Characterization of Fenvalerate Residues in Dairy Cattle and Poultry

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The chemical nature and magnitude of [^{14}C]fenvalerate residues in the milk, egg, fat, liver, kidney, and muscle tissues in dairy cows and laying hens were examined after extended periods of oral exposure. Dosing levels represented 2 to greater than 100 times the maximum dietary burden. Rapid absorption and distribution of the unchanged fenvalerate residues in the milk (primarily in the cream fraction), egg yolk, body fat, and muscle tissues were observed. Extensive degradation/metabolism of [^{14}C]-fenvalerate (labeled with ^{14}C at the chlorophenyl and/or phenoxyphenyl moiety) was observed in the liver and kidney tissues. Tissue residues were also shown to dissipate rapidly from the test animals when treated diets were replaced with uncontaminated feeds. The overall metabolic pathway of fenvalerate, mainly via ester cleavage, is consistent among dairy cow, laying hen, and other laboratory animals.

INTRODUCTION

Fenvalerate [1, cyano(3-phenoxyphenyl)methyl 4-chloro-α-(1-methylethyl)benzeneacetate, the active ingredient of Pydrin insecticide] and esfenvalerate (the insecticidally active 2-S, α-S isomer of fenvalerate, active ingredient of Asana insecticide) are effective synthetic pyrethroids. They control a wide range of economically important pests on the major field, vegetable, tree fruit, and nut crops (Ohno et al., 1977).

The environmental and metabolic fate of fenvalerate and esfenvalerate has been extensively investigated. With its extended field residual activities compared to those of other commercial pyrethroids and increased wide use patterns (the U.S. label includes more than 50 crops), it is important that the potential for the transfer of fenvalerate residues from animal feed items to livestock is adequately understood. This paper presents results from animal feeding studies that examined the chemical nature and the magnitude of fenvalerate residues in livestock's (cattle and poultry) milk, egg, fat, and meat. This information provides a better understanding of its comparative metabolism in different animal species and the basis for the establishment of tolerance for fenvalerate residues in these animal products.

MATERIALS AND METHODS

Test Materials and Reference Standards. Radiolabeled fenvalerate and appropriate reference standards were synthesized by the Biological Science Researh Center, Shell Agricultural Chemical Co., Modesto, CA. Two preparations of [^{14}C]fenvalerate, one labeled at the chlorophenyl and the other at the phenoxyphenyl moiety, were used. Radiochemical purities were >97% as determined by thin-layer chromatography (TLC), autoradiography, and liquid scintillation counting (LSC). Authentic standards included CPIA [2, 4-chloro-α-(1-methylethyl)benzeneacetic acid], 2-OH-CPIA [α and β isomers, 3 and 4, respectively, of 4-chloro-α-(2-hydroxy-1-methylethyl)benzeneacetic acid], PBacid [5, 3-phenoxybenzoic acid], and 4'-OH-PBacid [6, 3-(4-hydroxyphenoxy)benzoic acid]. Chemical structures of these compounds are presented in Figure 1.

Cattle Feeding Study. Lactating Guernsey cows (400–650-kg body weight), obtained from local suppliers, were used in the feeding study. In addition to the appropriate control animals (received untreated dairy rations), four main treatment groups were included. Detailed testing parameters are presented in Table I.

[^{14}C]Fenvalerate was incorporated into dairy grain concentrates at the nominal concentrations of 2, 180, and 1140 ppm. On the basis of total daily feed consumption, the above nominal concentrations were equivalent to an average daily dietary intake of 0.11–0.15, 11, and 79 ppm of fenvalerate residues, respectively. Animals from the 0.11 and 11 ppm treatment groups were exposed to [^{14}C-*phenoxyphenyl*]fenvalerate. Animals from the 79 ppm treatment group were exposed to an equal mixture of both [^{14}C-*chlorophenyl*]- and [^{14}C-*phenoxyphenyl*]fenvalerate. The highest dose tested was 79 ppm. It represents approximately twice the maximum fenvalerate residues in the dairy cattle's diet under a worst-case Pydrin insecticide use scenario. A more realistic estimation based on anticipated fenvalerate residues in the animal feed items resulted from Pydrin insecticide applications showed the 79 ppm dosing level represents approximately 8–12 times the anticipated beef and dairy cattle dietary burden.

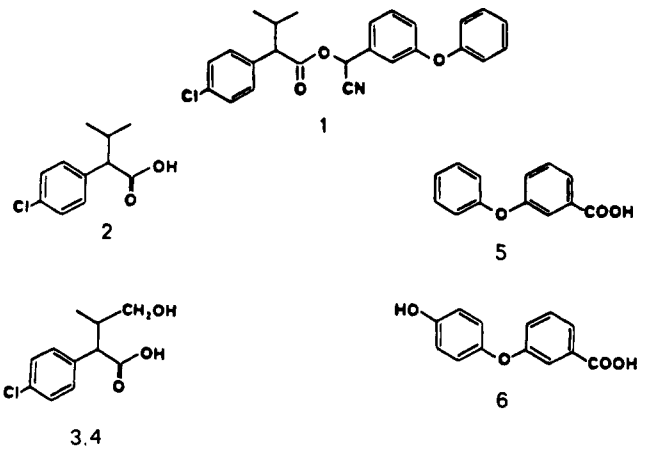

Figure 1. Chemical structures of fenvalerate and metabolites.

Test animals each received 0.5 kg of the treated concentrates and a weighed portion of untreated alfalfa cubes twice daily, immediately after the morning and afternoon milkings. Animals were acclimated for a minimum of 7 days prior to dosing and were monitored by veterinarians during the in-life phase. Test animals were placed individually in stainless steel stanchions except for an occasional exercise period. The stanchion areas are equipped with steel floor grates which were partially covered with heavy rubber mats; this allowed the collection of feces with minimum cross-contamination. In-dwelling catheters were used periodically to obtain uncontaminated urine samples.

Milk samples were collected twice daily (morning and afternoon). Whole milk was further fractionated by centrifugation/chilling into cream and skim milk prior to radioanalysis and residue analysis. Twelve to 24 h after the last dosing, treated and control animals were sacrificed. Samples of quadriceps muscle, gastrocnemius muscle, subcutaneous fat, mesenteric fat,

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Table I. Testing Parameters for the Fenvalerate Cattle Feeding Study

treatment group: test material:	I [^{14}C]chlorophenyl	II [^{14}C]phenoxyphenyl	III [^{14}C]chlorophenyl	IV [^{14}C]chlorophenyl/ [^{14}C]phenoxyphenyl
sp act., μCi/mg	2.2	2.4	0.16	0.21
dose level, ppm	0.11	0.15	11	79
animals				
treated	3	3	3	5
control	2	2	2	2
dosing schedule, days	21	21	28	21
depuration schedule, days	none	none	none	up to 20

Table II. Testing Parameters for the Fenvalerate Poultry Feeding Study

treatment group: test material:	I [^{14}C]chlorophenyl	II [^{14}C]chlorophenyl	III [^{14}C]chlorophenyl	IV [^{14}C]chlorophenyl/ [^{14}]phenoxyphenyl
sp act., μCi/mg	1.7	0.49	0.15	6.6
dose level, ppm	9	29	86	160
animals				
treated	34	6	6	20
control	3	3	4	5
dosing schedule, days	up to 50	23	23	5
depuration schedule, days	up to 57	none	none	none

kidney, and liver tissues were collected. All samples were stored frozen (−4 °C) until analysis.

Poultry Feeding Study. White Leghorn hens (1-year-old, 1.3–1.5-kg body weight), obtained from local suppliers, were used in the feeding study. In addition to the appropriate control hens, four main treatment groups were included. Detailed testing parameters are presented in Table II.

^{14}C-Labeled test materials were administered either by direct capsule intubation (18 mg/hen per day) or incorporated in daily rations. Treatment levels of 9, 29, and 86 ppm in the diet corresponded to approximately 2, 5, and 14 times the maximum fenvalerate residue in the poultry diet under the worst-case Pydrin insecticide use scenario. A more realistic estimation based on the anticipated fenvalerate residue resulted from Pydrin insecticide applications, 86 ppm feeding level, represented greater than 110 times the maximum anticipated poultry dietary burden.

In one of the treatment groups, hens were administered via capsule 18 mg of an equal mixture of [^{14}C-*chlorophenyl*]- and [^{14}C-*phenoxyphenyl*]fenvalerate (equivalent to 160 ppm dietary burden) daily for 5 consecutive days. All hens were sacrificed 18 h after the last capsule was administered. In all other treatment groups, hens were exposed to layer mash treated with a nominal concentration of approximately 10, 30, and 100 ppm of [^{14}C-*chlorophenyl*]fenvalerate. Hens were acclimated for a minimum of 7 days prior to dosing and were monitored closely by veterinarians during the in-life phase. Test animals were held in batteries of wire cages at all times. Each battery consisted of six or more individual cages which permit collection of eggs from each individual hen.

Eggs were collected daily. Hens were sacrificed by cervical dislocation at various time intervals during the exposure and depuration phase. Each hen was then dipped into water (175 °F) for approximately 10 min. The feathers were removed and the carcasses skinned. Fifty grams, or as much as possible, of fat, gizzard, liver, and white and dark tissues was collected. Egg whites and yolks were separated prior to analysis.

Sample Processing and Characterization. Fenvalerate residues in the milk, egg, fat, and meat were characterized by both radiometric and chromatographic procedures.

Radioactive residues in the whole milk, cream, skim milk, egg yolk, egg white, and cow and chicken tissues (approximately 100-mg aliquot/subsample) were analyzed by combustion in a Packard Model 306B sample oxidizer. Background and combustion efficiencies of individual tissues, egg, and milk were determined with control animals and [^{14}C]fenvalerate solution as the calibration standard. Oxidizer solution included Carbo-Sorb and Permafluor V (Packard Instrument Co.) 10:12 mL mixture. Radioactivity was quantitated in 15 mL of Aquasol 2 scintillation solution (New England Nuclear) in a Packard Model 2660 liquid scintillation system. Tissue residues are reported as parts per million (ppm) equivalent of the administered [^{14}C]fenvalerate based on tissue wet weight.

Fenvalerate residues in the milk, egg, and tissues were also determined by electron-capture gas–liquid chromatography (GLC). The detailed method description is available in the *Pesticide Analytical Manual* (U.S. Food and Drug Administration, 1987). Milk (approximately 25 mL, whole, cream, and skim milk) was extracted with methylene chloride, followed by an acetone extraction of the milk solids. Residues in the acetone phase were recovered by hexane-solvent partitioning. The combined methylene chloride and hexane extracts were concentrated. Residual material was solubilized with hexane and partitioned with acetonitrile. The acetonitrile phase was further partitioned with hexane and then diluted with sodium chloride solution. Fenvalerate residue was recovered from the sodium chloride/acetonitrile solution by hexane partitioning. The final hexane phase was concentrated, cleaned up by an activated Florisil column, and analyzed by GLC.

Aliquots of the egg and tissue samples (approximately 25 g, liver, kidney, and muscle) were homogenized in a Waring Blendor with hexane–2-propanol (3:1) solvent mixture. 2-Propanol in the tissue-solvent homogenate was removed from the hexane phase following partitioning with water. Fat tissues (10–20 g) were homogenized twice in the Waring Blendor with hexane (200 mL) and sodium sulfate (20 g). Fenvalerate residues in the egg and tissue hexane extract, after concentration and cleanup by Florisil column, were analyzed by GLC as described below.

Chromatographic Conditions. Operation conditions for the GLC analyses were as follows: 4 ft × 2 mm i.d. glass tube column (no glass wool at inlet) packed with 3% Dexsil 300 on 100/200-mesh Supelcoport in a Varian 3700 gas chromatograph equipped with a ^{63}Ni electron-capture detector. Instrumental conditions were as follows: column temperature, 280 °C; inlet temperature 280 °C; detector temperature, 300 °C; carrier gas, argon–methane; flow rate, 20 mL/min. Two fenvalerate diastereomers were separated with the corresponding retention times of approximately 4.4 and 4.8 min.

The chemical nature of ^{14}C residues recovered in the milk, egg, and animal tissues was also analyzed by two-dimensional TLC (silica gel F-254, 0.25 mm, E. Merck) and confirmed by mass spectrometry (Finnigan 3200 GC/mass spectrometer with a 12 m × 0.3 mm SE-30 WCOT glass column). The TLC R_f values of fenvalerate and reference standards in several TLC solvent systems and its mass spectral information had been previously reported (Lee et al., 1985). The distribution pattern of ^{14}C residues on the TLC plate was visualized by autoradiography on Kodak SB-5 single-coated X-ray film.

RESULTS AND DISCUSSION

Cow Feeding Studies. *Characterization of Milk, Fat, and Muscle Residues.* To generate sufficient residues for characterization, the chemical nature of [^{14}C]fenvalerate equivalent residues in dairy cow's milk and tissues was

Table III. Distribution Profile of Fenvalerate Residues in the Cow Liver and Kidney Tissues (79 ppm Treatment Group, 21-Day Feeding)

	% of total tissue ^{14}C residues					
	liver			kidney		
extractable residues	83			92		
organic-extractable		39			82	
fenvalerate (1)			1			17
CPIA (2)			36			26
PBacid (5)						10
others[a]			2			29
water-soluble		44			10	
CPIA (2)			14			
2-OH-CPIA (3, 4)			3			
PBacid (5)			16			
others[a,b]			11			
tissue-bound residues	17			8		
connective residues		7				
TCA precipitates		10				

[a] Radioactivity associated with the origin of the TLC plate and other minor radiolabeled materials. [b] Include radioactive residues remaining with aqueous phase after acid hydrolysis and organic solvent extraction.

investigated from samples obtained from the 79 ppm treatment group. Test animals were exposed to feed items treated with a mixture of [^{14}C-*chlorophenyl*]- and [^{14}C-*phenoxyphenyl*]fenvalerate. ^{14}C residues in the whole milk, muscle, liver, kidney, and fat were 0.50, 0.29, 2.2, 1.6, and 2.6 ppm, respectively, at the termination of the 21-day dosing phase. Animal excreta were not examined in this study.

The majority of the ^{14}C residues in the milk were localized in the cream fraction (>95% of the total milk residues). The total amount of ^{14}C residues in the skim milk was below the quantitation limit of 0.01 ppm. Radioanalysis and GLC determination were consistent and showed greater than 95% of the ^{14}C residues in the cream was fenvalerate. [^{14}C]Fenvalerate accounted for greater than 90% of the total ^{14}C residues in the subcutaneous and mesenteric fat and muscle tissue. No significant metabolite/degradation product, greater than 5% of the total tissue/milk ^{14}C residues, was detected.

Characterization of Cow Liver Tissues. Liver tissues contained approximately 2 ppm of [^{14}C]fenvalerate equivalent residues at the termination of the dosing phase. Extensive efforts were carried out to fractionate, characterize, and identify significant extractable and tissue-bound residues after enzymatic and acid/base hydrolysis treatments.

Residue distribution data (Table III) showed the majority of the ^{14}C liver residues was recovered in the tissue homogenate (83% of the total ^{14}C residues). Tissue-bound residue (17%) was further fractionated in the connective tissues (7%) and trichloroacetic acid protein precipitates fraction (10%).

Organic-extractable residues (39%) in the liver tissue homogenate were recovered by chloroform-solvent partitioning. TLC autoradiography and GC/MS analyses showed the presence of a trace level of [^{14}C]fenvalerate [*m/z* 419 (M^+), 225, 181, 169, 167, 154, 127, 125, <1% of the total liver residue]. CPIA (2), the primary ester cleavage product of [^{14}C-*chlorophenyl*]fenvalerate, was the primary organic-extractable metabolite identified. CPIA was confirmed by GC/MS as the corresponding methyl ester [*m/z* 226 (M^+), 186, 184, 169, 167, 154, 152, 127, 125, 117, 115, 91, 89].

Water-soluble residues, representing 44% of the total liver ^{14}C residues, were recovered by chloroform-solvent partitioning after acid hydrolysis treatment (pH 2, 37 °C for 4 h). From the [^{14}C]chlorophenyl moiety, CPIA (2) and 2-OH-CPIA (3 and 4) were the major products [confirmed by GC/MS as the corresponding lactone; *m/z* 210 (M^+), 168, 166, 153, 151, 131, 127, 125, 117, 116, 115, 91] identified. PBacid [5, identified as the corresponding methyl ester; *m/z* 228 (M^+), 173, 169, 141, 115, 98, 77] was the major product observed with the [^{14}C]phenoxyphenyl moiety. Several minor products were also observed in the organic-extractable and from the acid hydrolysis fractions.

Characterization of Cow Kidney Tissues. Kidney tissues contained approximately 1.6 ppm of [^{14}C]fenvalerate equivalent residues. Greater than 80% of the kidney residues were recovered by organic-solvent extraction (Table III). TLC autoradiography and GC/MS analyses showed in addition to [^{14}C]fenvalerate (17% of the tissue residues) CPIA (2) and PBacid (5) were identified as major metabolites. At least six minor products were also observed.

Table IV. Magnitude of [^{14}C]Fenvalerate Residues in the Whole Milk Samples from the Three Dosing Groups during the Exposure and Depuration Phases

	[^{14}C]fenvalerate equivalent residues, ppm, at feeding level of		
	0.11–0.15 ppm	10.9 ppm	79.4 ppm
exposure period, days			
1	<0.001	0.02 ± 0.01	0.11 ± 0.04
3	<0.001	0.07 ± 0.01	0.49 ± 0.01
5			0.48 ± 0.07
6	0.002	0.09 ± 0.04	
7			0.52 ± 0.06
9	0.002	0.07 ± 0.01	0.52 ± 0.06
11			0.51 ± 0.07
12	0.001	0.08 ± 0.01	
13			0.52 ± 0.08
15	0.002	0.08 ± 0.01	0.50 ± 0.08
17			0.59 ± 0.13
18	0.002	0.07 ± 0.02	
19			0.55 ± 0.10
21	0.002	0.08 ± 0.02	0.50 ± 0.10
24		0.06 ± 0.01	
27		0.06 ± 0.01	
depuration period, days			
1			0.31 ± 0.04
2			0.12 ± 0.01
3			0.06
4			<0.06

Magnitude of Residues in Milk. [^{14}C]Fenvalerate accounts for greater than 90% of the total ^{14}C residues in the milk fat/cream fraction. Excellent accountability of the ^{14}C residues in all of the milk samples from the various treatment groups during the dosing and depuration phase between direct radioassay and GLC analyses were obtained. [^{14}C]Fenvalerate residues plateaued rapidly in the milk after 3–7 days of dietary exposure. The maximum concentrations reached approximately 0.002, 0.09, and 0.6 ppm at the 0.15, 11, and 79 ppm feeding groups, respectively (Table IV). [^{14}C]Fenvalerate residues dissipated rapidly to below the quantitation limit (<0.06 ppm) within 4 days when cows from the 79 ppm treatment group were fed untreated feed after the termination of the 21-day exposure period. The plot of milk residue concentration vs feeding level showed the total [^{14}C]fenvalerate residues in the whole milk (and the cream) were linear (regression correlation r^2 = 1.00) within the three dose levels tested in this study.

Magnitude of Residues in Fat, Muscle, Liver, and Kidney. Plots of fenvalerate residues vs feeding levels showed the total [^{14}C]fenvalerate equivalent residues in the various tissues were linear (regression correlation r^2 = 0.94–1.00) within the three dose levels tested (Table V). Except for the fat tissue residues, [^{14}C]fenvalerate dissipated rapidly in the liver, kidney, and muscle during the depuration phase.

Table V. Magnitude of [^{14}C]Fenvalerate Residues in the Various Cow Tissues from the Three Dosing Groups during the Exposure and Depuration Phases

	[^{14}C]fenvalerate equivalent residues, ppm			
	exposure phase		depuration phase	
	21 days	28 days	10 days	20 days
feeding level, 0.10–0.15 ppm				
fat	0.01			
muscle	<0.01			
liver	<0.01			
kidney	<0.01			
feeding level, 11 ppm				
fat		0.68–0.79		
muscle		<0.04–0.06		
liver		0.34		
kidney		0.18		
feeding level, 79 ppm				
fat	1.8–3.4		2.2–2.7	1.8–2.4
muscle	0.3		0.14–0.18	0.08–0.12
liver	2.2		0.68	0.48
kidney	1.6		0.32	0.10

Table VI. Magnitude of [^{14}C]Fenvalerate Residues in the Eggs and Various Tissues in Chicken after Five Consecutive Dosings of [^{14}C-*chlorophenyl*]- and [^{14}C-*phenoxyphenyl*]Fenvalerate (18 mg/Hen)

	total [^{14}C]fenvalerate residues, ppm	
	[^{14}C]chlorophenyl	[^{14}C]phenoxyphenyl
egg yolk	1.3	1.0
albumen	<0.2	<0.2
muscles	<0.2	<0.2
fat	0.5	0.5
liver	2.4	1.0

Table VII. Chemical Nature and Distribution of [^{14}C]Fenvalerate Residues in the Chicken Egg Yolk, Fat, and Liver Tissues (18 mg/Hen, 5 Consecutive Days)

	% of total tissue ^{14}C residues					
	yolk		fat		liver	
	acid[a]	alcohol[b]	acid	alcohol	acid	alcohol
fenvalerate (1)	52	70	81	85	<1	<1
CPIA (2)	8				38	
CPIA conjugates					10	
2-OH-CPIA (3, 4)					4	
PBacid (5)						12
PBacid conjugates						3
minor fraction[c]	30	24	16	13	27	45
unextractable residues	10	6	3	2	20	39

[a] [^{14}C]chlorophenyl. [b] [^{14}C]phenoxyphenyl. [c] Includes minor metabolites and solvent extracts.

Poultry Feeding Studies. *Characterization of Egg, Fat, and Muscle Residues.* The chemical nature of [^{14}C]-fenvalerate equivalent residues in the chicken egg (yolk and albumen) and tissues was investigated using samples from the 160 ppm treatment group. Test animals were administered via capsule (18 mg/animal) for 5 consecutive days with both [^{14}C-*chlorophenyl*]- and [^{14}C-*phenoxyphenyl*]fenvalerate. Distribution of ^{14}C residues in the eggs and tissues, 18 h after the last dosing, is presented in Table VI.

^{14}C residues were localized primarily in the yolk. ^{14}C residues in the albumen were below the quantitation limit. [^{14}C]Fenvalerate was identified by TLC and GLC as the major component (50–80%) of the egg yolk ^{14}C residues. CPIA (2, 8%) was the major metabolite identified (Table VII). Greater than 80% of the ^{14}C residues in the fat tissues were identified by TLC and GLC as the parent molecule. ^{14}C residues in the other chicken tissues were negligible.

Characterization of Liver Residues. Chicken liver contained 2.4 and 1.0 ppm of [^{14}C-*chlorophenyl*]- and [^{14}C-*phenoxyphenyl*]fenvalerate residues, respectively. Initial fractionation data showed approximately 50% of the total liver ^{14}C residues could be recovered by solvent extractions. Only a trace level of [^{14}C]fenvalerate was observed (<1%). CPIA (2, free and conjugates) and PBacid (5, free and conjugates) were major components recovered from the [^{14}C-*chlorophenyl*]- and [^{14}C-*phenoxyphenyl*]fenvalerate-treated liver tissues (Table VII).

Approximately 50% of the ^{14}C residues associated with the liver tissues was characterized by tissue-bound materials. Enzymatic treatment of the liver TCA protein precipitates with chymotrypsin released 4–6% of the total ^{14}C residues. CPIA (2) and PBacid (5) were identified in this fraction. Less than 1% of the liver ^{14}C residues were released by peptidase enzyme treatment.

Approximately 4–5% of the liver ^{14}C residues in the remaining bound fraction following enzyme treatment were recovered by vigorous treatment with hot methanol. However, this treatment also released a large amount of proteinaceous and lipid materials; thus, further qualitative characterization of ^{14}C residues in these viscous materials was not successful.

Sodium hydroxide tissue solubilization recovered 8–15% of the liver residues. In the [^{14}C-*chlorophenyl*]fenvalerate treatment group, chromatographic characterization of the organic-extractable residues, after acidification, showed the presence of CPIA (2) and 2-OH-CPIA (3, 4) as the predominant products. Virtually all of the sodium hydroxide released radioactivity from the [^{14}C-*phenoxyphenyl*]fenvalerate treatment group was associated either with the proteinaceous materials reprecipitated during the acidification of the sodium hydroxide solution or as water-soluble materials which could not be recovered by organic solvent extraction.

Magnitude of Residues in Egg. Greater than 60% of the total yolk residues was identified as the parent molecules. The level of ^{14}C residues in the chicken yolk plateaued rapidly after 14 days of exposure. The maximum concentrations were approximately 0.1, 0.3, and 1.2 ppm at the 9, 29, and 86 ppm feeding levels, respectively (Table VIII). ^{14}C residues in the egg yolk dissipated rapidly to less than 0.02 ppm when the hens from the 9.2 ppm treatment group were fed untreated feed for 8 days after 49 days of exposure. Total [^{14}C]fenvalerate equivalent residues in the egg yolk were linear (regression correlation $r^2 = 1.00$) within the three dose levels (9, 29, and 86 ppm) tested.

Magnitude of Residues in Fat, Liver, and Muscles. The amount of ^{14}C residues in the poultry (light and dark muscles), skin, and gizzard was negligible in all treatment groups (<0.02, 0.06, and 0.2 ppm) for the 9.2, 29, and 86 ppm treatment groups, respectively.

Liver tissues contained the highest level of ^{14}C residues, which plateaued after 14 days of dosing. The maximum ^{14}C residue levels in the 9.2, 29, and 86 ppm dose groups were 0.55, 0.64, and 2.6 ppm, respectively, after day 23. Liver residues depleted rapidly from 0.3 ppm after 50 days of dosing (at 9.2 ppm feeding level) to 0.07 ppm after 29 days of feeding on untreated ration. A similar profile was also observed in the fat tissues. Total [^{14}C]fenvalerate equivalent residues in the liver and fat tissues were linear (regression correlation r^2 = 0.95–0.96) within the three dose levels (9, 29, and 86 ppm) tested. Fat residues depleted rapidly from 0.08 ppm after 50 days of dosing (at the 9.2 ppm feeding level) to 0.03 ppm after 29 days of feeding on untreated rations.

Table VIII. Magnitude of [^{14}C]Fenvalerate Residues in the Egg Yolk, Body Fat, and Liver Tissues from Three Poultry Dosing Groups during the Exposure and Depuration Phases

	[^{14}C]fenvalerate equivalent residues, ppm								
	egg			fat			liver		
	9.2 ppm	29 ppm	86 ppm	9.2 ppm	29 ppm	86 ppm	9.2 ppm	29 ppm	86 ppm
feeding period, days									
7	0.09 ± 0.01	0.28 ± 0.08	1.1 ± 0.02	0.02			0.25 ± 0.10		
14	0.10 ± 0.03	0.32 ± 0.08	1.2 ± 0.30	0.03			0.29 ± 0.08		
21	0.10 ± 0.02	0.29 ± 0.09	0.99 ± 0.01						
23		0.27 ± 0.09	0.96 ± 0.10		0.17 ± 0.10	0.28 ± 0.05		0.64 ± 0.21	2.6 ● 0.35
28	0.09 ± 0.02			0.05 ± 0.02			0.30 ± 0.04		
35	0.10 ± 0.02								
42	0.09 ± 0.03			0.08 ± 0.01			0.55 ± 0.05		
49	0.11 ± 0.01			0.05 ± 0.01			0.30 ± 0.20		
depuration period, days									
1	0.10 ± 0.01								
4	0.07 ± 0.01								
8	<0.02			0.05 ± 0.01			0.13 ± 0.01		
15				0.04 ± 0.01			0.10 ± 0.07		
29				0.03 ± 0.01			0.07 ± 0.01		
57				0.03 ± 0.01			0.04 ± 0.02		

DISCUSSION

The chemical nature and magnitude of [^{14}C]fenvalerate residues in the milk, egg, fat, and tissues in the dairy cow and poultry were examined after an extended long-term feeding regimen. Although animal excreta were not analyzed in this current study, the metabolic fate of fenvalerate was well-defined on the basis of tissue residue characterization. Fenvalerate was the primary residue (>80%) recovered in the cream, whole milk, and fat samples. Fenvalerate had been reported earlier as the major product in cow's milk after oral dosing (Wszolek et al., 1980). The residue-transfer profile in the milk sample was consistent under oral or dermal/topical treatments (Frank et al., 1984). In the liver and kidney tissues, ester cleavage products, CPIA (2) and 2-OH-CPIA (3, 4) from the [^{14}C]chlorophenyl moiety and PBacid (5) and 3-OH-PBacid (6) from the [^{14}C]phenoxyphenyl moiety, were recovered as major degradation products. The overall metabolic pathway of fenvalerate in the dairy cow was consistent with that of cypermethrin (Croucher et al., 1985), fluvalinate (Quistad et al., 1982), and deltamethrin (Akhtar et al., 1986), other pyrethroids which contain the same α-cyanophenoxyphenyl moiety.

The metabolic fate of fenvalerate in various avian species had been reported (Mumtaz and Menzer, 1986; Akhtar et al., 1989). Fenvalerate was the major product recovered in the egg and fat. Liver residue profile showed the rapid and extensive metabolism of fenvalerate in the chicken. Ester cleavage again was the primary metabolic pathway of fenvalerate in the laying hen. The overall metabolic pathway of fenvalerate in the laying hen was consistent with that of cypermethrin (Hutson and Stoydin, 1987), fluvalinate (Staiger et al., 1982), and deltamethrin (Akhtar et al., 1985).

Although fenvalerate residues were found to distribute rapidly as the unchanged parent molecules in the milk cream, egg yolk, body fat, and muscle tissues, these fenvalerate residues were also dissipated rapidly from these tissues when test animals were placed on the untreated diet. No significant concentrations of fenvalerate metabolites (from the acid and alcohol portion of the parent molecule) were observed in the milk, egg, fat, and muscle tissues. The absorption and residue distribution profile showed a linear relationship between tissue residue levels and the corresponding dosing level tested. The level of fenvalerate residues in the various animal products is well below the allowable daily intake with adequate margin of safety, even under the worst-case dietary exposure scenario.

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