DATA EVALUATION RECORD

STUDY 4

CHEM 083701 Tetrachlorvinphos 164-A-SS

FORMULATION--00--ACTIVE INGREDIENT

STUDY ID 42848501

Krautter, G.R. 1993. The dissipation of $[^{14}C]$tetrachlorvinphos and its metabolites in manure from a beef cow following oral administration for 14 consecutive days. Laboratory Project No. 710; Laboratory Report No. 1520. Unpublished study performed by PTRL East, Inc., Richmond, KY, and submitted by Fermenta Animal Health Company for SRA International, Inc., Washington, DC.

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CONCLUSIONS:

Ancillary Study - Dissipation in Manure

1. The manure dissipation study was required to assess the potential for residues to be present following land application of manure from treated cows to agricultural fields prior to planting food crops.

2. Total residues of tetrachlorvinphos [beta isomer, (Z)-2-chloro-1-(2,4,5-trichlorophenyl)vinyl dimethyl phosphate] did not decline during 6 months of storage from composted manure collected throughout treatment from a cow treated orally at 70.4 mg ai/100 pounds/day for 14 days. Parent tetrachlorvinphos was not isolated in the compost samples at any sampling interval. The degradates identified in the compost samples were 1-(2,4,5-trichlorophenyl)-ethanol, 1-(2,4,5-trichlorophenyl)-2-chloroethanol, and 2,4,5-trichlorobenzoic acid. Eight additional degradates were isolated from the manure at 0.3 to 5.3 ppm but were not identified.

3. Eight unidentified degradates, isolated at up to 9.8% of the radioactivity recovered in the unextracted compost samples, were not identified. The unidentified compounds were not characterized following "exhaustive" extraction with strong acid or base extractants.

4. This study is scientifically sound and provides information on the dissipation of tetrachlorvinphos residues in cow manure.

METHODOLOGY:

Gelatin capsules containing cellulose powder were treated at 326.7 mg/capsule with uniformly phenyl ring-labeled [^{14}C]tetrachlorvinphos [beta isomer; (Z)-2-chloro-1-(2,4,5-trichlorophenyl)vinyl dimethyl phosphate; radiochemical purity 96.5-98.5%, specific activity 30.6 mCi/mMol, Shell]. A cross-bred beef cow (8 months old; 464-528 lbs), housed in a pen with a concrete floor and sawdust bedding, was fed one treated capsule per day for 14 consecutive days to provide a treatment rate of 70.4 mg ai/100 pounds of body weight (43.3 mg ai/kg feed) per day. Throughout the study, the cow was fed hay and a 16% protein concentrate and was provided with water *ad libitum*. Additionally, lighting in the facility was adjusted to a 16-hour light:8-hour dark photoperiod; temperature and relative humidity, monitored with a hygrothermograph, were 8-24 °C (17 ± 5 °C) and 52-80%, respectively.

Manure, consisting of urine, feces, and sawdust, was collected approximately 24 hours prior to the first treatment as a control sample. On each day of treatment, manure produced by the cow over the previous 24-hour period was placed in a large plastic tub, weighed, mixed with water, and homogenized by manual mixing using a hand trowel. Duplicate subsamples of the homogenized sample were analyzed by LSC following combustion; an additional subsample (200-300 g) was removed and stored frozen. In order to simulate normal agricultural practices for the storage of cow manure, the remaining portion of the daily sample was evenly layered into a manure pile box (2 x 2 x 2 feet) stored outdoors to allow for natural weathering. The frame of the box was constructed of treated lumber, the floor

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was constructed of plywood to allow for drainage, and the sides were covered with aluminum window screen to allow for aeration. The box was suspended above a circular steel tank to collect any leachate resulting from rainfall, and a plywood cover was placed over the steel tank to prevent warming of the tank by radiant heat.

Six compost cores were randomly collected vertically (in order that manure from each day's addition would be included in the samples) from the manure pile on the day the final daily manure sample was added to the compost (day 0), at 1 and 2 weeks, and at 3, 4, and 6 months. Sample cores were composited per collection interval; composited samples were homogenized with dry ice in a food processor, and triplicate subsamples were analyzed by LSC following combustion. The remainder of each sample was stored frozen for an unspecified period of time prior to extraction.

Subsamples (5 g) of the homogenized manure samples were extracted three times with acetonitrile:water (1:1, v:v) and twice with n-hexane, each time using a polytron homogenizer for 2 minutes; after each extraction, the slurries were centrifuged, and the extracts were decanted. Like extracts were combined, and aliquots of the acetonitrile:water and n-hexane extracts were analyzed by LSC. Subsamples of the extracted manures (post-extracted solids; PES) were analyzed by LSC following combustion. The solvent-extracted manures from the 0-day and 3-, 4-, and 6-month sampling intervals were Soxhlet-extracted with n-hexane for 18 hours; aliquots of the extracts were analyzed by LSC. The extracted manure was then refluxed with 6 N HCl followed by 6 N NaOH for 18 hours; after each refluxing procedure, the slurries were centrifuged and removed. The supernatants were partitioned three times against ethyl acetate; after each extraction, the organic phases were removed and combined. Aliquots of the aqueous and organic solutions were analyzed by LSC, and subsamples of the extracted manures (post-hydrolyzed solids; PHS) were analyzed by LSC following combustion.

Aliquots of the acetonitrile:water and n-hexane extracts were concentrated to dryness by rotary evaporation, and the resulting residues were dissolved in acetonitrile. Aliquots of the acetonitrile solutions were analyzed by reverse-phase HPLC using a Supelcosil LC-18 column eluted with a methanol:acetonitrile (1:1, v:v):0.01 M KH_2PO_4 buffer (pH 3) gradient; the column was equipped with UV (254 nm) and radioactive flow detection. Aliquots of selected aqueous and/or organic phases of the acid and base hydrolysates were concentrated to dryness under nitrogen by rotary evaporation, or by lyophilization, and the resulting residues were dissolved in acetonitrile. Aliquots of the acetonitrile solutions were analyzed by HPLC as previously described. Aliquots of HPLC eluate fractions corresponding to individual HPLC peaks from the acetonitrile:water and hexane extracts were analyzed by MS. An additional aliquot of the organic fraction of the base hydrolysate of the month-6 sample was analyzed by two-dimensional TLC on

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silica gel plates developed in ethyl acetate:methylene chloride (4:1, v:v) in the first direction and acetone:benzene (95:5, v:v) in the second direction. Radioactive areas were located by autoradiography, and 2-cm^2 areas were scraped from the plates and analyzed by LSC; unlabeled reference standards were cochromatographed with the samples and visualized under UV light. Sample results were reported on a dry solid basis.

DATA SUMMARY:

Total [^{14}C]tetrachlorvinphos residues did not dissipate during 6 months of outdoor storage in manure collected throughout treatment from a cow that had been treated orally with uniformly phenyl ring-labeled [^{14}C]tetrachlorvinphos (beta isomer, (Z)-2-chloro-1-(2,4,5-trichlorophenyl)vinyl dimethyl phosphate; radiochemical purity 96.5-98.5%) for 14 days at 70.4 mg ai/100 pounds of body weight (43.3 mg ai/kg feed) per day. Total [^{14}C]residues in the manure throughout the 6-month storage period were 39.1-57.3 μg/g, with no discernible pattern of decline (Table V). Parent tetrachlorvinphos was not isolated from the composted manure samples at any sampling interval. The degradates identified in the manure were:

1-(2,4,5-trichlorophenyl)-ethanol (SD 15509),

1-(2,4,5-trichlorophenyl)-2-chloroethanol (SD 15125), and

2,4,5-trichlorobenzoic acid (SD 15917)

(Tables VII-XII). 1-(2,4,5-Trichlorophenyl)-ethanol (SD 15509) decreased from 69.2% of the radioactivity recovered in the unextracted compost sample on the day the final daily manure sample was added to the compost (day 0) to 57.3% at 2 weeks, and 33.5-43.3% at 3 through 6 months. 1-(2,4,5-Trichlorophenyl)-2-chloroethanol (SD 15125) decreased from 7.1% at 0 days to 3.3% at 2 weeks, and was not detected at 3 through 6 months. 2,4,5-Trichlorobenzoic acid (SD 15917) was detected only at 6 months, at 10.6% of the recovered. Eight additional [^{14}C]degradates (M1-M8) were isolated during the 6-month storage, but were not identified. M1 was the only unidentified compound isolated at all sampling intervals (except 1 week), and ranged from 1.3 to 9.8% of the recovered (up to 5.3 ppm; reviewer-calculated) with no discernable pattern of formation or decline. M2 was a maximum of 3.8% of the recovered (2.1 ppm) at 4 months; M3 a maximum of 8.9% (4.8 ppm) at 3 months; M4 a maximum of 6.5% (2.6 ppm) at 1 week; M5 a maximum of 7.8% (3.7 ppm) at 2 weeks; M6 a maximum of 4.8% (2.3 ppm) at 2 weeks; M7 a maximum of 1.6% (0.7-0.8 ppm) at 0 days and 2 weeks; and M8 a maximum of 0.6% (0.3 ppm) at 6 months. Uncharacterized extractable [^{14}C]residues totaled $\leq$2.1% of the recovered throughout the study.

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Unextracted radioactivity was 9.2 and 23.0% of the recovered at 0 days and 6 months, respectively (Table VI).

Throughout the study, 84.6-103.2% of the radioactivity recovered in the unextracted compost samples was accounted for after extraction.

In the daily manure samples collected during the treatment period, 0.1% of the applied radioactivity was recovered after the first treatment, 0.9-1.6% after treatments 2 through 6, 1.7-2.9% after treatments 7 through 13, and 4.2% after treatment 14 (Appendix 8).

COMMENTS:

1. Eight minor [^{14}C]degradates, isolated at up to 9.8% of the radioactivity recovered in the unextracted manure samples, were unidentified. The unidentified compounds were not characterized following attempted extraction with strong acid (6N HCl) or strong base (6N NaOH) extractants.

2. Manure samples were stored frozen for an unspecified period of time prior to extraction, and extracts were refrigerated for an unspecified period prior to analysis. Actual storage lengths should have been provided. However, no dissipation of total residues was observed throughout the study.

3. Approximately 50% of the radioactivity recovered in the acetonitrile:water extracts was lost during the concentration step performed prior to HPLC or TLC analysis. To investigate the cause of the low recoveries, acetonitrile extracts of the day-0 samples were concentrated by rotary evaporation or under nitrogen; recoveries for both methods were >90%. The study author concluded from these results that the low recoveries from the acetonitrile:water extracts was due, not to a loss of volatiles, but to the limited solubility of the residues in the concentrated acetonitrile:water extracts. Results from HPLC analysis of the acetonitrile extracts reportedly agreed qualitatively and quantitatively with results from HPLC analysis of the acetonitrile:water extracts.

4. For verification of total radioactivity applied, duplicate treated capsules were extracted with toluene, then acetone, and aliquots of the extracts were analyzed by LSC. Extracts of additional capsules were analyzed by HPLC to establish stability throughout the treatment procedure; tetrachlorvinphos was 98.0-98.2% of the total radioactivity before treatment to the capsules, 98.3-98.5% after capsule treatment but before treatment to the cow, and 96.5-96.8% after treatment to the cow.

5. A proposed degradation pathway of tetrachlorvinphos residues in cow manure was provided in Figure 18.

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Pages 6 through 33 are not included in this copy.

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______ Identity of the source of product ingredients.

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REFERENCES

The following study was reviewed:

Krautter, G.R. 1993. The dissipation of [^{14}C]tetrachlorvinphos and its metabolites in manure from a beef cow following oral administration for 14 consecutive days. Laboratory Project No. 710; Laboratory Report No. 1520. Unpublished study performed by PTRL East, Inc., Richmond, KY, and submitted by Fermenta Animal Health Company for SRA International, Inc., Washington, DC. (42848501)

APPENDIX

TETRACHLORVINPHOS AND ITS DEGRADATES

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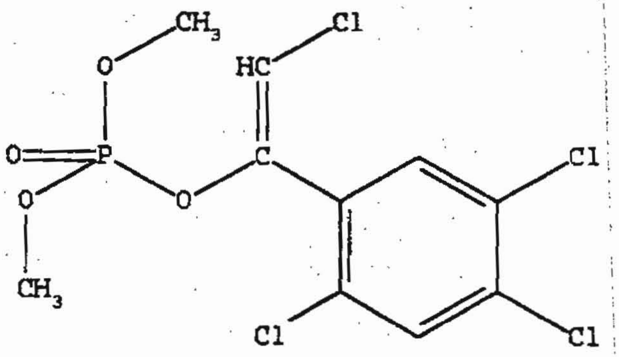
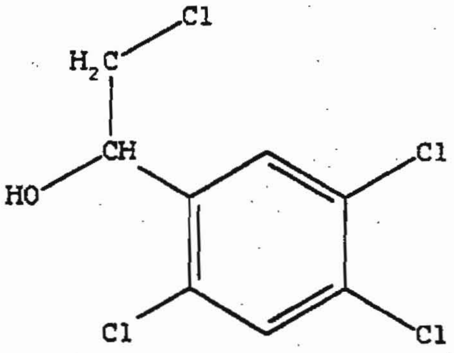


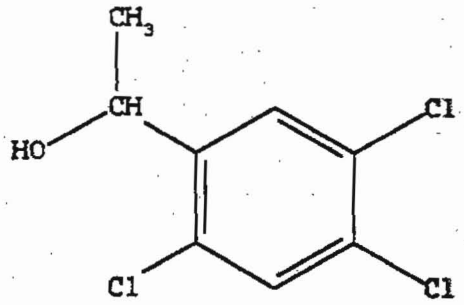
(Z)-2-Chloro-1-(2,4,5-trichlorophenyl)vinyl dimethyl phosphate

(Tetrachlorvinphos)



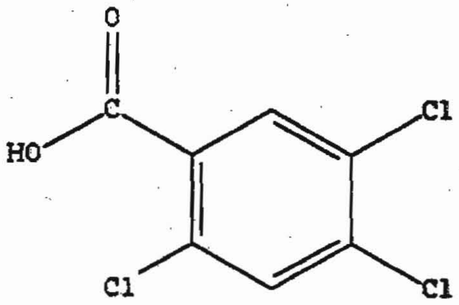
1-(2,4,5-Trichlorophenyl)-2-chloroethanol

(SD 15125)



1-(2,4,5-Trichlorophenyl)-ethanol

(SD 15509)



2,4,5-Trichlorobenzoic acid

(SD 15917)