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Sulfotepp, A Toxic Impurity in Formulations of Diazinon[1]

E. P. Meier, W. H. Dennis[2], A. B. Rosencrance, W. F. Randall, W. J. Cooper, and M. C. Warner
U.S. Army Medical Bioengineering Research and Development Laboratory, Fort Detrick, Frederick, Md. 21701

We have identified a toxic impurity, 0,0,0,0-tetraethyl dithiopyrophosphate (sulfotepp), in pesticide formulations of diazinon. Organophosphorus pesticides such as diazinon are widely used because of their acute toxicity to insect pests and short persistence after application. This allows the pesticide to be used with maximum immediate effect on the target species and minimum effect on the environment. However, their short persistence requires that these pesticides be used frequently to assure control of the target pest. As a result, relatively stable toxic impurities, such as sulfotepp, in these pesticides may concentrate in the environment and cause unanticipated health and ecological problems.

Human exposure in handling (manufacturing, formulation, application, etc.) a pesticide that contains toxic impurities may result in health hazards not anticipated from the known properties of the pesticide alone. For example, medical diagnosis and treatment for acute exposure to a pesticide can be in error due to effects caused by the toxic impurities. Chronic low level exposure to a pesticide can be in error due to effects caused by the toxic impurities. Chronic low level exposure to these toxic impurities may cause human health effects not anticipated from the known hazards of the pesticide. Toxic impurities can also affect the insecticidal properties of pesticide formulations. If the impurity is much more toxic than the pesticide, the toxicity of the formulation to insects may be primarily due to the impurity; and, entomological considerations in application of the pesticide may be in error.

We have been studying methods for the chemical degradation and disposal of pesticide wastes. Our studies with four different diazinon formulations (MEIER et al. 1976) demonstrated that acid hydrolysis (pH $\sim$2) significantly reduced the diazinon concentration (>99.9%); however, there was less than 50% reduction in the toxicity of the reaction mixture to aquatic organisms. The hydrolysis products have been identified as 6-isopropyl-4-methyl-2-pyrimidinol and diethyl thiophosphate (MEIER et al. 1976, FAUST & GOMMA 1972,

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[1] The opinions or assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Department of the Army or the Department of Defense.

[2] To whom correspondence should be addressed.

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MARGOT & GYSIN 1957). Aquatic bioassay data (Table 1) obtained with these compounds and another potential degradation product, diethyl phosphate, indicated that these products were not the cause of the residual toxicity of the reaction mixture. In reviewing the problem, we identified four potential causes of this high residual toxicity as:

1. Formulation "inert" ingredients that were toxic
2. Unidentified toxic products from the chemical degradation
3. Synergistic toxicity due to two or more ingredients
4. Unidentified toxic impurities

Similar reductions in the toxicity of the acid hydrolysis reaction mixtures were observed for four different diazinon formulations (technical standard, emulsifiable concentrate, oil solution and dust) with each of the individual aquatic species tested. Since each of the formulations had different "inert" ingredients we considered it unlikely that "inert" ingredients were the cause of the observed residual toxicity. The chemistry of the reaction had been thoroughly studied and it was unlikely that an unidentified product was responsible for this toxicity. Synergistic effects are complex and difficult to identify. Further study identified the cause; therefore, this alternative was not investigated.

TABLE 1. Aquatic Bioassay Data - 96 h (LC50) (mg/L)

	Test Animal			
Chemical	Fathead Minnow	Bluegill	Rainbow Trout	Daphnids[a]
Diazinon, Tech. Std.	10.3	0.12	1.35	0.0020
Sulfotepp	0.178	0.0016	0.018	0.00023
Pyrimidinol[b]	--	1200	--	1050
Diethyl phosphate	--	500	--	--
Diethyl thiophosphate	--	100	--	100

[a] 48 h EC50.

[b] 6-Isopropyl-4-methyl-2-pyrimidinol.

Careful analysis of the pesticide reaction mixtures and pesticide formulations led to the identification of the chemical species responsible for the residual toxicity observed in the reaction mixtures. The analyses were performed with a gas chromatograph equipped with a flame photometric detector and a 1.8 m glass column (2 mm ID) packed with 10% OV-17 on GC-Q (100/120 mesh). A temperature program of 180°C (held for 6 min) to 260°C at 30°C/min was employed to obtain a fast analysis for diazinon and any related impurities. The initial analysis of samples containing high concentrations of diazinon (∿500 mg/L) in hexane revealed several phosphorus-containing impurities. The impurities in these samples were present in very low concentrations (<1% of the diazinon concentration) and could not be detected by gas chromatography/mass spectrometry (g.c.m.s.). Therefore, neat samples of two pesticide formulations, the technical standard and the emulsifiable concentrate, were analyzed by g.c.m.s. The major impurity was identified as sulfotepp. The remaining impurities were present in much lower concentrations and were tentatively identified as the various non-toxic phosphate esters (diethyl thiophosphate, triethyl phosphate, etc.) commonly associated with organophosphate pesticides.

Sulfotepp was identified as an impurity in all of the diazinon formulations studied and was also observed in the reaction mixtures from acid hydrolysis of diazinon. The sulfotepp concentration in the reaction mixtures did not change with time during acid hydrolysis, indicating that it was not a product of the reaction and was stable under the reaction conditions (pH range of 1-2). The sulfotepp impurity may have resulted from degradation of diazinon after formulation or may have been introduced with the diazinon in preparing the formulations. To answer this question, eight different diazinon formulations were analyzed for sulfotepp (Table 2). A technical grade sample, Chem Service PS-90 (>92.4% purity), was used to prepare the standard curves for diazinon. An old (∿5 years) experimental formulation, AG 500, was analyzed to determine if age was a factor in the appearance of sulfotepp. Three standard military formulations of diazinon (0.5% oil solution, 48.2% emulsifiable concentrate and 2% dust) were analyzed to determine the concentration of sulfotepp in formulations used by the Army. In addition, three commercial formulations of diazinon were purchased from local stores and were analyzed to determine if sulfotepp was present in diazinon formulations used in the civilian sector. The commercial samples were not as old as any of the other formulations tested. A standard sample of sulfotepp (>96% purity) was prepared in the laboratory according to the method of TOY (1951). This pure material was used to obtain standard curves for analysis of sulfotepp in the formulations.

The results of these analyses (Table 2) demonstrate that sulfotepp is an impurity common to all formulations of diazinon. The concentration of sulfotepp was not a function of the age of the formulation. As a matter of fact, the oldest sample, AG 500, had a sulfotepp concentration lower than some of the other formulations analyzed. The reproducibility of the analysis can be seen in the data for the technical standard samples. We were not able to identify the source of sulfotepp in the various formulations. We do know that the technical standard does contain sulfotepp at a relatively high concentration. This would imply that the impurity is added with diazinon in preparation of the various pesticide formulations.

TABLE 2. Sulfotepp in Diazinon Formulations

Diazinon Formulation[a]	Diazinon (ppm)	Sulfotepp (ppm)	Sulfotepp[b] %
0.5% oil solution	409	1.9	0.46
48.2% e.c.	523	3.7	0.71
2% dust	704	1.4	0.20
48% e.c., AG 500[c]	553	2.0	0.36
25% e.c., commercial	532	2.2	0.41
25% e.c., commercial	516	2.1	0.41
4% dust, commercial	601	1.4	0.23
980 ppm standard		6.9	0.70
588 ppm standard		4.2	0.71
490 ppm standard		3.4	0.69
420 ppm standard		3.2	0.76
392 ppm standard		2.9	0.74

e.c. = emulsifiable concentrate.

[a] Except for standards, formulations were dissolved in hexane to yield ∿500 ppm diazinon.

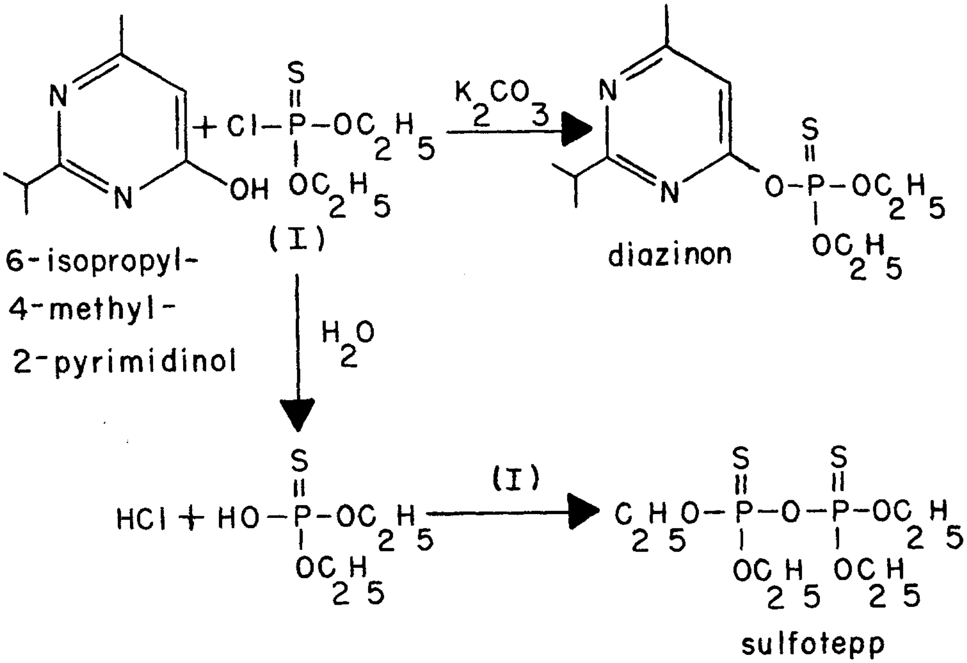
[b] Percent sulfotepp = sulfotepp (ppm) ÷ diazinon (ppm) x 100.

[c] Experimental formulation from a commercial source.

There are two potential sources of the sulfotepp impurity in diazinon. It may occur as the result of hydrolysis of diazinon on storage in the presence of water. MARGOT & GYSIN (1957) have observed the monothio analog under these conditions. However, our studies indicate that sulfotepp is not produced by this mechanism in commercially available diazinon formulations. A second source is the production of diazinon. During the production process diethyl thiophosphoryl chloride (I) is added to the pyrimidinol and the mixture is heated at reflux under anhydrous alkaline conditions

(Equation 1). Small amounts of water present during the synthesis of diazinon could react with the diethyl thiophosphoryl chloride in a mechanism similar to that used by TOY (1951) to produce sulfotepp. A similar argument could also be used to implicate sulfotepp as an impurity in the diethyl thiophosphoryl chloride that is introduced during synthesis of diazinon.

EQUATION I



Our aquatic bioassay data were obtained by exposing fathead minnows (*Pimephales promelas*), bluegill (*Lepomis macrochirus*), (*Salmo gairdneri*) and daphnids (*Daphnia magna*) to five or more concentrations of each compound in a static system. The test compounds were dissolved in acetone (diazinon and sulfotepp) or distilled water (6-isopropyl-4-methyl-2-pyrimidinol, diethyl phosphate and potassium diethyl thiophosphate) and diluted with well water (hardness = 192 mg/L as $CaCO_3$; total alkalinity = 138 mg/L as $CaCO_3$; and pH = 7.7) to produce the test solutions. At the end of each exposure the concentration at which 50% of the test animals survived (48-h EC50 for daphnids and 96-h LC50 for fish) was calculated following standard procedures (LITCHFIELD & WILCOXON 1949, FINNEY 1971, HARRIS 1959).

Our bioassay data (Table 1) show that sulfotepp is much more toxic than diazinon to the aquatic species tested. Sulfotepp is rated by EPA as a "highly toxic" substance, classed as less toxic than TEPP (tetraethyl pyrophosphate), but more toxic than parathion (MORGAN 1977). EPA has also classified sulfotepp as a "restricted use" pesticide (FEDERAL REGISTER 1978). Comparison of the qualifying toxic dose data (FAIRCHILD 1977) indicates that sulfotepp is much more toxic to mammals than diazinon.

Personal communications have indicated that a few people in the pesticide industry and EPA have known that sulfotepp is an impurity resulting from the production of diazinon. However, we have been unable to find any published reference where this fact has been made available to the pesticide user or the scientific community. A recent epidemiological study (DIGGORY et al. 1977) did find sulfotepp in flour that had been contaminated with parathion. Analysis of the parathion source showed that it had a sulfotepp/parathion ratio of 1.3 percent. The authors stated that sulfotepp is a known reaction by-product in the synthesis of parathion; however, no reference was provided.

Our analytical results indicate that sulfotepp is introduced as an impurity in diazinon during the preparation of the various pesticide formulations. If the impurity is introduced in the production process and can be eliminated by improved quality control procedures we feel that acid hydrolysis may be an acceptable method (MEIER et al. 1976) for chemical disposal of small quantities of diazinon wastes. If the impurity cannot be eliminated, the pesticide label for diazinon should list sulfotepp as an active ingredient so that the user is aware of its presence and can handle and use the pesticide accordingly.

The implications of these findings should be considered in evaluation of the impact of use of diazinon on health and the environment. Sulfotepp is much more toxic than diazinon and may even account for some of the insecticidal properties of diazinon formulations. As seen in our study, it is more stable to acid hydrolysis than diazinon. This may indicate that sulfotepp is more stable in the environment and that it may concentrate in areas where diazinon is used on a routine basis. Since little data are available on the environmental stability of sulfotepp, more effort is required to determine if it can concentrate to levels of environmental concern. In any case, the sulfotepp impurity in diazinon formulations does present a previously unidentified potential hazard to the health of the user and to the environment. If possible, the impurity should be removed during the production process; or, the EPA registration and pesticide labels should be modified to account for the presence of sulfotepp as an active ingredient in diazinon formulations.

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