttreatment and 47.0% (0.75 ppm) by 120 days posttreatment, and was 32.4% (0.52 ppm) at 357 days posttreatment (Table XX, p. 67). In the 9.6 ppm treated soil, the parent compound was initially detected at 95.1% (9.1 ppm) of the applied radioactivity, decreased to 66.3% (6.4 ppm) of the applied by 14 days posttreatment and 54.4% (5.2 ppm) by 120 days posttreatment, and was 36.2% (3.5 ppm) at 357 days posttreatment (Table XXI, p. 68). The major degradate

nicotinic acid (CGA-180777)

was initially detected in the 1.6 ppm treated soil at 1.5% (0.014 ppm) of the applied radioactivity at 3 days posttreatment, increased to a maximum of 16.5% (0.15 ppm) of the applied by 58 days posttreatment, decreased to 2.3% (0.021 ppm) by 92 days posttreatment and was last detected in one replicate at 0.5% (0.005 ppm) at 238 days posttreatment (Table XVII, pp. 62, 63). In the 9.6 ppm treated soil, CGA-180777 was initially detected at 0.3% (0.016 ppm) of the applied radioactivity at 0 days posttreatment, increased to a maximum of 13.9% (0.76 ppm) of the applied by 14 days posttreatment, then decreased to 12.6% (0.69 ppm) by 58 days posttreatment and was 0.1-2.2% (0.005-0.12 ppm) from 92 to 357 days posttreatment (Table XVIII, pp. 64, 65). The minor degradate CGA-359009 ("2U" in tables) was detected in the 1.6 ppm treated soil at all sampling intervals and was a maximum of 4.6% (0.079 ppm) of the applied radioactivity at 238 days posttreatment. CGA-359009 was observed in the 9.6 ppm treated soil at all sampling intervals and was a maximum of 7.7% (0.79 ppm) of the applied radioactivity at 182 days posttreatment. The

TEXT SEARCHABLE DOCUMENT 2011

minor degradate 6-hydroxy-nicotinic acid (CGA-319251) was detected in the 1.6 ppm treated soil in one replicate at 0.1% (0.001 ppm) of the applied at 92 days posttreatment and in the 9.6 ppm treated soil at 0.2% (0.012 ppm) at 58 (one replicate) and 182 days posttreatment. In the 1.6 ppm treated soil, 7 unknown minor degradates were detected at ≤4.6% of the applied radioactivity; in the 9.6 ppm treated soil, 8 unknown minor degradates were detected at ≤5.6% of the applied.

Residues in the NaOH extracts were not characterized due to the harsh nature of the extraction; total [^{14}C]residues in the NaOH extracts from 30 to 357 days posttreatment were 21.4-27.5% of the applied in the 1.6 ppm treated soil and 16.4-24.2% of the applied in the 9.6 ppm treated soil. Nonextractable [^{14}C]residues were maximums of 4.9% and 3.6% of the applied at 0 days posttreatment in the 1.6 ppm and 9.6 ppm treated soils, respectively. Bound residues were not further analyzed to determine their association with specific organic matter fractions. Radiolabeled $^{14}CO_2$ accounted for 1.6% and 3.8% of the applied radioactivity at 58 days posttreatment, and for maximums of 29.1% and 30.7% at 357 days for the 1.6 ppm and 9.6 ppm treated samples, respectively (reviewer-calculated; Tables XII, XIII; pp. 53-56).

Material balances during the incubation were 96.7-104.9% and 96.5-103.8% of the applied radioactivity for soils treated at 1.6 ppm and 9.6 ppm, respectively.

COMMENTS

1. A reasonable attempt was not made to extract degradates from the soil. Residues were extracted with two different solvents, acetonitrile:water and NaOH. The NaOH extractions were not characterized due to the harsh nature of the extraction and were 21.4-27.5% and 16.4-24.2% of the applied radioactivity in the 1.6 ppm and the 9.6 ppm treated soils, respectively, from 30 to 357 days posttreatment. Additional mild extraction solvents would have been appropriate in an attempt to extract additional residues for identification.

2. The study author used linear regression analysis of log transformed concentration data *vs.* cube-root transformed time data to determine the half-life of the parent compound, with the rationale that this regression best-fit the data. Biphasic degradation was observed when the data were analyzed using a first-order model; however, the rapid phase ended prior to the calculated half-life. The reviewer notes that the data (low dose application system) were variable around the half-life. The parent compound was 63.6% of the applied radioactivity at 30 days posttreatment, decreased to 55.2% by day 58, increased to 59.6% by day 92, and was 47.0% at day 120. Data from the high dose application system were also questionable, as the parent compound was present at 52.0-58.8% of the applied from 58-120 days posttreatment.

3. The study was submitted in partial fulfillment of Subdivision N Guidelines; only the

TEXT SEARCHABLE DOCUMENT 2011

pyridinyl ring was radiolabeled. An additional aerobic soil metabolism study was submitted (MRID 44024966) with a radiolabeled triazinyl ring.

4. The soil was treated at 1.6 ppm which is the proposed maximum seasonal use rate and at 9.6 ppm which was 6x the proposed maximum seasonal use rate. Exaggerated dose rate studies may be used to facilitate degradate identification, however, EPA requires that kinetic studies be conducted with the proposed maximum usage rate. The registrant-calculated half-lives were 101 days and 142 days for the 1.6 ppm and 9.6 ppm treated soils, respectively.

5. The maximum recommended use rate for pymetrozine is 5.0 oz a.i./A/application with a maximum of 10 applications per growing season (p. 35). The low dose rate of 1.6 ppm used in the study is approximately equal to the soil concentration in the 0- to 6-inch depth following the application of 50 oz a.i./A (the maximum total seasonal application rate).

6. The water solubility of pymetrozine at 20 °C is 270 mg/mL at pH 7.35 (p. 20).