ADME NTP Study S0375 Lead Ores

The contract laboratory used Alaskan lead ore concentrate for the test article.
Sex/Species: adult male F344 rats.
Vehicle: dosed feed, NRC-AIN-76A powder feed.

CASRN LEADORES

No radiolabel was used. Lead in feed was analyzed by an Inductively Coupled Argon Plasma Emission Spectrometer (220.35 nm). Blood samples and femurs were analyzed by a Graphite Furnace Atomic Absorption Spectrometer (283.3 nm).

Studies Performed:

- Rats were exposed to dosed feed with 0, 10, 30, or 100 ppm Alaskan lead ore concentrate for 30 days (n = 10 per group). Blood and bone (femur) was analyzed for lead on Day 30 and urine for delta-aminolevulinic acid (ALA) on Day 23.

This test article was one of four lead compounds tested together to determine the bioavailability of different chemical forms of lead. The other three test articles were lead (II) acetate, lead (II) oxide, and lead (II) sulfide (NTP studies S0195, S0248, and S0265, respectively).

All four of the test articles were sieved in an 8 inch 400 mesh US Standard Sieve. The fraction of lead ore that passed through the sieve (-400) was used in the study. For the Alaskan ore concentrate, the -400 fraction with particle sizes less than 38 microns was used in the feed preparations. The assay value for Alaskan lead ore concentrate used in formulating feed dosages was 61.1 ± 0.6% lead by weight. No significant differences were found in food consumption as a function of dose levels for any of the test chemicals.

The Alaskan lead ore concentrate was produced in mining activities as waste. Because the ore concentrate was not a single pure compound, but rather a mix of lead compounds, the small particle size fraction may not have the same lead composition as the unsieved concentrate.

Analysis of blood samples taken immediately prior to dosing and at the end of the dosing period showed substantial contamination of a significant number of the samples. For this reason, no conclusions can be made from the blood lead data (not shown).

On exposure day 23, each rat was transferred to an individual metabolism chamber with dosed feed and water for collection of urine for up to 24 hours to provide sufficient urine for analysis.

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Table 1

Concentration of ALA in Urine After
23 Days of Ingesting Alaskan Ore Concentrate in Feed[a,b]

Controls (0 ppm)		10 ppm Lead		30 ppm Lead		100 ppm Lead	
Animal No.	ALA (μg/mL)	Animal No.	ALA (μg/mL)	Animal No.	ALA (μg/mL)	Animal No.	ALA (μg/mL)
1D	11.0	11D	11.0	21D	10.8	31D	15.5
2D	12.3	12D	12.0	22D	12.7	32D	11.1
3D	11.7	13D	14.2	23D	12.4	33D	11.7
4D	14.6	14D	12.5	24D	14.7	34D	14.8
5D	13.2	15D	12.3	25D	11.8	35D	10.9
6D	10.0	16D	14.6	26D	12.4	36D	14.6
7D	13.5	17D	11.4	27D	11.9	37D	15.9
8D	7.3	18D	13.2	28D	9.7	38D	10.9
9D	9.6	19D	11.2	29D	12.2	39D	11.6
10D	12.0	20D	10.1	30D	10.7	40D	12.7
Mean	**11.5**		**12.3**		**11.9**		**12.9**
SD	2.1		1.4		1.4		2.0

Controls	Spiked Level	Found
1	10 μg/mL	9.9 μg/mL
2	20 μg/mL	21.0 μg/mL
3	40 μg/mL	41.9 μg/mL

[a] ALA - δ-amino levulinic acid.
[b] Data shown are averages of duplicate determinations for each sample.

Table 2

Uptake of Lead in Rat Femurs After 30 Days of Ingesting Alaskan Ore Concentrate in Feed

Dose Level: 0 ppm

Animal	Total Feed Consumption (g)	Femur Weight (g)	Total Lead in Femur (μg)	Femur [Pb] (μg/g)
1D	345.0	0.3681	0.03	0.07
2D	351.1	0.4097	0.07	0.17
3D	321.5	0.3014	0.02	0.08
4D	296.0	0.3474	0.04	0.11
5D	323.8	0.3373	0.06	0.17
6D	327.9	0.3612	0.03	0.07
7D	329.6	0.3535	0.00	0.00
8D	378.2	0.4102	0.01	0.03
9D	310.8	0.3270	0.18	0.54
10D	355.9	0.3985	0.02	0.06
Mean	**334.0**	**0.3614**	**0.05**	**0.13**
SD	22.7	0.0343	0.05	0.15
CV	6.8	9.4874	105.5	112.3

Dose Level: 30 ppm

Animal	Total Feed Consumption (g)	Femur Weight (g)	Total Lead in Femur (μg)	Femur [Pb] (μg/g)
21D	319.4	0.3409	7.02	20.60
22D	294.1	0.3235	2.50	7.72
23D	332.5	0.3726	1.46	3.93
24D	333.1	0.3523	2.15	6.11
25D	343.0	0.3690	3.68	9.96
26D	335.4	0.3112	2.15	6.90
27D	359.7	0.3887	1.85	4.75
28D	320.0	0.3439	1.88	5.48
29D	333.6	0.3531	3.33	9.42
30D	352.0	0.3119	3.34	10.70
Mean	**332.3**	**0.3467**	**2.94**	**8.6**
SD	17.4	0.0246	1.53	4.6
CV	5.2	7.0975	52.2	53.2

Dose Level: 10 ppm

Animal	Total Feed Consumption (g)	Femur Weight (g)	Total Lead in Femur (μg)	Femur [Pb] (μg/g)
11D	352.5	0.3845	0.70	1.81
12D	345.5	0.3923	0.40	1.02
13D	330.8	0.3533	2.31	6.53
14D	344.4	0.3687	2.49	6.75
15D	343.6	0.3606	0.26	0.71
16D	340.5	0.3635	0.51	1.41
17D	361.2	0.3479	0.40	1.15
18D	338.0	0.3735	0.38	1.03
19D	364.1	0.3778	7.48	19.80
20D	319.5	0.3312	0.56	1.70
Mean	**344.0**	**0.3653**	**1.55**	**4.2**
SD	12.6	0.0172	2.12	5.6
CV	3.7	4.7154	137.1	134.3

Dose Level: 100 ppm

Animal	Total Feed Consumption (g)	Femur Weight (g)	Total Lead in Femur (μg)	Femur [Pb] (μg/g)
31D	326.1	0.3614	6.65	18.4
32D	347.7	0.3634	5.01	13.8
33D	356.5	0.3660	3.70	10.1
34D	330.8	0.3668	1.87	5.1
35D	368.7	0.3763	5.49	14.6
36D	349.2	0.3506	5.61	16.0
37D	359.0	0.3629	3.30	9.1
38D	340.4	0.3561	5.80	16.3
39D	386.2	0.4102	4.35	10.6
40D	332.4	0.3291	7.40	22.5
Mean	**349.7**	**0.3643**	**4.92**	**13.7**
SD	17.7	0.0194	1.57	4.8
CV	5.1	5.3	31.8	35.1

Table 3

Correlations of Femur Pb Uptake with Dose

Compound	Regression Equation[a,b]	Correlation Coefficient (r^2)
Lead Acetate	$[Pb]_{femur} = 2.64 \times Dose + 1.24$	0.9938
Lead Oxide	$[Pb]_{femur} = 1.64 \times Dose - 3.53$	0.9953
Lead Sulfide	$[Pb]_{femur} = 0.10 \times Dose + 0.54$	0.9626
Alaskan Ore Concentrate	$[Pb]_{femur} = 0.12 \times Dose + 2.40$	0.8733

[a] Dose in μg Pb/g feed; $[Pb]_{femur}$ in μg Pb/g femur (fresh weight).
[b] Slopes of the regression equations for lead acetate and lead oxide studies were statistically different from each other and from those of the other test compounds. Slopes of the regression equations for lead sulfide and Alaskan lead ore concentrate were not statistically different from each other.