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DATA EVALUATION RECORD

STUDY 1

CHEM 060101

Thiabendazole

§161-2

FORMULATION--00--ACTIVE INGREDIENT

STUDY ID 43328305

Flynn, J. 1994. Determination of the aqueous photolysis rate of ¹⁴C-thiabendazole. ABC Final Report No. 41285. Unpublished study performed by ABC Laboratories, Inc., Columbia, MO, and submitted by Merck and Company, Inc., Rahway, NJ.

DIRECT REVIEW TIME = 25

REVIEWED BY: M. Anderson

TITLE: Staff Scientist

EDITED BY: K. Ferguson
C. Padova

TITLE: Task Leader
Staff Scientist

APPROVED BY: W. Spangler

TITLE: Project Manager

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

APPROVED BY: J. Breithaupt
TITLE: Agronomist
ORG: EFGWB/EFED/OPP
TEL: 703-305-5925

SIGNATURE:

DRAFT

CONCLUSIONS:

Degradation - Photodegradation in Water

1. This study can be used to fulfill data requirements.
2. Thiabendazole [2-(thiazol-4-yl)benzimidazole] photodegraded with a half-life of 29.0 hours in aqueous 0.1 M acetate buffer solutions (pH 5) that were continuously irradiated for 96 hours at 23 C using a filtered xenon arc lamp. The xenon lamp had an emission spectrum and a measured intensity (310-740 nm; 0.466-23.1 x 10¹⁹ photons/cm²·day) that approximated that of natural sunlight at 40°N when the sun was at the equinox; the intensity of the light received by the samples was approximately half the intensity of the lamp. In contrast,


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thiabendazole did not degrade in the dark controls. Benzimidazole-2-carboxamide, benzimidazole, and benzimidazole-2-carboxylic acid were identified in the irradiated solutions.

3. This study is acceptable and fulfills EPA Data Requirements for Registering Pesticides by providing information on the photodegradation of phenyl ring-labeled [U-¹⁴C]thiabendazole [2-(thiazol-4-yl)-benzimidazole] in an aqueous 0.1 M acetate buffer (pH 5) solution that was irradiated using a xenon arc lamp.
4. No additional information on the photodegradation of thiabendazole in pH 5 buffer solution is needed at this time.

METHODOLOGY:

Phenyl ring-labeled [U-¹⁴C]thiabendazole [2-(thiazol-4-yl)-benzimidazole; radiochemical purity 98.4%, specific activity 57.40 uCi/mg, Merck], dissolved in methanol, was concentrated to near dryness under nitrogen, then diluted with an aqueous 0.1 M acetate buffer (pH 5) solution; the concentration of thiabendazole in the final buffer solution was approximately 10 ug/mL. Aliquots of the treated solution were transferred to quartz glass tubes (13 x 100 mm) "so as to minimize headspace", and the tubes were sealed with polyethylene caps. Half of the sample tubes were wrapped in aluminum foil to serve as dark controls [page 70]. All of the tubes were placed inside a temperature-controlled environmental chamber maintained at 22.5-23.2 C. Within the chamber, the tubes were positioned roughly parallel to the light source, so that the solutions received "approximately one-half the intensity of sunlight at equinox 40°N" (Figure 3). The chamber was irradiated continuously for 96 hours using an Atlas xenon arc lamp equipped with borosilicate glass filters; the xenon lamp had an emission spectrum between 310 and 740 nm and a measured intensity of $0.466-23.1 \times 10^{19}$ photons/cm²·day, which approximated sunlight at 40°N when the sun was at equinox ($0.618-19.9 \times 10^{19}$ photons/cm²·day; Tables I and II, and Figure 4). Duplicate tubes of the irradiated and dark control test solutions were collected at 0, 6, 12, 18, 24, 36, 48, 72, and 96 hours posttreatment. The pH of the test solutions was determined at each sampling interval.

Aliquots of the test samples were analyzed for total radioactivity using LSC. Additional aliquots were analyzed by HPLC for thiabendazole and its degradates using Phenomenex Primesphere C-18 HC columns eluted with gradients of 0.1 M NaH₂SO₄ plus 0.01 M NaClO₄ in water:methanol (70:30 to 0:100 or 90:10 to 0:100, v:v; Methods 1 and 2, respectively); the columns were equipped with UV (279 nm) and radioactivity detection. [¹⁴C]Compounds were identified by comparison to the retention times of unlabeled reference standards of thiabendazole, benzimidazole, benzimidazole-2-carboxamide, benzimidazole-2-carboxylic acid, and 5-hydroxy thiabendazole. Eluate fractions of all samples from HPLC Method 1 and of the 96-hour

samples from HPLC Method 2 were collected, and aliquots were analyzed by LSC.

Material adsorbed to the quartz sample tubes was desorbed by sonicating the tubes twice with methanol for 5 minutes per desorption; the extracts were combined, and aliquots were analyzed by LSC.

To generate sufficient material to allow degradate identification, additional pH 5 buffer solution was treated at approximately 10 ug/mL, and aliquots were irradiated as described. Samples were collected daily through 4 days posttreatment. Aliquots of the irradiated solutions were analyzed by HPLC Method 2; eluate fractions were collected, and corresponding "Regions of Interest (ROI)" were combined for all samples. For further chromatographic separation, eluate fractions corresponding to Regions 1 and 3 were individually analyzed by HPLC using an Alltech MM C-8 column eluted with acidified (0.1% acetic acid) water:acetonitrile (100:0 to 0:100, v:v); the column was equipped with UV (279 nm) and radioactivity detection. No additional characterization analysis was attempted for these regions or Region 4. To remove buffer salts and other impurities, eluate fractions corresponding to regions 2, 5, 6, 7, and 8 were individually analyzed by HPLC using a Phenomenex Primesphere C-18 HC column eluted with water:methanol (100:0 to 0:100, v:v); the resulting eluate fractions were concentrated to near-dryness under nitrogen, then diluted with methanol, and the methanol solutions were analyzed by direct-probe MS.

DATA SUMMARY:

Phenyl ring-labeled [U-¹⁴C]thiabendazole [2-(thiazol-4-yl)-benzimidazole; radiochemical purity 98.4%], at 10 ug/mL, photodegraded with a registrant-calculated half-life of 29.0 hours in aqueous 0.1 M acetate buffer solutions (pH 5) that were continuously irradiated for 96 hours at 22.5-23.2 C using a borosilicate-filtered xenon arc lamp (Table IX). The xenon lamp had an emission spectrum and a measured intensity (310-740 nm; $0.466-23.1 \times 10^{19}$ photons/cm²·day) that approximated that of natural sunlight at 40°N when the sun was at the equinox ($0.618-19.9 \times 10^{19}$ photons/cm²·day; Tables I and II, and Figure 4); the intensity of the light received by the samples was approximately half the intensity of the lamp. In contrast, [¹⁴C]thiabendazole did not degrade in the dark controls.

Benzimidazole-2-carboxamide,

benzimidazole, and

benzimidazole-2-carboxylic acid,

were identified in the irradiated solutions.

In the irradiated samples, [¹⁴C]thiabendazole averaged 96.8% of the applied immediately posttreatment, 51.2% at 24 hours, 37.3% at 36 hours, and 10.4% at 96 hours (Table X). Uncharacterized [¹⁴C]residues in the sample tube extracts (i.e. [¹⁴C]residues that had adsorbed to the sample tubes) were maximums of 9.02-11.5% of the applied at 36 and 48 hours posttreatment (Table VI). At 96 hours posttreatment, benzimidazole-2-carboxamide averaged 10.22% of the applied and benzimidazole averaged 6.49%; benzimidazole-2-carboxylic acid and at least one unidentified [¹⁴C]compound totaled 9.98%; and additional unidentified [¹⁴C]compounds or uncharacterized [¹⁴C]residues totaled \leq 8.59% in distinct HPLC regions (Table XI). Material balances were 99.4-109% of the applied through 48 hours posttreatment and 94.6-98.5% at 72 and 96 hours (Table VI).

In the dark controls, thiabendazole averaged 98.1-102% of the applied throughout the study (Table VIII). Material balances were 98.3-105% of the applied through 96 hours posttreatment, with no discernible pattern of loss (Table VII).

COMMENTS:

1. [¹⁴C]Residues adsorbed to the walls of the sample tubes totaled 9.02-11.5% of the applied at 36 and 48 hours posttreatment. These residues were not characterized; rather, the study author assumed that the distribution of [¹⁴C]residues adsorbed to the tubes mirrored the distribution of [¹⁴C]residues in solution. However, since no significant adsorption to the tube walls was noticed in the dark controls and since adsorption to the tube walls in the irradiated samples increased as the concentration of thiabendazole decreased, it is probable that the adsorbed material contained little or no thiabendazole and was instead a composed primarily of thiabendazole degradates.
2. Based on the concentration of total [¹⁴C]residues in solution as measured by LSC following sampling and the sum of the [¹⁴C]residues quantified following HPLC, up to 27% of the applied radioactivity was not accounted for following the HPLC Method 1 analysis of the irradiated samples and 33% of the applied (96 hours) was not accounted for during HPLC Method 2 analysis (reviewer-calculated; average sample recovery from Table VI minus HPLC recovery in Table X, and sample recovery from Table VI minus HPLC recovery in Table XI). However, HPLC column recoveries for Method 1 were reported to be \geq 89.0% of the applied for the irradiated samples (no column recoveries were reported for Method 2). The source of the discrepancy between the LSC measurements, the HPLC measurements, and the reported HPLC recoveries could not be resolved.
3. According to the study author, the HPLC gradient system employed in Method 1 was "expanded" in Method 2 in order to improve resolution between thiabendazole degradates. Results reported for all sampling intervals from Method 1 were according to "Regions of Interest",

rather than for individual compounds. Unfortunately, although information provided within the study suggest that the samples collected at all sampling intervals were analyzed by Method 2, only quantitative data for those collected at 96 hours were provided.

4. The reported half-life, 29 hours, is equivalent to 1.2 days of natural sunlight, assuming 12 hours of sunlight each day.
5. The identities of thiabendazole, benzimidazole, and benzimidazole-2-carboxamide in the test solutions were confirmed by MS analysis. No attempt was made to confirm the identity of benzimidazole-2-carboxylic acid by MS.
6. Tentative identification information provided in Table XI for chromatographic regions 3 and 4 (Method 2) were inadvertently reversed. Narrative information provided throughout the study indicate that region 3 contained benzimidazole-2-carboxylic acid and at least one additional compound; region 4, which was composed of several components, contained a total concentration that was considered too low to warrant further characterization analysis.
7. The adsorption spectrum of thiabendazole in pH 5 buffer solution was provided in Figure 5.
8. Thiabendazole was reported to have an aqueous solubility of 3.84% at pH 2.2.
9. During the study, the pH of the test solutions was 5.01-5.06.
10. The buffer solution was made using filter-sterilized water, but there was no indication that the buffer solution, once made, was sterilized prior to use. Bacterial and fungal plate count analyses were performed on test solutions collected at the initiation of the study and at 96 hours posttreatment. Bacterial counts were determined using plate count agar, and fungal counts were determined using Sabouraud agar containing rose bengal and tetracycline. It was reported that the test solutions were sterile throughout the study.

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