NTP Study S0817 N-Methylolacrylamide

Contract laboratory synonym is N-(hydroxymethyl)acrylamide (HMA).
Sex/Species: adult male F344 rats and B6C3F1 mice.
Vehicle: oral gavage, water; dosed water, water; intraperitoneal, water.

CASRN 924-42-5
Radiolabeled with carbon-14 at the hydroxymethyl group; N-Methylolacrylamide, [methyl-^{14}C]-

Studies performed

1. Single 150 mg/kg intraperitoneal administration in mice with sacrifice 72 hours postdose.

2. Single 150 mg/kg oral gavage dose in mice with sacrifice 72 hours postdose.

3. Single 1.50 mg/kg oral gavage dose in mice with sacrifice 72 hours postdose.

4. Single 150 mg/kg oral gavage dose following 7- and 14-day drinking water exposure to unlabeled HMA (500 ppm) in mice.

5. Single 150 mg/kg oral gavage dose in rats with sacrifice 72 hours postdose.

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Table 1

Disposition of Radioactivity 72 h after an ip Dose of [^{14}C]HMA (150 mg/kg) to Male B6C3F$_1$ Mice[a]

Cumulative Excretion of Radioactivity

End of Collection Period	Percent of Dose Recovered in:				Total
	Urine	Breath Volatiles	CO_2	Feces	
8 h	26.3 ± 24.0	0.01 ± 0.00	6.86 ± 0.65		33.2 ± 24.2
24 h	50.2 ± 17.6	0.10 ± 0.04	8.38 ± 0.72	1.41 ± 0.67	60.1 ± 16.9
48 h	59.7 ± 18.0	0.19 ± 0.12	9.26 ± 0.94	2.52 ± 1.05	71.6 ± 17.1
72 h	72.6 ± 7.11	0.24 ± 0.17	9.80 ± 1.12	4.08 ± 2.29	86.7 ± 4.7

Distribution in Tissues

Tissue	ng-eq HMA per g Tissue	Tissue/Blood Ratio	% Dose in Total Tissue
Adipose	5250 ± 2630	0.25 ± 0.15	0.29 ± 0.19
Blood	22700 ± 3270	Unity	1.17 ± 0.14
Brain	7560 ± 1120	0.335 ± 0.035	0.10 ± 0.001
Epididymis	9570 ± 2020	0.424 ± 0.073	0.02 ± 0.00
Heart	9470 ± 1350	0.422 ± 0.062	0.04 ± 0.01
Kidney	13400 ± 2200	0.590 ± 0.028	0.16 ± 0.03
Liver	11700 ± 1310	0.520 ± 0.038	0.39 ± 0.10
Lung	11900 ± 1410	0.535 ± 0.097	0.05 ± 0.01
Muscle	6150 ± 280	0.276 ± 0.048	1.89 ± 0.18
Forestomach	11300 ± 936	0.507 ± 0.097	0.01 ± 0.00
Glandular Stomach	9800 ± 1020	0.438 ± 0.061	0.03 ± 0.00
Small Intestine[b]			0.20 ± 0.02
Cecum[b]			0.05 ± 0.01
Large Intestine[b]			0.06 ± 0.02
Skin	5680 ± 834	0.253 ± 0.033	0.56 ± 0.10
Spleen	12500 ± 1130	0.557 ± 0.058	0.02 ± 0.01
Testis	6010 ± 606	0.267 ± 0.019	0.04 ± 0.01
		Total in tissues	4.77 ± 0.29

[a] N=4
[b] Includes contents

Table 2

Disposition of Radioactivity 72 h after an Oral Dose of [^{14}C]HMA (150 mg/kg) to Male B6C3F$_1$ Mice[a]

Cumulative Excretion of Radioactivity

End of Collection Period	Percent of Dose Recovered in:				Total
	Urine	Breath Volatiles	CO_2	Feces	
8 h	18.0 ± 21.0	0.024 ± 0.016	6.98 ± 1.02		25.0 ± 21.6
24 h	27.8 ± 31.4	0.13 ± 0.07	9.00 ± 0.88	16.3 ± 18.4	53.2 ± 18.7
48 h	31.0 ± 32.8	0.25 ± 0.10	9.86 ± 0.95	20.7 ± 19.2	61.8 ± 16.3
72 h	42.9 ± 34.6	0.33 ± 0.11	11.0 ± 1.62	24.9 ± 22.1	79.1 ± 12.3

Distribution in Tissues

Tissue	ng-eq HMA per g Tissue	Tissue/Blood Ratio	% Dose in Total Tissue
Adipose	3180 ± 1050	0.16 ± 0.04	0.16 ± 0.06
Blood	19400 ± 2490	Unity	0.91 ± 0.09
Brain	7590 ± 770	0.40 ± 0.05	0.09 ± 0.01
Epididymis	8300 ± 1470	0.43 ± 0.03	0.02 ± 0.00
Heart	9310 ± 1840	0.48 ± 0.08	0.03 ± 0.01
Kidney	15300 ± 2100	0.80 ± 0.14	0.16 ± 0.03
Liver	12000 ± 1390	0.63 ± 0.09	0.35 ± 0.08
Lung	11900 ± 2320	0.61 ± 0.08	0.05 ± 0.01
Muscle	6090 ± 671	0.32 ± 0.03	1.69 ± 0.16
Forestomach	9480 ± 1070	0.49 ± 0.07	0.01 ± 0.00
Glandular Stomach	11300 ± 1980	0.59 ± 0.10	0.02 ± 0.01
Small Intestine[b]			0.23 ± 0.06
Cecum[b]			0.10 ± 0.09
Large Intestine[b]			0.08 ± 0.06
Skin	4930 ± 534	0.26 ± 0.03	0.44 ± 0.04
Spleen	11200 ± 2210	0.58 ± 0.10	0.02 ± 0.00
Testis	6040 ± 717	0.31 ± 0.03	0.03 ± 0.00
		Total in tissues	3.74 ± 1.09

[a] N=4

[b] Includes contents

Table 3

Disposition of Radioactivity 72 h after an Oral Dose of [^{14}C]HMA (1.5 mg/kg) to Male B6C3F$_1$ Mice[a]

Cumulative Excretion of Radioactivity

End of Collection Period	Percent of Dose Recovered in: Urine	CO_2	Feces	Total
8 h	11.9 ± 23.8	6.39 ± 0.86		18.3 ± 24.5
24 h	42.4 ± 17.3	8.14 ± 0.71	6.73 ± 5.06	57.3 ± 13.7
48 h	47.4 ± 19.2	9.00 ± 0.66	9.41 ± 7.38	65.8 ± 12.5
72 h	56.7 ± 15.5	9.48 ± 0.70	10.1 ± 7.60	76.3 ± 8.72

Distribution in Tissues

Tissue	ng-eq HMA per g Tissue	Tissue/Blood Ratio	% Dose in Total Tissue
Adipose	27.2 ± 8.72	0.207 ± 0.0854	0.18 ± 0.05
Blood	137 ± 18.3	Unity	0.69 ± 0.15
Brain	58.8 ± 7.70	0.434 ± 0.322	0.08 ± 0.01
Epididymis	75.0 ± 8.29	0.557 ± 0.0975	0.01 ± 0.00
Heart	93.4 ± 4.87	0.692 ± 0.0868	0.03 ± 0.01
Kidney	136 ± 18.8	1.00 ± 0.141	0.14 ± 0.02
Liver	97.2 ± 11.5	0.717 ± 0.0866	0.32 ± 0.10
Lung	113 ± 33.3	0.824 ± 0.182	0.05 ± 0.02
Muscle	54.4 ± 8.32	0.401 ± 0.0624	1.62 ± 0.29
Forestomach	86.7 ± 2.36	0.646 ± 0.106	0.01 ± 0.00
Glandular Stomach	95.5 ± 9.1118	0.717 ± 0.178	0.03 ± 0.00
Small Intestine[b]			0.22 ± 0.04
Cecum[b]			0.27 ± 0.05
Large Intestine[b]			0.34 ± 0.05
Skin	45.9 ± 11.6	0.339 ± 0.0839	0.44 ± 0.07
Spleen	109 ± 14.5	0.806 ± 0.143	0.02 ± 0.00
Testis	46.6 ± 7.57	0.345 ± 0.0674	0.02 ± 0.00
		Total in tissues	3.98 ± 0.61

[a] N=4

[b] Includes contents

Table 4

Disposition of Radioactivity 72 h after an Oral Dose of [^{14}C]HMA (150 mg/kg) to Male B6C3F$_1$ Mice that had been Provided HMA in Drinking Water (500 ppm) for 7 Days[a]

Cumulative Excretion of Radioactivity

End of Collection Period	Percent of Dose Recovered in:			
	Urine	CO_2	Feces	Total
8 h	26.4 ± 18.8	6.07 ± 2.03		32.4 ± 18.3
24 h	41.1 ± 27.5	7.68 ± 2.15	12.1 ± 12.8	60.9 ± 13.5
48 h	47.9 ± 31.4	8.38 ± 2.23	17.2 ± 12.2	73.5 ± 17.4
72 h	57.2 ± 26.2	8.67 ± 2.33	19.8 ± 13.8	85.6 ± 10.5

Distribution in Tissues

Tissue	ng-eq HMA per g Tissue	Tissue/Blood Ratio	% Dose in Total Tissue
Adipose	3200 ± 1132	0.207 ± 0.053	0.192 ± 0.080
Blood	15169 ± 1659	Unity	0.764 ± 0.082
Brain	5673 ± 636	0.374 ± 0.023	0.071 ± 0.004
Epididymis	7756 ± 1238	0.511 ± 0.059	0.009 ± 0.000
Heart	7626 ± 1874	0.500 ± 0.090	0.032 ± 0.007
Kidney	9735 ± 1822	0.643 ± 0.116	0.116 ± 0.024
Liver	7983 ± 2054	0.526 ± 0.13	0.280 ± 0.071
Lung	9387 ± 3115	0.610 ± 0.150	0.045 ± 0.041
Muscle	4856 ± 889	0.319 ± 0.039	1.44 ± 0.22
Forestomach	7504 ± 2410	0.493 ± 0.150	0.010 ± 0.005
Glandular Stomach	6717 ± 1539	0.442 ± 0.095	0.017 ± 0.003
Small Intestine[b]			0.175 ± 0.068
Cecum[b]			0.042 ± 0.020
Large Intestine[b]			0.038 ± 0.007
Skin	4693 ± 1815	0.305 ± 0.091	0.443 ± 0.132
Spleen	8000 ± 2280	0.522 ± 0.115	0.013 ± 0.003
Testis	4798 ± 867	0.316 ± 0.039	0.026 ± 0.001
		Total in tissues	3.71 ± 0.61

[a] The radiolabeled dose was administered on the morning of Day 8. Mice were provided plain tap water during the 72 h following administration of the radiolabeled dose. N=4

[b] Includes contents

Table 5

Disposition of Radioactivity 72 h after an Oral Dose of [^{14}C]HMA (150 mg/kg) to Male B6C3F$_1$ Mice that had been Provided HMA in Drinking Water (500 ppm) for 14 Days[a]

Cumulative Excretion of Radioactivity

End of Collection Period	Percent of Dose Recovered In:			
	Urine	CO_2	Feces	Total
8 h	20.0 ± 13.8	6.50 ± 0.62		26.5 ± 14.3
24 h	35.1 ± 14.2	8.39 ± 0.42	8.33 ± 5.79	49.8 ± 12.5
48 h	41.9 ± 15.2	9.32 ± 0.41	11.7 ± 5.42	60.1 ± 12.4
72 h	59.6 ± 10.1	9.75 ± 0.41	16.4 ± 8.87	81.7 ± 6.32

Distribution in Tissues

Tissue	ng-eq HMA per g Tissue	Tissue/Blood Ratio	% Dose in Total Tissue
Adipose	3950 ± 1742	0.286 ± 0.128	0.244 ± 0.163
Blood	14051 ± 2443	Unity	0.718 ± 0.045
Brain	5748 ± 1288	0.411 ± 0.081	0.068 ± 0.011
Epididymis	8945 ± 224	0.649 ± 0.099	0.011 ± 0.004
Heart	7866 ± 2768	0.548 ± 0.094	0.034 ± 0.018
Kidney	12184 ± 2245	0.866 ± 0.044	0.142 ± 0.018
Liver	8099 ± 1527	0.575 ± 0.033	0.316 ± 0.053
Lung	9058 ± 1585	0.645 ± 0.046	0.042 ± 0.005
Muscle	5240 ± 927	0.374 ± 0.042	1.592 ± 0.244
Forestomach	9068 ± 4392	0.622 ± 0.196	0.014 ± 0.006
Glandular Stomach	8779 ± 2886	0.613 ± 0.091	0.024 ± 0.005
Small Intestine[b]			0.195 ± 0.063
Cecum[b]			0.034 ± 0.010
Large Intestine[b]			0.042 ± 0.007
Skin	4364 ± 945	0.315 ± 0.074	0.431 ± 0.107
Spleen	9225 ± 1175	0.668 ± 0.117	0.017 ± 0.004
Testis	5234 ± 756	0.378 ± 0.062	0.027 ± 0.004
		Total in tissues	3.95 ± 0.61

[a] The radiolabeled dose was administered on the morning of Day 15. Mice were provided plain tap water during the 72 h following administration of the radiolabeled dose. N=4

[b] Includes contents

Table 6

Disposition of Radioactivity 72 h after an Oral Dose of [^{14}C]HMA (150 mg/kg) to Male F-344 Rats[a]

Cumulative Excretion of Radioactivity

End of Collection Period	Percent of Dose Recovered in:				
	Urine	Breath	CO_2	Feces	Total
8 h	44.2 ± 4.4	0.00 ± 0.00	2.15 ± 0.09		46.4 ± 4.4
24 h	72.1 ± 1.0	0.01 ± 0.00	3.64 ± 0.06	0.70 ± 0.56	76.5 ± 0.7
48 h	77.1 ± 1.3	0.02 ± 0.01	4.22 ± 0.04	1.10 ± 0.65	82.5 ± 0.6
72 h	79.1 ± 1.4	0.02 ± 0.01	4.49 ± 0.05	1.20 ± 0.62	84.8 ± 0.8

Distribution in Tissues

Tissue	ng-eq HMA per g Tissue	Tissue/Blood Ratio	% Dose in Total Tissue
Adipose	2850 ± 880	0.023 ± 0.007	0.126 ± 0.035
Blood	124000 ± 3770	Unity	4.11 ± 0.22
Brain	10900 ± 958	0.088 ± 0.009	0.060 ± 0.003
Epididymis	21000 ± 5180	0.168 ± 0.038	0.027 ± 0.009
Heart	24600 ± 2370	0.199 ± 0.020	0.048 ± 0.005
Kidney	24200 ± 2250	0.195 ± 0.016	0.114 ± 0.004
Liver	25600 ± 3110	0.206 ± 0.026	0.594 ± 0.044
Lung	30400 ± 1240	0.245 ± 0.012	0.070 ± 0.003
Muscle	10000 ± 1490	0.081 ± 0.011	3.06 ± 0.41
Forestomach	17900 ± 2810	0.144 ± 0.025	0.019 ± 0.003
Glandular Stomach	12700 ± 2400	0.103 ± 0.020	0.020 ± 0.004
Small Intestine[b]			0.129 ± 0.006
Cecum[b]			0.038 ± 0.004
Large Intestine[b]			0.058 ± 0.005
Skin	25500 ± 5660	0.206 ± 0.048	2.74 ± 0.54
Spleen	60800 ± 7720	0.490 ± 0.050	0.088 ± 0.013
Testis	8990 ± 918	0.073 ± 0.009	0.069 ± 0.005
		Total in tissues	11.3 ± 0.9

[a] N=4

[b] Includes contents