

soy proteins may belong to the class of nucleoproteins. The higher amount of phytic acid P in the glycinin fraction suggests that it may be forming a complex with soy protein as indicated earlier (DiCarlo et al., 1955). Such a complex is reported to be resistant to digestion by proteolytic enzymes (Barre, 1956).

The different phosphorus compounds in the protein fractions responded favorably to the application of soil phosphorus but the level of 112 kg of P_2O_5 /ha did not prove to be beneficial to the phosphorus composition of albumin fraction. The percentage increase in total P, phytic acid P, nucleic acid P, and inorganic P of the glycinin fraction was observed to be 24–25, 18–21, 25–29, and 30, respectively, from the application of 56 kg of P_2O_5 /ha and 47–53, 28–31, 55–57, and 54–58, respectively, from an application of 112 kg of P_2O_5 /ha. The corresponding values for the albumin fraction were 14, 24, 20, and 5 from 56 kg of P_2O_5 /ha. These observations suggest that phosphorus compounds of the glycinin fraction are mostly affected by the phosphorus nutrition, the response being higher in nucleic acid P and inorganic P. The total P of other protein fractions has also responded favorably under the influence of P. O'Dell and Savage (1960) observed that soy protein contained about 0.5% phytic acid P. The acid-precipitated protein was reported to contain 0.5–0.8% P or about 90% of the P extracted from the meal (Smith and Rackis, 1957).

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COMMUNICATIONS

Distribution and Excretion Rates of ^{14}C -Labeled Permethrin Isomers Administered Orally to Four Lactating Goats for 10 Days

Permethrin [3-phenoxybenzyl 3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate] ^{14}C -labeled isomers were administered orally to four goats. Each goat received one of the following ^{14}C isomers of permethrin daily for 10 days: *trans*-(±)-permethrin labeled in the acid or alcohol moiety or *cis*-(±)-permethrin labeled in the acid or alcohol moiety. Radiocarbon was rapidly excreted in each instance. The major pathway for the elimination of radiocarbon of the *cis* isomers was the feces (51.7–67.4%), whereas that for the elimination of radiocarbon of the *trans* isomers was the urine (72.1–79.4%). Recovery in the milk from any treatment was less than 1% of the total radiocarbon dose. Twenty hours after the final dose, detectable levels of radiocarbon were found in most tissues, but none was higher than 0.04 ppm for the *trans* isomers or 0.25 ppm for the *cis* isomers.

Permethrin [3-phenoxybenzyl *cis,trans*-(±)-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate], a new photostable synthetic pyrethroid, has been highly effective in controlling stable flies, *Stomoxys calcitrans* L., and horn flies, *Haematobia irritans* L., when applied as a spray to cattle (Schmidt et al., 1976). Because the prospects for wide use of permethrin on livestock are good, possible residues in meat and milk should be determined. Residues of isomers are of special interest because permethrin is a

mixture of *trans* (FMC 30960) and *cis* (FMC 45812) isomers.

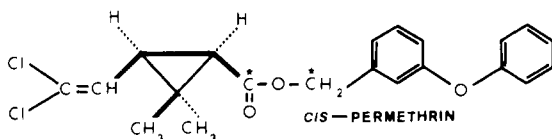
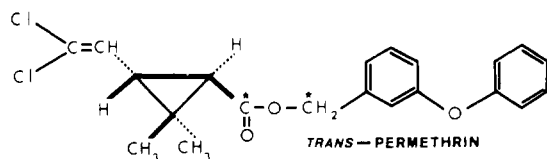
When the metabolism of permethrin in rats and mice was studied (Elliott et al., 1976; Gaughan et al., 1977), the findings indicated that with [1*R,trans*]- and [1*R,cis*]-acid labeled in the side chain (Cl_2 $^{14}C=CH-$) or alcohol labeled at the α - $^{14}CH_2$ of permethrin, their hydrolysis products and metabolites were excreted from the body in a short time and were not retained in the tissues. The current study

was initiated to determine whether goats likewise show the rapid excretion rates of *cis* and *trans* isomers of permethrin.

MATERIALS AND METHODS

Chemicals. FMC Corporation (Middleport, N.Y.) provided the following ^{14}C -labeled permethrin isomers that were in each case >98% radiochemically pure: FMC 30960, *trans*-(±)-permethrin labeled in the acid moiety ^{14}CO (54.8 mCi/mmol); FMC 30960, *trans*-(±)-permethrin labeled in the alcohol moiety $^{14}\text{CH}_2$ (57.01 mCi/mmol); FMC 45812, *cis*-(±)-permethrin labeled in the acid moiety ^{14}CO (54.8 mCi/mmol); FMC 45812, *cis*-(±)-permethrin labeled in the alcohol moiety $^{14}\text{CH}_2$ (57.01 mCi/mmol).

The ^{14}C -labeled isomers were subsequently diluted with the same unlabeled permethrin isomer to the following specific activities: *trans*-(±)-permethrin labeled in the acid moiety 5.85 mCi/mmol [*trans*-(±)-acid]; *trans*-(±)-per-



methrin labeled in the alcohol moiety, 5.67 mCi/mmol [*trans*-(±)-alcohol]; *cis*-(±)-permethrin labeled in the acid moiety, 5.85 mCi/mmol *cis*-(±)-acid]; *cis*-(±)-permethrin labeled in the alcohol moiety, 5.67 mCi/mmol [*cis*-(±)-alcohol].

Treatment and Sample Collection. Four lactating Nubian and Nubian-Saanen cross goats were housed in individual metabolism stalls. A specific amount of a ^{14}C -labeled plus unlabeled isomer was added to a small amount of crushed grain in a gelatin capsule. The treatment was administered by use of a balling gun orally to each goat daily for 10 consecutive days. The daily treatments were: goat A: *trans*-(±)-permethrin, 10.077 mg of unlabeled, and 0.15 mCi of ^{14}C acid labeled: equivalent to 0.22 mg/kg body weight; goat B: *cis*-(±)-permethrin, 10.035 mg of unlabeled, and 0.15 mCi of ^{14}C alcohol labeled: equivalent to 0.28 mg/kg body weight; goat C: *trans*-(±)-permethrin, 9.93 mg of unlabeled, and 0.14 mCi of ^{14}C alcohol labeled: equivalent to 0.20 mg/kg body weight; goat D: *cis*-(±)-permethrin, 10.077 mg of unlabeled, and 0.15 mCi of ^{14}C acid labeled: equivalent to 0.22 mg/kg body weight.

After treatment, urine, milk, and feces were collected from each animal at 12-h intervals. The samples were pooled into 24-h samples, subsampled, and frozen for subsequent analysis. The samples of urine were collected by use of retention catheters from which the urine flowed into reservoirs submerged in a 10 °C water bath. Ten-milliliter blood samples were taken once daily and at 2, 4, 8, 16, and 24 h after both the first and the final treatment. The goats were handmilked at approximately 12-h intervals.

The possible loss of ^{14}C through respiration was monitored in the following way. A face mask with a side flutter valve was shaped to the nose of the goat and securely attached to the goat's head. The gases were pulled from

Table I. Total Equivalents of Permethrin in Blood of Goats during and after Ten Daily Oral Administrations of [^{14}C]-Acid- and [^{14}C]-Alcohol-Labeled *cis*- and *trans*-Permethrin

Hour after treatment	Equivalents of permethrin in indicated sample as ppb			
	Goat A Trans acid	Goat B Cis alcohol	Goat C Trans alcohol	Goat D Cis acid
2	8	0	4	63
4	22	0	9	74
8	35	10	4	24
16	21	12	5	6
24	17	13	2	7
48	17	19	3	8
72	14	24	3	8
96	19	25	1	9
120	14	21	3	7
144	13	24	3	8
168	14	28	2	13
192	14	26	1	20
216	14	27	1	11
218	18	26	3	42
220	25	28	6	88
224	31	39	14	33
232	18	31	6	14
240	10	26	1	10
Slaughter	10	24	1	9

Table II. Total Equivalents of Permethrin in Milk of Goats during and after Ten Daily Oral Administrations of [^{14}C]-Acid- and [^{14}C]-Alcohol-Labeled *cis*- and *trans*-Permethrin

Hour after treatment	Equivalents of permethrin in indicated sample as μg (ppb)			
	Goat A Trans acid	Goat B Cis alcohol	Goat C Trans alcohol	Goat D Cis acid
24	8.97	26.28	12.46	50.81
	(7)	(21)	(5)	(23)
48	11.31	54.50	21.14	63.07
	(10)	(44)	(9)	(31)
72	19.46	62.46	23.34	69.90
	(11)	(52)	(10)	(33)
96	21.15	70.21	22.64	59.79
	(12)	(60)	(10)	(30)
120	18.06	59.84	23.84	53.24
	(11)	(55)	(11)	(25)
144	16.37	49.65	26.26	62.69
	(10)	(46)	(12)	(29)
168	18.15	51.01	25.05	59.23
	(10)	(47)	(11)	(29)
192	18.99	54.41	28.97	77.01
	(10)	(50)	(12)	(37)
216	18.99	51.69	25.75	86.18
	(10)	(52)	(11)	(45)
240	16.94	50.04	28.17	79.82
	(10)	(49)	(11)	(40)
	168.39	530.09	237.62	661.74
Total μg % of dose recov.	0.17	0.53	0.24	0.66

the mask through a flex hose by means of a pump operating at 35 L/min but capable of moving 163 L of air/min (Gast Mfg. Co.). Through a system of splitters and flow meters, 4% of the respired air gases was diverted into a series of two traps containing ethanolamine. The expired gases were trapped for 1 h on alternate days at 3 and 5 h after treatment. Aliquots of the trapping solution were added to Insta-gel (Packard) and counted by liquid scintillation techniques (Isc, Beckman LS-150).

Crushed grain was fed twice daily at milking time; alfalfa hay and water were available ad libitum.

Table III. Total Equivalents of Permethrin in Urine of Goats during and after Ten Daily Oral Administrations of [¹⁴C]-Acid- and [¹⁴C]-Alcohol-Labeled *cis*- and *trans*-Permethrin

Hour after treatment	Equivalents of permethrin in indicated sample as μg (ppm)			
	Goat A Trans acid	Goat B Cis alcohol	Goat C Trans alcohol	Goat D Cis acid
24	4484.53 (3.31)	2777.22 (2.15)	5237.34 (4.36)	2402.32 (2.19)
48	7285.27 (5.13)	3517.46 (3.07)	3438.00 (4.02)	2585.90 (2.31)
72	8246.51 (4.66)	4039.22 (3.22)	17747.65 (8.55)	2596.10 (1.16)
96	7307.63 (5.45)	4037.57 (3.45)	7546.41 (5.31)	2476.80 (0.86)
120	7763.04 (6.02)	4294.37 (3.38)	8718.80 (4.38)	2297.99 (0.97)
144	7020.18 (5.85)	4413.17 (3.43)	7392.79 (3.89)	2473.34 (1.05)
168	7992.19 (6.22)	2290.28 (2.12)	7113.63 (5.08)	2222.10 (1.39)
192	7606.12 (5.59)	3572.16 (2.28)	7107.39 (4.24)	2859.87 (1.52)
216	7425.72 (5.87)	3659.35 (2.25)	7562.10 (4.03)	3270.74 (1.53)
240	7299.11 (5.41)	3801.81 (1.90)	7390.78 (3.44)	2734.49 (1.08)
Slaughter	263.96 (1.82)	174.66 (0.92)	137.42 (1.46)	28.91 (0.17)
Total μg % of dose recov.	72694.26 72.1	36577.27 36.4	79392.31 79.4	25948.56 25.8

Table IV. Total Equivalents of Permethrin in Feces of Goats during and after Ten Daily Oral Administrations of [¹⁴C]-Acid- and [¹⁴C]-Alcohol-Labeled *cis*- and *trans*-Permethrin

Hour after treatment	Equivalents of permethrin in indicated sample as μg (ppm)			
	Goat A Trans acid	Goat B Cis alcohol	Goat C Trans alcohol	Goat D Cis acid
24	10.85 (0.03)	674.20 (0.93)	408.74 (0.39)	4314.70 (3.35)
48	398.05 (0.6)	3699.21 (6.34)	654.30 (0.89)	5855.61 (6.45)
72	1484.30 (1.58)	4926.78 (8.24)	1081.85 (1.20)	7506.47 (7.16)
96	1378.29 (1.37)	6243.86 (7.26)	1520.97 (1.51)	7608.93 (5.05)
120	1758.74 (1.9)	8833.23 (11.04)	1164.34 (1.28)	8308.36 (4.68)
144	2430.01 (2.02)	4377.68 (5.12)	1060.63 (0.95)	8369.93 (4.41)
168	1812.36 (1.49)	4808.66 (7.03)	2034.13 (1.97)	2577.85 (1.77)
192	2443.11 (1.8)	5807.26 (8.05)	1391.10 (1.32)	5635.72 (3.92)
216	1627.74 (1.41)	5267.37 (6.69)	1535.66 (1.40)	8963.54 (5.71)
240	1783.07 (1.39)	7227.34 (8.56)	1405.89 (1.20)	8830.20 (4.80)
Total μg % of dose recov.	15126.52 15.0	51865.59 51.7	12257.61 12.3	67971.31 67.5

The goats were slaughtered 24 h after the tenth treatment. Selected tissues and organs were collected, and the weights of organs were determined for calculation of total radioactive residue. Samples of all tissues were ground, frozen for subsequent analysis. The gut, rumen, and stomach were emptied, and the contents were weighed and subsampled.

Radioassay. Radiocarbon in the urine and milk was determined by pipetting aliquots (1 mL or less, depending on the activity) into 15 mL of Insta-gel and counted by lsc. Samples of blood, feces, rumen, stomach, gut contents, and tissues were combusted in a tricarb 306 oxidizer (Packard) and counted by lsc. Blood (200 μL) was placed on a combustion pad, and 200 μL of Combustaid (Packard) was added just before combustion. Lyophilized feces,

rumen, stomach, and gut contents were powdered in a micromill (Chemical Rubber), and 100-mg samples were pressed into pellets before combustion. Lean tissues (400 mg) were weighed into combustion cones and combusted wet after the addition of 200 μL of Combustaid. Samples of fat (200 mg) were mixed with equal amounts of cellulose powder before combustion. The sensitivity limit of the combustion procedure used was 0.001 ppm permethrin equivalents.

RESULTS AND DISCUSSION

The residence time of permethrin ¹⁴C isomers in the goats was short. Most radiocarbon had been eliminated from the previous treatment before the next dose was administered. The excretion for both ¹⁴C *trans* and ¹⁴C

Table V. Total Equivalents of Permethrin in Tissues of Goats after Ten Daily Oral Administrations of [^{14}C]-Acid- and [^{14}C]-Alcohol-Labeled *cis*- and *trans*-Permethrin

Tissue	Equivalents of permethrin in indicated sample as ppm			
	Goat A Trans acid	Goat B Cis alcohol	Goat C Trans alcohol	Goat D Cis acid
Bladder	0.028	0.032	0.004	0.024
Bone	0.009	0.048	0.006	0.049
Brain	0.002	0.015	0.003	0.006
Fat, kidney	0.025	0.242	0.019	0.218
Fat, omental	0.022	0.252	0.013	0.242
Gallbladder	0.022	0.068	0.026	0.053
Gland, adrenal	0.008	0.029	0.007	0.059
Gland, pituitary	0.007	0.028	0.004	0.009
Gland, thyroid	0.005	0.044	0.003	0.048
Heart	0.009	0.014	0.005	0.024
Kidney	0.027	0.047	0.034	0.048
Liver	0.040	0.132	0.010	0.121
Lung	0.012	0.016	0.002	0.216
Muscle, leg	0.005	0.005	0.002	0.006
Muscle, tenderloin	0.003	0.010	0.001	0.006
Ovaries, oviducts and uterus	0.017	0.018	0.001	0.012
Skin	0.007	0.012	0.003	0.010
Spleen	0.008	0.010	0.002	0.019
Bile	0.128	2.260	0.102	0.139
Content, intestinal	0.310	2.310	0.290	0.310
Content, rumenal	0.290	1.250	0.980	0.030
Content, stomach	0.168	0.107	0.200	0.010

cis isomers during a 24-h collection was almost quantitative, although the rates were different.

Absorption of ^{14}C trans acid into the blood reached maximum levels at 8 h after the first dose (Table I). *Cis* acid, trans alcohol, and *cis* alcohol had maximum levels at 4, 8, and 8 h after the final dose; 24-h ranges were 7–20, 1–3, and 13–28 ppb, respectively.

The residues in the milk were highest for the *cis* ^{14}C isomers; ranges were 0.03–0.09 and 0.01–0.03 ppm for the trans isomers (Table II). The total recovery in the milk from each treatment was less than 1%.

The major pathway for the elimination of radiocarbon of the trans isomers was the urine (72.1–79.4%) (Table III). Only 25.8–36.4% of the *cis* isomers were eliminated by this route. The rate of elimination in the urine of each goat reached a plateau at about 48 h and generally maintained this level until slaughter.

The major pathway for the elimination of radiocarbon of the *cis* isomers was the feces (51.7–67.4%) (Table IV).

Values to only 15% of the trans isomers were eliminated in the feces. The percentage of elimination by each pathway was almost reversed for the two isomers.

Only 4% of the total expired gases from the goats was trapped during the sampling periods; however, no detectable radiocarbon was found in ethanolamine traps.

The levels of radiocarbon in the fat of the goats receiving the *cis* isomers were about 10 \times higher than levels in the fat of the goats receiving the trans isomers (Table V). There were no appreciable differences between the amounts of radioactivity found in the fat around the kidney and those found in omental fat.

We attribute the high levels of radiocarbon in the bone of the goats treated with *cis* isomers to the fact that the fat in the bone marrow was not removed from the bone before quantitation. Although levels of radiocarbon were detected in most tissues, none were higher than 0.04 ppm for the ^{14}C trans isomer or 0.25 ppm for ^{14}C *cis* isomer treatments. We believe that the high level of radiocarbon found in the lung tissue of the *cis* acid treated goat was probably due to slaughter contamination.

The recovery of the radiocarbon from *trans*-[acid- ^{14}C]permethrin was 90.4%; from *trans*-[alcohol- ^{14}C]permethrin, 94.6%; from *cis*-[acid- ^{14}C]permethrin, 96.5%; and from *cis*-[alcohol- ^{14}C]permethrin, 95.1%. (The recoveries are based on total weight of organs, feces, gastrointestinal tract contents, and volumes of urine and milk.)

All goats maintained a high level of milk production throughout the test, and no appreciable change was observed in volume and amount of excreta. The tissues removed at slaughter appeared normal by gross examination.

A complete metabolism study is being conducted and will be reported when completed.

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LaWanda M. Hunt*
 Bennye N. Gilbert

U.S. Livestock Insects Laboratory
 Agricultural Research Service
 U.S. Department of Agriculture
 Kerrville, Texas 78028

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