ADME NTP Study S0075 N-(3-Chloroallyl)hexaminium chloride

The contractor abbreviated the test article as CHC.
Sex/Species: male F344 rats.
Vehicles: intravenous, water; oral, water.

CASRN 4080-31-3

Radiolabeled with carbon-14 uniformly in the 1,3,5,7-triaza-1-azoniaadamantane moiety; N-(3-Chloroallyl)hexaminium(UL-^{14}C) chloride

Studies Performed:

- Single 1.86, 9.51, or 46.6 mg/kg oral gavage dose to rats with sacrifice 72 hours postdose.

- Single 9.95 mg/kg intravenous dose to rats with sacrifice 24 hours postdose.

Unlabeled CHC was the *cis* isomer. The radiolabeled [^{14}C]CHC was a mixture of *cis* and *trans* isomers.

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Table 1

Disposition of Radioactivity from [^{14}C] CHC

in Rats Dosed Orally 72 hr Prior to Sacrifice

Sample	Time After Dosing, hr	Dose: High (46.6 mg/kg) % of Dose	High (46.6 mg/kg) nCi/g or ml	(Medium (9.51 mg/kg) % of Dose	(Medium (9.51 mg/kg) nCi/g or ml	Low (1.86 mg/kg) % of Dose	Low (1.86 mg/kg) nCi/g or ml
		(Group Mean ± S.D. for 3 Rats Per Dose Group)					
CO_2	1	1.45 ± 0.32	-[a]	1.69 ± 0.18	-	3.39 ± 0.38	-
	2	6.14 ± 1.26	-	4.15 ± 0.84	-	5.44 ± 0.55	-
	4	14.1 ± 0.8	-	10.6 ± 1.3	-	10.4 ± 0.9	-
	8	11.2 ± 0.8	-	9.20 ± 0.72	-	7.37 ± 0.26	-
	12	3.80 ± 0.82	-	2.66 ± 0.24	-	2.02 ± 0.19	-
	24	2.17 ± 0.41	-	2.20 ± 0.22	-	1.81 ± 0.12	-
	48	1.70 ± 0.10	-	1.48 ± 0.11	-	1.30 ± 0.10	-
	72	0.562 ± 0.051	-	0.532 ± 0.036	-	0.469 ± 0.129	-
Total		41.1 ± 0.9	-	32.6 ± 1.1	-	32.1 ± 1.6	-
Formaldehyde	1	<0.001	-	<0.001	-	<0.001	-
	2	0.009 ± 0.010	-	0.002 ± 0.001	-	0.009 ± 0.009	-
	4	0.027 ± 0.013	-	0.007 ± 0.001	-	0.010 ± 0.007	-
	8	0.018 ± 0.003	-	0.039 ± 0.035	-	0.020 ± 0.006	-
	12	0.004 ± 0.007	-	0.021 ± 0.017	-	0.014 ± 0.004	-
	24	0.015 ± 0.006	-	0.028 ± 0.014	-	0.023 ± 0.007	-
	48	0.003 ± 0.003	-	0.015 ± 0.004	-	0.002 ± 0.002	-
	72	0.001	-	0.002 ± 0.003	-	0.001	-
Total		0.076 ± 0.029	-	0.115 ± 0.069	-	0.078 ± 0.007	-
Urine	24	25.5 ± 1.0	-	35.8 ± 1.2	-	31.3 ± 9.7	-
	48	1.02 ± 0.08	-	1.09 ± 0.21	-	1.06 ± 0.06	-
	72	0.520 ± 0.073	-	0.487 ± 0.086	-	0.515 ± 0.051	-
Total		27.0 ± 1.1	-	37.3 ± 1.1	-	32.9 ± 9.8	-
Feces	24	8.30 ± 0.93	-	8.00 ± 0.89	-	15.3 ± 9.2	-
	48	1.15 ± 0.25	-	1.54 ± 0.55	-	1.26 ± 0.49	-
	72	0.418 ± 0.043	-	0.328 ± 0.015	-	0.342 ± 0.215	-
Total		9.86 ± 0.86	-	9.87 ± 0.50	-	16.9 ± 9.5	-
Gut contents		0.757 ± 0.026	-	0.705 ± 0.016	-	0.786 ± 0.022	-
Gut tissue		0.388 ± 0.031	18.8 ± 0.6	0.378 ± 0.037	18.3 ± 1.4	0.350 ± 0.023	16.6 ± 1.2
Liver		1.29 ± 0.06	28.7 ± 2.9	1.08 ± 0.14	26.6 ± 4.0	1.13 ± 0.07	26.9 ± 2.8
Lungs		0.086 ± 0.008	20.7 ± 1.5	0.74 ± 0.006	18.9 ± 1.0	0.083 ± 0.004	20.2 ± 0.2
Kidneys		0.247 ± 0.024	33.5 ± 5.2	0.227 ± 0.024	31.8 ± 3.2	0.253 ± 0.023	34.0 ± 2.0
Fat[b]		0.305 ± 0.068	4.46 ± 0.95	0.225 ± 0.061	3.44 ± 0.92	0.315 ± 0.089	4.51 ± 1.26
Plasma[c]		0.331 ± 0.042	6.81 ± 1.21	0.269 ± 0.017	5.75 ± 0.36	0.285 ± 0.032	5.71 ± 0.59
Whole blood[d]		0.802 ± 0.027	9.12 ± 0.74	0.647 ± 0.011	7.70 ± 0.13	0.702 ± 0.078	7.83 ± 0.67
Total Recovery		81.9 ± 0.6	-	83.2 ± 0.5	-	85.6 ± 1.2	-

[a] Not applicable or not determined

[b] Considered to be 7% of body weight

[c] Considered to be 5% of body weight; not included in total

[d] Considered to be 9% of body weight

Table 2

Disposition of Radioactivity in Rats Dosed Intravenously with [^{14}C] CHC (9.95 mg/kg) 24 hr Prior to Sacrifice

Sample		% of Dose	nCi/g or ml
		(Group Mean ± S.D. for 3 Rats)	
CO_2	1 hr	15.4 ± 1.6	-[a]
	2 hr	8.29 ± 1.02	-
	4 hr	3.25 ± 0.48	-
	8 hr	1.74 ± 0.15	-
	12 hr	0.765 ± 0.057	-
	24 hr	0.860 ± 0.241	-
	Total	30.3 ± 1.9	-
Urine		50.4 ± 1.8	-
Feces		1.22 ± 0.88	-
Gut contents		2.07 ± 0.56	-
Gut tissue		1.16 ± 0.12	88.3 ± 9.8
Liver		2.13 ± 0.18	110 ± 27
Lungs		0.153 ± 0.003	60.9 ± 1.4
Kidneys		0.515 ± 0.050	127 ± 15
Fat[b]		0.261 ± 0.058	7.26 ± 1.73
Plasma[c]		0.535 ± 0.051	20.8 ± 2.0
Whole blood[d]		0.827 ± 0.045	17.8 ± 1.2
Tail		0.134 ± 0.039	32.5 ± 9.4
Total Recovery		89.0 ± 2.7	-

[a] Not applicable or not determined

[b] Considered to be 7% of body weight

[c] Considered to be 5% of body weight; not included in total

[d] Considered to be 9% of body weight