

ADME NTP Study S0108 Butanal oxime

The contract laboratory abbreviation for the test article is BOX.

Sex/Species: male F344 rats.

Vehicles: intravenous, isotonic saline; oral, water; dermal, acetone.

CASRN 110-69-0

Radiolabeled with carbon-14 in the 1 position; Butanol oxime, [1-¹⁴C, E and Z isomers]-

Studies Performed:

1. Single 1.98 mg BOX/kg oral gavage dose with sacrifice 72 hours postdose.
2. Single 20.0 mg BOX/kg oral gavage dose with sacrifice 72 hours postdose.
3. Single 2.00 mg BOX/kg intravenous dose with sacrifice 72 hours postdose.
4. Single 2.21mg BOX/kg dermal dose with sacrifice 72 hours postdose.
5. Single 20.8 mg BOX/kg dermal dose with sacrifice 72 hours postdose.
6. Single 20.0 mg BOX/kg oral administration with no pretreatment, pretreatment with 1-aminobenzotriazole (inhibitor of cytochrome P-450), or pretreatment with pentachlorophenol (inhibitor of sulfation) and sacrifice 24 hours post radiolabeled dose.

An additional *in vitro* test of volatilization of butanal oxime from skin (not shown) was performed. It resulted in a total recovery of radioactivity from the skin 3 minutes after dermal application of butanal oxime of $30.0 \pm 1.9\%$ and $36.2 \pm 0.9\%$ for the 2 and 20 mg/kg equivalent, respectively

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Table 1

Cumulative Excretion
of Radioactivity 72 Hours After Oral Administration
of ^{14}C -BOX to Male F-344 Rats (N=3)

End of Collection Period (h)	% of Dose Appearing in:				Total
	Urine	Breath	CO ₂	Feces	
			<u>1.98 mg/kg</u>		
2		2.6 ± 2.8	15.0 ± 3.7		17.5 ± 5.9
4		2.8 ± 2.9	24.0 ± 3.7		26.8 ± 5.4
8	31.4 ± 2.1	3.1 ± 3.0	29.2 ± 2.5	0.1 ± 0.1	63.9 ± 4.2
12		3.3 ± 3.0	30.8 ± 2.1		34.2 ± 3.7
24	<u>36.4 ± 3.1</u>	3.7 ± 3.0	32.1 ± 2.1	0.5 ± 0.3	<u>72.7 ± 2.2</u>
48	39.6 ± 4.5	3.9 ± 3.0	33.5 ± 2.1	1.2 ± 0.5	78.1 ± 2.1
72	42.0 ± 4.2	4.0 ± 3.1	34.2 ± 2.1	1.9 ± 0.7	82.1 ± 2.1
			<u>20.0 mg/kg</u>		
2		1.8 ± 0.3	7.1 ± 1.6		8.9 ± 1.9
4		2.2 ± 0.4	11.1 ± 2.4		13.3 ± 2.9
8	22.8 ± 2.5	2.4 ± 0.5	20.8 ± 3.6	0.2 ± 0.1	46.2 ± 6.2
12		2.5 ± 0.5	26.0 ± 2.6		28.6 ± 2.7
24	<u>36.9 ± 3.2</u>	2.7 ± 0.5	29.2 ± 1.3	0.9 ± 0.5	<u>69.8 ± 2.8</u>
48	42.3 ± 3.6	2.9 ± 0.5	30.2 ± 1.5	1.5 ± 0.2	76.9 ± 2.6
72	44.7 ± 3.2	2.9 ± 0.5	30.7 ± 1.5	1.9 ± 0.5	80.2 ± 1.9

Table 2

**Tissue Distribution
of Radioactivity 72 Hours after Oral Administration
of ¹⁴C-BOX to Male F-344 Rats (N=3)**

Tissue	ng-eq BOX per g Tissue	Tissue Blood Ratio	% Dose in Total Tissue
1.98 mg/kg			
Adipose	93 ± 20	0.17 ± 0.05	0.32 ± 0.06
Blood	558 ± 65	Unity	1.41 ± 0.16
Kidney	505 ± 11	0.92 ± 0.12	0.17 ± 0.01
Liver	822 ± 20	1.49 ± 0.16	1.45 ± 0.15
Muscle	152 ± 29	0.27 ± 0.03	3.56 ± 0.60
Skin	624 ± 87	1.12 ± 0.07	5.18 ± 0.77
Testis	175 ± 12	0.32 ± 0.02	0.09 ± 0.01
20.0 mg/kg			
Adipose	573 ± 94	0.17 ± 0.04	0.20 ± 0.03
Blood	3436 ± 291	Unity	0.89 ± 0.07
Kidney	2843 ± 176	0.83 ± 0.04	0.10 ± 0.01
Liver	3330 ± 73	0.98 ± 0.10	0.65 ± 0.07
Muscle	1134 ± 50	0.33 ± 0.02	2.72 ± 0.10
Skin	4723 ± 503	1.39 ± 0.25	4.02 ± 0.44
Testis	2002 ± 11	0.59 ± 0.05	0.11 ± 0.01

Table 3

Cumulative Excretion
of Radioactivity 72 Hours After Intravenous Administration
of ^{14}C -BOX (2.00 mg/kg) to Male F-344 Rats (N=3)

End of Collection Period (h)	% of Dose Appearing in:				
	Urine	Breath	CO ₂	Feces	Total
2		0.7 ± 0.1	5.3 ± 0.1		6.0 ± 0.1
4		1.0 ± 0.0	9.1 ± 0.5		10.0 ± 0.4
8	33.7 ± 1.0	1.3 ± 0.1	11.5 ± 0.6	0.1 ± 0.1	46.5 ± 1.3
12		1.5 ± 0.1	12.2 ± 0.6		13.7 ± 0.5
24	43.8 ± 1.7	1.9 ± 0.1	13.0 ± 0.6	1.0 ± 0.2	59.8 ± 1.7
48	48.3 ± 1.7	2.1 ± 0.1	13.6 ± 0.8	2.2 ± 0.3	66.2 ± 1.5
72	52.7 ± 0.5	2.2 ± 0.1	14.1 ± 0.8	2.9 ± 0.2	71.9 ± 0.2

Table 4

Tissue Distribution
of Radioactivity 72 Hours after Intravenous Administration
of ¹⁴C-BOX (2.00 mg/kg) to Male F-344 Rats (N=3)

Tissue	ng-eq DEA [sic] per g Tissue	Tissue Blood Ratio	% Dose in Total Tissue
Adipose	97 ± 4	0.15 ± 0.03	0.34 ± .02
Blood	668 ± 116	Unity	1.72 ± .24
Kidney	514 ± 35	0.78 ± 0.12	0.18 ± .01
Liver	873 ± 30	1.33 ± 0.24	1.59 ± .06
Muscle	179 ± 29	0.27 ± 0.06	4.25 ± .67
Skin	885 ± 95	1.34 ± 0.19	7.45 ± .64
Testis	309 ± 40	0.47 ± 0.04	0.17 ± .01

Table 5

Disposition of Radioactivity 72 Hours After Dermal Application
of [¹⁴C]BOX to Male F-344 Rats (N=3)

	% of Dose	
	20.8 mg/kg	2.21 mg/kg
<u>Absorbed</u>		
Tissues	2.4 ± 0.6	1.6 ± 0.8
Dose site	0.9 ± 0.2	1.3 ± 0.4
Feces	0.7 ± 0.4	0.2 ± 0.1
Urine	7.4 ± 1.9	3.5 ± 1.3
CO ₂	4.6 ± 2.9	1.5 ± 0.5
Total	16.0 ± 3.2	8.2 ± 2.3
<u>Unabsorbed</u>		
Appliance	3.0 ± 0.6	1.7 ± 0.2
Skin wash	1.6 ± 0.6	0.8 ± 1.1
Gauze	2.9 ± 0.5	1.5 ± 1.8
Total	7.5 ± 1.7	4.1 ± 2.6
Volatiles Traps	51.1 ± 4.5	18.7 ± 1.0
<u>Total Recovery</u>	74.6 ± 8.7	30.9 ± 1.16

Table 6

Cumulative Excretion
of Radioactivity 72 Hours After Dermal Application
of ^{14}C -BOX to Male F-344 Rats (N=3)

End of Collection Period (h)	% of Dose Appearing in:				Total
	Urine	Breath	CO ₂	Feces	
			<u>2.21 mg/kg</u>		
2		3.7 ± 2.4	0.1 ± 0.1		3.8 ± 2.5
4		8.7 ± 0.2	0.4 ± 0.1		9.0 ± 0.2
8	1.3 ± 0.3	12.5 ± 0.2	0.6 ± 0.1	0.0 ± 0.1	14.4 ± 0.5
12		14.0 ± 0.4	0.7 ± 0.1		14.7 ± 0.4
24	2.0 ± 0.4	15.3 ± 0.6	0.8 ± 0.2	0.1 ± 0.1	18.3 ± 0.0
48	2.9 ± 1.1	17.6 ± 1.0	1.2 ± 0.4	0.2 ± 0.1	21.8 ± 2.5
72	3.5 ± 1.2	18.7 ± 1.0	1.5 ± 0.5	0.3 ± 0.1	23.9 ± 2.7
			<u>20.8 mg/kg</u>		
2		10.9 ± 1.1	1.5 ± 2.0		12.3 ± 3.0
4		22.1 ± 2.0	1.8 ± 1.9		23.9 ± 3.8
8	2.1 ± 0.3	35.1 ± 2.9	2.3 ± 1.7	0.2 ± 0.1	39.6 ± 4.2
12		41.4 ± 3.3	2.6 ± 1.6		44.0 ± 4.9
24	5.3 ± 1.7	47.0 ± 3.2	3.6 ± 2.5	0.4 ± 0.3	56.3 ± 4.7
48	6.5 ± 2.0	49.6 ± 3.8	4.4 ± 2.9	0.6 ± 0.4	61.1 ± 5.8
72	7.4 ± 1.9	51.1 ± 4.5	4.6 ± 2.9	0.7 ± 0.4	63.9 ± 6.7

Table 7

Tissue Distribution
of Radioactivity 72 Hours after Dermal Application
of ^{14}C -BOX to Male F-344 Rats (N=3)

Tissue	ng-eq BOX per g Tissue	Tissue Blood Ratio	% Dose in Total Tissue
20.8 mg/kg			
Adipose	164 ± 44	0.15 ± 0.01	0.05 ± 0.02
Blood	1109 ± 266	Unity	0.27 ± 0.07
Kidney	1264 ± 311	1.14 ± 0.03	0.05 ± 0.01
Liver	1270 ± 68	1.20 ± 0.33	0.24 ± 0.07
Muscle	279 ± 25	0.26 ± 0.04	0.63 ± 0.08
Skin	1402 ± 362	1.26 ± 0.06	1.13 ± 0.34
Testis	509 ± 46	0.47 ± 0.09	0.03 ± 0.01
2.21 mg/kg			
Adipose	10 ± 6	0.10 ± 0.00	0.03 ± 0.02
Blood	101 ± 61	Unity	0.23 ± 0.14
Kidney	148 ± 57	1.62 ± 0.38	0.04 ± 0.01
Liver	134 ± 46	1.51 ± 0.42	0.19 ± 0.05
Muscle	19 ± 9	0.19 ± 0.04	0.40 ± 0.19
Skin	95 ± 48	0.98 ± 0.12	0.71 ± 0.35
Testis	31 ± 12	0.34 ± 0.08	0.01 ± 0.01

Table 8

Distribution of Radioactivity in Excreta Collected for 24 Hours
after Oral Administration of ¹⁴C-BOX (20 mg/kg) to Rats*

	Urine	Volatiles	CO ₂
no pretreatment with inhibitor [§]	36.9 ± 3.2	2.7 ± 0.5	29.2 ± 1.3
pretreatment with 1-aminobenzotriazole [†]	16.6 ± 0.4	13.0 ± 0.5	50.4 ± 0.9
pretreatment with pentachlorophenol [†]	44.1 ± 2.4	3.2 ± 0.1	26.4 ± 0.4

* Values are means ± standard deviation.

§ N = 3

† N = 2