

ADME NTP Study S0044 Diethyl phthalate

The contractor used the abbreviation DEP for the test article in the comparison tables.

Sex/Species: male F344 rats.

Vehicle: dermal, absolute ethanol.

CASRN 84-66-2

Radiolabeled with carbon-14 in the phthalyl moiety; Diethyl phthalate, [¹⁴C-U-phthalyl]

Studies Performed:

- Single 5, 50, or 166.7 mg/kg dermal dose to rats with covered dose site and sacrifice 7 days postdose. (n = 3 per dose)
- Single 5 mg/kg dermal dose to rats with uncovered dose site and sacrifice 7 days postdose. (n = 3)

This study was part of a series to compare excretion profiles and tissue distributions of nine phthalate esters. To view the comparison excretion profiles see the NTP Study S0043 on dimethyl phthalate. Daily excretion data for the 5 mg/kg dermal dose with uncovered dose site was given only in a figure and is not shown here.

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Table 1. Excretion Profile of diethyl phthalate (low dose level) in the urine and the feces after dermal application to the rat*

Time (hr)	% Dose Excreted		
	Urine	Feces	Urine & Feces ($\Sigma\bar{X}$)
24	16.4 ± 0.6	0.56 ± 0.39	16.96
48	6.3 ± 3.58	0.3 ± 0.19	6.6
72	2.6 ± 1.55	0.095 ± 0.06	2.69
96	1.6 ± 1.29	0.2 ± 0.13	1.8
120	1 ± 0.96	0.185 ± 0.16	1.185
144	1.45 ± 0.83	0.24 ± 0.19	1.69
168	0.82 ± 0.4	0.31 ± 0.39	1.13
Total	30.26 ± 8.7	1.87 ± 0.76	32.13

*Male F-344 rats (200 ± 20 gm) received Diethyl phthalate in ethanol dermally (5 mg/Kg). The skin was covered with a perforated plastic cap. Data points are the mean ± standard deviation. The percentage of dose excreted represents the fraction of the dose found (as ¹⁴C-equivalent) relative to the total ¹⁴C-equivalent applied.

Table 2. Excretion profile of diethyl phthalate (medium dose level) in the urine and the feces after dermal application to the rat*

Time (hr)	% Dose Excreted		
	Urine	Feces	Urine & Feces ($\Sigma\bar{X}$)
24	23.9 ± 8.4	1.03 ± 0.55	24.93
48	10.8 ± 2.6	0.795 ± 0.35	11.59
72	7.2 ± 0.55	0.29 ± 0.04	7.49
96	2.5 ± 1.16	0.1 ± 0.03	2.6
120	1.9 ± 1.45	0.09 ± 0.01	1.99
144	0.74 ± 0.6	0.058 ± 0.007	0.798
168	0.57 ± 0.46	0.04 ± 0.009	0.61
Total	47.8 ± 7.	2.42 ± 0.88	50.22

*Male F-344 rats (200 ± 20 gm) received diethyl phthalate in ethanol dermally (50 mg/Kg). The skin was covered with a perforated plastic cap. Data points are the mean ± standard deviation. The percentage of dose excreted represents the fraction of the dose found (as ¹⁴C-equivalent) relative to the total ¹⁴C-equivalent applied.

Table 3. Excretion profile of diethyl phthalate (high dose level) in the urine and the feces after dermal application to the rat*

Time (hr)	% Dose Excreted		
	Urine	Feces	Urine & Feces ($\Sigma\bar{X}$)
24	19.06 ± 11.9	1.168 ± 0.45	20.228
48	13.5 ± 5.67	0.67 ± 0.42	14.17
72	6.67 ± 0.75	0.41 ± 0.1	7.08
96	3.22 ± 0.39	0.39 ± 0.13	3.61
120	2.65 ± 0.72	0.34 ± 0.11	2.99
144	2.03 ± 0.95	0.31 ± 0.06	2.34
168	1.53 ± 0.68	0.35 ± 0.05	1.88
Total	48.7 ± 15.8	3.64 ± 1.17	52.34

*Male F-344 rats (200 ± 20 gm) received diethyl phthalate in ethanol dermally (166.7 mg/Kg). The skin was covered with a perforated plastic cap. Data points are the mean ± standard deviation. The percentage of dose excreted represents the fraction of the dose found (as ¹⁴C-equivalent) relative to the total ¹⁴C-equivalent applied.

Table 4. Body tissue distribution of 7 days of exposure to diethylphthalate

Tissue	% Dose Found ($\bar{X} \pm$ S.D., n = 3)							
	Low Dose 5 mg/kg (Capped)		Low Dose 5 mg/kg (Uncapped)		Medium Dose 50 mg/kg		High Dose 166.7 mg/kg	
Brain	0.005 ±	0.004	0.003 ±	0.001	0.002 ±	0.001	0.009 ±	0.002
Lung	0.003 ±	0.002	0.002 ±	0.001	0.002 ±	0.001	0.004 ±	0.001
Liver	0.012 ±	0.004	0.014 ±	0.011	0.008 ±	0.005	0.021 ±	0.003
Spleen	0.037 ±	0.061	0.002 ±	0.001	0.001 ±	0.001	0.002 ±	0.00
Small Intestine	0.003 ±	0.003	0.007 ±	0.003	0.004 ±	0.002	0.012 ±	0.005
Kidney	0.005 ±	0.003	0.005 ±	0.001	0.004 ±	0.001	0.009 ±	0.003
Testis	0.002 ±	0.002	0.006 ±	0.001	0.002 ±	0.00	0.005 ±	0.003
Fat	0.073 ±	0.069	0.138 ±	0.03	0.033 ±	0.029	0.108 ±	0.013
Muscle	0.155 ±	0.136	0.213 ±	0.022	0.137 ±	0.072	0.349 ±	0.095
Skin	0.072 ±	0.063	0.164 ±	0.062	0.061 ±	0.018	0.307 ±	0.313
Spinal Cord	0.001 ±	0.001	0.002 ±	0.001			0.002 ±	0.001
Blood	0.05 ±	0.015	0.026 ±	0.007	0.004 ±	0.005	0.064 ±	0.009
Skin of Application	26.85 ±	22.8	1.09 ±	0.996	33.67 ±	24.28	15.94 ±	15.3
Plastic Cap	14.4 ±	4.7	---		4.774 ±	3.153	9.26 ±	8.64
Total Recovery*	73.85 ±	21.3	26.194 ±	3.1	88.588 ±	19.137	77.57 ±	11.6

*Total recovery represents the sum of the % dose found in the urine, the feces, the tissues and the plastic cap (if any) after 7 days of exposure

Table 5. Total percentage recovery of the dose applied on the skin of the rat of the phthalate ester, Diethyl phthalate.^{a,b,c,d}

Low Dose (covered) ^e	Low Dose (uncovered)	Medium Dose (covered) ^e	High Dose (covered) ^e
73.85 ± 21.377	26.194 ± 3.1	88.58 ± 19.1	77.57 ± 11.6

^aTotal recovery represents the sum of the % dose found in the urine, the feces, the tissues, and the plastic cap (if any) in 7 days of exposure to the phthalate ester.

^bData represents the mean ± standard deviation.

^cDoses were 5 mg/kg for the low dose, 50 mg/kg for the medium dose, and 166.7 mg/kg for the high dose.

^dn = 3

^eA plastic cap was used to cover the dose site.