

ADME NTP Study S0131 Thiophene

The contract laboratory did not use an abbreviation for the test article.

Sex/Species: young adult male F344 rats.

CASRN 110-02-1

Radiolabeled with carbon-14 in the 2- and 5- positions; Thiophene, [2,5-¹⁴C]-

Study Performed:

- Single 8000 ppm thiophene exposure for 1 hour by nose-only inhalation with sacrifice 72 hours post-exposure.

Two rats died as a result of exposure, and of the remaining eight out of the original ten, two were used for serial blood collection, one for both serial blood and urine and feces collection, two for urine and feces collection and three for radioactivity in the expired air collection. No ¹⁴CO₂ was detected (less than twice background of the system) in the exhaled air. The majority (73.9%) of the retained thiophene was eliminated unchanged in the exhaled air as volatiles.

Toxicokinetics:

The rates of elimination of compound equivalents from plasma and blood cells were calculated by fitting simple exponential functions to the concentration-time curves for mean data. Elimination of thiophene-derived radioactivity from plasma between 1 and 12 hours was monophasic with a half-time of circa 3.6 hours. Elimination of thiophene-equivalents from blood cells after 1 hour following exposure was biphasic with half-times of circa 2.9 hours and circa 9.1 days. No other modeling was performed.

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TABLE 1

Exhalation of ^{14}C -thiophene by male Fischer-344 rats after
inhalation of ^{14}C -thiophene at ca. 8000 ppm for 60 min

<u>Time</u> (hr) ^a	Mean \pm SD ^{14}C -Thiophene <u>Equivalents Exhaled (μmol)</u> ^b
0-1	110.01 \pm 2.55
1-2	101.29 \pm 29.38
2-3	51.67 \pm 7.79
3-4	39.53 \pm 14.29
4-5	24.63 \pm 7.67
5-6	15.83 \pm 3.97
6-7	11.08 \pm 5.25
7-8	2.95 \pm 2.56
8-12	1.73 \pm 1.46
12-24	0.98 \pm 0.05
24-32	0.29 \pm 0.12
32-48	0.20 \pm 0.13
48-56	0.06 \pm 0.05
56-72	0.10 \pm 0.05

Footnotes defined on the following page.

TABLE 1 (continued) Cumulative Exhaled

<u>Time (hr)</u> ^a	<u>Mean ± SD ¹⁴C-Thiophene Equivalents Exhaled (μmol)</u> ^b
0-1	110.01 ± 2.55
0-2	211.30 ± 29.48
0-3	262.97 ± 21.75
0-4	302.50 ± 13.48
0-5	327.14 ± 7.14
0-6	342.97 ± 6.32
0-7	354.05 ± 8.22
0-8	357.00 ± 9.63
0-12	358.73 ± 10.52
0-24	359.72 ± 10.50
0-32	360.00 ± 10.62
0-48	360.20 ± 10.70
0-56	360.26 ± 10.72
0-72	360.36 ± 10.76

^a Time after the end of the exposure period.

^b Mean of data from 3 rats.

TABLE 2

Urinary and fecal excretion of ¹⁴C-radioactivity by male Fischer-344 rats after inhalation of ¹⁴C-thiophene at ca. 8000 ppm for 60 min

<u>Time (hr)</u> ^a	<u>Urine</u>	<u>Feces</u>
	<u>Mean ± SD ¹⁴C-Thiophene</u>	<u>Equivalents Excreted (μmol)</u>
0-4	37.7 ± 8.6	0.16 ± 0.22
4-8	45.1 ± 5.1	0.28 ± 0.49
8-12	27.2 ± 5.2	0.21 ± 0.25
12-24	6.2 ± 1.7	1.38 ± 0.65
24-48	3.2 ± 0.7	0.64 ± 0.1
48-72	1.3 ± 0.3	0.09 ± 0.01
	<u>Mean ± SD ¹⁴C-Thiophene Equivalents Excreted (Cumulative μmol)</u> ^b	
0-4	37.7 ± 8.6	0.16 ± 0.22
0-8	82.8 ± 8.1	0.45 ± 0.41
0-12	110.0 ± 6.0	0.65 ± 0.64
0-24	116.2 ± 6.6	2.03 ± 0.26
0-48	119.5 ± 7.2	2.67 ± 0.25
0-72	120.7 ± 7.6	2.76 ± 0.26

^a Time after the end of the exposure period.

^b Mean of data from 3 rats.

TABLE 3

Concentration of ^{14}C -thiophene equivalents in tissues of male Fischer-344 rats at 72 hr^a after inhalation of ^{14}C -thiophene at 8000 ppm for 60 min

<u>Tissue</u>	<u>Mean \pm SD Concentration (nmol/g)</u> ^b
Plasma	# ^c
Blood Cells	317.18 \pm 59.7
Liver	75.3 \pm 8.9
Kidney	55.5 \pm 6.5
Heart	56.1 \pm 12.0
Lung	49.0 \pm 4.6
Brain	10.5 \pm 1.7
Fat	16.6 \pm 6.3
Skeletal Muscle	11.3 \pm 1.0
Nasal Passage	43.8 \pm 9.4
Larynx/Trachea	29.8 \pm 6.1

^a Time after the end of the exposure period.

^b Mean of data from 3 rats.

^c Mean \pm SD not calculable because radioactivity in all samples was less than twice background for the system.

TABLE 4

Concentration of ¹⁴C-thiophene equivalents in plasma of male
Fischer-344 rats after inhalation of ¹⁴C-thiophene at
ca. 8000 ppm for 60 min.

Time ^a	Rat			Mean ± SD
	930	932	933	
	Concentration (nmol/g)			
5 (min)	408.80	374.30	352.40	378.50 ± 28.43
15	* ^b	442.50	376.30	409.40
30	347.50	277.40	264.70	296.53 ± 44.59
1 (hr)	537.20	162.80	243.90	314.63 ± 196.97
2	379.20	234.10	210.20	274.50 ± 91.46
4	185.80	175.40	120.40	160.53 ± 35.14
6	138.20	167.00	102.80	136.00 ± 32.16
8	111.00	78.70	141.50	110.40 ± 31.4
12	30.10	43.30	29.50	34.30 ± 7.8
24	- ^c	-	-	# ^d
48	-	-	-	#
72	-	-	-	#

^a Time after the end of the exposure period.

^b Sample not collected.

^c Radioactivity less than twice background for the system.

^d Mean ± SD not calculable because radioactivity in all samples was less than twice background for the system.

TABLE 5

Concentration of ¹⁴C-thiophene equivalents in blood cells of male Fischer-344 rats after inhalation of ¹⁴C-thiophene at ca. 8000 ppm for 60 min.

Time ^a	Rat			Mean ± SD
	930	932	933	
	Concentration (nmol/g)			
5 (min)	2382.81	1692.06	1590.44	1888.44 ± 431.14
15	* ^b	2497.27	1635.01	2066.14
30	1402.31	1381.27	1095.20	1292.93 ± 171.56
1 (hr)	1890.54	1336.11	1209.06	1478.57 ± 362.39
2	1051.11	1070.72	599.71	907.18 ± 266.46
4	720.23	599.36	514.98	611.52 ± 103.16
6	384.24	434.51	421.08	413.28 ± 26.03
8	486.81	438.32	657.59	527.57 ± 115.18
12	430.24	519.02	443.90	464.39 ± 47.80
24	415.14	458.64	414.43	429.40 ± 25.32
48	428.10	511.17	388.99	442.75 ± 62.39
72	327.07	489.18	379.61	398.62 ± 82.71

^a Time after the end of the exposure period.

^b Sample not collected.