DATA EVALUATION RECORD

STUDY 2

CHEM 030703 Naptalam sodium salt §161-2
FORMULATION--00--ACTIVE INGREDIENT

STUDY ID 41385401
Gaydosh, K.A. 1989. Aqueous photolysis of naptalam. Uniroyal Project No. 8992. Unpublished study performed and submitted by Uniroyal Chemical Company, Inc., Middlebury, CT.

DIRECT REVIEW TIME = 5

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CONCLUSIONS:

Degradation - Photodegradation in Water

1. This study cannot be used to fulfill data requirements at this time.

2. Naptalam photodegraded with half-lives of 6.2-6.9 days (149-164 hours) in sterile aqueous pH 7 buffered 0.001 and 0.01 M phosphate solutions, and 10.3 days (248 hours) in 0.1 M phosphate solutions that were continuously irradiated with a xenon arc lamp at 25 C. Naptalam did not degrade in similar solutions incubated in the dark. The major degradate in the irradiated solutions was 1-naphthylamine; N-1-naphthylphthalimide was also identified.

3. This study is scientifically sound, but does not meet Subdivision N guidelines for the following reasons:

the study author failed to account for all of the radioactivity as analyzed by HPLC/LSC; following HPLC analysis, 14-23% of the applied radioactivity was unidentified;

the treatment rate was not specified;

the test substance was incompletely characterized;

the photolysis apparatus was not adequately described;

the radiant intensity of the xenon light source was not measured; and

the absorption spectra of the pesticide in the test solutions were not provided.

4. In order for this study to fulfill the photodegradation in water data requirement, the registrant must characterize the unidentified radioactivity, report the treatment rate used for the study, report the position of the radiolabel on the test substance, provide a more complete description of the photolysis apparatus used, measure the radiant intensity that reached the test solutions, and provide absorption spectra of the pesticide in the test solutions.

METHODOLOGY:

Aliquots of sterile (boiled for 15 minutes) aqueous 0.001, 0.01, and 0.1 M phosphate buffered (pH 7) solutions were placed in sterile 20-mL glass vials; four vials were prepared at each buffer concentration. [^{14}C]Naptalam (sodium salt, radiochemical purity 97.6%, specific activity 11.86 mCi/mmole, Uniroyal Chemical) was added to each vial at an unspecified treatment rate, and the vials were capped; two vials at each concentration were then wrapped in aluminum foil to serve as dark controls. The vials (wrapped and unwrapped) were placed in a recirculating waterbath maintained at 25 C and irradiated continuously using a xenon arc lamp (Heraeus Suntest) with the "output set at 890 Watt/m^2"; the photolysis apparatus was not further described. The spectral distribution of the light source was similar to sunlight (Appendix III). Aliquots (1 mL) were taken from the vials at 0, 12, 24, 36, 48, 120, 240, and 360 hours (0.5, 1, 1.5, 2, 5, 10, and 15 days) posttreatment.

Aliquots of each sample were analyzed for total radioactivity using LSC. The solutions were also analyzed for naptalam and its degradates by HPLC using a mobile phase of 0.1% trifluroacetic acid in water:acetonitrile with a linear gradient in the water:acetonitrile from 90:10 (v:v) to 50:50 (v:v); detection was by UV absorbance (280-282 nm) and radioactivity monitoring. Unlabeled reference standards were cochromatographed with the samples.

DATA SUMMARY:

[^{14}C]Naptalam (sodium salt, radiochemical purity 97.6%), at an unspecified concentration, photodegraded with reviewer-calculated

half-lives of 6.2-6.9 days (149-164 hours) in sterile aqueous buffered (pH 7) 0.001 and 0.01 M phosphate solutions, and 10.3 days (248 hours) in 0.1 M phosphate solutions that were irradiated continuously for 15 days (360 hours) with a xenon arc lamp at 25 C. The xenon lamp was set to emit 890 Watt/m^2 with a spectral distribution reported to be similar to sunlight; actual intensity was not measured. In contrast, naptalam was stable in the test solutions that were incubated in the dark, comprising 96.6-97.4% of the applied radioactivity at 15 days (360 hours) posttreatment (Appendix I). The major degradate in the irradiated solutions was

1-naphthylamine

(Tables I, III, and V). At 15 days posttreatment in the 0.001 and 0.01 M phosphate solutions, naptalam (as determined by HPLC/LSC analysis) comprised 18.6-21.3% of the applied radioactivity, 1-naphthylamine comprised 47.5-49.8%, and

N-1-naphthylphthalimide

comprised 7.3-7.5%; 14-23% of the applied radioactivity was not accounted for. At 15 days posttreatment in the 0.1 M phosphate solutions, naptalam comprised 35.8% of the applied, 1-naphthylamine comprised 37.4%, N-1-naphthylphthalimide comprised 9.1%, and 17.7% of the applied was not accounted for.

Material balances ranged from 84.7 to 107.8% of the applied during the study (Appendix II).

COMMENTS:

1. The study author failed to account for all of the radioactivity as analyzed by HPLC/LSC. Following HPLC/LSC analysis of solutions at 360 hours posttreatment, approximately 75% of the applied radioactivity was accounted for in the 0.01 and 0.001 M buffer solutions (Tables III and V) out of a total recovered (as determined by LSC alone) of approximately 98 and 89%, respectively (Appendix II). The study author provided no explanation for the deficit.

2. The treatment rate was not specified. It was reported that "Using a sterile HPLC syringe, added 125 uL of the Napthalam solution to each 20 mL vial of buffer solution." It was not reported what the concentration of the [^{14}C]naptalam stock solution was; therefore, the treatment rate could not be determined.

3. The position of the radiolabel on the test substance was not specified.

4. The photolysis apparatus was not adequately described. The distance from the xenon arc lamp to the test solutions was not reported, and it was not specified if radiation below 290 nm was filtered out.

5. The radiant intensity of the xenon light source at the sample position was not measured. Since the samples were placed in a waterbath, the intensity should be measured at the sample position in the waterbath because the water may reduce the amount of light that reaches the samples. In a photodegradation on soil study (Study 3, MRID 41385402), the samples were also placed in a waterbath. In that study, the xenon light source was set to emit 820 Watt/m^2, but the measured intensity in the waterbath at the sample position was 700-750 Watt/m^2.

6. The absorption spectra of the pesticide in the test solutions were not provided.

7. It was not specified if single, duplicate, or triplicate aliquots of the test solutions were analyzed using LSC and HPLC.

8. Using the data provided and first-order linear regression where x = time and y = ln(concentration of naptalam), the reviewer calculated the half-lives of naptalam to be 164.4 hours [6.9 days] (r^2 = 0.993), 149.1 hours [6.2 days] (r^2 = 0.998), and 248.1 hours [10.4 days] (r^2 = 0.997) in 0.001 M, 0.01 M, and 0.1 M phosphate buffer solutions, respectively. The half-lives reported by the study author were 148.4, 144.2, and 248.3 hours, respectively (Tables II, IV, and VI).

9. EFGWB prefers that [^{14}C]residues in samples be separated by chromatographic methods (such as TLC, HPLC, or GC) with at least three solvent systems of different polarity, and that specific compounds isolated by chromatography be identified using a confirmatory method such as MS in addition to comparison with the R_f of reference standards.

   In this study, the sample extracts were analyzed using HPLC with a linear gradient between two solvent systems. Radioactive peaks were identified only by comparison with the retention times of known reference standards chromatographed on the same column.

Table I - CHARACTERIZATION OF ALANAP IN 0.1 M KH_2PO_4 AS DETERMINED BY HPLC/LSC ANALYSIS

TIME (HOURS)[a]	% OF APPLIED RADIOACTIVITY IDENTIFIED AS ALPHA-NAPTHALAMINE	IDENTIFIED AS ALANAP	IDENTIFIED AS ALANAP-IMIDE
0	ND[b]	96.9	ND
12	ND	95.3	ND
24	2.1	90.4	3.4
36	2.9	88.5	4.1
48	4.5	85.6	4.6
120	14.7	66.3	7.7
240	27.2	50.0	9.4
360	37.4	35.8	9.1

[a] 1 Day = 12 hours sunlight

[b] ND = Not detected

Table II - CALCULATION OF HALF-LIFE OF PHOTOLYZED ^{14}C-ALANAP IN 0.1 M KH_2PO_4

	X (HOURS)	% ^{14}C IDENTIFIED AS ALANAP	LN Y (% ^{14}C IDENTIFIED AS ALANAP / 100)
Experimental	0	96.9	- 0.0315
	12	95.3	- 0.0481
	24	90.4	- 0.1009
	36	88.5	- 0.1222
	48	85.6	- 0.1555
	120	66.3	- 0.4110
	240	50.0	- 0.6931
	360	35.8	- 0.0272
Calculated Best Fit Line:	40		- 0.1423
	200		- 0.5887
	360		- 1.0351
50% Degradation		48.5	- 0.7236

Statistics: 1/2 life = 248.3 hours

Slope = - 0.0028

y-intercept = - 0.0308

Correlation coefficient = - 0.9986

Table III - CHARACTERIZATION OF ALANAP IN 0.01 M KH_2PO_4 AS DETERMINED BY HPLC/LSC ANALYSIS

	% OF APPLIED RADIOACTIVITY		
TIME (HOURS)[a]	IDENTIFIED AS ALPHA-NAPTHALAMINE	IDENTIFIED AS ALANAP	IDENTIFIED AS ALANAP-IMIDE
0	ND[b]	97.7	ND
12	2.3	91.9	2.6
24	3.9	85.7	3.5
36	6.3	81.4	5.1
48	9.7	75.9	6.2
120	20.0	52.5	9.2
240	43.1	30.3	9.7
360	49.8	18.6	7.3

[a] 1 Day = 12 hours sunlight

[b] ND = Not detected

Table IV - CALCULATION OF HALF-LIFE OF PHOTOLYZED ^{14}C-ALANAP IN 0.01 M KH_2PO_4

	X HOURS	% ^{14}C IDENTIFIED AS ALANAP	LN Y = % ^{14}C IDENTIFIED AS ALANAP / 100
Experimental	0	97.7	- 0.0233
	12	91.9	- 0.0845
	24	85.7	- 0.1543
	36	81.4	- 0.2058
	48	75.9	- 0.2758
	120	52.5	- 0.6444
	240	30.3	- 1.1940
	360	18.6	- 1.6820
Calculated Best Fit Line:	40		- 0.2310
	200		- 0.9745
	360		- 1.7180
50% Degradation		48.9	- 0.7154

Statistics: 1/2 life = 144.2 hours

Slope = - 0.0046

y-intercept = - 0.0404

Correlation coefficient = 0.9990

Table V - CHARACTERIZATION OF ALANAP IN 0.001 M KH_2PO_4 AS DETERMINED BY HPLC/LSC ANALYSIS

	% OF APPLIED RADIOACTIVITY		
TIME (HOURS)[a]	IDENTIFIED AS ALPHA-NAPTHALAMINE	IDENTIFIED AS ALANAP	IDENTIFIED AS ALANAP-IMIDE
0	ND[b]	99.0	ND
12	2.5	90.3	2.7
24	4.6	82.8	6.8
36	9.1	77.3	5.7
48	10.8	71.9	6.7
120	24.8	56.3	8.4
240	40.0	31.6	8.0
360	47.5	21.3	7.5

[a] 1 Day = 12 hours sunlight

[b] ND = Not detected

Table VI - CALCULATION OF HALF-LIFE OF PHOTOLYZED ^{14}C-ALANAP IN 0.001 M KH_2PO_4

	X HOURS	% ^{14}C IDENTIFIED AS ALANAP	LN Y = % ^{14}C IDENTIFIED AS ALANAP / 100
Experimental	0	99.0	- 0.0101
	12	90.3	- 0.1020
	24	82.8	- 0.1887
	36	77.3	- 0.2575
	48	71.9	- 0.3299
	120	56.3	- 0.5745
	240	31.6	- 1.1520
	360	21.3	- 1.5465
Calculated Best Fit Line:	40		- 0.2462
	200		- 0.9205
	360		- 1.5948
50% Degradation		49.5	- 0.7032

Statistics: 1/2 life = 148.4 hours

Slope = - 0.0042

y-intercept = - 0.0777

Correlation coefficient = - 0.9964

APPENDIX I

Characterization of Control Samples of ALANAP photolyzed in 0.1M, 0.01 M and 0.001 M KH_2PO_4 as determined by HPLC/LSC analysis

	% ALANAP IN CONCENTRATION OF KH_2PO_4		
TIME (HOURS)	0.1 M	0.01 M	0.001 M
0	96.3	98.2	97.4
12	98.4	96.4	98.6
24	97.2	96.5	98.6
36	97.6	98.3	96.5
48	97.8	96.3	96.5
120	97.7	98.5	94.0
240	96.9	97.7	95.9
360	97.1	97.4	96.6

APPENDIX II

Material Balance of Samples of ALANAP photolyzed in 0.1 M, 0.01 M and 0.001 M KH_2PO_4 [a]

$0.1\ M\ KH_2PO_4$

TIME (HOURS)	% MATERIAL BALANCE A	B	Control A
0	93.5	98.9	95.8
12	95.1	95.4	98.4
24	95.7	100.1	99.4
36	95.9	107.8	106.6
48	94.9	92.7	98.2
120	94.7	86.4	89.8
240	91.3	89.9	99.3
360	88.0	87.5	93.1

$0.01\ M\ KH_2PO_4$

TIME (HOURS)	% MATERIAL BALANCE A	B	Control A
0	98.2	94.0	92.9
12	100.5	88.4	91.3
24	105.1	94.2	91.1
36	106.6	94.1	96.5
48	107.7	89.3	95.3
120	104.1	89.4	96.3
240	96.7	98.6	93.0
360	98.1	97.9	96.8

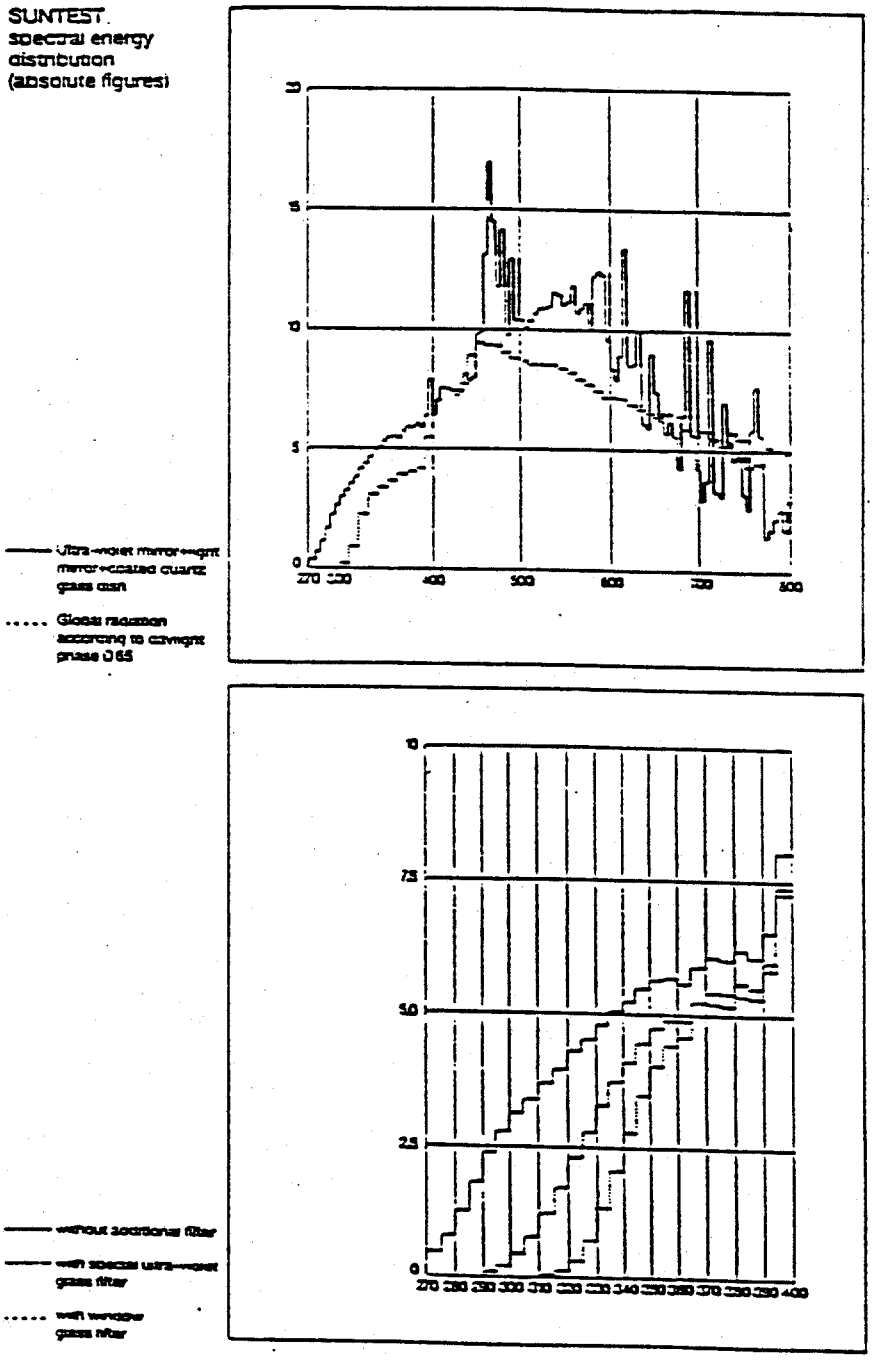
$0.001\ M\ KH_2PO_4$

TIME (HOURS)	% MATERIAL BALANCE A	B	Control A
0	94.7	96.6	92.8
12	97.3	90.6	86.2
24	97.8	94.5	92.3
36	93.0	93.6	84.7
48	91.1	90.4	86.2
120	102.0	102.6	100.5
240	97.4	100.8	95.9
360	88.4	90.4	99.8

[a] Material Balance $\frac{\text{dpm}/\mu L \text{ initial solution}}{\text{dpm}/\mu L \text{ photolyzed solution}} \times 100$

APPENDIX III

The spectral distribution of the xenon burner used. Graphs were supplied by instrument manufacturer.



STUDY AUTHOR(S)'S RESULTS AND/OR CONCLUSIONS

RESULTS AND DISCUSSION

An aqueous photolysis study was conducted in 0.1 M, 0.01 M and 0.001 M KH_2PO_4 solutions at pH 7.0 with ^{14}C-napthalam (ALANAP). The samples were photolyzed for a period equivalent to 30 days of sunlight (12 hours of sunlight equals 1 day) with sample aliquots removed at various time points. The degradation of the parent compound and metabolite formation under photolysis were monitored by high pressure liquid chromatography (HPLC) and liquid scintillation counting (LSC).

At zero time, the 0.1 M KH_2PO_4 solution treated with ^{14}C-napthalam contained 96.9% ALANAP. The metabolites were first detected after 24 hours of direct sunlight with 2.1% attributed to the alpha-napthalamine and 3.4% to the ALANAP-imide. Breakdown of the parent compound continued and sample aliquots removed at 120 hours were found to contain 66.3% ALANAP, 14.7% of the amine and 7.7% of the imide. At the final time point of 360 hours, 35.8% of the applied radioactivity was present as ALANAP while 37.4% and 9.1% were identified as the amine and imide respectively (Figure 3 and Figure 4).

The half-life of napthalam photolyzed in 0.1 M KH_2PO_4 was calculated to be 248 hours using linear regression. Figure 5 shows the best fit line of ^{14}C-napthalam photolyzed in 0.1 M KH_2PO_4 versus time.

The second set of samples to be analyzed were those photolyzed in a solution of 0.01 M KH_2PO_4. Initially, at time point zero, HPLC/LSC profile analysis showed 97.7% ALANAP to be present in the sample. Alpha-napthalamine and ALANAP-imide were not detected at this time. At 120 hours, 52.5% was identified as ALANAP with 20.0% and 9.2% being attributed to the amine and imide products respectively. Upon

RESULTS AND DISCUSSION (Continued)

completion of photolysis, 360 hours, ALANAP was identified as 18.6% of the radioactivity. The presence of the amine increased to 49.8% while the imide was detected at 7.3% (Figure 6 and Figure 7).

The half-life of napthalam photolyzed in 0.01 M KH_2PO_4 was calculated to be 144 hours linear regression analysis. Figure 8 visualizes the best fit line of ^{14}C-napthalam photolyzed in 0.01 M KH_2PO_4 versus time.

The final samples analyzed were photolyzed in a solution of 0.001 M KH_2PO_4. At zero hour (initial time point) 99.0% of the applied radioactivity was identified as ALANAP. Again, the metabolites were not detected. After 120 hours of photolysis, 56.3% of the parent compound remained. Alpha-napthalamine was present at 24.8% while 8.4% was identified as ALANAP-imide. At 360 hours, only 21.3% of the ^{14}C-ALANAP remained in the sample. Forty-seven and one-half percent formed the amine metabolite and 7.5% was produced as ALANAP-imide (Figure 9 and Figure 10).

The half-life of napthalam photolyzed in 0.001 M KH_2PO_4 was calculated by linear regression analysis to be 148.4 hours. Figure 11 shows the best fit line of ^{14}C-napthalam photolyzed in 0.001 M KH_2PO_4 versus time.