

ADME NTP Study S0129 Chlorpheniramine maleate

Sex/Species: male F344 rats.

Vehicle: intravenous, not specified; oral, water.

CASRN 113-92-8

Radiolabeled with carbon-14, no specified location; [¹⁴C]Chlorpheniramine maleate

Studies Performed:

- Single 2 mg/kg intravenous dose to rats with sacrifice at 0.25, 0.5, 1, 2, 4, 8, 12, 24, 48, 72, 144, or 216 hours postdose. (n = 3 per time point)
- Single 2 or 20 mg/kg oral gavage dose to rats with sacrifice 9 days postdose. (n = 3 per group)

For the tables with μ Moles chlorpheniramine* in the titles, it is the μ Mole chlorpheniramine maleate equivalents as total ¹⁴C that was measured.

Toxicokinetics:

Parent chlorpheniramine maleate data for the blood percentage dose versus time was best described by the two exponential equation $X = Ae^{-\alpha t} + Be^{-\beta t}$ ($p < 0.01$). The parent data of organ percentage dose versus time was best described by the one exponential equation $X = Ae^{-\alpha t}$ ($p < 0.05$) (Table 15).

The data for tissues using % dose of total ¹⁴C chlorpheniramine equivalents versus time was fit to the equation $X = \sum_{i=1}^n A_i e^{-b_i t}$ where blood used $n=3$ and the rest of the tissues used $n=2$. (Table 16)

The data for intestinal contents was fitted to the equation $X = A_1 e^{-b_2 t} + A_2 e^{-b_3 t} - (A_1 + A_2) e^{-b_1 t}$ reflecting the appearance of ¹⁴C into the intestinal contents. For skin, muscle and fat, the point at 5=9 days is higher than the value at 5=6 days. These terminal half-lives have large errors due to the data variability. The correlation coefficient is represented by r .

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Table 1. Percentage of dose found in excreta vs time from male Fisher 344 rats (n=3) orally administered chlorpheniramine maleate.

Time (Days)	Dose = 2.0 mg/kg ^a			
	Urine(%) ^b	Feces(%) ^b	Urine(%) ^b	Feces(%) ^b
1	49.35±12.9	11.54±7.3	44.91±9.0	0.35±0.2
2	9.21±3.6	7.64±6.9	11.53±3.4	9.19±2.0
3	3.94±1.2	6.89±4.2	4.30±1.9	
4	2.07±0.8	2.92±1.6	2.04±0.8	7.61±5.1
5	1.21±0.3	3.06±1.2	1.42±0.5	1.81±0.7
6	0.98±0.4	2.02±1.1	0.95±0.2	1.16±0.9
7	0.54±0.1	1.08±0.9	0.54±0.1	0.95±0.2
8	0.42±0.1	1.06±0.1	0.33±0.1	0.44±0.3
9	0.18±0.05	0.27±0.05	0.31±0.05	0.44±0.2
Cumulative	67.9±13.5	36.48±11.2	66.33±9.9	28.42±6.0
total % dose excreted ^c	104.38±17.5		94.75±11.6	

^a All doses include a ¹⁴C tracer ≈ 50μCi/kg.

^b Percentages are the mean of three rats ± standard deviation.

^c Analysis of variance between the low and high dose shows no significant difference between the doses (significance of F = 0.817).

Table 2 . Percentage of dose found in major body tissues and excreta nine days after oral administration of chlorpheniramine maleate to male Fisher 344 rats.

Tissue or Excreta	% Dose \pm Standard Deviation ^a	
	Dose = 2.0 mg/kg ^b	Dose = 20 mg/kg ^b
Brain	.0054 \pm .0010	.0076 \pm .0030
Liver	.3947 \pm .0963	.2385 \pm .0605
Lung	.0108 \pm .0036	.0095 \pm .0034
Kidney	.0704 \pm .0155	.0512 \pm .0138
Spleen	.0029 \pm .0003	.0035 \pm .0013
Fat	.1754 \pm .0657	.2080 \pm .0202
Small Intestine	.0339 \pm .0243	.0229 \pm .0041
Large Intestine	.0807 \pm .1043	.0260 \pm .0088
Muscle	.6691 \pm .1112	.8209 \pm .1702
Blood ^c	.1802 \pm .0475	.1388 \pm .0204
Urine ^d	67.90 \pm 13.5	66.33 \pm 9.9
Feces ^d	36.48 \pm 11.2	28.42 \pm 6.0
total % dose recovered ^e	106.00 \pm 17.54	96.28 \pm 11.58

^a % dose is the mean % dose recovered from three animals \pm standard deviation.

^b Dose includes a ¹⁴C tracer \approx 50 μ Ci/kg.

^c Blood samples were obtained via cardiac puncture just prior to termination.

^d Reported value is the cumulative % dose excreted over 9 days.

^e Analysis of variance between the low and high dose shows no significant difference between doses. [Significance of F_(excreta) = 0.817; significance of F_(tissues) = 0.851].

Table 3. μ Moles Chlorpheniramine* Excreted Over Nine Days Following Oral Administration of 2.0 mg/kg Chlorpheniramine Maleate.

Rat #	3	4	5	Mean	S.D.
Day	moles $\times 10^2$				
Urine					
1	29.37	28.17	45.69	34.41	±9.79
2	6.21	4.86	8.34	6.47	±1.75
3	2.58	2.22	3.49	2.76	±0.65
4	1.08	1.09	2.16	1.44	±0.62
5	0.99	1.25	0.89	1.04	±0.19
6	0.64	0.48	0.95	0.69	±0.24
7	0.40	0.25	0.50	0.38	±0.13
8	0.18	0.33	0.23	0.25	±0.08
9	0.09	0.14	0.15	0.13	±0.03
Feces					
1	12.32	4.09	-	(8.20)	
2	10.24	5.60	0.22	5.35	±5.0
3	3.66	2.58	8.36	4.87	±3.1
4	3.52	1.14	1.58	2.08	±1.3
5	1.67	1.62	3.14	2.28	±0.98
6	1.79	0.50	2.04	1.44	±0.83
7	0.06	0.96	1.19	0.74	±0.60
8	-	0.73	0.71	(0.72)	
9	0.16	0.16	0.23	0.183	±0.04
Total μ moles	74.96	56.17	79.87		
μ moles dose	73.83	64.51	71.68		
% recovery	101%	87.07%	111%		

* As total ^{14}C equivalents.

Table 4. μ Moles Chlorpheniramine* Excreted Over Nine Days Following Oral Administration of 20 mg/kg Chlorpheniramine Maleate.

Rat #	6	7	8	
Day	$\mu\text{moles} \times 10^2$			Mean \pm S.D.
<u>Urine</u>				
1	373.6	269.0	243.2	295.3 \pm 69.0
2	92.68	77.43	56.74	75.62 \pm 18.0
3	28.60	32.67	23.78	28.35 \pm 4.45
4	10.97	17.67	10.90	13.18 \pm 3.89
5	8.80	11.29	7.74	9.28 \pm 1.82
6	5.23	7.07	6.20	6.17 \pm 0.92
7	2.71	4.10	3.56	3.46 \pm 0.70
8	2.13	2.66	1.78	2.19 \pm 0.44
9	1.97	2.32	1.73	2.01 \pm 0.30
<u>Feces</u>				
1	3.97	1.04	1.97	2.33 \pm 1.50
2	72.64	63.34	44.75	60.24 \pm 14.2
3	62.14	31.86	34.53	42.84 \pm 16.76
4	45.02	81.58	20.70	49.10 \pm 30.6
5	13.88	15.41	15.79	15.03 \pm 1.01
6	12.36	-	3.43	(7.89)
7	7.73	4.96	5.99	6.23 \pm 1.40
8	1.99	4.93	1.45	2.79 \pm 1.87
9	2.24	3.60	2.71	2.85 \pm 0.69
Total μ moles	748.66	620.85	486.69	
μ moles dose	693.88	620.84	647.36	
% recovery	108%	100%	74.0%	

* As total ^{14}C equivalents

Table 5 μ Moles Chlorpheniramine* Remaining in Tissues Nine Days Following Oral Administration of 2.0 mg/kg and 20 mg/kg Chlorpheniramine Maleate.

Tissues	μ moles x 10			Mean +S.D.
Low Dose (2.0 mg/kg)				
Rat #	3	4	5	
Brain	0.004	0.003	0.004	0.004±0.001
Liver	0.373	0.219	0.241	0.278±0.08
Lung	0.010	0.005	0.006	0.007±0.003
Kidney	0.057	0.033	0.058	0.049±0.014
Spleen	0.002	0.002	0.002	0.002±0.00
Fat	0.183	0.077	0.112	0.124±0.054
Small Intestine	0.046	0.013	0.141	0.067±0.066
Large Intestine	0.148	0.013	0.014	0.058±0.078
Muscle	0.485	0.362	0.512	0.453±0.080
Blood		0.022	0.153	(0.088)
High Dose (20 mg/kg)				
Rat #	6	7	8	
Brain	0.067	0.055	0.036	0.053±0.02
Liver	14.87	1.53	0.148	5.52±8.13
Lung	0.076	0.72	0.039	0.278±0.38
Kidney	0.366	0.397	0.242	0.335±0.08
Spleen	0.021	0.031	0.016	0.023±0.01
Fat	1.58	1.17	1.35	1.37±0.21
Small Intestine	0.180	0.112	0.157	0.15±0.03
Large Intestine	0.228	0.179	0.105	0.171±0.06
Muscle	5.22	6.29	4.53	5.35±0.89
Blood	0.967	0.979	0.767	0.904±0.12

* As total ^{14}C equivalents.

Table 6. Tissue to Blood Ratios 9 Days Following Oral Administration of 2.0 mg/kg and 20 mg/kg Chlorpheniramine Maleate.

<u>Low Dose (2 mg/kg)</u>				
<u>Rat #</u>	<u>3*</u>	<u>4</u>	<u>5</u>	<u>Mean ±S.D.</u>
<u>Tissues</u>				
Brain	-	0.35	0.27	(0.31)
Liver	-	10.70	8.84	(9.77)
Lung	-	0.93	0.99	(0.96)
Kidney	-	4.61	5.52	(5.07)
Spleen	-	1.76	1.89	(1.83)
Fat	-	1.06	0.95	(1.01)
Small Intestine	-	1.09	0.78	(0.94)
Large Intestine	-	1.63	1.12	(1.38)
Muscle	-	0.69	0.66	(0.68)
Blood	-	1	1	1
<u>High Dose (20 mg/kg)</u>				
<u>Rat #</u>	<u>6</u>	<u>7</u>	<u>8</u>	<u>Mean ±S.D.</u>
<u>Tissues</u>				
Brain	0.80	0.62	0.51	0.64±0.15
Liver	10.60	7.91	7.99	8.83±1.53
Lung	1.92	1.84	1.38	1.71±0.29
Kidney	6.10	5.06	4.29	5.15±0.91
Spleen	2.53	2.10	2.14	2.26±0.24
Fat	2.09	1.53	2.26	1.96±0.38
Small Intestine	1.86	1.34	1.95	1.72±0.33
Large Intestine	2.21	2.16	2.58	2.32±0.23
Muscle	0.97	1.15	1.06	1.06±0.09
Blood	1	1	1	1

No blood could be recovered due to technical error.

Table 7. Percentage of Dose as Parent Chlorpheniramine in Urine and Feces 3 Days After the Administration of Chlorpheniramine Maleate (2 mg/kg).

Rat #	14	15	16	
Urine	Percentage of Dose			Mean ±S.D.
Day 1	1.38×10^{-2}	7.11×10^{-2}	1.72×10^{-1}	$8.56 \times 10^{-2} \pm 8.01 \times 10^{-2}$
Day 2	I.S.	1.57×10^{-2}	9.03×10^{-3}	$1.24 \times 10^{-2} \pm 4.71 \times 10^{-3}$
Day 3	7.52×10^{-1}	3.40×10^{-3}	5.90×10^{-3}	$3.35 \times 10^{-3} \pm 2.57 \times 10^{-3}$
Feces	Percentage of Dose			Mean S.D.
Day 1	2.25×10^{-3}	2.88×10^{-4}	1.34×10^{-3}	$1.29 \times 10^{-3} \pm 9.82 \times 10^{-4}$
Day 2	1.64×10^{-4}	2.93×10^{-4}	6.40×10^{-4}	$3.66 \times 10^{-4} \pm 2.46 \times 10^{-4}$
Day 3	1.37×10^{-4}	1.29×10^{-4}	2.40×10^{-4}	$1.69 \times 10^{-4} \pm 6.19 \times 10^{-5}$

I.S. - Insufficient sample for analysis

Table 8.

Summary of Percent of Dose as Parent Chlorpheniramine in Selected Tissues vs Time After a Single iv Dose of Chlorpheniramine Maleate (2 mg/kg)

TIME Tissue	15 min	30 min	1 hour	2 hour	4 hour	8 hour
Brain	0.337±0.05	0.491±0.156				
Lung	1.98±1.36	1.15±0.30	0.974±0.665	0.313±0.181	0.124±0.076	0.035±0.025
Liver	5.24±2.75	5.43±0.19	3.13±1.34	0.786±0.113	0.285±0.107	0.0231±0.0117*
Kidney	1.49±0.25	1.39±0.36	0.421±0.099	0.190±0.028	0.108±0.040	0.0160±0.0056
Small Intestine	1.46±0.23	2.04±0.84	1.11±0.17	0.344±0.089	0.141±0.011	0.0319±0.0104
Muscle	13.50±0.32*	14.18±1.71	6.19±1.43	3.42±1.40*	1.83±0.064	0.483±0.255*
Skin	2.82±0.99	3.21±0.28	2.12±0.98	0.993±0.157	0.587±0.087	0.219±0.0635
Blood	1.47±0.26	0.884±0.13	0.425±0.21	0.154±0.04	0.050±0.028	N.D.

N.D. none detected

Average data ±Std. Dev. of n=3 rats except * where n=2.

Table 9. Summary of $\mu\text{Moles Chlorpheniramine}^*$ Found in Tissues Following iv Injection of 2.0 mg/kg Chlorpheniramine Maleate.

	$\mu\text{moles chlorpheniramine} \times 10^2$					
	15 min	30 min	1 hr	2 hrs	4 hrs	8 hrs
Brain	0.97±0.34	0.762±0.42	0.466±0.07	0.317±0.03	0.217±0.03	0.138±0.01
Lung	3.45±2.0	3.03±0.51	4.34±2.33	3.19±0.95	2.69±0.46	2.15±0.85
Liver	9.14±0.4	10.46±1.68	11.80±0.09	7.00±1.21	4.97±1.03	3.88±0.23
Kidney	2.50±0.23	2.38±0.07	3.04±0.20	2.32±0.19	1.66±0.28	1.06±0.12
Small Intestine	2.69±0.51	4.66±2.15	3.51±0.51	3.42±0.42	2.42±0.35	2.16±0.62
Large Intestine	0.68±0.28	0.664±0.13	0.649±0.11	0.489±0.02	0.512±0.17	0.568±0.35
Fat	1.71±0.40	2.13±0.26	1.58±0.05	1.15±0.11	0.902±0.29	0.484±0.03
Muscle	26.46±4.8	21.56±2.03	26.14±1.60	18.53±2.2	10.96±1.76	6.45±1.04
Skin	4.98±1.2	5.83±0.61	5.62±0.61	4.98±0.68	2.85±0.36	1.90±0.19
Blood	1.41±0.21	1.09±0.10	1.35±0.05	0.827±0.02	0.539±0.15	0.495±0.06
Injection Site	2.80±2.1	2.19±1.55	3.00±3.3	0.505±0.02	0.618±0.79	0.179±0.06
Intestinal Contents	2.58±0.57	3.03±0.90	7.21±0.36	8.28±2.71	11.96±1.99	15.78±0.21
Bladder Contents	(0.178)	(1.193)	(1.17)	-	(6.62)	(7.69)
Feces	-	-	-	-	-	-
Urine	-	-	-	-	-	-

* As total ^{14}C equivalents.

Table 10. Summary of μ Moles Chlorpheniramine Found in Tissues Following iv Injection of 2.0 mg/kg Chlorpheniramine Maleate.

	μ moles chlorpheniramine $\times 10^2$					
	12 hrs	24 hrs	2 days	3 days	6 days	9 days
Brain	0.139 \pm 0.02	0.023 \pm 0.004	0.014 \pm 0.01	0.003 \pm 0.001	0.005 \pm 0.01	0.002 \pm 0.001
Lung	2.12 \pm 1.31	0.194 \pm 0.05	0.074 \pm 0.05	0.016 \pm 0.015	0.007 \pm 0.01	0.004 \pm 0.001
Liver	3.52 \pm 0.38	1.37 \pm 0.24	0.743 \pm 0.17	0.517 \pm 0.08	0.266 \pm 0.04	0.144 \pm 0.03
Kidney	0.859 \pm 0.14	0.197 \pm 0.03	0.096 \pm 0.05	0.038 \pm 0.01	0.023 \pm 0.01	0.017 \pm 0.002
Small Intestine	2.43 \pm 0.78	0.773 \pm 0.56	0.185 \pm 0.05	0.056 \pm 0.02	0.030 \pm 0.01	0.011 \pm 0.004
Large Intestine	0.531 \pm 0.11	0.516 \pm 0.49	0.124 \pm 0.10	0.032 \pm 0.02	0.016 \pm 0.01	0.007 \pm 0.00
Fat	0.651 \pm 0.25	0.272 \pm 0.03	0.180 \pm 0.06	0.121 \pm 0.03	0.083 \pm 0.01	0.153 \pm 0.07
Muscle	5.99 \pm 1.24	1.37 \pm 0.22	0.661 \pm 0.28	0.298 \pm 0.12	0.189 \pm 0.02	0.281 \pm 0.16
Skin	1.83 \pm 0.48	0.521 \pm 0.01	0.304 \pm 0.11	0.194 \pm 0.04	0.155 \pm 0.03	0.282 \pm 0.25
Blood	0.619 \pm 0.06	0.215 \pm 0.04	0.115 \pm 0.04	0.067 \pm 0.01	0.055 \pm 0.01	0.048 \pm 0.003
Injection Site	0.481 \pm 0.27	0.038 \pm 0.03	0.079 \pm 0.06	0.037 \pm 0.03	0.033 \pm 0.02	0.037 \pm 0.008
Intestinal Contents	16.79 \pm 1.1	5.43 \pm 2.57	2.22 \pm 0.22	0.602 \pm 0.36	0.241 \pm 0.10	-
Bladder Contents	2.29 \pm 2.5	-	-	-	-	-
Feces	-	11.43 \pm 2.31	17.04 \pm 2.33	19.18 \pm 2.35	20.58 \pm 2.35	21.01 \pm 2.35
Urine	-	36.17 \pm 2.52	39.74 \pm 2.53	40.75 \pm 2.53	41.77 \pm 2.55	42.41 \pm 2.55

* As total 14 C equivalents.

Table 11. μ Moles Chlorpheniramine* Excreted vs Time Following iv Administration of 2.0 mg/kg Chlorpheniramine Maleate.

Rat #	14	15	16	
Day	$\mu\text{moles} \times 10^2$			Mean \pm S.D.
<u>Urine</u>				
1	33.94	38.91	35.66	36.17 \pm 2.52
2	3.41	3.83	3.47	3.57 \pm 0.23
3	1.06	0.897	1.07	1.01 \pm 0.10
4	0.333	0.414	0.504	0.417 \pm 0.08
5	0.291	0.325	0.476	0.364 \pm 0.09
6	0.231	0.215	0.273	0.240 \pm 0.03
7	0.232	0.152	0.239	0.208 \pm 0.05
8	0.338	0.389	0.235	0.321 \pm 0.08
9	0.127	0.079	0.120	0.109 \pm 0.03
<u>Feces</u>				
1	9.34	11.03	13.91	11.43 \pm 2.31
2	5.85	5.85	5.23	5.64 \pm 0.36
3	2.20	2.31	1.82	2.11 \pm 0.26
4	0.718	0.761	0.812	0.764 \pm 0.047
5	0.312	0.438	0.390	0.380 \pm 0.064
6	0.193	0.310	0.256	0.253 \pm 0.059
7	0.167	0.187	0.174	0.176 \pm 0.010
8	0.126	0.102	0.147	0.125 \pm 0.023
9	0.112	0.134	0.151	0.132 \pm 0.020

* As total ^{14}C equivalents

Table 12. Tissue (g):Blood (ml) Ratios \pm S.D. Following iv Administration of 2.0 mg/kg Chlorpheniramine Maleate (n=3).

Time	15 min	30 min	1 hr	2 hrs	4 hrs	8 hrs	12 hrs	24 hrs	2 days	3 days	6 days	9 days
Tissue												
Brain	8.90 ± 1.51	7.55 ± 3.96	4.52 ± 0.90	3.89 ± 0.07	4.32 ± 0.62	3.01 ± 0.41	2.53 ± 0.52	1.24 ± 0.09	0.71 ± 0.27	0.46 ± 0.11	0.81 ± 0.68	0.58 ± 0.14
Lung	35.90 ± 5.27	49.80 ± 15.71	58.27 ± 2.141	66.29 ± 19.50	84.39 ± 19.66	68.86 ± 22.8	52.50 ± 24.06	14.00 ± 2.14	8.36 ± 5.19	3.22 ± 2.14	2.01 ± 0.68	1.50 ± 0.25
Liver	14.84 ± 2.38	21.30 ± 3.15	20.86 ± 0.29	19.83 ± 3.92	21.11 ± 0.54	18.94 ± 4.85	12.88 ± 3.53	12.47 ± 1.04	14.72 ± 2.02	15.26 ± 1.95	9.60 ± 1.19	5.82 ± 1.45
Small Intestine	11.09 ± 2.43	17.87 ± 7.48	16.13 ± 5.40	17.44 ± 2.35	19.21 ± 6.62	19.15 ± 6.48	15.50 ± 5.36	11.62 ± 7.68	5.35 ± 1.68	2.58 ± 0.87	1.62 ± 0.24	0.73 ± 0.07
Large Intestine	4.39 ± 2.05	5.38 ± 1.22	5.13 ± 0.93	5.06 ± 0.81	9.21 ± 5.97	9.41 ± 6.14	6.95 ± 1.52	14.03 ± 4.53	7.67 ± 2.81	3.07 ± 1.06	1.89 ± 0.04	1.15 ± 0.17
Fat	1.60 ± 0.54	2.52 ± 0.17	1.52 ± 0.08	1.79 ± 0.14	2.25 ± 0.90	1.26 ± 0.18	1.39 ± 0.64	1.64 ± 0.16	2.32 ± 1.51	2.30 ± 0.60	1.99 ± 0.54	4.12 ± 1.97
Muscle	3.38 ± 0.51	3.56 ± 0.03	3.53 ± 0.22	4.03 ± 0.58	3.76 ± 0.67	2.35 ± 0.20	1.77 ± 0.50	1.16 ± 0.20	1.01 ± 0.15	0.79 ± 0.28	0.62 ± 0.11	1.04 ± 0.56
Skin	1.97 ± 0.25	3.01 ± 0.16	2.37 ± 0.23	3.39 ± 0.54	3.06 ± 0.45	1.84 ± 0.39	1.71 ± 0.57	1.39 ± 0.24	1.54 ± 0.52	1.61 ± 0.18	1.57 ± 0.12	3.19 ± 2.71
Blood	1	1	1	1	1	1	1	1	1	1	1	1

Table 13. Percentage of Dose Found in Excreta vs Time after IV Administration of 2.0 mg/kg Chlorpheneramine Maleate to Male Fisher 344 Rats (n = 3).

Time (Days)	Percent of Dose ± Standard Deviation		
	Urine	Feces	Total
1	51.98±0.81	16.45±3.4	68.43±3.49
2	5.14±0.05	8.13±0.60	13.27±0.60
3	1.46±0.22	3.03±0.34	4.49±0.40
4	0.60±0.12	1.10±0.08	1.70±0.14
5	0.52±0.14	0.54±0.06	1.06±0.15
6	0.35±0.06	0.36±0.06	0.71±0.08
7	0.30±0.08	0.25±0.01	0.55±0.08
8	0.46±0.10	0.18±0.04	0.64±0.11
9	<u>0.15±0.05</u>	<u>0.19±0.03</u>	<u>0.34±0.06</u>
Cumulative	60.96±0.87	30.23±3.5	91.19±3.6

Table 14. Summary of the % Dose Recovered in Tissues and Excreta vs Time from Rats (n=3) following iv Administration of 2 mg/kg Chlorpheniramine Maleate.

	15 minutes	30 minutes	1 hour	2 hours	4 hours	8 hours	12 hours	24 hours	2 days	3 days	6 days	9 days
Brain	1.37 ±0.69	1.07 ±0.50	0.53 ±0.08	0.49 ±0.03	0.24 ±0.17	0.21 ±0.02	0.20 ±0.03	0.04 ±0.01	0.01 ±0.01	<0.01 ±0.003	<0.01 ±0.001	<0.01 ±0.001
Lung	4.50 ±2.16	4.40 ±1.07	4.89 ±2.49	5.00 ±1.71	4.02 ±0.52	3.22 ±1.33	3.11 ±1.9	0.30 ±0.08	0.13 ±0.10	0.03 ±0.02	0.01 ±0.004	<0.01 ±0.001
Liver	12.46 ±2.23	14.91 ±1.17	13.41 ±0.49	10.79 ±1.36	7.44 ±0.92	5.78 ±0.16	5.16 ±0.56	2.14 ±0.35	1.23 ±0.12	0.84 ±0.06	0.43 ±0.07	0.21 ±0.04
Kidney	3.40 ±0.53	3.42 ±0.20	3.45 ±0.22	3.61 ±0.34	2.48 ±0.21	1.59 ±0.21	1.26 ±0.21	0.31 ±0.04	0.17 ±0.10	0.06 ±0.01	0.04 ±0.01	0.02 ±0.002
Small Intestine	3.60 ±0.33	6.66 ±3.04	3.99 ±0.72	5.32 ±0.83	3.69 ±0.77	3.21 ±0.84	3.58 ±1.2	1.22 ±0.92	0.30 ±0.05	0.09 ±0.03	0.05 ±0.01	0.02 ±0.003
Large Intestine	0.92 ±0.35	0.95 ±0.09	0.74 ±0.12	0.76 ±0.07	0.77 ±0.25	0.86 ±0.56	0.78 ±0.18	0.81 ±0.76	0.21 ±0.18	0.05 ±0.03	0.03 ±0.004	0.01 ±0.001
Fat	2.40 ±1.03	3.05 ±0.12	1.79 ±0.11	1.80 ±0.27	1.38 ±0.55	0.72 ±0.03	0.96 ±0.38	0.42 ±0.04	0.31 ±0.14	0.19 ±0.03	0.13 ±0.03	0.22 ±0.09
Muscle	35.33 ±0.75	30.87 ±1.5	29.68 ±2.0	28.72 ±2.90	16.39 ±1.15	9.65 ±1.90	8.80 ±1.9	2.15 ±0.34	1.10 ±0.50	0.47 ±0.14	0.31 ±0.05	0.41 ±0.24
Skin	6.64 ±0.78	8.34 ±0.15	6.38 ±0.64	7.70 ±0.69	4.27 ±0.24	2.84 ±0.38	2.69 ±0.72	0.82 ±0.02	0.53 ±0.24	0.32 ±0.08	0.25 ±0.04	0.39 ±0.33
Blood	1.91 ±0.27	1.56 ±0.06	1.53 ±0.03	1.29 ±0.09	0.80 ±0.16	0.74 ±0.11	0.91 ±0.07	0.34 ±0.05	0.19 ±0.07	0.11 ±0.02	0.09 ±0.01	0.07 ±0.003
Intestinal Contents	3.50 ±0.83	4.35 ±1.31	8.20 ±0.07	12.72 ±3.67	18.01 ±2.93	23.51 ±0.80	24.64 ±2.0	8.45 ±3.9	3.75 ±0.57	0.97 ±0.59	0.39 ±0.15	0.19 ±0.03
Bladder Contents	0.24 ±0.07	1.58 ±1.76	(1.38)	--	9.66 ±4.12	4.49 ±1.3	3.37 ±3.6	--	--	--	--	--
Injection Site	3.67 ±2.45	3.08 ±2.2	3.49 ±3.9	0.79 ±0.07	0.87 ±1.07	0.26 ±0.08	0.71 ±0.42	0.06 ±0.04	0.14 ±0.11	0.06 ±0.04	0.05 ±0.03	0.05 ±0.01

Table 14. Summary of the % Dose Recovered in Tissues and Excreta vs Time from Rats (n=3) following iv Administration of 2 mg/kg Chlorpheniramine Maleate.--(Continued).

	15 minutes	30 minutes	1 hour	2 hours	4 hours	8 hours	12 hours	24 hours	2 days	3 days	6 days	9 days
Urine (cumulative)	**	**	**	**	**	**	**	51.98 ±0.81	57.12 ±0.81	58.58 ±0.84	60.05 ±0.86	60.96 ±0.87
Feces	--	--	--	--	--	--	--	16.45 ±3.4	24.58 ±3.45	27.61 ±3.46	29.61 ±3.47	30.04 ±3.50
Total % Dose Recovered	79.87 ±3.25	83.70 ±2.91	78.55 ±5.94	78.98 ±2.95	66.90 ±10.27	55.58 ±2.85	56.17 ±12.03	85.48 ±5.14	89.79 ±3.97	89.51 ±3.66	91.46 ±3.58	92.62 ±3.61

* Percent dose for time points 15 minutes thru 12 hours excludes dose in excreta.

** Urine was not collected at these time points and probably accounts for the lower recoveries.

Table 15. Parent chlorpheniramine.

Organ	A %	α min^{-1}	$T_{1/2}^{\alpha}$ min.	B %	β min^{-1}	$T_{1/2}^{\beta}$ min.	r
Lung	1.417 ± 0.353	0.008354 ± 0.001101	83.0 ± 10.9	-	-	-	0.967
Liver	5.665 ± 1.120	0.011831 ± 0.000874	58.6 ± 4.3	-	-	-	0.989
Kidney	1.108 ± 0.329	0.009283 ± 0.001314	74.7 ± 10.6	-	-	-	0.962
Small Intestine	1.651 ± 0.394	0.008767 ± 0.001054	79.1 ± 9.5	-	-	-	0.972
Muscle	11.895 ± 2.349	0.007061 ± 0.000873	98.2 ± 12.1	-	-	-	0.971
Skin	2.852 ± 0.446	0.005706 ± 0.000692	121.5 ± 14.7	-	-	-	0.972
Blood	2.009 ± 0.136	0.0393 ± 0.00401	17.7 ± 1.8	0.376 ± 0.070	0.00843 ± 0.000829	82.3 ± 8.1	1.000

Table 16. Total ^{14}C in Tissue.

	A_1 %	b_1 hr^{-1}	$T_{1/2}^{b1}$ hr	A_2 %	b_2 hr^{-1}	$T_{1/2}^{b2}$ hr	A_3 %	b_3 hr^{-1}	$T_{1/2}^{b3}$ hr	r
Blood	3.578 ± 7.402	5.013 ± 7.065	0.138 ± 0.195	0.918 ± 0.201	0.04649 ± 0.02074	14.91 ± 6.65	0.095 ± 0.105	0.001221 ± 0.006043	567.69 ± 2809.61	0.975
Muscle	-	-	-	31.339 ± 3.983	0.12423 ± 0.01643	5.58 ± 0.74	0.785 ± 0.243	0.004059 ± 0.002153	170.77 ± 90.58	0.993
Skin	-	-	-	7.143 ± 0.788	0.10760 ± 0.01602	6.44 ± 0.96	0.367 ± 0.098	0.0005694 ± 0.0018512	1217.33 ± 3957.71	0.990
Brain	1.433 ± 0.657	1.6112 ± 0.8424	0.430 ± 0.225	0.386 ± 0.073	0.97869 ± 0.00760	8.81 ± 0.85	-	-	-	0.991
Liver	-	-	-	11.686 ± 0.794	0.11662 ± 0.01323	5.94 ± 0.67	1.836 ± 0.235	0.010082 ± 0.000912	68.75 ± 6.22	0.998
Fat	-	-	-	2.007 ± 0.330	0.10709 ± 0.02951	6.47 ± 1.78	0.242 ± 0.081	0.001586 ± 0.002359	437.04 ± 650.05	0.973
Kidney	-	-	-	3.632 ± 0.356	0.10961 ± 0.01302	6.32 ± 0.75	0.159 ± 0.041	0.009698 ± 0.001740	71.47 ± 12.82	0.996
Lung	-	-	-	5.461 ± 0.927	0.09593 ± 0.01707	7.23 ± 1.29	0.083 ± 0.100	0.014856 ± 0.009542	46.66 ± 29.97	0.990
Small Intestine	-	-	-	5.242 ± 0.582	0.06692 ± 0.00888	10.36 ± 1.37	0.123 ± 0.095	0.007924 ± 0.004270	87.47 ± 47.14	0.994
Intestinal Content	41.031 ± 11.415	0.30943 ± 0.07937	-	1.131 ± 0.906	0.06074 ± 0.01121	11.41 ± 2.11	-	0.008099 ± 0.004330	85.58 ± 45.76	0.994