1-14-75

Environmental Chemistry Review for Captan (N-((tri-chloromethyl)thio)-4-cyclohexene-1,2-dicarboximide

Reg. No. - 239-533
Company Name - Ortho Chevron Chemical Co.
Application Date - 5/22/73

I. INTRODUCTION

See review of 8/17/73 and 10/4/73. This submission, dated 11/15/74, is in response to our letter of 12/27/73 requesting 70-15 data.

The Captan 50W fungicide is for use on taro in Hawaii only.

Physical and chemical properties

mp:	174-176 °C
crystal density:	1.7324 at 20 °C
water solubility:	0.5 - 3.3 ppm (25 °C); degradation is rapid

II. DIRECTIONS FOR USE

See review dated 8/17/73.

III. DISCUSSION OF DATA

1. Analytical methods

(a) extraction with methylene chloride and GLC-EC analysis

(b) colorimetric (427 mu) - react with pyridine-tetraethylammonium hydroxide

2. The Soil Metabolism of Carbonyl- ^{14}C-Captan (ref. 2)

An Oakley (Calif.) sandy loam (67% sand, 17% silt, 16% clay, 1.78% OM, pH = 6.8) was fortified with carbonyl- ^{14}C-Captan at 5.33 ppm (dry wt. basis), moistened to facilitate microbial activity, covered and kept at ambient temperature on the lab bench. Hot CO_2 was collected in an ethanolamine trap and other volatile metabolites were collected in a methoxyethanol trap.

Soil aliquots were analyzed by combustion and counting and by acidifying an aliquot to pH = 2 and extracting 5 times with ethyl acetate. Aliquots of the extract were counted, and spotted on TLC plates for 2-D development. Spot visualization and quantitation was by fluorescence, autoradiography and other chemical techniques and identification was by co-chromatography. The remaining

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soil was extracted 3 times with water and an aliquot of the extract was counted. An aliquot of the remaining soil was combusted for ^{14}C assay. The soil residue was then extracted for humic acid using a method described in the literature.*

Samples were taken at about 5-7 day intervals for 322 days.

Results

1) CO_2 was the only volatile metabolite found.

2) Liberation of $^{14}CO_2$

Day interval	% of ^{14}C dose (total)
0-1	1.01
1-3	5.61
3-7	20.36
10-14	45.65
17-21	63.40
24-28	75.04
43-45	85.23
85-91	90.23
175-182	93.14
316-322	94.98

3) Soil Extraction Distribution Data

Day	% of Applied Dose				
	EtOAc	Water	Soil	$^{14}CO_2$	Total
0	95.7	0.35	0.42	-----	96.4
7	85.1	1.33	3.90	20.4	110.2
14	75.8	1.84	5.06	45.7	128.4
37	24.7	2.65	9.68	82.4	119.9
63	11.15	2.50	12.73	88.1	114.5
122	2.90	1.45	7.58	91.5	103.4
244	0.66	0.59	5.69	94.2	101.2

*The soil residue remaining after water extraction is extracted with NaOH. The NaOH extract is acidified producing 3 fractions: (1) CO_2 gas, (2) a supernatant and (3) a precipitate. The supernatant is then extracted with ether giving an ether phase and an aqueous phase.

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4) Residue distribution after extraction with EtOAc and Water (% of initial dose) in days

Fraction	0	7	14	63	181	244
Soil residue (unextracted)	0.17	0.21	0.70	1.62	1.27	1.02
NaOH extract	0.39	3.71	4.92	11.87	6.61	6.59
Humic acid	0	0.14	0.49	1.42	0.45	0.94
Supernatant (fulvic acid fraction)	0.40	3.29	4.22	7.74	5.72	5.04
Ether phase	0.26	1.69	1.04	1.55	0.76	0.76
Aqueous phase	0.07	1.11	2.59	6.15	4.05	3.31

5) Identification of metabolites and % of initial dose (ppm) at indicated day

Compound	0	7	14	63	244
Captan (parent)	93.1 (4.97)	0.94(0.05)	0.78(0.041)	0.30(0.015)	
THPI	3.41 (0.091)	66.0(1.77)	38.0(1.02)	0.70(0.019)	0.18(0.005)
THPI-Epox		1.57(0.046)		1.26(0.037)	
Diol		0.18(0.006)	0.59(0.02)		
THPAm		11.8(0.354)	16.8(0.503)	1.32(0.042)	
THPAl		1.19(0.036)	3.19(0.096)	0.23(0.007)	
CO_2		20.4	45.7	88.1	94.2
Total	96.5	102.1	105.1	91.9	94.6

Conclusions

1) Hot CO_2 released from carbonyl-labelled captan is the major soil degradation product. After 2-3 weeks, about 50% of the applied activity is released as hot CO_2.

2) The amount of activity extracted with EtOAc drops from 95.7% at day 0 to less than 1% at day 244. Water extractable activity remains between 0.3 and 2.7% during the first 244 days. The amount not extractable with EtOAc or water climbs from 0.4% at day 0 to 12.7% at day 63 and then drops to 5.7% at day 244.

   Hot CO_2 accounts for most of the activity and at day 244 represents 94.2% of the applied activity.

3) Extraction of the soil residue with NaOH showed the activity associated with the humic acid fraction reached a maximum on day 63 of 1.4%. The activity in the fulvic acid fraction also maximized on day 63 at 7.7%.

4) Major soil metabolites found were THPI (tetrahydrophthalimide) and THPAm (tetrahydrophthalamic acid). The THPI reached a high of 66% of the applied activity in the first week but dropped to less than 1% after 9 weeks. The THPAm reached a maximum of 16.8% at around 2 weeks and declined to less than 1.3% after 9 weeks.

Other metabolites identified (and never reached an individual % greater than 4% of the applied activity) are: THPI-Epox, Diol (5,6-dihydroxyhexahydrophthalimide) and THPAl (tetrahydrophthalic acid). These eventually degraded releasing CO_2.

There are other spots on the TLC plates but they were not identified.

5) This type study does not account for the ring portion of the molecule.

3. Stability of Captan in Silt Loam - a comparative study (literature) ref. 4
(Burchfield, H.P. Contributions from Boyce Thompson Institute Vol. 20 1959 p.205)

A 5% Captan-pyrophilite dust mixture was added to moist and air-dried loam top soil which 2-3 years earlier was composted with manure, 5-10-5 fertilizer and limestone. Captan (and 3 other fungicides-dyrene, dichlone and 1-fluoro-2,4-dinitrobenzene (FDNB)) was added to the moist and dry soil samples (pH = 6.4; 17.5% water when moist and pH = 6.2; 1.6% water when air-dry) at rates of 10 and 100 ug ai/gm soil. The soils were mixed, jarred and mountained at 26 ± 2 °C. The Captan-fortified soil was analyzed by extraction with dichloromethane and determined colorimetrically (427 mu) by reaction with tetraethyl-ammonium hydroxide.

The hydrolysis rate of Captan and the other fungicides in water containing 1% acetone, 5 ug/ml of fungicide and buffered to pH = 7.0 at 29 °C was studied. Captan hydrolysis was also determined in the absence of buffer.

The disappearance of Captan from 200 ul of a solution of Captan at a concentration of 2000 ug/ml in 20 ml of a solution of glutathione containing 40.8 ug glutathione/ml buffered to pH = 7 under an N_2 atmosphere and kept at 29 °C was studied. The reaction was stopped at a pre-set time by adding some $AgNO_3$ solution to precipitate the glutathione and buffer. The resultant suspension was extracted with dichloromethane and analyzed for residual Captan.

The solubilities of the fungicides in water containing 1% acetone was also studied.

Results

Fungicide	half-life in days: dry soil	moist soil	in pH7 buffer	water sol (ug/ml)
Captan	>50	3.5	0.1	8-70
Dyrene	2.5	0.5	20	10
Dichlone	>50	1	5	7
FDNB	>50	0.5	20	400

Conclusions

1) Captan degrades faster in moist soil than in dry soil. This is indicative of microbial degradation.

2) Captan readily degrades in solution (water with 1% acetone) buffered at pH = 7.

4. Stability of Captan in Microaerophillic Taro Soil (Ref. 1)

A 7 kg. sample of air-dried taro paddy soil was fortified with 0.656 gm of Captan 50W (0.328 gm ai) placed in an open 5-gallon can and water added to 100% capacity. Additional water was added to a depth of 6". A control was maintained.

Each day, the 6" of water covering the soil was siphoned off for analysis, a soil sample was taken for analysis and the water was replaced with fresh water.

The method of analysis was not described.

Results

Day	Average ppm of Captan: Water: Control	Water: Treated	Soil: Control	Soil: Treated
0				46.4
1	ND	< .0008	0.26	5.7
4	ND	ND	0.07	0.16
7	ND	ND	0.08	0.08

ND = not detected

Conclusions

1) Fresh water daily replaced the water covering the soil. It would have been better if this water was only sampled instead of entirely replaced. Replacing the water may have altered the rate of degradation.

2) This was not a labeled study and a material balance was not submitted as suggested in our ltr. of 12/27/73.

3) This study shows captan to degrade quickly in soil under water with a half-life of less than one day.

4) Degradation products and their formation and decline were not monitored.

5. Photodegradation of Captan, Phaltan and Difolatan (ref. 6)

This study was carried out by Ortho to ascertain the validity of a French report on the photodegradation of Captan, Phaltan and Difolatan. The French report shows the following photodegradation of Captan:

Sunlight exposure (hours)	% degradation	UV exposure (hours)	% degradation
8	17	4	39
16	30	6	53
24	51	12	61
32	62	24	76
		36	78

% Degradation of Captan, Phaltan and Difolatan from 8 hours exposure to UV light

Captan	64%
Phaltan	33%
Difolatan	88%

In the French study the compounds were placed on polyethylene sheets and exposed to a germicidal UV lamp. Additional Captan samples were exposed to sunlight. Degradation was measured by punching a disc from the polyethylene sheet, placing it on agar seeded with Penicillium expansum spores and measuring the zone of growth inhibition.

In this study, conducted by Ortho, acetone solutions of the fungicides were placed in Petri dishes and polyethylene coasters and evaporated leaving 10 mg. of fungicide. These were exposed for 3 and 7 days to sunlight. Under UV light

Captan was on polyethylene and Phaltan and Difolatan were on glass. The samples were exposed at 12" to a mercury lamp emitting 10.4 watts at 2537 A UV.

Difolatan was assayed by TLC, a benzidine-tetraethylammonium hydroxide colorimetric method and a bioassay technique using Monlinia fructicola spores. Captan and Phaltan were assayed using a resorcinol-colorimetric method.

Results

1) % Recovery After UV Exposure

Compound	Exposure time (hrs.)	% Recovery
Captan	15.38	97.3
Phaltan	17.38	99.3
Difolatan	16.45	107
Difolatan	59	107

2) % Recovery After Sunlight Exposure

Compound	Surface	Exposure (days) 0	3	7
Captan	Glass	109.5	93.0	89.5
Captan	Polyeth.	92.0	87.5	83.2
Phaltan	Glass	93.5	96.5	99.7
Phaltan	Polyeth.	89.5	89.6	89.3
Difolatan	Glass	93.0	92.0	105.0
Difolatan	Polyeth.	87.0	91.7	94.3

3) When Difolatan samples at concentrations of 1.0, 0.3 and 0.1 ppm were exposed to UV light for up to 59 hours or sunlight for up to 3 days, degradation was only minor as measured by spore germination inhibition. The LD_{50} of the spores is 0.03 ppm.

Conclusion

1) The results reported by Ortho grossly conflict with the French test results.

2) Degradation of Captan by sunlight occurs but only to the extent of 10-17% after 7 days exposure. Degradation on the polyethylene surface was generally 5-10% greater than on the glass surface for all three fungicides tested.

3) The UV exposure, caused less degradation than the sunlight exposure for the same exposure time.

6. Alkaline Hydrolysis of Captan (ref. 5, pg. 8)

Pure captan was suspended in solutions of buffered pH's of 7.6, 9.5 and 11.5. The test was run at different temperatures but only the results at 20 °C were submitted.

Degradation was followed by analysis for chloride ion.

Results

1) Hydrolysis is more complete at higher pH.

2) After 35 hrs., there is 5% hydrolysis at pH 7.6, 30% at pH 9.5 and 84% at pH 11.4.

Conclusion

1) Captan hydrolyzes at basic pH's, the more basic the solution, the more hydrolysis within a given time.

2) Metabolites were not identified.

7. Heat Effects on Suspended Captan in Water (ref. 5, pg. 6)

Pure captan was suspended in distilled water at 4 temperatures - 100 °C, 80 °C, 60 °C and 42 °C. Degradation was monitored by analysis for chloride ion. The 2% suspension was maintained by periodic shaking. Other studies were run in buffered solutions of pH 3 and 5.

Results

1) If more than 2% captan is in the suspension, the rate of decomposition falls. At 2% and below, the rate is constant.

2) At 100 °C, captan is totally degraded in 2½ hrs.

3) Degradation rate varies with temperature; higher temperatures bring quicker degradation.

4) Degradation products: hydrogen sulfide, thiosulfate, sulfites, tetrahydrophthalimide, tetrahydrophthalic acid and its monoamide, CO_2 and HCl.

5) The results were the same in buffered solutions of pH 3 and 5.

Conclusions

1) When more than 2% captan is in suspension, degradation is impeded. This indicates that the captan particles congregate leaving less surface area for degradation.

2) The results of the degradation of captan at 80 °C, 60 °C and 42 °C were not submitted.

3) This study was done on pure captan. Heat effects on the product in suspension cannot be determined from this study.

4) Under acidic conditions Captan will degrade to H_2S, sulfites, THPI, THPAl, THPAm, CO_2, HCl and thiosulfates which should further degrade to S and SO_2.

8. The Water Solubility of Difolatan, Captan and Phaltan (reference 3)

About 200 mg of fungicide were added to 100 ml of deionized water in a jar, capped and tumbled for one day. After tumbling, portions of the suspension were centrifuged at 1800 rpm for 2 hrs. The supernatant was placed in 3 separate vials. One vial was analyzed immediately, one just after the first analysis, the next vial was analyzed at 4 hrs. and the last one 22 hrs. after centrifugation stopped.

Analysis was done by extracting the fungicide solution with benzene and injecting into a GLC using an EC detector.

Results

1)

	Difolatan	Captan	Phaltan
Solubility in water at 25 °C in ppm at 0 time	1.4	3.3	1.25

The fungicides decomposed rapidly in solution with half-lives of 5 hrs. (Phaltan), 7 hrs. (Captan) and 9 hrs. (Difolatan).

Conclusion

The solubility of Captan in deionized water at 25 °C is 3.3 ppm. It also degrades rapidly in the water with a half-life of 7 hrs. Since degradation in water is so rapid, the solubility value was determined by extrapolation back to 0 time.

9) ^{14}C-Difolatan in a Model Aquatic Ecosystem (reference 7)

Two tanks (2.4 in. m diameter) were filled with about 200 kg of air-dried soil (>90% sand, 3.9% OM, CEC = 2.19 and pH = 6.1) to 2.5 cm. In one tank, rice seed treated with ^{14}C-Difolatan (specific activity 1075 dpm/µg) at a rate of 1872 mg/kg was spread over the surface of the soil at 200 lb. seed/acre thereby applying Difolatan at 0.375 lb./acre. Both tanks were then filled with 712 liters of aerated well water (pH = 7.1, total hardness 39 mg/l as $CaCO_3$, temp = 15 ± 2.0°C) to a depth of 15.2 cm.

After 7 days equilibration, 75 channel catfish (average 8.2 gm and 80 mm) and 75 crayfish (average 30 gm and 75 mm) were placed in each system.

Water, fish, crayfish and soil were sampled on days 1, 3, 7, 10, 14, 21, and 28. Remaining crayfish were placed in a clean, flowing water system and sampled on days 1, 3, 7, 10 and 14.

Analysis was done on the edible portion of the fish (muscle) and crayfish (tail) by combustion and counting. (Catfish edible and non-edible portions were analyzed for activity after day 10, but all the results were not reported). The water activity was counted directly and the soil was dried and analyzed radiometrically.

The detection limits were 0.005 ppm for catfish, crayfish and soil and 0.001 ppm for water.

Results

1) ^{14}C-residue calculated as Difolatan (ppm)

Day	Soil	Water	Crayfish Edibles (CF)	Catfish Edibles (CF)
1	0.158	0.336	0.016 (0.05)	0.289 (0.86)
3	0.278	0.300	0.055 (0.18)	0.213 (0.71)
7	0.187	0.304	0.263 (0.87)	0.200 (0.66)
10	0.168	0.334	0.183 (0.55)	0.282 (0.84)
14	0.212	0.332	0.178 (0.54)	0.195 (0.59)
21	0.188	0.339	0.088 (0.26)	0.244 (0.72)
28	0.138	0.363	0.087 (0.24)	0.233 (0.64)

2) The crayfish showed slow elimination of activity during the 14 days of withdrawal. However, a leveling off plateau was not reached, so activity may be retained by the crayfish.

3) On day 10, activity found in the catfish non-edibles (viscera) was 0.74 ppm and in the muscle was 0.28 ppm.

Conclusions - Note: The study was on Difolatan, not Captan.

1) All the data for the catfish viscera are not reported. Therefore, residues in the whole fish cannot be calculated.

2) The activity in the soil and water remained at a relatively constant level during the 28 day uptake period, and was only 25-35% higher than the residues found in the crayfish and catfish.

3) The CF values for the crayfish edibles were 0.1 to 0.9 and the CF values for the catfish edibles were 0.6 to 0.9.

4) On day 22, catfish mortality was first noticed. By day 28, all the catfish were dead. This occurred with a CF value in the edibles of less than 1.

5) This information is in review with difolatan.

10. The Chemistry of Captan (reference 5)

a) Captan is not hygroscopic.

b) On dry distillation at 200°C, captan breaks down to thiophosgene, tetrahydrophthalimide and related products.

c) Captan solutions readily react with amines, hydrazines, hydroxylamine, semicarbazides, oximes, sulfites and sulfur dioxide.

d) Toluene and xylene solutions of captan form color bodies at elevated temperatures.

e) Solutions of captan in DMF or benzene in presence of peroxides break down.

f) Stability to light

Thin layers of recrystallized captan (dry, moist and mixed with clay fillers) were exposed for 24 hours to a 100 watt H-6 mercury lamp one foot away. There was no evidence of degradation by checking the melting point, bio-assay, weight loss of the captan or reduction in fungotoxicity.

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g) Dry Heat

Pure captan at 100°C slowly decomposes over several days. At 80°C, captan is stable for a week. At 200°C, decomposition is instantaneous.

Conclusions

1) The above results are for pure captan, not for any formulation thereof.

2) The chemically reactive site on the captan molecule is the trichloromethyl group.

3) The light stability study indicates captan to be stable. However, before a final conclusion can be made we will need additional experimental information.

4) Pure captan is stable under average room conditions.

11. Degradation Products

a) tetrahydrophthalimide (THPI, 151)
soil, water (pH 7 or less)

b) tetrahydrophthalamic acid (THPAm, 169)
soil, water (pH 7 or less)

c) tetrahydrophthalimide epoxide (THPI-epox, 167)
soil

d) 5,6-dihydroxyhexahydrophthalimide (Diol, 185)
soil

e) tetrahydrophthalic acid (THPAl, 170)
soil, water (pH 7 or less)

f) hydrogen sulfide
water (pH 7 or less)

g) thiosulfates
water (pH 7 or less)

h) sulfites
water (pH 7 or less)

i) CO_2
soil, water (pH 7 or less)

j) HCl
water (pH 7 or less)

IV. CONCLUSIONS

1. Aerobic soil degradation of Captan occurs readily. Carbon dioxide is a primary volatile degradation product. The half-life of Captan under aerobic soil lab conditions is 2-3 weeks.

   Major soil (aerobic) metabolites identified were THPI and THPAm. Minor metabolites found were THPI-epox, Diol and THPAl. [See 11. Degradation Products].

   Captan degrades much slower in dry soil than moist soil indicating soil microbial degradation.

2. Captan readily degrades in soil under water. The half-life is less than one day.

3. Captan exposure to sunlight causes 10-17% degradation after 7 days exposure.

4. Captan hydrolyzes under basic conditions. The higher the pH, the greater the hydrolysis rate and the more hydrolysis within a given time period.

5. Difolatan (very similar in structure to Captan) accumulates to less than 1X in the edibles of catfish and crayfish. (There was 100% catfish mortality by day 28.)

6. Captan degrades under acidic conditions to hydrogen sulfide, thiosulfates (which should further break down to S and SO_2), sulfites, THPI, THPAl, THPAm, CO_2 and HCl.

7. Captan is soluble in neutral water only to the extent of ~3 ppm.

V. RECOMMENDATIONS

1. ~~Object to Registration~~ Object to registration - The fish accumulation study on difolatan cannot be used to support the aquatic use of captan. The fish accumulation study as previously requested is needed. See enclosure. (PM enclose V-37-38 of the draft guidelines.)

2. It has been brought to our attention that water from treated taro fields may be drained into adjacent marsh areas containing crabs which are harvested for commercial use. There should be a caution on the label such as "Do not use in areas where water is drained and/or discharged into adjacent marsh areas containing crabs." A crab accumulation study will be needed to determine if this caution can be deleted.

3. Concerning the study titled "Stability of Captan in Micro-aerophillic Taro Soil" (reference 1), submit the identity of the degradation products and indicate their formation and decline in ppm.

4. Concerning the study on the effect of heat on the decomposition of captan (reference 5, page 6) submit degradation data on the % of captan remaining versus time for the water suspensions of captan at 80°C, 60°C and 42°C. Also, submit the results of the studies run in buffered solutions of pH 3 and 5.

5. What was the wavelength range of the light used on the study of the stability of captan to UV light (reference 5, page 4)?

3/5/75

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