

ADME NTP Study S0210 Decabromodiphenyl Ether

The contractor abbreviated the test article as DBBE.

Sex/Species: adult male F344 rats.

Vehicles: intravenous, tetrahydrofuran:Emulphor:water (2:1:2, v/v); dosed feed, powdered Wayne Lab-Blox feed.

CASRN 1163-19-5

Radiolabeled with carbon-14 uniformly in the rings; Decabromodiphenyl Ether, [U-¹⁴C]-

Studies Performed:

- Repeat dosed feed study with rats fed unlabeled DBBE on days 1-7 and 9-11 in the amounts 5.11, 2.54, 0.473, 0.251, 0.0496, or 0.0238% of the diet for groups 1-6, respectively, and on day 8 with [¹⁴C]DBBE in similar amounts with sacrifice 72 hours after the day 8 [¹⁴C]DBBE dose. (See Table 1 for doses; Experiment A; n=3 per group)
- Repeat 10-12 day dosed feed studies with groups 1-6 (See Table 3 for doses)
 1. Repeat 4.80% dosed feed study with rats fed unlabeled DBBE on days 1-7 and day 9 and on day 8 with [¹⁴C]DBBE in similar amounts with sacrifice on day 10. (Group 1; Experiment C; n=3)
 2. Repeat 4.80% dosed feed study with rats fed unlabeled DBBE on days 1-7 and day 9 and on day 8 with [¹⁴C]DBBE in similar amounts with sacrifice on day 11. (Group 2; Experiment C; n=3)
 3. Repeat 4.80% dosed feed study with rats fed unlabeled DBBE on days 1-7 and day 9 and on day 8 with [¹⁴C]DBBE in similar amounts with sacrifice on day 12. (Group 3; Experiment C; n=3)
 4. Repeat 0.0277% dosed feed study with rats fed unlabeled DBBE on days 1-7 and day 9 and on day 8 with [¹⁴C]DBBE in similar amounts with sacrifice on day 10. (Group 4; Experiment C; n=3)
 5. Repeat 0.0277% dosed feed study with rats fed unlabeled DBBE on days 1-7 and day 9 and on day 8 with [¹⁴C]DBBE in similar amounts with sacrifice on day 11. (Group 5; Experiment C; n=3)
 6. Repeat 0.0277% dosed feed study with rats fed unlabeled DBBE on days 1-7 and day 9 and on day 8 with [¹⁴C]DBBE in similar amounts with sacrifice on day 12. (Group 6; Experiment C; n=3)
- Single 1.07 mg/kg intravenous dose to rats with sacrifice 72 hours postdose. (Experiment D; n=3)

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Table 1 (Experiment A)
Food Consumption, DBBE Content of the Diet,
and DBBE Consumed by Rats

Rat Group	Food Consumed (g/day)	DBBE Content of Feed			[¹⁴ C] DBBE Consumed on Day 8	
		%	nCi/g		mg	nCi
I	14.4 ± 1.0 ^{a,b}	5.11 ^c	4.86 ^d	214 ± 5 ^d	716 ± 58	3150 ± 250
II	15.1 ± 1.1	2.54	2.44	219 ± 28	370 ± 10	3320 ± 90
III	16.5 ± 0.7	0.473	0.500	232 ± 23	78.0 ± 5.1	3620 ± 240
IV	17.1 ± 0.3	0.251	0.249	212 ± 19	43.9 ± 2.4	3740 ± 200
V	16.9 ± 0.5	0.0496	0.0521	206 ± 8	8.72 ± 0.40	3460 ± 160
VI	17.0 ± 1.5	0.0238	0.0261	215 ± 23	4.37 ± 0.68	3610 ± 560

^aThe numbers are the means ± std. dev. for 3 rats.

^bSignificantly less ($P < 0.025$) than values for Groups III, IV, V, and VI.

^cContent of the feed containing unlabeled DBBE and fed on Days 1-7 and 9-11; the values are the averages of those derived by analysis before and after feeding.

^dContent of the feed containing [¹⁴C] DBBE and fed on Day 8. The values for % DBBE are averages of those derived by analysis before and after feeding.

Table 2 (Experiment A)

Disposition of Radioactivity from [¹⁴C] DBBE in Rats
 Fed Unlabeled DBBE in the Diet on Days 1-7 and
 9-11 and [¹⁴C] DBBE in the Diet on Day 8

Rat Group	Feces (Days 8-12)	Liver (Day 12)	Fat ^a (Day 12)
	(% of dose)		
I	95.5 ± 9.9 ^b	0.008 ± 0.002	0.096 ± 0.041
II	93.0 ± 5.0	0.006 ± 0.001	0.088 ± 0.022
III	91.3 ± 4.0	0.011 ± 0.003	0.126 ± 0.017
IV	101 ± 4	0.016 ± 0.003	0.090 ± 0.027
V	100 ± 1	0.043 ± 0.010	0.161 ± 0.026
VI	97.7 ± 5.8	0.064 ± 0.003	0.157 ± 0.007

^aConsidered to be 7% of total body weight.

^bThe numbers are the means ± std. dev. for 3 rats.

Table 3 (Experiment C)
 Food Consumption, DBBE Content of the Diet,
 and DBBE Consumed by Rats

Rat Group	Food Consumed (g/day)	DBBE Content of Feed			[¹⁴ C] DBBE Consumed on Day 8	
		%		nCi/g	mg	nCi
I	12.6 + 2.3 ^a	4.80 ^b	4.85 ^c	219 + 9 ^c	755 + 129 ^a	3410 + 580 ^a
II	12.9 + 2.7	4.80	4.85	219 + 9	794 + 32	3590 + 140
III	13.8 + 2.5	4.80	4.85	219 + 9	744 + 250	3360 + 1130
IV	14.3 + 2.3	0.0277	0.0259	215 + 5	3.70 + 0.07	3070 + 60
V	15.7 + 2.0	0.0277	0.0259	215 + 5	4.27 + 0.51	3540 + 420
VI	15.8 + 2.4	0.0277	0.0259	215 + 5	4.06 + 1.15	3370 + 960

^aThe numbers are the means + std. dev. for 3 rats.

^bContent of unlabeled DBBE in the feed on Days 1-7 and 9 (Groups I and IV), Days 1-7 and Days 9-10 (Groups II and V), and Days 1-7 and Days 9-11 (Groups III and VI). Values are the averages of those derived by analysis before and after feeding.

^cContent of [¹⁴C]DBBE in the feed for Day 8. Values for % DBBE are averages of those derived by analysis before and after feeding. The values for nCi/g are the means + std. dev. for four separate determinations.

Table 4 (Experiment C)

Disposition of Radioactivity from [¹⁴C]DBBE in Rats Fed Unlabeled DBBE in the Diet on Days 1-7 and 9, on Days 1-7 and Days 9-10, and on Days 1-7 and 9-11, with [¹⁴C]DBBE in the Diet on Day 8

	Group I (Sacrifice Day = 10)		Group II (Sacrifice Day = 11)		Group III (Sacrifice Day = 12)		Group IV (Sacrifice Day = 10)		Group V (Sacrifice Day = 11)		Group VI (Sacrifice Day = 12)	
	% of Dose	nCi/g or ml	% of Dose	nCi/g or ml	% of Dose	nCi/g or ml	% of Dose	nCi/g or ml	% of Dose	nCi/g or ml	% of Dose	nCi/g or ml
Urine	0.004 ± 0.002 ^f	§	0.007 ± 0.003	-	0.008 ± 0.005	-	0.012 ± 0.005	-	0.011 ± 0.003	-	0.012 ± 0.007	-
Feces	85.3 ± 7.1	-	85.6 ± 4.5	-	85.1 ± 5.5	-	86.4 ± 8.5	-	83.9 ± 0.9	-	82.5 ± 4.7	-
Gut contents	3.32 ± 1.85	-	0.552 ± 0.873	-	0.059 ± 0.039	-	1.82 ± 0.36	-	0.518 ± 0.413	-	0.093 ± 0.029	-
Gut tissue	0.031 ± 0.016	0.255 ± 0.132	0.012 ± 0.011	0.095 ± 0.086	0.001 ± 0.001	0.013 ± 0.011	0.038 ± 0.004	0.302 ± 0.023	0.021 ± 0.000	0.181 ± 0.023	0.011 ± 0.001	0.107 ± 0.024
Liver	0.007 ± 0.001	0.019 ± 0.005	0.007 ± 0.006	0.019 ± 0.015	0.016 ± 0.006	0.040 ± 0.004	0.449 ± 0.010	1.62 ± 0.012	0.213 ± 0.016	0.846 ± 0.057	0.109 ± 0.029	0.440 ± 0.203
Kidneys	<0.001	0.007 ± 0.004	<0.001	0.009 ± 0.003	<0.001	0.009 ± 0.005	0.016 ± 0.002	0.407 ± 0.015	0.016 ± 0.000	0.430 ± 0.066	0.013 ± 0.001	0.295 ± 0.059
Lungs	<0.001	0.015 ± 0.006	<0.001	0.010 ± 0.006	0.001 ± 0.001	0.022 ± 0.005	0.011 ± 0.001	0.457 ± 0.022	0.007 ± 0.000	0.321 ± 0.051	0.004 ± 0.001	0.167 ± 0.055
Spleen	<0.001	0.031 ± 0.018	<0.001	0.038 ± 0.025	<0.001	0.022 ± 0.011	0.003 ± 0.001	0.273 ± 0.030	0.002 ± 0.000	0.160 ± 0.017	0.001 ± 0.000	0.074 ± 0.028
Brain	<0.001	<0.01	<0.001	<0.01	<0.001	<0.01	<0.001	<0.01	<0.001	<0.01	<0.001	<0.01
Muscle ^a	0.015 ± 0.014	0.005 ± 0.005	0.014 ± 0.005	0.006 ± 0.002	0.008 ± 0.012	0.004 ± 0.006	0.198 ± 0.024	0.008 ± 0.001	0.244 ± 0.018	0.009 ± 0.001	0.248 ± 0.007	0.008 ± 0.002
Skin ^b	0.099 ± 0.018	0.115 ± 0.024	0.049 ± 0.017	0.061 ± 0.023	0.036 ± 0.013	0.038 ± 0.008	0.252 ± 0.018	0.257 ± 0.022	0.207 ± 0.031	0.232 ± 0.062	0.138 ± 0.018	0.144 ± 0.042
Fat ^c	0.040 ± 0.015	0.107 ± 0.036	0.018 ± 0.004	0.049 ± 0.010	0.012 ± 0.012	0.025 ± 0.022	0.062 ± 0.033	0.145 ± 0.073	0.077 ± 0.022	0.198 ± 0.073	0.048 ± 0.001	0.115 ± 0.026
Blood ^d	0.003 ± 0.001	0.008 ± 0.002	0.001 ± 0.002	0.003 ± 0.004	0.014 ± 0.011	0.023 ± 0.009	0.043 ± 0.006	0.077 ± 0.009	0.024 ± 0.010	0.048 ± 0.023	0.028 ± 0.008	0.050 ± 0.024
Plasma ^e	0.001 ± 0.001	0.003 ± 0.003	0.001 ± 0.001	0.002 ± 0.002	0.006 ± 0.002	0.019 ± 0.003	0.035 ± 0.004	0.112 ± 0.010	0.019 ± 0.006	0.087 ± 0.019	0.021 ± 0.004	0.068 ± 0.007
Total Recovery	88.8		88.3		85.3		89.3		85.3		83.2	

^a Considered to be 50% of body weight.^b Considered to be 18% of body weight.^c Considered to be 7% of body weight.^d Considered to be 9% of body weight.^e Considered to be 5% of body weight.^f The numbers are THP means ± std. dev. for 3 rats.[§] Not calculated.

Table 5 (Experiment D)

Distribution of Radioactivity from
 $[^{14}\text{C}]$ DBBE for Rats Dosed Intravenously
 72 Hr Previously with 1.07 mg/kg

Tissue or Sample	% of Dose	nCi/g or ml
Urine	0.129 \pm 0.007 ^f	<u>g</u>
Feces	70.0 \pm 2.5	-
Gut contents	4.21 \pm 1.71	-
Gut tissue	0.853 \pm 0.127	-
Tail	9.50 \pm 0.89	-
Liver	4.27 \pm 1.05	15.1 \pm 3.9
Kidneys	0.697 \pm 0.073	13.7 \pm 1.4
Lungs	0.361 \pm 0.030	13.3 \pm 1.4
Spleen	0.027 \pm 0.004	1.78 \pm 0.42
Brain	0.047 \pm 0.003	0.69 \pm 0.04
Muscle ^a	12.9 \pm 1.1	4.32 \pm 0.68
Skin ^b	7.25 \pm 0.76	7.53 \pm 0.41
Fat ^c	2.99 \pm 1.94	7.33 \pm 5.25
Blood ^d	0.732 \pm 0.053	1.36 \pm 0.17
Plasma ^e	0.589 \pm 0.068	1.97 \pm 0.35

^aConsidered to be 50% of body weight.

^bConsidered to be 16% of body weight.

^cConsidered to be 7% of body weight.

^dConsidered to be 9% of body weight.

^eConsidered to be 5% of body weight.

^fThe numbers are the means \pm std. dev. for 3 rats.

^gNot calculated.