

Biotransformation and Deposition of Residues of Fenthion and Oxidative Metabolites in the Fat of Cattle

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Yearling steers conditioned on either a low- or high-energy ration for 14 weeks were treated with a pouron formulation of 3% fenthion (Tiguvon, *O,O*-dimethyl *O*-[3-methyl-4-(methylthio)phenyl] phosphorothioate). When these steers were slaughtered at 3 or 10 days posttreatment, the omental, renal, and subcutaneous fat was collected and analyzed for fenthion and five oxidative metabolites. Residues of fenthion, fenthion sulfoxide, fenthion sulfone, and fenthion oxygen analogue were found in all samples at 3 days posttreatment. At 10 days posttreatment, no fenthion sulfone was present, the other two metabolites were found, and unchanged fenthion was found in the greatest concentration. Residues of fenthion oxygen analogue sulfoxide and fenthion oxygen analogue sulfone were not found in any samples. The levels of residues in the fat of steers on the low-energy ration were greater than the levels in the fat of steers on the high-energy ration.

Two species of cattle grubs, *Hypoderma lineatum* and *H. bovis*, cause considerable economic damage to cattle because the larvae migrate through the body of the host, locate below the skin of the back, and then cut breathing holes in the skin. One approved method of treating animals for control of these flies is to pour an undiluted formulation of fenthion (Tiguvon) along the backline of the animal during the period before the larvae reach the back (Campbell et al., 1973; Loomis et al., 1973). The material then acts systemically to kill the migrating larvae before they can do extensive damage to the tissue and hide. Because of its lipophilic properties, fenthion is primarily deposited in the fatty tissue of exposed animals (Möllhoff, 1971). Also, as with other organophosphorus compounds containing a thioether linkage, fenthion (P=S,S) has several oxidative metabolites including the sulfoxide (P=S,SO), the sulfone (P=S,SO₂), the oxygen analogue (P=O,S), the oxygen analogue sulfoxide (P=O,SO), and the oxygen analogue sulfone (P=O,SO₂).

The objectives of this study therefore were to: (1) determine the individual residues of fenthion and five oxidative metabolites in the fat of cattle taken from three body locations and (2) determine the effect of nutrition on biotransformation and residue deposition of the parent compound and its oxidative metabolites. Little data are available in the literature on the effect of the quantity of fat available on levels of the residues deposited.

MATERIALS AND METHODS

Reagents. Tiguvon pouron contains fenthion 3.0% active ingredient (AI), *O,O*-dimethyl *O*-[3-methyl-4-(methylthio)phenyl] phosphorothioate. According to our analysis, P=S,S accounts for 2.97% of the AI and P=S,SO accounts for 0.03%. Analytical standards for fenthion and the oxidative metabolites were supplied by Mobay Chemical Corp., Kansas City, MO.

Apparatus. A gas chromatograph (Model 220, Tracor, Austin, TX) equipped with a flame photometric detector, a phosphorus specific filter, and a 4 mm i.d. × 1.22 m borosilicate glass column packed with 3% OV-1 coated on Chromosorb 750 (80–100 mesh) was used to determine residues of P=S,S, P=S,SO, P=S,SO₂, P=O,S, and P=O,SO₂ in the fat extracts. A liquid chromatograph (Model 204, Waters Associates, Milford, MA) equipped

Table I. Amount of Pouron Formulation Used per Steer and Milligram of AI/Kilogram of Bodyweight

animal no.	grp ^a	time to slaughter, ^b days	wt of animal at treatment, kg	wt of pouron, g ^c	treatment, mg of AI/kg ^d
405	I	3	240.9	57.79	7.19
407	I	3	257.7	76.20	8.87
456	II	3	334.1	98.78	8.87
474	II	3	315.9	93.41	8.87
447	I	10	238.6	57.12	7.19
476	I	10	242.7	71.64	8.87
408	II	10	320.5	94.75	8.87
444	II	10	334.5	98.92	8.87
449	II	0	331.8	0	0
400	I	0	276.0	0	0

^a Group I was fed a low-energy ration and group II was fed a high-energy ration for 14 weeks before treatment. ^b Number of days from treatment. ^c Recommended treatment of Tiguvon is 0.5 fluid oz/100 lb of bodyweight (8.87 mg/kg). ^d AI, active ingredients.

with a universal injector, 6000A pump, a Model 440 UV absorbance detector fitted with a 254-nm filter, and a 4 mm i.d. × 0.3 m stainless steel column packed with μ Bondapak C 18 was used to analyze for P=O,SO.

Selection and Conditioning of Animals. Ten Hereford steers from 13 to 15 months old from our Camp Stanley, TX, herd were selected for the study. All steers selected were from Hereford cows, had been sired by the same Hereford bull, and had been reared under similar conditions. The average weight per steer at the start of the study was 228.9 ± 8.9 kg. For this experiment, the steers were separated into two groups of five each. The animals in group I were fed a low-energy ration consisting of 0.9 kg of grain and ample hay per steer per day, a ration that allowed the steers to gain weight slowly while depositing little body fat. The animals in group II were fed a high-energy ration consisting of 3.6 kg of grain and ample hay per steer per day, a diet similar to that fed in a commercial feedlot. The two groups were placed in separate pens and had free access to water at all times. Both groups were maintained on the test rations for approximately 14 weeks before treatment. The bodyweight of each steer was recorded weekly throughout the study.

Treatment of Animals. Two steers from group I and four steers from group II were treated with the pouron formulation at the rate (0.5 fluid oz/100-lb bodyweight) recommended by the manufacturer. Two other steers from

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Table II. Residues^a of Fenthion and Its Oxidative Metabolites in Fat of Treated and Untreated Steers

animal no.	grp ^b	time to slaughter, days	residues, ppm ^c of			
			P=S,S	P=O,S	P=S, SO	P=S, SO ₂
Omental Fat						
405	I	3	3.23	0.07	0.09	0.34
407	I	3	3.19	0.13	<0.05	0.20
456	II	3	2.95	0.11	<0.05	0.12
474	II	3	2.44	0.05	<0.05	0.13
447	I	10	1.05	<0.01	0.15	<0.05
476	I	10	0.29	0.08	<0.05	<0.05
408	II	10	0.52	<0.01	<0.05	<0.05
444	II	10	0.75	<0.01	<0.05	<0.05
449 ^d	II	0	<0.01	<0.01	<0.05	<0.05
Renal Fat						
405	I	3	4.07	0.06	0.05	0.34
407	I	3	4.58	0.08	<0.05	0.22
456	II	3	3.36	0.10	<0.05	0.16
474	II	3	3.02	0.04	<0.05	0.14
447	I	10	1.11	0.01	0.14	<0.05
476	I	10	0.12	0.03	<0.05	<0.05
408	II	10	0.45	<0.01	<0.05	<0.05
444	II	10	0.49	<0.01	<0.05	<0.05
449 ^d	II	0	<0.01	<0.01	<0.05	<0.05
Subcutaneous Fat						
405	I	3	2.26	0.10	0.09	0.57
407	I	3	4.67	0.10	<0.05	0.35
456	II	3	2.73	0.16	<0.05	0.21
474	II	3	2.69	0.04	<0.05	0.15
447	I	10	1.57	0.01	0.21	<0.05
476	I	10	0.98	0.04	0.06	<0.05
408	II	10	0.63	<0.01	<0.05	<0.05
444	II	10	0.79	<0.01	<0.05	<0.05
449 ^d	II	0	<0.01	<0.01	<0.05	<0.05

^a Values presented are averages of triplicate samples.

^b Steers in group I were on a low-energy ration and were allowed to gain only a minimum of fat. Steers in group II were on a high-energy ration. ^c Calculations of ppm were based on extracted fat in sample. ^d This animal was untreated and served as a control.

group I were treated at 80% of the recommended rate. The fifth steer in each group was untreated and served as a control. The steers were weighed on the day of treatment, treated by pouring the material along the back, and then housed in individual stalls in a well-ventilated barn. At no time were the steers allowed to come in contact with one another. The treatment information and the time of slaughter after treatment is given in Table I.

Collection and Analysis of Samples. The treated steers were slaughtered at either 3 or 10 days posttreatment. A control steer was slaughtered at the same time. Samples of omental, renal, and subcutaneous fat were collected from each animal for residue analysis. Extreme care was taken to prevent contamination between animals or samples. Samples were individually packaged in plastic bags, labeled, and stored at -20 °C until analyzed.

The residues of fenthion and oxidative metabolites in the fat samples were determined by the method of Wright and Riner (1978). This method is a modification of the method of Bowman and Beroza (1968) which was used to determine residues of these compounds in corn, grass, and milk. The residues were extracted from fat in boiling hexane, dried with sodium sulfate, partitioned into acetonitrile, and then concentrated. The various components were then eluted from a cleanup column by different mixtures of isopropyl alcohol, acetone, and benzene. The fractions were concentrated and subjected to quantitation by gas chromatography with a flame photometric detector

or by a liquid chromatograph with an ultraviolet detector. Residue analyses were run in triplicate. Recoveries from fortified samples averaged 92%, and the relative standard deviation of the method was less than 8.3% for all six compounds. Detection limits ranged from 6 ppb for P=S,S to 250 ppb for P=O,SO₂. The residues (ppm) were based on the weight of extracted fat.

RESULTS AND DISCUSSION

The steers in both groups gained weight during the 14-week pretreatment period. The steers in group I had an average gain of 14.8 kg/steer (1.1 kg/steer per week) while the steers in group II had an average gain of 91.5 kg/steer (6.5 kg/steer per week). At slaughter, the steers in group II had much more adipose tissue than did those in group I.

The residues of fenthion and metabolites in the fat samples are reported in Table II. No residues of P=O,SO or P=O,SO₂ could be detected in any fat samples, but residues of P=S,S, P=O,S, and P=S,SO, and P=S,SO₂ were found in fat from all three body locations at 3 days posttreatment. This result is similar to that obtained by Brady and Arthur (1961) who found that thiophosphate and thiophenyl oxidation of fenthion formed five oxidative metabolites in rats, insects, and cotton plants. Also, Knowles and Arthur (1966) found the parent compound (P=S,S) and two oxidative metabolites of fenthion (P=O,S and P=S,SO) in tissues of dairy cattle treated dermally.

At 10 days posttreatment in our study, no residues of P=S,SO₂ could be found, but residues of P=S,SO had increased, probably due to the oxidation of a portion of the P=S,S residue present.

Fenthion was by far the most abundant of the compounds recovered at both 3 and 10 days posttreatment; it accounted for 90.4% of the total residues. At 3 days posttreatment, average recoveries of P=S,SO₂, P=O,S, and P=S,SO were 6.6, 2.5, and 1.0%, respectively. At 10 days posttreatment, average recoveries for P=S,SO₂, P=O,S, and P=S,SO were 0, 1.8, and 7.3%, respectively.

Residues were greater in the fat of the steers on the low-energy ration than in the fat of steers on the high-energy ration. Residues were also greater in the fat of the two steers of group I that were treated with 80% of the recommended amount of fenthion. Because more fat was available in the steers in group II, residues were lower in these animals (dilution effect of the additional fat). The quantity of fat available did not appear to affect the biotransformation of fenthion.

No residues of fenthion or metabolites were detected in adipose tissue from the control steers.

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