MRID 44767601 (7-31-01)

DATA EVALUATION RECORD

STUDY 1

CHEM 013803 MSMA §162-1
CAS No. 2163-80-6
FORMULATION--00--ACTIVE INGREDIENT

STUDY ID 44767601

Peel, D. 1996. Aerobic soil metabolism of [^{14}C]MSMA. PTRL Project No.: 884; PTRL Report No.: 1881. Unpublished study performed by PTRL East, Inc., Richmond, KY. Sponsored by the MAA Research Task Force Three, Mentor, Ohio.

DIRECT REVIEW TIME =

REVIEWED BY: Kathleen Ferguson
TITLE: Senior Staff Scientist
SIGNATURE:
DATE:

EDITED BY: Andrew Glucksman
TITLE: Staff Scientist
SIGNATURE:
DATE:

EDITED BY: Joan Harlin
TITLE: Senior Staff Scientist
SIGNATURE:
DATE:

ORG: Dynamac Corporation
Rockville, MD
TEL: 301-417-9800

EDITED AND APPROVED BY: Alex Clem
TITLE: Environmental Scientist
ORG: ERB3/EFED/OPP
TEL: 703-305-5773

SIGNATURE: Alex Clem 7/31/01

ADMINISTRATIVE CONCLUSIONS

This study ***satisfies*** the data requirement for the aerobic soil metabolism of MSMA. However, the registrant should regard the critical elements cited in this data evaluation report, and consider their applicability to future submissions.

SCIENTIFIC ABSTRACT

Metabolism - Aerobic Soil (Note: All data reported as percentages of the applied dose represent percentages of the actual dose, and are the means of two replicates unless otherwise noted.)

Methyl-labeled [^{14}C]MSMA (monosodium methanearsonate), at 6.1 ppm, degraded with a reviewer-calculated first-order kinetics regression half-life of approximately 240 days (95% confidence interval 170 to 420 days; $r^2 = 0.76$; 0-365 day data) in a sandy loam soil that was incubated in the dark at 25°C and 75% of field moisture capacity for 1 year (based on data in attached Table IX and Figure 7). The degradation of [^{14}C]MSMA could also be described by a two-compartment (biphasic) model. By inspection of the data and figure, the DT50 was approximately 60 days, but after this time metabolism slowed to the extent that approximately 35% of the applied dose remained after one year. **Cacodylic acid** was the only major arsenic-containing metabolite. Its concentration increased steadily, reaching approximately 30-35% of the applied dose after one year.

Based on HPLC analysis, the MSMA was initially 96.2% of the applied radioactivity, was 78.2% at 14 days posttreatment, was 61.5% at 1 month, was 51.2% at 2 months, and was 35.1% at 12 months. The major degradate, cacodylic acid, was 12.2% of the applied radioactivity at 1 month posttreatment and increased from 17.1% to a maximum of 31.9% at 2-12 months. An unidentified minor [^{14}C]compound was isolated at 0.2% (single replicate) and 0.3% (single replicate) of the applied radioactivity at 3 and 7 days posttreatment, respectively. $^{14}CO_2$ was initially 2.5% of the applied radioactivity at 3 days posttreatment, increased to 10.7% by 14 days, was a maximum of 19.9% at 9 months, and was 19.4% at 12 months (reviewer-calculated means). CO_2 was the only volatile compound detected during the study. Unextracted [^{14}C]residues in the soil were initially (time 0) 1.9% of the applied radioactivity, were a maximum of 12.2% at 4 months posttreatment, and were 9.8% at 12 months.

Material balances ranged from 87.1 to 103% of the applied (mean 95.4 ± 4.1%) throughout the study, with no pattern of loss.

METHODOLOGY

Air-dried, sieved (2 mm) sandy loam soil (71.2% sand, 21.2% silt, 7.6% clay, 0.25% organic carbon, pH 7.0, CEC 3.40 meq/100 g, native arsenic 0.19 ppm; Table 1, p. 36), collected from

Madera County, California, was weighed (50 g) into 500-mL sterile Erlenmeyer flasks equipped with inlet and outlet tubes, and treated with methyl-labeled [^{14}C]MSMA (monosodium methanearsonate; Figure 1, p. 64; radiochemical purity ≥98.0%, p. 30; specific activity 2.4 mCi/mMol; Lot No. ICNCFQ2289, Wil Research Laboratories, p. 14), dissolved in water, at an application rate of 6.1 ppm (p. 16). The soil was moistened to 75% of the moisture content at 0.33 bar. Additional flasks (single replicates) of untreated control soils were prepared by the same method. All flasks were sealed with ground glass stoppers and transferred to an incubator and maintained in the dark at 24-26°C (mean 25.0 ± 0.2°C). Duplicate flasks of treated soil were analyzed at 0, 3, 7, and 14 days, and 1, 2, 3, 4, 6, 9, and 12 months posttreatment (p. 16). Untreated controls were analyzed at 0 days and 1, 3, 6, 9, and 12 months posttreatment. The soil was remoistened to 75% of 0.33 bar approximately every 14 days and at each sampling interval. Prior to each sampling interval and at approximately 14-day intervals, oxygen was drawn (120 mL/minute for 10 minutes) through the sample flasks and into a series of two gas dispersion tubes containing 0.01M potassium iodide/iodine (KI/I_2; both treated and untreated samples) and 10% sodium hydroxide (treated samples only) trapping solutions (p. 17; Figure 1, p. 96). The KI/I_2 solutions for each flask were sealed and stored after use, and reused for subsequent trapping. The KI/I_2 solutions were reequilibrated with solid I_2 as needed, and replaced with fresh solutions after the 6-month sampling interval. The NaOH solutions were similarly reused until a significant accumulation of radioactivity had occurred, at which time the trapping solutions were replaced.

At each sampling interval, subsamples (10 g) were transferred to centrifuge tubes. Selected samples (days 0-14) were extracted twice with 1N NH_4OH for 30 minutes per extraction, followed by a reflux extraction with 1N NH_4OH for 1 hour. Selected samples (months 1-12) were extracted by refluxing with 1N NH_4OH for 2 hours. The samples were centrifuged, supernatants were decanted, and replicate extracts were combined and vacuum filtered (Whatman No. 1). Aliquots of the filtrate were vortexed or sonicated, syringe filtered (0.2 µm), and analyzed by HPLC (Supelcosil LC amino column; 25 cm x 4.6 mm; 5-µm diameter particle size; Supelco, Inc.) using a mobile phase gradient of acetonitrile:50% aqueous acetonitrile:2% aqueous acetic acid (100:0:0 to 0:100:0 to 0:0:100, v:v:v) with radioactive flow detection. [^{14}C]Compounds were identified by comparison of sample retention times to known retention times of radiolabeled reference standards of the parent compound and the potential degradate cacodylic acid. Selected samples (days 7 and 14; months 1-12) were concentrated by rotary evaporation and aliquots were radioassayed (method not specified). Selected sample extracts (days 0 and 3) and concentrated extracts (days 7 and 14) were cleaned-up using an AG 50W Cation Exchange (CE) Resin column (Bio-Rad Laboratories, Inc.); eluents were analyzed by HPLC as described previously. Selected concentrated extracts (months 1-14) were cleaned up using a Varian Amino (NH_2) 6-cc Bond Elut column (Varian Sample Preparation Products); aliquots of the eluents were radioassayed (method not specified). Additionally, the eluents were concentrated by rotary evaporation and stored frozen at -20°C for up to 15 days prior to analysis by HPLC as described previously. Selected concentrated sample extracts (month 12) were co-chromatographed with either the radiolabeled reference standards of the test compound or the potential degradate cacodylic acid (p. 33).

3

To confirm compound identities, selected concentrated soil extracts (months 4 and 12) were analyzed by one-dimensional TLC on silica gel plates developed with ethyl acetate:17.4N glacial acetic acid:water (3:2:1, v:v:v). Extracts were co-chromatographed with radiolabeled reference standards of the test compound and cacodylic acid, which were visualized using radioimage scanning. Radiolabeled residues were scraped from the plates, extracted with methanol, and the extracts were quantified by LSC. Recovery of [^{14}C]residues was determined for each TLC plate.

Aliquots of the extracts were analyzed for total radioactivity using LSC, and portions of the extracted soil were analyzed for unextracted [^{14}C]residues using LSC following combustion. The soil was extracted within 20 days of sample collection, and extracts were analyzed within 15 days following generation (p. 105). Extracts and the extracted soil were stored at -20°C when not in use (p. 19). Total [^{14}C]residues in subsamples of each soil at the initiation and termination of the study were determined by LSC following combustion (p. 18).

A portion (5.5 g wet weight) of the unextracted treated and untreated soils were each analyzed for total arsenic (p. 21). The soil was digested by heating in hydrochloric acid:deionized ultra-filtered water:nitric acid solution (5:4:1, v:v:v) until most of the liquid had evaporated and the soil was only damp. After cooling, aqueous 50% hydrochloric acid was added to the soil and the solution was heated for an additional 5 minutes. The mixture was vacuum-filtered (Whatman No. 50), and the flask and filter were rinsed with water. The extract solution was analyzed by a MHS-10 Mercury Hydride System (Perkin-Elmer Model 3100) on an atomic absorption spectrometer (p. 21).

The KI/I_2 trapping solutions were analyzed by graphite furnace atomic absorption spectroscopy for total arsenic (p. 21). The 10% NaOH trapping solutions were analyzed using LSC; barium chloride precipitation was used to confirm the presence of $^{14}CO_2$ in the NaOH solutions (p. 17).

To determine viability of the soils at the initiation and termination of the study, soil samples were diluted and plated on selective media for aerobic bacteria, actinomycetes, and fungi. Plates were visualized for microbial growth; the data indicated that soils were viable (Table II, p. 37).

DATA SUMMARY/RESULTS (Note: All data reported as percentages of the applied represent percentages of the actual application, and are the means of two replicates unless otherwise noted..)

Methyl-labeled [^{14}C]MSMA (monosodium methanearsonate; radiochemical purity ≥98.0%), at 6.1 ppm, degraded with a reviewer-calculated first-order kinetics regression half-life of approximately 240 days (95% confidence interval 170 to 420 days; $r^2 = 0.76$; 0-365 day data) in sandy loam soil that was incubated in the dark at an average 25.0 ± 0.2°C and 75% of field moisture capacity for 1 year (based on data in the attached Table IX from p. 57-59 of the submission). The degradation of [^{14}C]MSMA could also be described by a two-compartment (biphasic) model. By inspection of the data in Table IX and Figure 7 (p. 70, attached), the DT50

4

was approximately 60 days, but after this time metabolism slowed to the extent that approximately 35% of the applied dose remained after one year. Cacodylic acid was the only major arsenic-containing metabolite. Its concentration increased steadily, reaching approximately 30-35% of the applied dose after one year.

Based on HPLC analysis, the test compound was initially 96.2% of the applied radioactivity, was 78.2% at 14 days posttreatment, was 61.5% at 1 month, was 51.2% at 2 months, and was 35.1% at 12 months (Table IX, pp. 57-59; Figure 7, p. 70).

The major degradate

cacodylic acid (Figure 1, p. 64)

was initially 12.2% of the applied at 1 month posttreatment and increased from 17.1% to a maximum of 31.9% at 2-12 months posttreatment (Table IX, pp. 57-59; Figure 7, p. 70).

An unidentified minor [^{14}C]compound (designated in data tables as "Unknown A"; retention time 39.2-39.9 minutes) was isolated at 0.2% (single replicate) and 0.3% (single replicate) of the applied at 3 and 7 days posttreatment, respectively.

$^{14}CO_2$ initially accounted for 2.5% of the applied radioactivity at 3 days posttreatment, increased to 10.7% by 14 days, was a maximum of 19.9% at 9 months, and was 19.4% at 12 months (reviewer-calculated means; Table VIII, pp. 55, 56). CO_2 was the only volatile compound detected during the study (p. 31).

Unextracted [^{14}C]residues in the soil were initially (time 0) present at 1.9% of the applied radioactivity, were a maximum of 12.2% at 4 months, and were 9.8% at 12 months.

Material balances ranged from 87.1 to 103% of the applied (mean 95.4 ± 4.1%) throughout the study, with no pattern of loss (Table VIII, pp. 55, 56).

The concentration of arsenic in the treated soil remained constant throughout the experiment, with no increasing or decreasing trend (Appendix 7, Table I, p. 103). The percentage of arsenic in the KI/I_2 trapping solutions for the treated soil was variable (0.1-0.7%), but at 12 months did not exceed concentrations associated with the untreated controls (p. 104).

COMMENTS AND DEFICIENCIES/DEVIATIONS

1. Radiochromatograms were not provided for the 3- and 7-day sampling intervals, although an unidentified compound was isolated from the extracts at these intervals. MSMA and cacodylic acid were the only [^{14}C]compounds that were present on the radiochromatograms that were provided for review.

2. Limits of quantitation and detection were not reported for HPLC and TLC analysis. It is necessary that both limits of quantitation and detection be reported to allow the reviewer to evaluate the adequacy of the test method for the determination of the parent compound and its degradates.

3. The combustion efficiency was not reported. Additionally, the study author did not state whether samples were corrected for combustion efficiency.

4. The proposed maximum application rate was not reported.

5. Organic matter fractionation was not performed.

6. The identification of MSMA and cacodylic acid was confirmed by comparison to reference standards using HPLC and one-dimensional TLC. A single solvent was used with each method.

ATTACHMENT 1
Tables and Figures cited in DER

THE FOLLOWING ATTACHMENT IS NOT AVAILABLE ELECTRONICALLY
SEE THE FILE COPY

Page_____ is not included in this copy.

Pages 8 through 17 are not included.

The material not included contains the following type of information:

_____ Identity of product inert ingredients.

_____ Identity of product impurities.

_____ Description of the product manufacturing process.

_____ Description of quality control procedures.

_____ Identity of the source of product ingredients.

_____ Sales or other commercial/financial information.

_____ A draft product label.

_____ The product confidential statement of formula.

_____ Information about a pending registration action.

✓ FIFRA registration data.

_____ The document is a duplicate of page(s) _____.

_____ The document is not responsive to the request.

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.