ADME NTP Study S0077 4-Chloronitrobenzene

The contract laboratory abbreviation is 4-CNB.
Sex/Species: Young adult male F344 rats (10-12 weeks old, weighing between 200-225 g at randomization).
Vehicle: topical application (dermal) acetone.

CASRN 100-00-5

Radiolabeled with carbon-14 in the ring; 4-Chloronitrobenzene, [Ring-^{14}C]-

Studies performed:

Single dermal administrations of 0.65, 6.5, or 65 mg/kg [^{14}C]4-CNB (with dose site covered) to rats sacrificed at 72 hours postdose. **The is the first study (S0077)** of a four-part study on 4-chloronitrobenzene (4-CNB).

Companion studies:

The second study (S0105) examined the effect of the single oral administration (gastric intubation) of 2, 20, or 200 mg/kg [^{14}C]4-chloronitrobenzene in 11-week old male F344 rats.

The third study (S0779) investigated the effect of 11-day repeated daily dosing of 65 mg/kg 4-CNB by oral administration (gastric intubation) on young adult F344 rats (9 weeks old). Rats were sacrificed on Day 12.

A fourth study (S0363) investigated the effect of 11-day repeated daily dosing of 65 mg/kg 4-CNB by oral administration (gastric intubation) on geratric rats (male F344 rats, approximately 19 months old). The same dosing and sampling regime as for S0779 was used.

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Table 1: Urinary excretion of ^{14}C radioactivity by male Fischer 344 rats after dermal administration of [^{14}C]4-CNB at 0.65, 6.5 and 65 mg/kg

	Dose level (mg/kg)		
	0.65	6.5	65
Time (hr)	Dose excreted (%)[a]		
0-4	1.1 ± 2.0	1.7 ± 1.0	0.3 ± 0.3
4-8	6.3 ± 1.2	5.8 ± 3.7	1.7 ± 0.8
8-24	18.7 ± 2.9	20.0 ± 5.2	10.4 ± 0.7
24-48	12.7 ± 3.0	11.8 ± 2.0	20.3 ± 4.3
48-72	4.5 ± 1.6	3.7 ± 0.8	12.7 ± 5.3
	Dose excreted (cumulative %)		
0-4	1.1 ± 2.0	1.7 ± 1.0	0.3 ± 0.3
0-8	7.5 ± 2.0	7.5 ± 2.7	2.0 ± 0.7
0-24	26.1 ± 1.0	27.5 ± 7.4	12.4 ± 1.2
0-48	38.8 ± 3.8	39.3 ± 8.2	32.7 ± 4.3
0-72	43.4 ± 5.3	43.0 ± 8.8	45.4 ± 9.2

[a]Values are means of data from three animals ± SD.

Table 2: Fecal excretion of ^{14}C radioactivity by male Fischer 344 rats after dermal administration of [^{14}C]4-CNB at 0.65, 6.5 and 65 mg/kg

	Dose level (mg/kg)		
	0.65	6.5	65
Time (hr)	Dose excreted (%)[a]		
0-4	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.1
4-8	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
8-24	1.3 ± 0.5	2.7 ± 1.5	1.1 ± 0.8
24-48	1.9 ± 0 7	3.2 ± 0.8	5.2 ± 1.3
48-72	2.3 ± 0.1	2.3 ± 0.8	6.0 ± 2.1
	Dose excreted (cumulative %)		
0-4	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.1
0-8	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
0-24	1.3 ± 0 5	2 7 ± 1.5	1.1 ± 0.7
0-48	3.1 ± 0 5	5 9 ± 2 2	6.3 ± 0.7
0-72	5.4 ± 0.6	8.3 ± 2.5	12.2 ± 1.5

[a]Values are means of data from three animals ± SD.

Table 3: Collection of ^{14}C radioactivity in ethanol from male Fischer 344 rats after dermal administration of [^{14}C]4-CNB at 0.65, 6.5 and 65 mg/kg

	Dose level (mg/kg)		
	0.65	6.5	65
Time (hr)	Dose excreted (%)[a]		
0-4	0.9 ± 0.6	0.7 ± 0.4	0.9 ± 0.3
4-8	0.7 ± 0 4	0.9 ± 0.4	0.7 ± 0.4
8-24	3.0 ± 1.4	3.3 ± 1.4	4.3 ± 2.6
24-32	1.6 ± 0.5	2.0 ± 0.8	2.0 ± 1.1
32-48	2.9 ± 1.0	4.1 ± 1.2	3.1 ± 1.6
48-56	1.7 ± 0.3	2.1 ± 0.6	1.4 ± 0.7
56-72	2.6 ± 0.7	2.1 ± 0.3	2.6 ± 1.1
	Dose excreted (cumulative %)		
0-4	0.9 ± 0.6	0.7 ± 0.4	0.9 ± 0.3
0-8	1.6 ± 1.0	1.6 ± 0.8	1.6 ± 0.7
0-24	4.6 ± 2.4	4.9 ± 2.2	5.8 ± 3.2
0-32	6.2 ± 2.1	6.9 ± 3.0	7.9 ± 4.2
0-48	9.1 ± 1.6	11.0 ± 4.1	11.0 ± 5.8
0-56	10.8 ± 1.3	13.0 ± 4.7	12.3 ± 6.5
0-72	13.4 ± 0.6	15.1 ± 5.0	14.9 ± 7.6

[a]Values are means ± SD from 3 animals per group.

Table 4: Recovery of ^{14}C radioactivity at 72 hr after dermal application of [^{14}C]4-CNB to male Fischer 344 rats at 0.65, 6.5 and 65 mg/kg

	Dose level (mg/kg)		
	0.65	6.5	65
Sample	**Dose excreted (%)[a]**		
Exposed skin	0.8 ± 0.3	1.3 ± 1.0	1.3 ± 1.1
Protective device	15.4 ± 4.6	7.7 ± 3.5	8.8 ± 3.2
Gauze	0.3 ± 0.1	0.3 ± 0.2	0.3 ± 0.1
Ethanol trap	13.4 ± 0.6	15.1 ± 5.0	14.9 ± 7.6
Urine	43.4 ± 5.3	43.0 ± 8.8	45.4 ± 9.2
Feces	5.4 ± 0.6	8.3 ± 2.5	12.2 ± 1.5
Cagewash	2.6 ± 1.0	1.9 ± 1.0	4.6 ± 1.3
Total unabsorbed[a]	29.9 ± 4.2	24.4 ± 9.6	25.3 ± 9.3
Total absorbed[b]	51.3 ± 6.1	53.2 ± 10.3	62.2 ± 9.7
Total recovered	81.2 ± 6.7	77.6 ± 1.2	87.5 ± 7.2

[a] Total unabsorbed represents radioactivity recovered in exposed skin, protective device, gauze and ethanol traps. N = 3 animals per group.
[b] Total absorbed represents radioactivity recovered in urine, feces and cagewash.