ADME NTP Study S0069 Crotonaldehyde

Sex/Species: adult male F344 rats.
Vehicle: intravenous, 10% ethanol in water or 2% ethanol in water; oral, 10% ethanol in water.

CASRN 4170-30-3

Radiolabeled with carbon-14 at all carbons; Crotonaldehyde, [U-^{14}C]-

Studies Performed:

- Single 2.6-2.9 mg/kg intravenous dose to rats with sacrifice 0.25, 0.75, 2, 6, 24, or 72 hours postdose (vehicle is 10% ethanol in water; n=3-4).
- Single 2.9 mg/kg intravenous dose to rats with sacrifice 24 hours postdose (vehicle is 2% ethanol in water; n=4).
- Single 0.67 mg/kg oral gavage dose to rats with sacrifice 72 hours postdose (n=3).
- Single 3.3 mg/kg oral gavage dose to rats with sacrifice 72 hours postdose (n=3).
- Single 35 mg/kg oral gavage dose to rats with sacrifice 72 hours postdose (n=4).

Note on Accessibility: Persons with disabilities or using assistive technology may find some documents are not fully accessible. For assistance, contact Central Data Management or use our contact form and identify the documents/pages for which access is required. We will assist you in accessing the content of the files. NIEHS has helpful information on accessibility.

Table 1

Recovery of Total Radioactivity After Administration of [^{14}C]Crotonaldehyde to Male Fischer 344 Rats (% Dose)[a]

Time (h)	Route	Dose (mg/kg)	Urine	Breath CO_2	Breath Volatiles	Feces	Major Selected Tissues & Blood[b,c]	Total
0.25	IV	2.8	N/A[d]	N/A		N/A	55 ± 1	
0.75	IV	2.8	N/A	N/A		N/A	37 ± 3	
2	IV	2.8	N/A	N/A		N/A	18 ± 0.3	
6	IV	2.6	39 ± 5	35 ± 6	1.3 ± 0.8	N/A	10 ± 0.5	82 ± 4
24	IV	2.8	50 ± 9	34 ± 7		0.55 ± 0.25	7.4 ± 0.4	90 ± 4
24[e]	IV	2.9	45 ± 5	36 ± 1		0.5 ± 0.1	8.7 ± 0.9	88 ± 4
72	IV	2.8	(39 ± 6)[f]	43 ± 4		N/A	4.8 ± 0.5	(88 ± 4)[f]
72	IV	2.8	48 ± 7	41 ± 2		0.27 ± 0.12	N/A	
72	Oral	0.67	39 ± 4[b]	47 ± 5[b]		6.6 ± 0.9[b]	6.2 ± 0.7	99 ± 8[b]
72	Oral	3.3	34 ± 2[b]	49 ± 7[b]		5.6 ± 3.8[b]	N/A	
72	Oral	35	38 ± 3	44 ± 5	0.26 ± 0.19	6.9 ± 0.2	4.7 ± 0.2	93 ± 4

[a] Mean ± SD for four animals except where noted.

[b] Mean ± SD for three animals.

[c] Major tissues are considered to be skin, muscle, adipose, and liver. Skin is assumed to be 15% of total body weight; muscle, 50%; and adipose, 10%.

[d] N/A: Samples were not obtained (or analyzed).

[e] Dose was administered in 2% ethanol.

[f] Due to loss of a portion of some samples, actual value is higher than that shown.

Table 2

Cumulative Excretion of Total ^{14}C After Oral Administration of [^{14}C]Crotonaldehyde to Male Fischer 344 Rats (% Dose)

Dose (mg/kg)	35[a]				3.3[b]				0.67[b]			
Excreta	Urine	Breath	Feces	Total	Urine	Breath	Feces	Total	Urine	Breath	Feces	Total
Time (h)												
12	27 ± 10	33 ± 5	d	60 ± 11	32.8 ± 5.6[a]	43.6 ± 5.5[a]	d	76.5 ± 9.6[a]	37.0 ± 4.7	41.0 ± 4.6	d	78.0 ± 7.7
24	35 ± 4	39 ± 4	2.9 ± 2.6	77 ± 7	32.9 ± 2.3	e	5.1 ± 3.7	81.8 ± 5.0	38.7 ± 4.9	44.7 ± 5.2[c]	5.8 ± 1.2	87.4 ± 9.9[c]
36	37 ± 3	42 ± 4		81 ± 4	33.3 ± 2.1	45.4 ± 6.7		83.7 ± 4.9	39.0 ± 4.0	45.0 ± 4.6		89.8 ± 7.1
48	37 ± 3	43 ± 5	5.6 ± 1.1	86 ± 3	33.4 ± 2.1	47.9 ± 6.7[e]	5.5 ± 3.8	86.7 ± 4.8	39.1 ± 4.0	45.7 ± 4.7	6.4 ± 0.9	91.2 ± 7.2
72	38 ± 3	44 ± 5	6.9 ± 0.2	89 ± 3	34.0 ± 1.6	49.1 ± 6.9	5.6 ± 3.8	88.7 ± 4.6	39.4 ± 4.1	46.8 ± 5.0	6.6 ± 0.9	92.8 ± 7.5

[a]Values are mean ± SD for four animals.

[b]Values are mean ± SD for three animals, except where noted otherwise.

[c]Values are mean ± range for two animals.

[d]First feces collection was 0-24 h.

[e]The 12-24 h and the 36-48 h breath samples were accidentally combined before analysis. The percent dose excreted for this combined sample is recorded as one sample, 36-48 h.

Table 3

Cumulative Excretion of Total ^{14}C After Intravenous Administration of [^{14}C]Crotonaldehyde to Male Fischer 344 Rats (% Dose)

Dose (mg/kg)	2.8[a]				2.8[b]			
Excreta	Urine	Breath	Feces	Total	Urine	Breath	Feces	Total
Time (h)								
0-1	(9.4 ± 7.2)[c]	16.2 ± 2.2	d	25.7 ± 5.4	1.4 ± 1.3	16.6 ± 0.3	e	18.0 ± 1.1
1-2	(13.9 ± 10.5)[c]	26.1 ± 3.2		40.0 ± 7.7	18.0 ± 16.4	26.0 ± 0.5		44.0 ± 16.0
2-4	(22.8 ± 8.0)[c]	32.0 ± 4.0		54.8 ± 9.3		31.1 ± 1.3		
4-6	(28.9 ± 8.7)[c]	34.4 ± 4.4		63.3 ± 8.0	40.2 ± 7.0	33.3 ± 1.4		73.5 ± 6.7
6-12	(36.3 ± 6.0)[c]	37.4 ± 4.4		73.9 ± 5.4	45.4 ± 7.2	36.4 ± 1.8		81.9 ± 6.1
12-24	(38.0 ± 5.7)[c]	39.2 ± 4.8		77.2 ± 5.5	46.8 ± 6.7	38.2 ± 2.2		85.0 ± 5.5
24-36	(38.4 ± 5.7)[c]	40.3 ± 4.7		78.8 ± 5.5	47.2 ± 6.7	39.3 ± 2.3		86.6 ± 5.4
36-48	(38.7 ± 5.7)[c]	41.0 ± 4.9		79.7 ± 5.5	47.4 ± 6.6	40.0 ± 2.3		87.5 ± 5.4
48-72	(39.0 ± 5.6)[c]	42.0 ± 5.0		81.0 ± 5.7	47.7 ± 6.6	40.9 ± 2.5	0.27 ± 0.12	88.8 ± 5.0

(continued)

Table 3 (continued)

Cumulative Excretion of Total ^{14}C After Intravenous Administration of [^{14}C]Crotonaldehyde to Male Fischer 344 Rats (% Dose)

Dose (mg/kg)	2.8[a]				2.6[a]			
Excreta	Urine	Breath	Feces	Total	Urine	Breath[f]	Feces	Total
Time (h)								
0-1	0.4 ± 0.8	14.6 ± 3.1	e	15.0 ± 2.9	10.4 ± 10.1	16.4 ± 4.0	d	27.6 ± 11.8
0-2	5.0 ± 10.0	22.4 ± 3.4		27.4 ± 7.3	16.6 ± 11.6	24.5 ± 1.9		42.3 ± 11.5
2-4	21.9 ± 17.6	27.7 ± 5.1		49.5 ± 14.2	32.9 ± 6.1	31.3 ± 1.1		65.5 ± 6.3
4-6	27.1 ± 18.1	30.1 ± 6.0		57.2 ± 14.2	38.7 ± 4.7	33.5 ± 0.8		73.5 ± 5.3
6-12	40.6 ± 7.3	32.8 ± 6.3		73.4 ± 3.8				
12-24	50.0 ± 8.7	34.4 ± 6.7	0.55 ± 0.25	82.0 ± 4.2				

[a]Values are mean ± SD for four animals. There are two groups sacrificed at 72 hours for which excreta was collected.

[b]Values are mean ± SD for three animals.

[c]Part of the 1 h and 4 h urine samples were lost for some animals. Therefore actual cumulative values are somewhat higher than shown.

[d] Feces not analyzed.

[e] Feces analyzed as one combined sample, 0-72 h.

[f]Values are for excretion in breath as CO_2. Excretion in breath as volatiles was 0.82 ± 0.47 for 0-1 h, and 1.3 _).8 for 1-2 h collection.

Table 4

Cumulative Excretion of Total ^{14}C After Intravenous Administration of [^{14}C]Crotonaldehyde to Male Fischer 344 Rats (% Dose)[a]

Dose (mg/kg)	2.8				2.9			
Vehicle	10% Ethanol				2% Ethanol			
Excreta	Urine	Breath	Feces	Total	Urine	Breath	Feces	Total
Time (h)								
0-1	0.42 ± 0.85	14.6 ± 3.1	N/A[b]	15.0 ± 2.9	2.5 ± 5.0	16.4 ± 1.9	N/A[b]	18.9 ± 5.5
1-2	5.0 ± 10.0	22.4 ± 3.4	N/A	27.4 ± 7.3	13.5 ± 15.1	22.4 ± 3.9	N/A	35.9 ± 18.7
2-4	21.9 ± 17.6	27.7 ± 5.1	N/A	49.5 ± 14.2	28.8 ± 8.4	27.8 ± 2.0	N/A	56.5 ± 9.3
4-6	27.1 ± 18.1	30.1 ± 6.0	N/A	57.2 ± 14.2	33.8 ± 6.4	30.6 ± 2.6	N/A	63.2 ± 7.2
6-12	40.6 ± 7.3	32.8 ± 6.3	N/A	73.4 ± 3.8	38.2 ± 5.8	32.4 ± 1.4	N/A	70.6 ± 6.1
12-24	50.0 ± 8.7	34.4 ± 6.7	0.55 ± 0.25	82.0 ± 4.2	45.2 ± 5.3	35.8 ± 1.0	0.5 ± 0.1	81.4 ± 5.2

[a] Values are mean ± SD for four animals. (Two groups sacrificed at 24 hours but with different vehicles.)

[b] Feces analyzed as one combined sample, 0-72 h.

Table 5

Amount of ^{14}C-Labeled Compounds in Tissues 24 h After Intravenous Administration of [^{14}C]Crotonaldehyde to Fischer 344 Male Rats[a]

Dose (mg/kg)	2.8			2.9		
Dose Vehicle	10% EtOH/H_2O			2% EtOH/H_2O		
Tissue	ng-eq Cmpd per g Tissue	TRB[d]	% Dose	ng-eq Cmpd per g Tissue	TRB[d]	% Dose
I. Blood	606 ± 149	1.0 ± 0	1.4 ± 0.3	782 ± 112	1.0 ± 0	1.7 ± 0.3
II. Major Tissues						
Skin - Ear	344 ± 71	0.62 ± 0.31		344 ± 51	0.44 ± 0.03	
Neck	310 ± 105	0.57 ± 0.36		295 ± 39	0.38 ± 0.07	
Abdomen	342 ± 160	0.64 ± 0.48		413 ± 81	0.53 ± 0.06	
Hindquarters	388 ± 87	0.70 ± 0.36		406 ± 35	0.53 ± 0.11	
Average	346 ± 106	0.63 ± 0.38	1.9 ± 0.6	364 ± 39	0.47 ± 0.06	1.9 ± 0.2
Muscle - Neck	191 ± 25	0.32 ± 0.06		218 ± 39	0.28 ± 0.08	
Abdomen	149 ± 9	0.26 ± 0.09		179 ± 23	0.23 ± 0.03	
Hindleg	159 ± 12	0.27 ± 0.05		159 ± 10	0.20 ± 0.02	
Average	166 ± 10	0.28 ± 0.07	3.0 ± 0.1	185 ± 15	0.24 ± 0.04	3.2 ± 0.3
Adipose - Kidney	147 ± 23	0.25 ± 0.04		236 ± 71	0.30 ± 0.05	
Epididymis	109 ± 27	0.19 ± 0.07		157 ± 74	0.20 ± 0.09	
Mesenteric	208 ± 79	0.35 ± 0.13		433 ± 190	0.54 ± 0.16	
Average	155 ± 41	0.26 ± 0.08	0.56 ± 0.13	276 ± 104	0.34 ± 0.09	0.97 ± 0.38
Liver	456 ± 46	0.80 ± 0.28	0.68 ± 0.07	537 ± 53	0.70 ± 0.16	0.77 ± 0.09

(continued)

Table 5 (continued)

Amount of ^{14}C-Labeled Compounds in Tissues 24 h After Intravenous Administration of [^{14}C]Crotonaldehyde to Fischer 344 Male Rats[a]

Dose (mg/kg)	2.8			2.9		
Dose Vehicle	10% EtOH/H_2O			2% EtOH/H_2O		
Tissue	ng-eq Cmpd per g Tissue	TRB[d]	% Dose	ng-eq Cmpd per g Tissue	TRB[d]	% Dose
III. GI Tract Tissues						
Esophagus	533 ± 86	0.90 ± 0.19	0.014 ± 0.002	939 ± 399	1.2 ± 0.66	0.030 ± 0.010
Stomach	385 ± 61	0.68 ± 0.30	0.058 ± 0.010	386 ± 83	0.49 ± 0.05	0.071 ± 0.013
Small Intestine	490 ± 87	0.87 ± 0.41	0.22 ± 0.06	445 ± 68	0.57 ± 0.04	0.19 ± 0.04
Cecum	268 ± 116	0.50 ± 0.36	0.033 ± 0.007	278 ± 26	0.36 ± 0.02	0.042 ± 0.004
Large Intestine	542 ± 113	0.96 ± 0.40	0.083 ± 0.016	579[c]	0.63[c]	0.077[c]
IV. Reproductive Tissues						
Testes	176 ± 30	0.31 ± 0.14	0.068 ± 0.012	172 ± 18	0.22 ± 0.03	0.062 ± 0.008
Seminal Vesicles	315 ± 46	0.56 ± 0.24	0.034 ± 0.006	316 ± 12	0.41 ± 0.05	0.027 ± 0.012
Prostate	415 ± 46	0.73 ± 0.29	0.014 ± 0.002	344 ± 128	0.44 ± 0.16	0.015 ± 0.005
V. Other Tissues						
Trachea	916 ± 118	1.5 ± 0.2	0.019 ± 0.006	1059 ± 357	1.3 ± 0.26	0.019 ± 0.010
Lungs	921 ± 76	1.6 ± 0.3	0.15 ± 0.01	974 ± 99	1.2 ± 0.2	0.16 ± 0.01
Adrenals	609 ± 82	1.1 ± 0.4	0.0065 ± 0.0012	816 ± 114	1.0 ± 0.01	0.0074 ± 0.0007
Spleen	612 ± 73	1.0 ± 0.3	0.044 ± 0.006	632 ± 83	0.81 ± 0.04	0.051 ± 0.012
Kidneys	421 ± 89	0.75 ± 0.38	0.12 ± 0.02	432 ± 68	0.55 ± 0.06	0.12 ± 0.02
Eyes	163 ± 41	0.29 ± 0.16[b]	0.0067 ± 0.0023[b]	223 ± 33	0.29 ± 0.06	0.0084 ± 0.0009
Brain	282 ± 126[b]	0.50 ± 0.08[b]	0.073 ± 0.029[b]	343 ± 29[b]	0.44 ± 0.06[b]	0.085 ± 0.008
Heart	340 ± 84[b]	0.60 ± 0.06[b]	0.039 ± 0.011[b]	320 ± 17[b]	0.40 ± 0.05[b]	0.035 ± 0.0004[b]

[a]Values are mean + SD for 3 animals.
[b]Mean ± range for 2 animals.
[c]Values for 1 animal.
[d]Tissue:blood ratio.

Table 6

Concentration of ^{14}C-Labeled Compounds in Tissues 72 h After Oral Administration of [^{14}C]Crotonaldehyde to Fischer 344 Male Rats (ng-eq/g)[a]

Dose (mg/kg)		35	0.67
I.	Blood	2350 ± 180	42 ± 7
II.	Major Tissues		
	Skin - Ear	4680 ± 350	86 ± 8
	Neck	2190 ± 450	98 ± 25
	Abdomen	3180 ± 500	65 ± 31
	Hindquarters	2790 ± 1000	54 ± 13
	Average	3210 ± 300	76 ± 16
	Muscle - Neck	1510 ± 70	37 ± 10
	Abdomen	910 ± 150	25 ± 5
	Hindquarters	990 ± 230	22 ± 9
	Average	1140 ± 100	28 ± 8
	Adipose - Kidney	1470 ± 450	15 ± 6[b]
	Epididymis	1120 ± 190	20 ± 2
	Mesenteric	2660 ± 710	46 ± 5
	Average	1750 ± 320	25 ± 5
	Liver	6790 ± 1200	281 ± 113
III.	GI Tract Tissues		
	Esophagus	7030 ± 550	189 ± 62
	Stomach	9220 ± 1430	570 ± 209
	Small Intestine	4680 ± 810	32 ± 7
	Cecum	2190 ± 610	12 ± 10
	Large Intestine	3620 ± 170	30 ± 19
IV.	Reproductive Tissues		
	Testes	2280 ± 780	29 ± 6
	Seminal Vesicles	3360 ± 730	60 ± 8
	Prostrate	3250 ± 110	54 ± 4
V.	Other Tissues		
	Trachea	4650 ± 1640	98 ± 22
	Lungs	4390 ± 1730	67 ± 7
	Adrenals	10800 ± 120	138 ± 1
	Spleen	4700 ± 290	74 ± 6
	Kidneys	4730 ± 180	69 ± 6
	Eyes	1190 ± 10[b]	20 ± 2
	Brain	2230 ± 90	30 ± 9
	Heart	2360[c]	46 ± 14

[a] Values are mean + SD for 3 animals.

[b] Mean ± range for 2 animals.

[c] Value for 1 animal.

Table 7

Tissue-Blood Ratios of ^{14}C-Labeled Compounds After Oral Administration of [^{14}C]Crotonaldehyde to Fischer 344 Male Rats (TBR)[a]

Dose (mg/kg)		35	0.67
I.	Blood	1.0 ± 0.0	1.0 ± 0.0
II.	Major Tissues		
	Skin - Ear	2.0 ± 0.1	2.1 ± 0.2
	Neck	0.94 ± 0.25	2.3 ± 0.6
	Abdomen	1.3 ± 0.1	1.5 ± 0.4
	Hindquarters	1.2 ± 0.5	1.3 ± 0.1
	Average	1.4 ± 0.2	1.8 ± 0.2
	Muscle - Neck	0.64 ± 0.03	0.87 ± 0.12
	Abdomen	0.39 ± 0.08	0.60 ± 0.02
	Hindleg	0.42 ± 0.06	0.50 ± 0.12
	Average	0.48 ± 0.03	0.66 ± 0.08
	Adipose - Kidney	0.62 ± 0.15	0.36 ± 0.20[b]
	Epididymis	0.48 ± 0.11	0.48 ± 0.08
	Mesenteric	1.1 ± 0.3	1.1 ± 0.3
	Average	0.75 ± 0.14	0.61 ± 0.16
	Liver	2.9 ± 0.5	7.1 ± 3.5
III.	GI Tract Tissues		
	Esophagus	3.0 ± 0.2	4.4 ± 1.0
	Stomach	3.9 ± 0.6	14 ± 5
	Small Intestine	2.0 ± 0.3	0.76 ± 0.02
	Cecum	0.94 ± 0.28	0.27 ± 0.19
	Large Intestine	1.5 ± 0.1	0.68 ± 0.31
IV.	Reproductive Tissues		
	Testes	0.98 ± 0.35	0.69 ± 0.03
	Seminal Vesicles	1.4 ± 0.3	1.4 ± 0.05
	Prostate	1.4 ± 0.1	1.3 ± 0.1
V.	Other Tissues		
	Trachea	2.0 ± 0.7	2.3 ± 0.1
	Lungs	1.8 ± 0.6	1.6 ± 0.1
	Adrenals	4.6 ± 0.3	3.4 ± 0.6
	Spleen	2.0 ± 0.1	1.8 ± 0.1
	Kidneys	2.0 ± 0.2	1.7 ± 0.1
	Eyes	0.49 ± 0.03[b]	0.48 ± 0.03
	Brain	0.95 ± 0.04	0.70 ± 0.08
	Heart	0.92[c]	1.1 ± 0.1

[a]Values are the mean for 3 rats ± SD.

[b]Mean + range for 2 animals.

[c]Value for 1 animal.

Table 8

Amount of ^{14}C-Labeled Compounds in Tissues 72 h After Oral Administration of [^{14}C]Crotonaldehyde to Fischer 344 Male Rats (% Dose)[a]

Dose (mg/kg)		35	0.67
I.	Blood	0.43 ± 0.1	0.41 ± 0.06
II.	Major Tissues		
	Skin	1.4 ± 0.2	1.8 ± 0.3
	Muscle	1.6 ± 0.1	2.2 ± 0.5
	Adipose	0.51 ± 0.10	0.39 ± 0.07
	Liver	0.66 ± 0.12	1.5 ± 0.7
III.	GI Tract Tissues		
	Esophagus	0.017 ± 0.001	0.022 ± 0.004
	Stomach	0.16 ± 0.03	0.83 ± 0.20
	Small Intestine	0.13 ± 0.01	0.10 ± 0.02
	Cecum	0.022 ± 0.005	0.021 ± 0.008
	Large Intestine	0.041 ± 0.003	0.034 ± 0.004
IV.	Reproductive Tissues		
	Testes	0.070 ± 0.026	0.046 ± 0.003
	Seminal Vesicles	0.018 ± 0.005	0.020 ± 0.002
	Prostate	0.012 ± 0.006	0.010 ± 0.003
V.	Other Tissues		
	Trachea	0.0097 ± 0.0038	0.0099 ± 0.0022
	Lungs	0.044 ± 0.009	0.040 ± 0.003
	Adrenals	0.0043 ± 0.0008	0.0047 ± 0.0007
	Spleen	0.027 ± 0.001	0.022 ± 0.003
	Kidneys	0.094 ± 0.005	0.080 ± 0.007
	Eyes	0.0032 ± 0.0004[b]	0.0032 ± 0.0003
	Brain	0.041 ± 0.002	0.030 ± 0.008
	Heart	0.018[c]	0.023 ± 0.010

[a]Values are mean ± SD for 3 animals.

[b]Mean ± range for 2 animals.

[c]Values for 1 animal.

[d]Adipose assumed to be 10% of body weight; muscle, 50% of body weight; and skin, 15% of body weight.

Table 9

Concentration of ^{14}C-Labeled Compounds in Tissues After Intravenous Administration of 2.6 - 2.9 mg/kg of [^{14}C]Crotonaldehyde to Fischer 344 Male Rats (ng-eq/g)[a]

	Time (h)	0.25	0.75	2	6	24	72
I.	Blood	11400 ± 100	5820 ± 630	2370 ± 70	950 ± 88	606 ± 149	371 ± 96
II.	Major Tissues						
	Skin - Ear	1200 ± 80	1010 ± 32	516 ± 14	383 ± 23	344 ± 71	264 ± 29
	Neck	1180 ± 50	1070 ± 100	482 ± 92	325 ± 102	310 ± 105	193 ± 66
	Abdomen	1430 ± 90	1260 ± 150	731 ± 187	368 ± 70	342 ± 160	182 ± 36
	Hindquarters	927 ± 139	954 ± 36	692 ± 65	403 ± 2[b]	388 ± 87	196 ± 5
	Average	1160 ± 60	1070 ± 19	605 ± 32	366 ± 12	346 ± 106	209 ± 28
	Muscle - Neck	1190 ± 20	839 ± 71	385[c]	228 ± 56	191 ± 25	122 ± 19
	Abdomen	974 ± 158[b]	746 ± 57	382 ± 47	230 ± 18	149 ± 9	133 ± 27
	Hindquarters	910 ± 24	750 ± 44	357 ± 34	156 ± 23	159 ± 12	98 ± 11
	Average	1030 ± 40	778 ± 52	376 ± 29	205 ± 28	166 ± 10	118 ± 19
	Adipose - Kidney	248 ± 94	136 ± 26	99 ± 41[b]	94 ± 27	147 ± 23	55 ± 8
	Epididymis	263 ± 92	284 ± 196	109 ± 27	99 ± 40	109 ± 27	70 ± 23
	Mesenteric	733 ± 266	394 ± 153	281 ± 72	264 ± 66	208 ± 79	144 ± 35
	Average	414 ± 133	271 ± 69	176 ± 52	153 ± 37	155 ± 41	90 ± 20
	Liver	4150 ± 147	3490 ± 130	2120 ± 288	937 ± 147	456 ± 46	293 ± 25
III.	GI Tract Tissues						
	Esophagus	N/A	N/A	N/A	747 ± 139	533 ± 86	N/A
	Stomach	N/A	N/A	N/A	663 ± 56	385 ± 61	N/A
	Small Intestine	N/A	N/A	N/A	1240 ± 238	490 ± 87	N/A
	Cecum	N/A	N/A	N/A	695 ± 205	268 ± 116	N/A
	Large Intestine	N/A	N/A	N/A	995 ± 90	542 ± 113	N/A

(continued)

Table 9 (continued)

Concentration of ^{14}C-Labeled Compounds in Tissues After Intravenous Administration of 2.6 - 2.9 mg/kg of [^{14}C]Crotonaldehyde to Fischer 344 Male Rats (ng-eq/g)[a]

	Time (h)	0.25	0.75	2	6	24	72
IV.	Reproductive Tissues						
	Testes	N/A	N/A	N/A	303 ± 43	176 ± 30	N/A
	Seminal Vesicles	N/A	N/A	N/A	284 ± 180[b]	315 ± 46	N/A
	Prostate	N/A	N/A	N/A	728 ± 241[b]	415 ± 46	N/A
V.	Other Tissues						
	Trachea	N/A	N/A	N/A	1190 ± 240	916 ± 118	461 ± 63
	Lungs	N/A	N/A	N/A	1410 ± 270	921 ± 76	504 ± 39
	Adrenals	N/A	N/A	N/A	779 ± 42	609 ± 82	536 ± 70
	Spleen	N/A	N/A	N/A	944 ± 36	612 ± 73	N/A
	Kidneys	N/A	N/A	N/A	856 ± 79	421 ± 89	N/A
	Eyes	N/A	N/A	N/A	247 ± 21[b]	163 ± 41[b]	N/A
	Brain	N/A	N/A	N/A	631 ± 55[b]	282 ± 126[b]	N/A
	Heart	N/A	N/A	N/A	568 ± 35	340 ± 84[b]	N/A

[a]Values are mean ± SD for 3 animals.

[b]Mean ± range for 2 animals.

[c]Values for 1 animal.

Table 10

Tissue Blood Ratios of ^{14}C-Labeled Compounds in Tissues After Intravenous Administration of 2.6 - 2.9 mg/kg of [^{14}C]Crotonaldehyde to Fischer 344 Male Rats (TBR)[a]

Time (h)	0.25	0.75	2	6	24	72
I. Blood	1.0 ± 0.0	1.0 ± 0.0	1.0 ± 0.0	1.0 ± 0.0	1.0 ± 0.0	1.0 ± 0.0
II. Major Tissues						
Skin - Ear	0.10 ± 0.01	0.17 ± 0.02	0.22 ± 0.002	0.40 ± 0.03	0.62 ± 0.31	0.76 ± 0.31
Neck	0.10 ± 0.01	0.18 ± 0.03	0.20 ± 0.03	0.35 ± 0.13	0.57 ± 0.36	0.54 ± 0.17
Abdomen	0.12 ± 0.01	0.22 ± 0.02	0.31 ± 0.08	0.39 ± 0.06[b]	0.64 ± 0.48	0.51 ± 0.14
Hindquarters	0.08 ± 0.01	0.16 ± 0.01	0.29 ± 0.02	0.43 ± 0.05	0.70 ± 0.36	0.55 ± 0.15
Average	0.10 ± 0.01	0.18 ± 0.02	0.26 ± 0.02	0.39 ± 0.04	0.63 ± 0.38	0.59 ± 0.18
Muscle - Neck	0.10 ± 0.002	0.14 ± 0.02	0.17[c]	0.24 ± 0.08	0.32 ± 0.06	0.34 ± 0.08
Abdomen	0.08 ± 0.01[b]	0.13 ± 0.01	0.16 ± 0.02	0.24 ± 0.04	0.26 ± 0.09	0.37 ± 0.10
Hindquarters	0.080 ± 0.002	0.13 ± 0.02	0.15 ± 0.01	0.17 ± 0.04	0.27 ± 0.05	0.28 ± 0.08
Average	0.091 ± 0.004	0.13 ± 0.02	0.16 ± 0.01	0.22 ± 0.05	0.28 ± 0.07	0.33 ± 0.09
Adipose - Kidney	0.022 ± 0.008	0.023 ± 0.002	0.043 ± 0.019[b]	0.10 ± 0.03	0.25 ± 0.04	0.16 ± 0.07
Epididymis	0.023 ± 0.008	0.047 ± 0.027	0.046 ± 0.012	0.10 ± 0.04	0.19 ± 0.07	0.20 ± 0.08
Mesenteric	0.064 ± 0.024	0.068 ± 0.028	0.12 ± 0.03	0.28 ± 0.07	0.35 ± 0.13	0.42 ± 0.22
Average	0.036 ± 0.012	0.046 ± 0.008	0.074 ± 0.022	0.16 ± 0.04	0.26 ± 0.08	0.26 ± 0.12
Liver	0.36 ± 0.01	0.60 ± 0.08	0.89 ± 0.11	1.0 ± 0.2	0.80 ± 0.28	0.84 ± 0.32
III. GI Tract Tissues						
Esophagus	N/A	N/A	N/A	0.79 ± 0.17	0.90 ± 0.19	N/A
Stomach	N/A	N/A	N/A	0.70 ± 0.01	0.68 ± 0.30	N/A
Small Intestine	N/A	N/A	N/A	1.3 ± 0.2	0.87 ± 0.41	N/A
Cecum	N/A	N/A	N/A	0.73 ± 0.17	0.50 ± 0.36	N/A
Large Intestine	N/A	N/A	N/A	1.0 ± 0.02	0.96 ± 0.40	N/A

(continued)

Table 10 (continued)

Tissue Blood Ratios of ^{14}C-Labeled Compounds in Tissues After Intravenous Administration of 2.6 - 2.9 mg/kg of [^{14}C]Crotonaldehyde to Fischer 344 Male Rats (TBR)[a]

Time (h)	0.25	0.75	2	6	24	72
IV. Reproductive Tissues						
Testes	N/A	N/A	N/A	0.32 ± 0.02	0.31 ± 0.14	N/A
Seminal Vesicles	N/A	N/A	N/A	0.31 ± 0.22[b]	0.56 ± 0.24	N/A
Prostate	N/A	N/A	N/A	0.80 ± 0.21[b]	0.73 ± 0.29	N/A
V. Other Tissues						
Trachea	N/A	N/A	N/A	1.2 ± 0.2	1.5 ± 0.2	1.3 ± 0.2
Lungs	N/A	N/A	N/A	1.5 ± 0.4	1.6 ± 0.3	1.4 ± 0.4
Adrenals	N/A	N/A	N/A	0.82 ± 0.04	1.1 ± 0.4	1.5 ± 0.5
Spleen	N/A	N/A	N/A	1.0 ± 0.05	1.0 ± 0.2	N/A
Kidneys	N/A	N/A	N/A	0.90 ± 0.07	0.75 ± 0.38	N/A
Eyes	N/A	N/A	N/A	0.26 ± 0.01[b]	0.29 ± 0.16[b]	N/A
Brain	N/A	N/A	N/A	0.66 ± 0.03[b]	0.50 ± 0.08[b]	N/A
Heart	N/A	N/A	N/A	0.60 ± 0.05	0.60 ± 0.06[b]	N/A

[a]Values are mean + SD for 3 animals.

[b]Mean + range for 2 animals.

[c]Values for 1 animal.

Table 11

Amount of ^{14}C-Labeled Compound in Tissues After Intravenous Administration of 2.6 - 2.9 mg/kg of [^{14}C]Crotonaldehyde to Fischer 344 Male Rats (% Dose)[a]

Time (h)	0.25	0.75	2	6	24	72
I. Blood	25 ± 0.3	13 ± 2	5.1 ± 0.12	2.3 ± 0.2	1.4 ± 0.3	0.83 ± 0.19
II. Major Tissues						
Skin	6.0 ± 0.3	5.6 ± 0.2	3.1 ± 0.2	2.1 ± 0.1	1.9 ± 0.6	1.1 ± 0.2
Muscle	18 ± 0.7	14 ± 1	6.4 ± 0.5	4.0 ± 0.6	3.0 ± 0.1	2.1 ± 0.4
Adipose	1.4 ± 0.5	0.95 ± 0.26	0.60 ± 0.17	0.59 ± 0.14	0.56 ± 0.13	0.32 ± 0.08
Liver	5.0 ± 0.3	3.8 ± 0.3	2.8 ± 0.6	1.3 ± 0.2	0.68 ± 0.07	0.38 ± 0.04
III. GI Tract Tissues						
Esophagus	N/A	N/A	N/A	0.027 ± 0.007	0.014 ± 0.002	N/A
Stomach	N/A	N/A	N/A	0.11 ± 0.01	0.058 ± 0.010	N/A
Small Intestine	N/A	N/A	N/A	0.52 ± 0.08	0.22 ± 0.06	N/A
Cecum	N/A	N/A	N/A	0.071 ± 0.011	0.033 ± 0.007	N/A
Large Intestine	N/A	N/A	N/A	0.19 ± 0.02	0.083 ± 0.016	N/A
IV. Reproductive Tissues						
Testes	N/A	N/A	N/A	0.12 ± 0.01	0.068 ± 0.012	N/A
Seminal Vesicles	N/A	N/A	N/A	0.032 ± 0.017[b]	0.034 ± 0.006	N/A
Prostate	N/A	N/A	N/A	0.026 ± 0.010[b]	0.014 ± 0.002	N/A

(continued)

Table 11 (continued)

Amount of ^{14}C-Labeled Compound in Tissues After Intravenous Administration of 2.6 - 2.9 mg/kg of [^{14}C]Crotonaldehyde to Fischer 344 Male Rats (% Dose)[a]

Time (h)	0.25	0.75	2	6	24	72
V. Other Tissues						
Trachea	N/A	N/A	N/A	0.026 ± 0.004	0.019 ± 0.006	0.011 ± 0.002
Lungs	N/A	N/A	N/A	0.24 ± 0.06	0.15 ± 0.01	0.074 ± 0.002
Adrenals	N/A	N/A	N/A	0.0066±0.0014	0.0065±0.0012	0.0027±0.0010
Spleen	N/A	N/A	N/A	0.072 ± 0.013	0.044 ± 0.006	N/A
Kidneys	N/A	N/A	N/A	0.25 ± 0.03	0.12 ± 0.02	N/A
Eyes	N/A	N/A	N/A	0.011 ± 0	0.0067 ± 0.002[b]	N/A
Brain	N/A	N/A	N/A	0.13 ± 0.02[b]	0.073 ± 0.029[b]	N/A
Heart	N/A	N/A	N/A	0.068 ± 0.003	0.039 ± 0.011[b]	N/A

[a]Values are mean ± SD for 3 animals.

[b]Mean ± range for 2 animals.

[c]Values for 1 animal.