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HERBICIDE TOXICOLOGY

Toxicology of Dalapon Sodium (2,2-Dichloropropionic Acid, Sodium Salt)

O. E. PAYNTER and T. W. TUSING

Hazleton Laboratories Inc., Falls Church, Va.

D. D. McCOLLISTER and V. K. ROWE

Biochemical Research Laboratories, The Dow Chemical Co., Midland, Mich.

Dalapon sodium, a plant growth regulator, is low in acute oral toxicity to laboratory animals, and cattle tolerate large doses without serious effect. Dogs receiving 100 mg. per kg. per day for 1 year and rats given 50 mg. per kg. per day for 2 years exhibited only slight, statistically significant increases in average kidney weights. Rats receiving 15 mg. per kg. per day for 2 years and dogs at 50 mg. per kg. per day for 1 year showed no significant differences from controls. There were small amounts of dalapon found in rat and dog tissues, and in the milk of lactating female rats as determined by chemical analyses. Reproduction and lactation were not affected in rats receiving diets equivalent to 150 mg. per kg. per day. Dalapon sodium presents no unusual handling problems in the field. These data provide a basis for judging the safety of the various residues likely to occur when this herbicide is used as directed on edible produce, or on soil in which food crops are grown.

DALAPON SODIUM is herbicidally active on grasses and cattails at relatively low rates. Controlled laboratory investigation has establishd that this herbicide is readily absorbed and translocated by active grass foliage. It is also absorbed by roots following soil application (*1*). As dalapon sodium may be used effectively for selective control of grasses in certain crops, the following studies were designed to obtain information from experimental animals upon which to base conclusions regarding the safety of any residues occurring in or on edible portions of such crops. Data were desired also for the purpose of making recommendations for safe handling of the material.

Material

Dalapon sodium is a white to tan-white, free-flowing, water-soluble powder with a melting point range of 193° to 197° C. The technical grade material was used in the acute oral studies. By chemical and infrared analyses of the original acid, and by hydrolysis assay techniques on the sodium salt, it was determined that this preparation had the following approximate composition:

83 to 85% 2,2-dichloropropionic acid, sodium salt
6% related chloropropionic acids, sodium salts
1% pyruvic acid, sodium salt
8% sodium chloride
2% undetermined

The sample used in both the subacute and chronic feeding studies was obtained from a large batch produced in May 1953. Twelve 1-pound bottles were sealed and stored under refrigeration, and a particular bottle was not opened until needed. Each time, a 25-gram sample was analyzed. Special attention was given to moisture content as an index of hygroscopy and to sodium pyruvate as an index of hydrolysis. These analytical results indicated that the 12 pounds of material had the following approximate composition and did not change significantly during the storage period:

65% 2,2-dichloropropionic acid, sodium salt
16% related chloropropionic acids, sodium salt
2% pyruvic acid, sodium salt
5% sodium chloride
5% water
7% undetermined

Acute Toxicity

Single oral doses of dalapon sodium dissolved in water were administered by intubation to five animal species in the following concentrations: rats: 10 and 50%; mice: 16%; guinea pigs: 10 and 50%; rabbits: 20%; New Hampshire red chickens: 30%. A total of 130 rats, 15 mice, 18 guinea pigs, 16 rabbits, and 10 chicks were divided into groups and received single doses ranging from 1.0 to 15.8 grams per kg. of body weight. All surviving animals were observed until it was certain that they had fully recovered—usually about 2 weeks. The acute oral LD_{50} with its 19/20 confidence limits was calculated for the five different animal species according to the "Moving Average" method of Thompson (*5*). The results are presented in Table I. Animals that died succumbed within a period of 2 hours to 1 day following administration. No gross pathological changes were found and the principal autopsy findings were a large quantity

Table I. Acute Oral LD_{50} Values for Dalapon Sodium

Species	Sex	LD_{50} 19/20 Confidence Limits, G./Kg.
Rat	Male	9.33 (8.46 to 10.3)
	Female	7.57 (6.88 to 8.35)
Mouse	Female	>4.6
Guinea pig	Female	3.86 (2.76 to 5.43)
Rabbit	Female	3.86 (2.30 to 6.50)
Chick	Mixed	5.66

of fluid and gas in the gastrointestinal tract. Autopsies of the surviving animals revealed no gross pathology which could be attributed to dalapon sodium.

Dermal and Eye Irritation Studies

Rabbits. Dalapon sodium and its solutions were bandaged repeatedly to the shaven abdomen—10 continuous applications in 14 days. The undiluted material produced moderate hyperemia and slight superficial necrosis after three or four applications. Healing was complete, without scarring, 1 week following the final application. On the abraded skin, prolonged contact resulted in necrosis. A 10% solution in water (equivalent to 25 pounds in 30 gallons) was only very slightly irritating to the intact or abraded skin, and a 1% solution in water (equivalent to 2.5 pounds in 30 gallons) caused no irritation whatsoever even after prolonged and repeated contact with either intact or abraded skin.

Observations of appearance, behavior, and body weight records made upon the rabbits during the various skin irritation tests revealed no evidence that dalapon sodium penetrated the intact skin in acutely or subacutely toxic amounts.

The dry, powdered material was placed in the eye of a rabbit. The immediate response was one of moderate pain and slight irritation of the conjunctival membranes. An hour later moderately severe conjunctivitis and corneal injury were observed. Healing was complete after several days with no indication of permanent damage. Washing the rabbit's eye immediately with a copious amount of water greatly alleviated the amount of irritation produced. A 10% aqueous solution caused only very slight pain and conjunctivitis when placed in the rabbit eye, whereas a 1% solution in water produced no reaction whatsoever.

Subacute Toxicity

Cattle. A heifer weighing 252 kg. and a bull suckling calf, approximately 3 weeks old and weighing 59.1 kg., were maintained under normal animal husbandry conditions. Each animal was given 1.0 gram per kg. of dalapon sodium dissolved in water by intubation on each of 10 successive days.

During the latter half and at the end of the experimental period, the heifer exhibited some abnormality, as evidenced by general lassitude, diarrhea, roughness of coat, loss of appetite, slight loss of weight, slowed pulse rate, mild cyanosis of the mucous membranes, and some discharge from the eyes. Four days after the last dose, the heifer appeared to be in good condition. The symptoms noted above were all absent except that the slowed pulse rate persisted and the discharge from the eyes was still excessive. At this time, the animal was sacrificed and autopsied. During the course of the study, the bull calf failed to exhibit any evidence of adverse effects and actually gained 6.8 kg. Twenty-four hours after the last dose, the calf was sacrificed and autopsied.

The organs and viscera of both animals appeared normal upon gross examination. Microscopic examination of sections from the rumen, reticulum, omasum, abomasum, lymph nodes, adrenals, duodenum, thyroid, heart, kidneys, liver, spleen, pancreas, lung, bladder, and gall bladder revealed these tissues to be within normal limits. The only possible exceptions were the kidneys of the bull calf, which showed slight cloudy swelling of the proximal convoluted tubules and hypertrophy or swelling of the glomerular cells with decreased glomerular spaces.

It is notable in the case of the heifer that recovery from the general nonspecific symptoms observed was prompt upon cessation of the dosing and that no evidence of organic injury was apparent at autopsy. The calf seemed to be particularly resistant to effects of the material.

Dogs. One male and one female mongrel dog were immunized, pre-experimentally, against rabies, given distemper serum, and were allowed to adjust to laboratory conditions and diet. Each animal was individually housed and observed daily for signs of systemic toxicity. Body weight and compound consumption were recorded at weekly intervals. Food was offered once a day and water was available at all times. Each animal was given dalapon sodium orally, by capsule, 5 days a week during an 80-day period. The dogs were weighed once a week and the doses for the week were adjusted according to their weight at that time. During the first 2 weeks, each dog received 50 mg. per kg. per day. Beginning with the third week, the dose for each dog was adjusted upward at weekly intervals during the remainder of the study until a maximum dosage of 1000 mg. per kg. per day was reached.

During the tenth week, the total daily dose of dalapon sodium was administered in two divided doses in an attempt to reduce the occurrence of vomiting; however, vomiting occurred in both dogs two or three times during the eleventh week while receiving the 1000 mg. per kg. per day dosage level. To prevent marked disturbances in nutrition and secondary metabolic changes associated with frequent vomiting, the study was terminated.

Complete blood counts, sedimentation rates, cell volumes, blood urea nitrogen determinations, bromosulphalein liver function tests, and urinalyses were conducted on each dog initially and at termination. At 81 days the dogs were sacrificed by exsanguination under Pentothal anesthesia and autopsied. Liver, kidney, spleen, and testes were weighed.

The total amount of dalapon sodium administered to the male and female dogs was 199.58 and 161.0 grams, respectively. Both dogs maintained good appetites and exhibited good nutrition during the study. Except for vomiting by both dogs, there were no gross signs of systemic toxicity associated with the oral administration of dalapon sodium in doses ranging from 50 to 1000 mg. per kg. per day.

The results of hematological and biochemical studies and urinalyses obtained prior to sacrifice revealed no specific changes or alterations in values as compared with values from similar studies obtained initially from both dogs.

On autopsy, gross inspection of the viscera and body cavities revealed no specific findings in either dog which could be associated with the oral administration of dalapon sodium. Organ–body weight ratios of liver, kidneys, spleen, or testes for both dogs were within normal limits.

Rats. Groups of 10 male and 10 female rats (Wistar-Dow strain) each were maintained for 97 days on diets containing 0.0 (control), 0.0115, 0.0346, 0.115, 0.346, or 1.15% of dalapon sodium. In the male rats, there was no effect, whatsoever, at the 0.115% level—equivalent to an average of about 115 mg. per kg. per day for young growing animals—or below. In the female rats, there were slight, statistically significant increases in average kidney weights at the 0.115 and 0.0346% dietary levels, but no other differences from the control values were indicated by any criterion, including histopathological examination. At the higher concentrations, 0.346 and 1.15%, there was no evidence of adverse effect as judged by mortality and food consumption records, hematological examination, or average weights and microscopic examination of the lungs, heart, and spleen. Growth retardation, increases in average weight of liver and kidneys, and slight histopathological changes in the liver and kidneys were the principal findings of significance.

One-Year Oral Administration

Dogs. Twelve mongrel dogs were selected at random in December, 1953, and immunized, pre-experimentally, against rabies, given distemper serum and a vermifuge, and allowed to adapt to laboratory conditions and diet. They were then divided into four groups of two males and one female, each group receiving either 0, 15, 50, or 100 mg. per kg. per day of dalapon sodium. The compound was administered by capsule, 5 days a week, for 52 weeks.

The dogs were housed in individual cages and observed closely for signs of

systemic toxicity. Body weights were recorded weekly and compound consumption was recorded daily. Food was offered once a day, with water available at all times.

Complete blood counts, hematocrits, sedimentation rates, blood urea nitrogen determinations, bromosulphalein liver function tests, and urinalyses were conducted on each dog initially and at the end of the thirteenth, twenty-sixth, and fifty-second week.

Following ether anesthesia, each dog was sacrificed by exsanguination and gross autopsies were performed. Weights of the lungs, heart, liver, spleen, and kidneys were determined for each animal. The weights of the testes were also obtained. Sections from thyroid, lung, heart, liver, kidney, adrenal, pancreas, spleen, lymph nodes, bone marrow, urinary bladder, and gonads from each animal were examined microscopically.

The test dogs exhibited normal behavior, gained weight, and exhibited no untoward reactions attributable to the test material. The results of hematological and biochemical studies and urinalyses indicated no significant alterations. Average organ-body weight ratios (Table II) were normal when compared to the controls except for a statistically significant increase in average kidney weight in those dogs that received the 100 mg. per kg. per day dosages of the chemical. Histopathological examination of the tissues from the control dogs and from the dogs that had received dalapon sodium revealed no significant difference, even in the slightly heavy kidneys of the dogs on the high dosage level.

Table II. Average Weights of Various Organs, as Per Cent of Terminal Body Weights with Standard Deviations, Taken from Dogs Which Received Dalapon Sodium for 1 Year

Level, Mg./Kg./Day	Weight, Kg.	Lungs, %	Heart, %	Liver, %	Spleen, %	Kidneys, %	Testes, %
Control	9.33 ±0.82	0.67 ±0.12	0.64 ±0.05	2.51 ±0.23	0.16 ±0.02	0.42 ±0.03	0.17 ±0.03
15	9.87 ±1.85	0.70 ±0.18	0.77 ±0.07	2.91 ±0.24	0.20 ±0.03	0.43 ±0.02	0.16 ±0.00
50	8.43 ±1.79	0.62 ±0.06	0.88 ±0.23	2.80 ±0.09	0.20 ±0.07	0.46 ±0.01	0.18 ±0.00
100	9.60 ±1.21	0.73 ±0.15	0.85 ±0.22	2.83 ±0.15	0.23 ±0.05	0.56 ±0.03	0.21 ±0.00

Table III. Average Weights of Various Organs, as Per Cent of Terminal Body Weights with Standard Deviations, Taken from Rats Maintained for 2 Years on Diets Containing Dalapon Sodium

Diet Level, %	Sex	Number of Rats	Body Weight, G.	Liver, %	Kidneys, %	Testes, %
Control	M	15	488 ±60	2.88 ±0.37	0.64 ±0.06	0.73 ±0.10
0.01	M	16	491 ±65	2.79 ±0.38	0.66 ±0.10	0.64 ±0.15
0.03	M	15	463 ±94	2.59 ±0.33	0.68 ±0.14	0.60 ±0.15
0.10	M	15	473 ±58	2.91 ±0.25	0.71[a] ±0.20	0.69 ±0.10
Control	F	12	336 ±39	3.54 ±0.46	0.68 ±0.09	... ...
0.01	F	15	326 ±66	3.35 ±0.43	0.80 ±0.27	... ...
0.03	F	13	353 ±64	3.51 ±0.10	0.70 ±0.14	... ...

[a] Statistically significant difference P = <0.05

Two-Year Feeding

Rats. Albino rats of the Carworth Farm strain were randomized in June 1953, and housed individually in wire mesh cages. Water and the appropriate diet, consisting of Purina Lab Chow, were available at all times. Weekly records were kept of the body weights, food consumption, general appearance, condition, and behavior of each rat.

The preliminary 97-day studies indicated that dietary levels of about 0.01%, 0.03%, and 0.1% were tolerated and that such levels would be suitable for long-term feeding studies. Mature rats of the Carworth strain receiving these dietary levels would be consuming approximately 5, 15, and 50 mg. per kg. per day, respectively. On this basis, the design for the first 13 weeks consisted of feeding weekly adjusted diets to approximate the above levels. Beginning with the fourteenth experimental week and continuing through the 104th week, dalapon sodium was added to the diet on a constant percentage basis as follows:

	Number of Rats		Dietary Level	
Group	Male	Female	%	P.p.m.
1	24	20	Control	0
2	24	20	0.01	100
3	24	20	0.03	300
4	24	..	0.1	1000

Complete blood counts and hemoglobin determinations were conducted on animals from each group at the following intervals: initially, five males and five females; at 13 weeks, three males and three females; at 26 weeks, two males and two females; at 52 weeks, three males and three females; and at 104 weeks, three males and three females. At the end of 26 weeks, two male and two female rats from each group were sacrificed, and after 52 weeks, two male rats from each group were sacrificed for histological study of representative tissue. At the end of 104 weeks, all surviving animals were sacrificed and gross autopsies were performed. All rats were sacrificed by exsanguination. At each interval when rats were sacrificed, organ weights of the liver, kidneys, and testes from the males, and the liver and kidneys from the females were determined. The histological findings in the tissues from representative male and female animals from each group were evaluated at the end of 104 weeks.

Growth, food consumption, and survival of the male and female rats at each dietary level were comparable to that of the control rats of corresponding sex during the 2-year period. The results of hematological studies conducted on the rats at intervals during the 2 years revealed no significant alterations in hemoglobin, cell counts, or peripheral blood smears. Gross examination of test and control rats sacrificed at 26, 52, and 104 weeks revealed no characteristic findings that could be attributed to the dietary feeding of dalapon sodium. The average kidney weight of the male test rats receiving the 0.1%—50 mg. per kg.—level showed a statistically significant increase when compared to the male control rats at the end of 2 years (Table III). The average liver and testes weights of these rats were not significantly different from the controls. Microscopic examination of the tissues, including the slightly heavier kidneys, revealed no evidence of adverse effect. In the groups of male and female rats maintained for 2 years on diets containing

Table IV. Summary of Results of Reproduction Study on Three Generations (2 Litters Each) of Rats Receiving Diets Containing Dalapon Sodium

Diet, %	Group	Fertility Index[a]	Gestation Index[b]	Viability Index[c]	Lactation Index[d]
Control	F_0	100	100	96	95
0.03	F_0	86	100	95	86
0.1	F_0	100	100	95	96
0.3	F_0	100	100	93	94
Control	F_{1b}	100	100	88	92
0.03	F_{1b}	100	100	86	100
0.1	F_{1b}	96	100	86	98
0.3	F_{1b}	100	100	89	99
Control	F_{2b}	100	96	87	82
0.03	F_{2b}	95	95	69	95
0.1	F_{2b}	100	100	81	99
0.3	F_{2b}	100	100	85	99

[a] Percentage of females achieving two pregnancies.
[b] Percentage of pregnancies yielding live litters.
[c] Percentage of rats born that survived for 5 days.
[d] Percentage of rats alive at 5 days that survived the 21 day lactation period.

0.03 or 0.01%, there were no differences whatsoever from control rats when judged by any criterion.

Reproduction Studies—Rats

Procedure. Groups of young albino rats (four male and 12 females per group) were started on diets containing 0.0 (control), 0.03, 0.1, or 0.3%. These animals were selected when approximately 90 days of age and each sex maintained in separate cages until the age of 110 days was reached. At this time, the males and females from each dietary group were placed together in large breeding cages. This comprised the parent generation (F_0). Parent rats and all descendant animals were maintained on the diets containing dalapon sodium throughout the entire experimental period.

When pregnancies were determined visually, or by palpation, the females were transferred to individual cages.

Records were kept of the number of young cast, including number born alive, born dead, or killed by mother. After 5 days, the number of pups per litter was reduced to eight if necessary, and the lactation period continued until 21 days. All of the pups were weighed at weaning. After 10 days, the females were returned to the breeding cage.

All pups from the F_{1a} litter (F_0 parents) were discarded at weaning. However, a sufficient number of rats was saved from the F_{1b} litters (F_0 parents) and maintained on their respective experimental diets for selection of four males and 12 females to be mated at 110 days to obtain generations F_{2a} and F_{2b}. F_{2a} animals were discarded when weaned. When the F_{2b} animals reached 110 days of age, four males and 12 females were mated to produce the third generation progeny (F_{3a} and F_{3b}) which then were discarded after weaning.

Results. Records for this experiment were kept in such a manner that indices of reproductive and lactating efficiency similar to those outlined by Oser and Oser (*2*) could be utilized. These included measures of fertility, gestation, viability, and lactation. In all, 2476 rats in 261 litters were involved in this experiment over a period of approximately 18 months. The results are presented in Table IV.

These show that continuous administration of dalapon sodium in the diet of rats through three generations of two litters each in concentrations as high as 0.3%—3000 p.p.m.—had no effect upon reproduction or lactation in these animals. Body weight records obtained at weaning and weekly thereafter for those rats allowed to mature for mating likewise did not indicate any evidence of adverse effects.

Table V. Summary of Tissue Analyses from Male and Female Rats Maintained for 2 Years on Diets Containing Dalapon Sodium and of Milk from Lactating Female Rats

Organ	Dosage, P.P.M. in Diet: 100	300	1000
	2,2-Dichloropropionic Acid, P.P.M.[a]		
Kidney	4.0	9.7	28.2
Liver	1.0	3.5	10.7
Muscle		2.9	7.5
Brain		2.6	5.4
Fat		0.5	1.4
Milk[b]		6.0	19.1

[a] Average net values after correction for blanks and recovery.
[b] From third generation lactating female rats. Milk samples for the rats maintained on diets containing 3000 p.p.m. of dalapon contained 29.3 p.p.m. of acid.

Tissue and Milk Analyses

Terminal tissues of dogs and rats from the long-term feeding studies were selected for analysis of dalapon sodium. The tissues were taken immediately upon autopsy, frozen immediately at dry ice temperature, and held at 0° C. or lower until analysis. In order to obtain enough tissues for the analyses, it was necessary to pool samples from several rats in most cases. The analyses were carried out by a modification of the method of Smith, Getzendaner, and Kutschinski (*4*) in which the compound is ether extracted, isolated chromatographically, hydrolyzed to pyruvic acid, converted to its 2,4-dinitrophenylhydrazone, and determined colorimetrically. The data are then expressed in terms of 2,2-dichloropropionic acid.

During the latter part of the reproduction studies, pooled samples of milk were obtained from lactating female rats that had been separated from their litters for a 24-hour period. Gentle suction from a pulsating pump was applied to the rat nipples through the flared end of a capillary tube, the milk being trapped in a small Erlenmeyer flask. The analyses were made using an isotope dilution method (*3*).

The results of the analyses of rat tissues and milk are given in Table V. Results of the dog tissue analyses are given in Table VI. On a dietary percentage basis, the repeated oral doses of 15, 50, or 100 mg. per kg. are equivalent for adult dogs to about 500, 1750, or 3500 p.p.m. of the total diet. The

Table VI. Summary of Tissue Analyses from Dogs Given Daily Doses (5 Days a Week) by Capsule of Dalapon Sodium for 1 Year

Organ	Sex	Dosage,[a] Mg./Kg./Day: 15	50	100
		2,2-Dichloropropionic Acid, P.P.M.[b]		
Kidney	M	23	21	78
	F	17	32	60
Liver	M	27	16	48
	F	17	27	57
Muscle	M	15	13	51
	F	12	27	35
Brain	M	11	9	25
	F	7	13	18
Fat	M	2	2	15
	F	1	4	5

[a] Equivalent to about 500, 1750, or 3500 p.p.m. in diet.
[b] Net parts per million corrected for blank and recovery.

2-year rats received diets containing 100, 300, or 1000 p.p.m. Comparison of tissue levels as parts per million of 2,2-dichloropropionic acid with dietary levels expressed as parts per million of dalapon sodium shows the results for the two species to be of the same order of magnitude. Quantitatively, the amounts occurring in the meat or other tissues were quite low in relation to the levels administered.

Practical Considerations for Handling and Use

The results of the studies reported here indicate that dalapon sodium is low in acute and subacute oral toxicity. The likelihood of human subjects, livestock, or wildlife ingesting sufficient amounts of the material to cause serious toxic effects is therefore extremely remote. However, salt-hungry stock have been known to ingest lethal amounts of sodium chloride, so it is recommended that dalapon sodium or strong solutions of it be kept in closed containers where it is unavailable to stock or wildlife.

Undiluted dalapon sodium may cause skin irritation, if it is allowed to remain on the skin for a prolonged period. Exposures of short durations are not likely to be injurious. Contact with dust, particularly when sweating, may cause a mild burning sensation. Prolonged contact with dilute aqueous solutions is not likely to cause any appreciable effect. Systemic effects due to absorption through the skin are not likely to occur. Because the ability of the material to cause irritation is markedly reduced by dilution with water, the prompt flooding of exposed areas with water will practically eliminate the possibility of irritation occurring as a result of skin contact.

The material in the solid form or in concentrated solutions is capable of causing appreciable pain, and irritation of the eyes, but is not likely to cause serious damage. Nevertheless, eye protection, such as safety glasses, should be worn when handling the salt or concentrated solutions. Solutions of less than 10% concentration are not likely to cause more than transient pain and inflammation. Prompt washing of contaminated eyes will markedly reduce the severity of any effect caused by the solid or strong solutions and practically eliminate the effect from dilute solutions.

Experience in the manufacturing, handling, and application of dalapon sodium has indicated that it presents no unusual problems. No incidences of irritation or other adverse effects have come to the attention of the authors thus far in the use of this product.

The results of the 2-year, life-span dietary feeding studies to rats, the reproduction and lactation studies in rats, and the 1-year repeated oral administration to dogs also show a low order of toxicity for this herbicidal material. Thus, these data provide a basis for judging the safety of the small amounts of dalapon sodium residues likely to occur when this herbicide is used as directed on edible crops, or on soil in which food crops are grown.

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INSECTICIDE RESIDUES

Colorimetric Determination of Residues of Phorate and Its Insecticidally Active Metabolites

PAUL A. GIANG and M. S. SCHECHTER

Entomology Research Division, Agricultural Research Service, U. S. Department of Agriculture, Beltsville, Md.

A colorimetric method, based on the chromatropic acid procedure for formaldehyde, has been developed for the estimation of Thimet (phorate) and its insecticidally active metabolites. The limit of detection of the method as indicated by results from analysis of 100-gram samples of treated plant leaves is about 0.10 p.p.m. and with larger samples it is even less. Although the method was developed for the determination of residues of phorate and related materials, it can also be applied with some minor modifications to the analysis of residues of any organic phosphorus insecticide that has a methylene linkage present in its molecule which will produce formaldehyde on hydrolysis.

PHORATE [the recently assigned generic name for *O,O*-diethyl *S*-(ethylthio)methyl phosphorodithioate, the major constituent of the commercial product, Thimet] has recently attracted wide interest as a systemic insecticide (*2, 7, 9*), although it also has considerable contact activity. Like many of the other organophosphorus insecticides, phorate is toxic to warm-blooded animals, being comparable to parathion in this respect (*2*).

In studies of the fate of phorate in plants, Bowman and Casida (*3*) and Metcalf, Fukuto, and March (*8*) found five oxidation products which are insecticidally active and which have high mammalian toxicity. These are the phorate oxygen analog, phorate sulfoxide, the phorate oxygen analog of the sulfoxide, phorate sulfone, and the phorate oxygen analog of sulfone.

Hydrolysis or any further oxidation results only in decomposition products that have little toxicity to insects or mammals. These authors found from in vitro enzymatic studies, that the sul-