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DATA EVALUATION RECORD

STUDY 2

CHEM 057701

Malathion

§161-2

FORMULATION--00--ACTIVE INGREDIENT

STUDY MRID 41673001

Carpenter, M. 1990. Determination of the photolysis rate of ¹⁴C-malathion in pH-4 aqueous solution. Laboratory Report No. 37574. Unpublished study performed by Analytical Bio-Chemistry Laboratories, Inc., Columbia, MO, and submitted by the Malathion Reregistration Task Force.

DIRECT REVIEW TIME = 9

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CONCLUSIONS:

Degradation - Photodegradation in Water

1. This study provides supplemental information that shows malathion is stable to aqueous photolysis since the half-lives were 71 and 98 days, respectively, in sensitized and non-sensitized solutions. The study is unacceptable at this time because data from the two TLC analyses and the HPLC analysis were not in agreement, suggesting that the methods may have been inadequate to accurately assess the concentration of malathion and its degradates in solution.
2. In order for this study to satisfy data requirements, the registrant must clarify the discrepancies between the different methods and provide accurate quantitative data.

3. Resolution of the problems associated with this study probably will not change the conclusion that malathion is stable to aqueous photolysis in water buffered to pH 4, since the half-lives were 71 and 98 days, respectively, in sensitized and non-sensitized solutions.
4. The section below listed as "REVIEWER'S COMMENTS", contains further details of the problems noted with the study.

METHODOLOGY:

Aliquots of a methanolic solution of [2,3-¹⁴C]malathion (radiochemical purity 94.9%, specific activity 8840 dpm/ug, Amersham) were transferred into two glass flasks, and the solvent was evaporated under nitrogen. To one flask was added 3.3 mL of acetone as a photosensitizer, and both flasks were brought to a volume of 330 mL with sterile aqueous pH 4 acetate buffer solution. The final concentrations of [¹⁴C]malathion were 9.49 ug/mL in the sensitized solution and 9.73 ug/mL in the nonsensitized solution; the final concentration of acetone in the sensitized solution was 1% by volume. Aliquots of the treated buffer solutions were transferred to sterile borosilicate tubes, which "were filled as completely as possible to minimize head space", and the tubes were sealed. To serve as dark controls, a portion of the sample tubes were wrapped in foil and placed in a closed box within a photolysis chamber (Figure 4; chamber not further characterized). The remaining sample tubes were placed in the same photolysis chamber, and the chamber was irradiated continuously using a xenon arc lamp. The intensity of the radiation from the lamp was measured prior to and after the irradiation period, and was stated to be approximately half that of natural sunlight at wavelengths between 290 and 750 nm (Table 1; Figure 3). The samples were maintained at 25 ± 1 C during the study. Duplicate tubes containing irradiated or dark control solutions were collected at 0, 1, 3, 7, 10, 14, 21, and 30 days posttreatment.

Aliquots of the sample solution were analyzed for total radioactivity by LSC. Additional aliquots of the sample solution were analyzed using one-dimensional TLC on silica gel plates developed in toluene:glacial acetic acid (80:20, v:v); [¹⁴C]residues were located and quantified using radioactive scanning. Aliquots of the day 30 irradiated samples were analyzed using TLC on silica gel plates developed in toluene:methanol (75:25, v:v); these samples were cochromatographed with reference standards of malathion and s-[1,2-di(carbethoxy)ethyl]-o-methyl-hydrogenphosphorodithioate (dicyclohexylammonium salt). [¹⁴C]Residues were located and quantified using radioactive scanning, and were identified by comparison to the standards. The day 30 irradiated samples were further analyzed using HPLC with a mobile phase consisting of a phosphate buffer:acetonitrile gradient from 75:25 to 45:55 (HPLC system not further characterized). HPLC results were compared to standards of malathion, malaoxon, o,o-dimethyl phosphorodithioic acid, mono-acid, di-acid, monoethyl maleate, diethyl maleate, diethyl mercaptosuccinate, diethyl fumarate, diethyl methylthiosuccinate, and s-[1,2-di(carbethoxy)ethyl]-o-methyl-hydrogenphosphorodithioate (dicyclohexylammonium salt).

DATA SUMMARY:

[2,3-¹⁴C]Malathion, at 9.5-9.7 ug/mL, degraded with registrant-calculated half-lives of 71.3 and 98 days in sterile pH 4 photosensitized (1% acetone) and nonsensitized aqueous buffer solutions, respectively, that were irradiated continuously with a xenon arc lamp at 25 ± 1 C for 30 days (Tables VI and VIII). The intensity of the radiation from the lamp was approximately half that of visible sunlight (290-750 nm). In contrast, [¹⁴C]malathion degraded with half-lives of 264-299 days in the dark controls (Tables VII and IX). During the study, the material balances of the sensitized solutions were $\geq 100\%$ of the applied and of the nonsensitized solutions were $\geq 96.3\%$ with no discernable pattern (Tables X-XIII).

At 30 days posttreatment, on TLC plates developed in toluene:glacial acetic acid (80:20, v:v), [¹⁴C]malathion comprised 74.9% of the radioactivity applied to the irradiated sensitized solutions, 80.3% of that applied to the irradiated nonsensitized solutions, 96.3% of that applied to the sensitized dark controls, and 92.1% of that applied to the nonsensitized dark controls (Tables VI-IX). Also on TLC plates developed in toluene:glacial acetic acid (80:20, v:v), no degradate comprised $\geq 10\%$ of the recovered radioactivity in the sensitized and nonsensitized dark control solutions (Tables II-V). One zone (R_f 0.21-0.34) in the sensitized irradiated solution at 30 days, comprised 17.2% of the recovered radioactivity which was not characterized; another zone (R_f 0.02-0.1) in the nonsensitized irradiated solution at 30 days, comprised 19.6% of the recovered radioactivity which was not characterized. The study author stated that two photoproducts were detected during the study that were tentatively identified as

the alpha and/or beta half esters of malathion (mono-acid) and o,o-dimethyl phosphorodithioic acid.

On TLC plates developed in toluene:methanol (75:25, v:v), the day 30 sensitized and nonsensitized irradiated solutions contained 52% and 56% of the recovered radioactivity, respectively, as malathion (Table XV). In the sensitized irradiated solution,

s-[1,2-di(carbethoxy)ethyl]-o-methylhydrogenphosphorodithioate-(dicyclohexylammonium salt)

was 14% of the recovered radioactivity, 13% was a discrete unknown, 3% remained at the origin, and 17% was described as "remainder"; the material balance was 91% of the applied radioactivity. In the nonsensitized irradiated solution, s-[1,2-di(carbethoxy)ethyl]-o-methylhydrogenphosphorodithioate(dicyclohexylammonium salt) was 33% of the recovered radioactivity, 3% remained at the origin, and 9% was described as "remainder"; the material balance was 102% of the applied.

Using HPLC, the day 30 sensitized and nonsensitized irradiated solutions contained 51.1% and 56.6% of the recovered radioactivity, respectively,

as malathion (Figures 15 and 16). In the sensitized irradiated solution,

s-[1,2-di(carbethoxy)ethyl]-o-methyl-hydrogen-phosphorodithioate(dicyclohexylammonium salt)

was 9.4% of the recovered radioactivity; minor peaks corresponding to

monoethyl maleate,

diethyl maleate,

malaoxon,

mono-acid,

diethyl mercaptosuccinate, and

diethyl fumarate

were also noted (Figure 16). In the nonsensitized irradiated solution, s-[1,2-di(carbethoxy)ethyl]-o-methyl-hydrogenphosphorodithioate(dicyclohexylammonium salt) was 32.1% of the recovered radioactivity; minor peaks corresponding to monoethyl maleate, diethyl maleate, mono-acid, and diethyl mercaptosuccinate were also noted (Figure 15).

REVIEWER'S COMMENTS:

1. Data from the two TLC analyses and the HPLC analysis were not in agreement, suggesting that the methods may have been inadequate to accurately assess the concentration of malathion and its degradates in solution. At 30 days posttreatment, the TLC method (toluene:glacial acetic acid) used to analyze the majority of samples found that 70-79% of the radioactivity recovered from the irradiated solutions was malathion (Tables II and IV).

In contrast, the TLC (toluene:methanol) and HPLC methods used only to analyze the day 30 samples found 51-57% of the recovered was malathion (Table XV; Figures 15 and 16). Also, the degradates identified by the various methods do not agree.

2. Degradates did not appear to have been adequately characterized. The study author stated that, using TLC with the toluene:glacial acetic acid solvent, two photoproducts were detected and tentatively identified as the alpha and/or beta half esters of malathion and o,o-dimethyl phosphorodithioic acid; however, these compounds were not quantified or related to zones on the TLC plates that were quantified. On the TLC plates developed in toluene:methanol, only the parent and s-[1,2-di(carbethoxy)ethyl]-o-methyl-hydrogen phosphorodithioate-(dicyclohexylammonium salt) were identified; one degradate, present at 13% of the recovered radioactivity, was not identified. In the HPLC analytical data, peaks were identified but not quantified.

3. The study author stated that malathion did not adsorb to glass surfaces, did not volatilize, and was stable when stored in solution in the refrigerator (4° C) or freezer (-20° C) for 7 days.
4. Material balances in the exposed systems varied from 100 to 106% in the sensitized solutions and from 96.3 to 102% in the non-sensitized solutions.

MALATHION

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Pages 6 through 27 are not included.

The material not included contains the following type of information:

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