

ADME NTP Study S0547 Trimethylolpropane triacrylate

The contract laboratory abbreviation for the test article is TMPTA.

Sex/Species: adult male F344 rats and B6C3F1 mice.

Vehicles: intravenous, Emulphor:ethanol:phosphate buffered saline (15:5:80); dermal, acetone.

CASRN 15625-89-5

Radiolabeled with carbon-14 on each carbon 1 of the triacrylate moieties;
[¹⁴C]Trimethylolpropane triacrylate.

Trimethylolpropane triacrylate Studies Performed:

1. Single 9.4 mg/kg intravenous dose in rats with sacrifice 72 hours postdose.
2. Single 1.7, 15.2, or 130 mg/kg dermal dose in rats with dose site covered and sacrifice 72 hours postdose.
3. Repeat dermal dose in rats with 37.5 mg non-radiolabeled TMPTA (144-156 mg TMPTA/kg) applied 24 hours prior to the 151 mg/kg radiolabeled dose. Rats were sacrificed 72 hours post radiolabeled dose.
4. Single 1.2 mg/kg dermal dose in mice with dose site covered and sacrifice 72 hours postdose.

The dose site was covered for all the dermal studies. The repeat dermal dose in rats is labeled as pre-exposed in the tables.

Serial blood collections were taken from 0 to 72 hours following intravenous administration of 9.4 mg/kg TMPTA in rats. However, no toxicokinetic analysis was performed.

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Table 1

Cumulative Excretion of Radiolabel by Male F-344 Rats 72 h after Intravenous Administration of [¹⁴C]TMPTA^a

Route	IV - Rat	
Dose	End of Collection	9.4 mg/kg
Excreta	Period (h)^b	(% Dose)
Urine	3	NC
	6	24.1 ± 2.6
	24	44.6 ± 4.9
	48	47.3 ± 4.5
	72	48.3 ± 4.4
	Cage Rinse	0.3 ± 0.1
Feces	3	NC
	6	0.0 ± 0.0
	24	6.1 ± 5.5
	48	8.1 ± 7.0
	72	8.7 ± 7.1
Exhaled CO ₂	3	6.4 ± 0.8
	6	12.9 ± 4.7
	24	18.6 ± 5.9
	48	19.8 ± 5.9
	72	20.1 ± 6.0
Total		77.4 ± 3.5

^a Values are mean ± SD for five animals.

^b Time points are referenced to time of administered iv dose.

NC Samples not collected for this time point.

Table 2

**Distribution of Radiolabel in Male F-344 Rats 72 h Following
Intravenous Exposure of [¹⁴C]TMPTA^a**

Dose		9.4 mg/kg			
Tissue Name	ng-eq TMPTA per g Tissue	Tissue Blood Ratio		Percent Dose In Total Tissue ^b	
Adipose	156 ± 47	0.01 ±	0.00	0.12 ±	0.04
Bladder	436 ± 80	0.03 ±	0.01	0.00 ±	0.00
Blood	13800 ± 1560	unity		5.01 ±	0.70
Brain	935 ± 370	0.07 ±	0.03	0.07 ±	0.03
Heart	3880 ± 700	0.28 ±	0.05	0.12 ±	0.03
Kidney	2530 ± 368	0.19 ±	0.04	0.20 ±	0.02
Liver	2390 ± 189	0.17 ±	0.01	0.93 ±	0.17
Lung	9570 ± 2050	0.70 ±	0.17	0.50 ±	0.18
Muscle	173 ± 31	0.01 ±	0.00	0.81 ±	0.26
Skin	276 ± 31	0.02 ±	0.00	0.49 ±	0.06
Spleen	7620 ± 1150	0.55 ±	0.06	0.20 ±	0.04
Testes	142 ± 26	0.01 ±	0.00	0.02 ±	0.00

^a Values are mean ± SD for five rats.

^b The percent dose was calculated using the following values for the mass of total tissue, expressed as percent of body weight: adipose, 7.0%; blood, 5.2%; muscle, 48%; and skin, 17%.

Cummulative % Dose Appearing in:	Following iv Bolus Dose of TMPTA
Residual Carcass	3.63 ± 0.2
Tail	1.07 ± 0.6
Selected Tissues	2.04 ± 0.3
Urine	48.6 ± 4.5
Feces	8.7 ± 7.1
Exhaled CO ₂	20.1 ± 6.0
72 h Blood	5.01 ± 0.7
Blood Samples for Assay	0.99 ± 0.2
Total	90.1 ± 2.6

Table 3

**Distribution of Radiolabel 72 h after Dermal Administration
of [¹⁴C]TMPTA^a**

Route	Pre-Exposed Rats 151 mg/kg	Rats 130 mg/kg	Rats 15.2 mg/kg	Rats 1.7 mg/kg	Mice 1.2 mg/kg
Absorbed					
Urine	5.8 ± 1.5	3.0 ± 0.4	12.1 ± 1.4	28.0 ± 1.2	16.5 ± 2.8
Cage Wash	0.4 ± 0.2	0.1 ± 0.0	0.9 ± 0.4	0.9 ± 0.4	2.0 ± 0.9
Feces	0.4 ± 0.2	0.2 ± 0.1	1.2 ± 0.2	2.51 ± 0.5	5.6 ± 4.2
Exhaled CO ₂	3.4 ± 1.1	1.4 ± 0.2	4.9 ± 0.8	13.1 ± 1.4	18.2 ± 5.4
Dose Site					
Acetone Extractable	8.5 ± 1.0	10.4 ± 5.1	8.0 ± 2.3	NC	NC
Non-extractable	2.6 ± 0.6	3.2 ± 1.3	3.3 ± 0.6	8.5 ± 1.4	30.8 ± 4.9
Selected Tissues	0.7 ± 0.3	0.2 ± 0.0	1.0 ± 0.1	0.4 ± 0.1	0.2 ± 0.1
Residual Carcass	3.6 ± 2.3	0.3 ± 0.0	1.2 ± 0.2	1.7 ± 0.3	1.7 ± 0.2
Total Absorbed	25.4 ± 4.4	18.7 ± 6.7	32.7 ± 4.6	55.1 ± 3.0	75.0 ± 2.4
Total Unabsorbed^b	65.3 ± 6.4	76.1 ± 6.3	57.0 ± 5.2	34.8 ± 4.8	20.9 ± 0.8
Total Recovery	90.7 ± 2.2	94.8 ± 2.3	89.7 ± 1.3	90.0 ± 2.9	95.9 ± 1.8

^a Values are mean ± SD for five rats and five mice. Four animals are being reported for the 1.7 mg/kg dermal study.

^b Total radioactivity in the appliance and skin wash.

NC Samples not collected for this time point.

Table 4

Cumulative Excretion of Radiolabel by Male F-344 Rats and B6C3F1 Mice 72 h after Administration of [¹⁴C]TMPTA^a

Route		Pre-Exposed Dermal	Dermal	Dermal
Dose		151 mg/kg	130 mg/kg	15.2 mg/kg
Excreta	End of Collection Period (h) ^b	(% Dose)	(% Dose)	(% Dose)
Urine	8	0.1 ± 0.0	0.1 ± 0.1	0.5 ± 0.1
	24	1.0 ± 0.2	0.6 ± 0.2	3.1 ± 0.3
	48	3.0 ± 0.8	1.7 ± 0.2	7.2 ± 1.1
	72	5.8 ± 1.5	3.0 ± 0.4	12.1 ± 1.4
	Cage Rinse	0.4 ± 0.2	0.1 ± 0.0	0.9 ± 0.4
Feces	8	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0
	24	0.1 ± 0.0	0.0 ± 0.0	0.3 ± 0.1
	48	0.2 ± 0.1	0.1 ± 0.0	0.8 ± 0.1
	72	0.4 ± 0.2	0.2 ± 0.1	1.2 ± 0.2
Exhaled CO ₂	8	0.1 ± 0.0	0.1 ± 0.0	0.4 ± 0.6
	24	0.5 ± 0.1	0.5 ± 0.0	1.5 ± 0.2
	48	1.7 ± 0.4	0.9 ± 0.2	3.1 ± 0.5
	72	3.5 ± 1.1	1.4 ± 0.2	4.9 ± 0.8
Total		10.1 ± 2.8	4.7 ± 0.6	19.2 ± 2.5

Route		Dermal - Rats	Dermal - Mice
Dose		1.7 mg/kg	1.2 mg/kg
Excreta	End of Collection Period (h) ^b	(% Dose)	(% Dose)
Urine	8	2.3 ± 0.8	0.8 ± 1.6
	24	10.6 ± 0.9	10.0 ± 2.5
	48	21.1 ± 0.8	14.3 ± 2.9
	72	28.0 ± 1.2	16.5 ± 2.8
	Cage Rinse	0.9 ± 0.4	2.0 ± 0.9
Feces	8	0.0 ± 0.0	NC
	24	0.9 ± 0.2	2.9 ± 2.6
	48	1.9 ± 0.4	4.3 ± 3.7
	72	2.5 ± 0.5	5.6 ± 4.2
Exhaled CO ₂	8	2.1 ± 0.4	8.3 ± 2.3
	24	6.6 ± 0.8	13.7 ± 4.0
	48	10.6 ± 1.1	16.7 ± 4.9
	72	13.1 ± 1.4	18.2 ± 5.4
Total		44.6 ± 2.7	42.4 ± 7.3

^a Values are mean ± SD for five rats.
^b Time points are referenced to time of dermal dosing.
 NC Samples not collected for this time point.

Table 5

Concentration of ^{14}C in Tissues of Male F-344 Rats 72 h Following Dermal Exposure of [^{14}C]TMPTA^a

Dose	Pre-Exposed 151 mg/kg					
Tissue Name	ng-eq TMPTA per g Tissue		Tissue Blood Ratio		Percent Dose in Total Tissue ^b	
Adipose	863	± 614	0.12	± 0.05	0.04	± 0.03
Bladder	6441	± 2780	1.24	± 1.11	0.00	± 0.00
Blood	6802	± 2776	unity		0.09	± 0.06
Brain	434	± 154	0.07	± 0.01	0.00	± 0.00
Heart	2655	± 1560	0.38	± 0.13	0.01	± 0.00
Kidney	20098	± 3447	3.29	± 1.08	0.09	± 0.02
Liver	3849	± 1384	0.59	± 0.08	0.08	± 0.03
Lung	3807	± 1332	0.58	± 0.06	0.02	± 0.01
Muscle	500	± 228	0.08	± 0.04	0.16	± 0.07
Skin	1630	± 1282	0.23	± 0.11	0.18	± 0.14
Spleen	3877	± 1477	0.58	± 0.06	0.01	± 0.00
Testes	674	± 393	0.10	± 0.03	0.00	± 0.00

Dose	130 mg/kg					
Tissue Name	ng-eq TMPTA per g Tissue		Tissue Blood Ratio		Percent Dose in Total Tissue ^b	
Adipose	94	± 35	0.08	± 0.04	0.01	± 0.00
Bladder	1705	± 810	1.49	± 0.76	0.00	± 0.00
Blood	1163	± 116	unity		0.01	± 0.01
Brain	78	± 11	0.07	± 0.01	0.00	± 0.00
Heart	468	± 46	0.40	± 0.03	0.00	± 0.00
Kidney	9636	± 2334	8.34	± 2.16	0.05	± 0.01
Liver	1201	± 225	1.04	± 0.24	0.03	± 0.01
Lung	668	± 104	0.58	± 0.09	0.00	± 0.00
Muscle	125	± 37	0.11	± 0.04	0.05	± 0.01
Skin	324	± 101	0.29	± 0.12	0.04	± 0.01
Spleen	698	± 164	0.60	± 0.12	0.00	± 0.00
Testes	196	± 127	0.18	± 0.13	0.00	± 0.00

Dose	15.2 mg/kg Dermal					
Tissue Name	ng-eq TMPTA per g Tissue		Tissue Blood Ratio		Percent Dose in Total Tissue ^b	
Adipose	75	± 45	0.14	± 0.10	0.03	± 0.02
Bladder	406	± 194	0.75	± 0.31	0.00	± 0.00
Blood	533	± 6	unity		0.18	± 0.02
Brain	62	± 47	0.11	± 0.07	0.00	± 0.00
Heart	255	± 14	0.48	± 0.03	0.01	± 0.00
Kidney	5910	± 715	11.1	± 0.9	0.28	± 0.03
Liver	480	± 47	0.90	± 0.06	0.12	± 0.01
Lung	321	± 40	0.60	± 0.03	0.01	± 0.00
Muscle	53	± 10	0.10	± 0.02	0.17	± 0.03
Skin	326	± 40	0.61	± 0.02	0.00	± 0.00
Spleen	166	± 8	0.31	± 0.03	0.19	± 0.01
Testes	114	± 46	0.21	± 0.08	0.01	± 0.00

^a Values are mean ± SD for five rats.

^b Percent dose was calculated using the following values for the mass of total tissue, expressed as percent of body weight: adipose, 7.0%; blood, 5.2%; muscle, 48%; and skin, 17%.

Table 6

Concentration of ^{14}C in Tissues of Male F-344 Rats and B6C3F1 Mice
72 h Following Dermal Exposure of [^{14}C]TMPTA^a

Dose	1.7 mg/kg Rats				
Tissue Name	ng-eq TMPTA per g Tissue	Tissue Blood Ratio		Percent Dose In Total Tissue ^b	
Adipose	11 ± 3	0.11 ±	0.05	0.04 ±	0.01
Bladder	89 ± 52	0.92 ±	0.64	0.00 ±	0.00
Blood	104 ± 29	unity		0.30 ±	0.09
Brain	7 ± 1	0.07 ±	0.02	0.00 ±	0.00
Heart	43 ± 21	0.40 ±	0.08	0.01 ±	0.01
Kidney	500 ± 86	4.98 ±	1.02	0.20 ±	0.04
Liver	66 ± 8	0.66 ±	0.14	0.12 ±	0.02
Lung	67 ± 31	0.63 ±	0.12	0.02 ±	0.01
Muscle	8 ± 1	0.08 ±	0.03	0.20 ±	0.03
Skin	22 ± 3	0.22 ±	0.03	0.20 ±	0.03
Spleen	69 ± 20	0.67 ±	0.13	0.01 ±	0.00
Testes	10 ± 2	0.11 ±	0.03	0.01 ±	0.00

Dose	1.2 mg/kg Mice				
Tissue Name	ng-eq TMPTA per g Tissue	Tissue Blood Ratio		Percent Dose In Total Tissue ^c	
Adipose	3 ± 3	0.14 ±	0.12	0.02 ±	0.02
Bladder	35 ± 16	2.07 ±	1.55	0.00 ±	0.00
Blood	20 ± 6	unity		0.12 ±	0.02
Brain	2 ± 1	0.09 ±	0.04	0.00 ±	0.00
Heart	8 ± 1	0.44 ±	0.14	0.00 ±	0.00
Kidney	36 ± 3	1.93 ±	0.55	0.05 ±	0.01
Liver	20 ± 4	1.04 ±	0.27	0.07 ±	0.02
Lung	18 ± 11	0.88 ±	0.50	0.01 ±	0.00
Muscle	4 ± 1	0.20 ±	0.08	0.13 ±	0.04
Skin	106 ± 23	5.52 ±	1.65	1.20 ±	0.31
Spleen	11 ± 2	0.56 ±	0.09	0.00 ±	0.00
Testes	4 ± 1	0.22 ±	0.04	0.00 ±	0.00

^a Values are mean ± SD for four rats and five mice.

^b For rats, the percent dose was calculated using the following values for the mass of total tissue, expressed as percent of body weight: adipose, 7.0%; blood, 5.2%; muscle, 48%, and skin, 17%.

^c For mice, the percent dose was calculated using the following values for the mass of total tissue, expressed as percent of body weight: adipose 9.6%; blood, 7.6%; muscle, 45.2%, and skin, 14.4%.

Table 7

Concentration of ¹⁴C in Blood of Male F-344 Rats Following iv Bolus Administration of 9.4 mg/kg TMPTA (ug-eq/g Blood)^a

0.08	15.2	24.3	39.7	27.0	33.5	27.9 ± 9.3
0.5	20.2	21.7	25.2	18.6	21.2	21.4 ± 2.4
1	12.9	22.0	16.9	10.8	19.7	16.5 ± 4.6
3	23.0	21.9	16.5	15.9	17.1	18.9 ± 3.3
6	22.1	20.7	20.0	14.9	16.6	18.9 ± 3.0
24	20.4	18.7	19.5	14.3	16.4	17.9 ± 2.5
48	17.6	17.1	17.0	12.6	15.4	15.9 ± 2.0
72	14.8	15.0	14.8	11.3	13.4	13.9 ± 1.6

a Mean ± SD for five rats.

b All time points referenced to time of administered iv dose.