Anaerobic Aquatic Metabolism of Pymetrozine

Report: Das, Y. (1996) CGA-215944: Metabolism of (Pyridinyl-5- (carbon-14)) CGA-215944 Under Anaerobic Aquatic Soil Conditions: Lab Project Number: 94012: 46-94. Unpublished study prepared by Innovative Scientific Services, Inc. 513 p.

Document No.: MRID 44024967

Guideline: OPPTS 835.4300

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 anaerobic aquatic metabolism of pymetrozine in flooded sandy loam soil; however, the pattern of decline of a major degradate CGA-180777 was not clearly demonstrated by the end of the study, and the test soils were flooded with reagent grade water rather than natural water. The NaOH soil extract contained a maximum of 18.3% of the applied and was not characterized.

PC Code: 101103

Reviewer: Jessica L. O. Joyce, Fate Scientist
U.S. EPA Date: Date: 2018.02.13 15:49:16 -05'00'

Rochelle F.H. Bohaty, Senior Scientist
U.S. EPA Date: 2018.02.08 08:34:51 -05'00'

TEXT SEARCHABLE DOCUMENT 2011

DATA EVALUATION RECORD

STUDY 5a

CHEM: 101103 Pymetrozine §162-3
CAS No. 123312-89-0
FORMULATION--00--ACTIVE INGREDIENT

STUDY ID 44024967
Das, Y. T. 1996. Metabolism of [pyridinyl-5-^{14}C]CGA-215944 under anaerobic aquatic soil conditions. Ciba-Geigy Study No: 46-94. Unpublished study performed by Innovative Scientific Services, Inc., Piscataway, NJ; and submitted by Ciba-Geigy Corporation, Greensboro, NC.

DIRECT REVIEW TIME = 44.5 Hours

REVIEWED BY:	E. A. Heger, M.S.	Signature:
TITLE:	Scientist	Date:
EDITED BY:	C. A. Little, Ph.D.	Signature:
TITLE:	Sr. Scientist/Asst. Project Manager	Date:
APPROVED BY:	P. H. Howard, Ph.D.	Signature:
TITLE:	Project Manager	Date:
ORG:	Syracuse Research Corp. Arlington, VA 22202	
TEL:	703/413-9369	

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

SIGNATURE:
EFED Share drive Copy

2087121

TEXT SEARCHABLE DOCUMENT 2011

CONCLUSIONS

Metabolism - Anaerobic Aquatic

1. This study is scientifically valid and provides useful information on the anaerobic aquatic metabolism of pymetrozine in flooded sandy loam soil.

2. These studies can be used to fulfill the Subdivision N Guidelines of EPA data requirements on anaerobic aquatic metabolism. However, note the following:

   (i) no clear pattern of decline of the major degradate CGA-180777 was observed by the end of study. However, no further action is needed as the studies were conducted to the maximum required period (approximately one year).

   (ii) the test soils were flooded with reagent grade water rather than natural water. Although Subdivision N Guidelines recommend the use of natural water, studies using reagent water should produce half-lives much longer than those reported in natural water, since the microbial activity in reagent water are presumably much less than in natural water.

3. Pyridinyl ring-labeled [5-^{14}C]pymetrozine, at nominal concentrations of 1.5 and 10.8 ppm, degraded with respective registrant-calculated half-lives of 69 ($r^2 = 0.98$) and 97 ($r^2 = 0.96$) days in anaerobic flooded sandy loam soil incubated in darkness at 25 °C for up to 176 and 357 days. All data, designated as percentages of the applied, were reported as percentages of the nominal application.

   In the water phase of the 1.5 ppm test system, the parent compound was 89.0% of the applied radioactivity at day 0, decreased to 49.8% of the applied by 3 days, was 42.4% at 7-14 days, and was 3.4% at 176 days posttreatment. The major degradate CGA-180777 was a maximum of 54.6% of the applied radioactivity at 176 days posttreatment. The minor degradates CGA-319251, CGA-359009 (designated "2U" in data tables), and eight unidentified degradates were each detected at ≤3.8% of the applied radioactivity. In the acetonitrile:water soil extract of the 1.5 ppm test system, the parent compound was detected at 12.8% of the applied radioactivity at day 0, was a maximum of 43.4% at 7 days posttreatment, and was 12.7% at 176 days posttreatment. The major degradate CGA-180777 was a maximum of 12.8% (day 120), and was 12.4% at 176 days posttreatment. The minor degradates CGA-319251, CGA-359009, and seven unidentified degradates were detected at ≤3.2% of the applied radioactivity. The NaOH soil extract contained a maximum of 18.3% of the applied radioactivity at 30 days posttreatment and was 11.0% of the applied at 176 days posttreatment; [^{14}C]residues were not characterized. Evolved $^{14}CO_2$ accounted for 1.5% of the applied radioactivity at 176 days posttreatment. The distribution of [^{14}C]residues between the soil and water fractions was not reported; however, the majority of the [^{14}C]residues was observed in the water phase from 0 to 3 days and 120 to 176 days posttreatment.

TEXT SEARCHABLE DOCUMENT 2011

In the water phase of the 10.8 ppm test system, the parent compound was 92.3% of the applied radioactivity at day 0, decreased to 52.8% of the applied by 14 days posttreatment and was 0.9% at 357 days. The major degradate CGA-180777 was a maximum of 67.8% of the applied radioactivity at 357 days posttreatment. The minor degradates CGA-319251, CGA-359009, and eight unidentified degradates were each detected at ≤3.4% of the applied radioactivity. In the acetonitrile:water soil extract of the 10.8 ppm test system, the parent compound was detected at 7.4% of the applied radioactivity at day 0, was a maximum of 36.6% by 7 days posttreatment, and was 7.0% at 357 days. The major degradate CGA-180777 was a maximum of 18.6% at 176 days posttreatment and was 16.6% at 357 days. The minor degradates CGA-319251, CGA-359009, and eight unidentified degradates were each detected at ≤2.8% of the applied radioactivity. The NaOH soil extract contained a maximum of 10.6% of the applied radioactivity at 30 days posttreatment, and was 5.4% of the applied at 357 days posttreatment; [^{14}C]residues were not characterized. Evolved $^{14}CO_2$ accounted for 2.5% of the applied radioactivity at 273 days posttreatment, and was 1.7% of the applied at 357 days. The distribution of [^{14}C]residues between the soil and water fractions was not reported; however, the majority of the [^{14}C]residues was observed in the water phase throughout the incubation.

METHODOLOGY

Samples (5 g) of sieved (2 mm) Hanford sandy loam soil (71% sand, 20% silt, 9% clay, 0.3% organic matter, pH 7.4, CEC 4.6 meq/100 g; Table II, p. 49) collected from Sanger, CA, were placed into borosilicate glass bottles and flooded with 10 mL of reagent-grade water (water characteristics were not reported); the final soil:water ratio was 1:2 (w:v, pp. 26-27). The soil/water systems were purged with hydrogen and nitrogen, and pre-incubated anaerobically (nitrogen atmosphere) in sealed test vessels in darkness at 25 °C for 22 days. Following the pre-incubation period, the soil/water samples were treated with pyridinyl ring-labeled [5-^{14}C]pymetrozine (6-methyl-4-(pyridin-3-yl-methylenamino)-4,5-dihydro-1,2,4-triazin-3(2H)-one; radiochemical purity 97.9%; specific activity 55.4 µCi/mg; p. 84), dissolved in acetonitrile, at a nominal rate of 1.5 or 10.8 ppm (p. 29). Treated flasks were purged with hydrogen and nitrogen, and incubated anaerobically (nitrogen atmosphere) in sealed test vessels in darkness at 25 ± 1 °C for up to 176 or 357 days, respectively. To trap volatiles, a 2.0 *N* potassium hydroxide volatile trap was used inside each test vessel (Figures 5, 7; pp. 88, 90). Soil/water samples treated at 1.5 ppm were removed for analysis at 0, 1, 3, 7, 14, 30, 58, 92, 120, and 176 days posttreatment (p. 30); samples treated at 10.8 ppm were removed for analysis at 0, 1, 3, 7, 14, 30, 58, 92, 120, 176, 273, and 357 days posttreatment. Triplicate samples (one for pH and redox potential determinations only) were analyzed for each test system at each sampling interval. To determine soil viability, additional vessels were analyzed at 0, 30, 58, 176, and 357 (10.8 ppm treatment only) days posttreatment for total anaerobic microbial populations in flooded soil (p. 30). Microbial populations were reported as CFU/g dry soil; data indicated that both test systems were viable at each sampling interval (Table VIII, p. 57).

TEXT SEARCHABLE DOCUMENT 2011

Soil/water samples were centrifuged, and the water phase was decanted and analyzed in triplicate for total radioactivity by LSC; the limit of detection was 0.2 ng (as parent pymetrozine; p. 32). Aliquots of the water phase were filtered (0.45 µm), concentrated by evaporation and/or lyophilization, and analyzed by reverse-phase HPLC (Zorbax SB-C18 column) using a mobile phase gradient of water:methanol (both with 0.05% trifluoroacetic acid, v:v; 100:0 to 95:5 to 0:100, v:v) with radioactive flow detection; the limit of quantitation was 0.01% of the injected radioactivity (p. 33). Samples were co-chromatographed with non-radiolabeled reference standards which were detected by UV light (220 nm). HPLC column recoveries (for water samples) based on LSC analysis of collected fractions were 96.5% to 105.0% (1.5 ppm test system) and 95.5% to 103.5% (10.8 ppm test system; p. 34). To confirm compound identities, samples were analyzed by HPLC/MS (Zorbax SB-C18 column) with a mobile phase gradient of water:methanol, (100:0 to 95:5 to 50:50, v:v) with the mass spectrometer in the atmospheric pressure chemical ionization mode (p. 35). Additional confirmational analyses were performed using two-dimensional TLC on silica gel plates developed perpendicularly with chloroform:methanol:ammonium hydroxide:water (80:30:2:4, v:v:v:v) and either ethyl acetate:methanol:water (75:15:10, v:v:v) or chloroform:methanol:formic acid:water (75:25:2:4, v:v:v:v; p. 34). Samples were co-chromatographed with nonradiolabeled reference standards which were visualized with UV light (254 nm); radiolabeled parent and degradates were located using a radioimaging scanner. Radioactivity was further quantified by scraping areas of radioactivity on TLC plates into vials, and dissolving the gel in deionized water and acetonitrile; triplicate aliquots of each solution were analyzed for total radioactivity by LSC (p. 35).

Soil samples were extracted three times by shaking and sonicating with acetonitrile:water (8:2, v:v); samples were centrifuged and the extract was decanted and combined (p. 32). Triplicate aliquots were analyzed for total radioactivity by LSC. Extracts were filtered, concentrated, and analyzed by HPLC as described above for the water samples. Column recoveries were 95.4-104.3% (1.5 ppm test system) and 95.0-105.0% (10.8 ppm test system). Parent and degradate compound identities were confirmed in selected samples by HPLC/MS or TLC as described above (p. 39). Soil samples were further extracted by agitating and sonicating at 80 °C with 1.0 *N* aqueous NaOH; samples were centrifuged and the extract decanted. The extraction was repeated and triplicate aliquots of the combined NaOH extracts were analyzed for total radioactivity by LSC. The NaOH extracts were analyzed by reverse-phase HPLC as described above; several polar compounds were separated, but not identified (p. 42). The water phase and the acetonitrile:water extracts were analyzed within 1 day of sampling (Tables VI, VII, pp. 55-56). The NaOH extractions were performed up to one month after sampling. Triplicate subsamples of post-extracted soil were analyzed for total radioactivity by LSC following combustion.

At each sampling interval, the head space of each test vessel was analyzed for total radioactivity by LSC following combustion (p. 31). Volatile traps (2.0 *N* potassium hydroxide) were removed for analysis at 100 (1.5 ppm test systems) or 100 and 191 (10.8

TEXT SEARCHABLE DOCUMENT 2011

ppm test systems) days posttreatment; triplicate aliquots were analyzed for total radioactivity by LSC. Precipitation of trap solutions with barium carbonate followed by re-analysis of the supernatant by LSC confirmed that all volatile compounds were present as $^{14}CO_2$ (p. 38).

To confirm the presence of anaerobic conditions, the redox potential was measured at each sampling interval in both test systems; pH was measured at each sampling interval following 58 days posttreatment (p. 29). The redox potentials were measured using a platinum electrode (E_o) and were corrected to normal hydrogen electrode potentials (E_{nhe}); data for both test systems indicate that anaerobic conditions were maintained throughout the incubation. In the 1.5 ppm test system, redox potentials were -411 to -751 mV (E_o) and -212 to -552 mV (E_{nhe}; Table IX, p. 58). In the 10.8 ppm test system, redox potentials were -296 to -756 mV (E_o) and -97 to -557 mV (E_{nhe}). The pH was 8.3 to 8.5 (1.5 ppm test system) and 8.3 to 8.9 (10.8 ppm test system; Table X, p. 59).

DATA SUMMARY

Pyridinyl ring-labeled [5-^{14}C]pymetrozine (radiochemical purity 97.9%), at nominal concentrations of 1.5 and 10.8 ppm, degraded with respective registrant-calculated half-lives of 69 (r^2 = 0.98) and 97 (r^2 = 0.96) days in anaerobic flooded sandy loam soil incubated in darkness at 25 ± 1 °C for up to 176 and 357 days, respectively (Tables XXVI, XXVII, pp. 82-83; Figures 62, 63, pp. 157-158). All data, designated as percentages of the applied, were reported as percentages of the nominal application.

Low Treatment Rate System (1.5 ppm)

In the water phase of the 1.5 ppm test system, the parent compound was 89.0% of the applied radioactivity at 0 days posttreatment, decreased to 49.8% of the applied by 3 days posttreatment, was 42.4% at 14-30 days and 19.8% at 58 days posttreatment, and decreased to 3.4% by 176 days posttreatment (Table XVII, p. 69). The major degradate

nicotinic acid (CGA-180777)

was sporadically detected at ≤0.2% of the applied radioactivity from 1 to 14 days posttreatment, was 2.1% of the applied at 30 days posttreatment, increased to 27.4% by 92 days posttreatment, and was a maximum of 54.6% at 176 days posttreatment. The minor degradates 6-hydroxy-nicotinic acid (CGA-319251); 1,2,4-triazine-3,5(2H, 4H)-dione, dihydro-6-methyl-4-[(3-pyridinylmethylene)amino]- (CGA-359009; designated "2U" in data tables); and eight unidentified degradates were each detected at ≤3.8% of the applied radioactivity. Uncharacterized [^{14}C]residues were a maximum of 1.4% of the applied radioactivity.

In the acetonitrile:water soil extract of the 1.5 ppm test system, the parent compound was

TEXT SEARCHABLE DOCUMENT 2011

initially detected at 12.8% of the applied radioactivity at 0 days posttreatment, increased to a maximum of 43.4% of the applied by 7 days posttreatment, was 21.6% at 120 days posttreatment, and was 12.7% at 176 days posttreatment (Table XXII, p. 76). The major degradate

nicotinic acid (CGA-180777)

was initially detected at 0.2% (single replicate) of the applied radioactivity at 14 days posttreatment, increased to 2.4% of the applied by 92 days posttreatment, and was 12.4-12.8% at 120-176 days posttreatment. The minor degradates CGA-319251, CGA-359009 (designate "2U" in the data tables), and seven unidentified degradates were each detected at ≤3.2% of the applied radioactivity. Uncharacterized [^{14}C]residues were a maximum of 0.8% of the applied radioactivity. The NaOH soil extract contained a maximum of 18.3% of the applied radioactivity at 30 days posttreatment and was 11.0% of the applied at 176 days posttreatment (Table XI, pp. 60-61); [^{14}C]residues were not characterized. Nonextractable [^{14}C]residues were a maximum of 1.7% of the applied radioactivity at 58 days posttreatment, and were 1.1% of the applied at 176 days posttreatment.

Evolved $^{14}CO_2$ accounted for 1.5% of the applied radioactivity at 176 days posttreatment (Table XI, pp. 60,61). The distribution of [^{14}C]residues between the soil and water fractions was not reported; however, the majority of the [^{14}C]residues was observed in the water phase from 0 to 3 days and 120 to 176 days posttreatment..

Material balances ranged from 100.6% to 106.3% of the applied radioactivity throughout the incubation period.

High Treatment Rate System (10.8 ppm)

In the water phase of the 10.8 ppm test system, the parent compound was 92.3% of the applied radioactivity at 0 days posttreatment, decreased to 52.8% of the applied by 14 days posttreatment, was 11.2% at 120 days posttreatment, and was 0.9% at 357 days posttreatment (Table XVIII, pp. 70-71). The major degradate

nicotinic acid (CGA-180777)

was 0.2-1.6% of the applied radioactivity at 1-14 days posttreatment, increased to 10.8% of the applied by 30 days posttreatment, was 33.4% at 90 days, and was a maximum of 67.8% at 357 days posttreatment. The minor degradates 6-hydroxy-nicotinic acid (CGA-319251); 1,2,4-triazine-3,5(2H, 4H)-dione, dihydro-6-methyl-4-[(3-pyridinylmethylene) amino]- (CGA-359009; designated "2U" in data tables); and eight unidentified degradates were each detected at ≤3.4% of the applied radioactivity. Uncharacterized [^{14}C]residues were a maximum of 3.0% of the applied radioactivity.

TEXT SEARCHABLE DOCUMENT 2011

In the acetonitrile:water soil extract of the 10.8 ppm test system, the parent compound was initially detected at 7.4% of the applied radioactivity at 0 days posttreatment, increased to a maximum of 36.6% of the applied by 7 days posttreatment, was 23.1% at 120 days posttreatment, and was 7.0% at 357 days posttreatment (Table XXIII, pp. 77-78). The major degradate

nicotinic acid (CGA-180777)

was sporadically detected at 0.0.2-3% (individual replicates) of the applied radioactivity at 1-14 days posttreatment, increased to 1.8% of the applied by 58 days, was a maximum of 18.6% at 176 days posttreatment, decreased to 10.6% by 273 days and then increased to 16.6% by 357 days posttreatment. The minor degradates CGA-319251, CGA-359009 (designated "2U" in the data tables), and eight unidentified degradates were each detected at ≤2.8% of the applied radioactivity. Uncharacterized [^{14}C]residues were a maximum of 1.0% of the applied radioactivity at 30 days posttreatment. The NaOH soil extract contained a maximum of 10.6% of the applied radioactivity at 30 days posttreatment, and was 5.4% of the applied at 357 days (Table XII, pp. 62-63); [^{14}C]residues were not characterized. Nonextractable [^{14}C]residues were a maximum of 1.6% of the applied radioactivity at 273 days posttreatment, and were 0.8% of the applied at 357 days posttreatment.

Evolved $^{14}CO_2$ accounted for 2.5% of the applied radioactivity at 273 days posttreatment, and was 1.7% of the applied at 357 days posttreatment (Table XII, pp. 62, 63). The distribution of [^{14}C]residues between the soil and water fractions was not reported; however, the majority of the [^{14}C]residues was observed in the water phase throughout the incubation.

Material balances were 102.6-107.2% of the applied radioactivity throughout the incubation period.

COMMENTS

1. The pattern of decline of the major degradate CGA-180777 was not clearly demonstrated in either test system studied. In the water phase of the 1.5 ppm test system, CGA-180777 was a maximum of 54.6% of the applied radioactivity at the final sampling interval (176 days posttreatment); in the soil extracts, the degradate was a maximum of 12.4-12.8% of the applied from 120-176 days posttreatment. In the water phase of the 10.8 ppm test system (see Comment #2), the degradate was a maximum of 67.8% of the applied at the final sampling interval (357 days posttreatment); in the soil extracts, the degradate was a maximum of 18.6% at day 176, but the pattern of decline was not apparent due to data variability observed for the final two sampling intervals. Subdivision N Guidelines require that the study be conducted until the formation and decline of degradates be clearly demonstrated, or for one year. Although the high treatment rate study (10.8 ppm) was conducted for approximately one year, exaggerated rate studies may not be used to

TEXT SEARCHABLE DOCUMENT 2011

determine kinetics information, as discussed in Comment #2 below.

2. The reviewer notes that the low treatment rate study was performed at the maximum seasonal label rate. Data obtained from the high (exaggerated) treatment rate study may be used for degradate identification purposes, but may not be used to provide kinetics information (USEPA. 1993. *Pesticide Reregistration Rejection Rate Analysis: Environmental Fate*. EPA 738-R-93-010, p. 67).

3. The test soil was flooded with reagent grade water rather than natural water. The microbial and chemical composition of natural water may alter the pattern or rate of degradation of pymetrozine as determined in this study; the use of reagent grade water is not recommended as it does not adequately represent a natural sediment/water system.

4. The registrant only reported residue data in the form of percentages of the applied or injected radioactivity. In future studies submitted to the EPA, it is necessary that residue data also be submitted in units of concentration, such as ppm.

5. The test soil was not flooded for 30 days prior to treatment with pymetrozine; however, redox measurements indicated that the systems were anaerobic at the time of treatment (Table IX, p. 58).

6. The reported water solubility of pymetrozine is 270 mg/mL (20 ^{o}C, pH 7.35; p. 84).

7. The maximum recommended use rate for pymetrozine is 5 oz. a.i./A/application, with a maximum of 10 applications per growing season (p. 44). The low dose rate of 1.5 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, which is the maximum total seasonal application rate.