FOR DU PONT USE ONLY

HASKELL LABORATORY

Common Name: Lead Oxide
Chemical Name: Lead Oxide[PbO] (9CI)
Synonyms: C.I. 77577
C.I. Pigment Yellow 46
Lead Monoxide
Lead Oxide Yellow
Lead Protoxide
Litharge
Plumbous Oxide
Massicot
Yellow Lead Ocher
CAS Registry No.: 1317-36-8
Chemical Structure:

Pb-O

Chemical and Physical Properties (1)

Appearance:	Yellow crystals
Molecular Weight:	223.21
Melting Point:	888°C
Density:	9.53
Solubility:	Insoluble in water and alcohol Soluble in acids and alkalies

Threshold Limit Value (2)

TWA = 0.15 mg/m^3 (as Lead)

TOXICITY

N 27659

A. Acute

1. Oral

- Lead oxide as a suspension in peanut oil was administered by intragastric intubation to two groups of ten male rats at dose levels of 17,000 and 25,000 mg/kg. One rat of ten died at each level. Clinical signs were soft feces and/or diarrhea containing lead oxide for two days, weight losses for as long as 12 days after dosing, emaciation and anorexia (17).

- Lead oxide dust, as a suspension in distilled water, was administered by intragastric intubation to male rats at dose levels from 670 mg/kg to 17,000 mg/kg. Rapid breathing occurred after dosing at 2,250 mg/kg dose level. Weights losses were noted for 1-3 days after dosing at 3,400 mg/kg and above. The lethal dose must be greater than 17,000 mg/kg (20).

- The lethal dose of lead oxide when fed to bees in honey was 0.32-0.50 mg per bee. Toxic symptoms included increased inertia, slow wing movements and inability to climb followed by paralysis, inability to feed and death (3).

2. Skin

- Lead oxide, when tested on the intact skin of male albino rabbits, produced no irritation in 24 or 48 hours (19).

- Lead oxide has been evaluated as safe for contact with intact or abraded skin. Irritancy was less than one on a scale of 1-4 (4).

- Lead oxide (29.5% by weight) is a component of a preparation useful in treating eczemas, allergies, inflammations, itching, infections, prurigo and of healing wounds (5).

3. Eye

- 0.1 ml of undiluted lead oxide dust was placed into the right conjunctival sac of 2 albino rabbits. After 20 seconds one treated eye was washed with water for 1 minute. The other rabbit's eye was not rinsed. Observations are as follows:

Conditions		Ocular Effects		
Dose	Treatment	Cornea	Iris	Conjunctiva
0.1 ml (129.4 mg)	Not Washed	None	None	Redness: mild 1 hr-2 days Discharge: slight 1-4 hrs Swelling: moderate at 1 hr, mild at 4 hr
0.1 ml (129.4 mg)	Washed	None	None	Redness: minimal 1-4 hrs Discharge: slight 1-4 hrs Swelling: mild 1-4 hrs

Lead oxide dust produced transient mild conjunctivitis with no iritic or corneal involvement in the rabbit eye (18).

4. Inhalation

- "Ten rabbits were exposed to a time-weighted average concentration of 3.72 mg/l lead oxide dust (98.3% respirable particle size) for a single one-hour exposure. No mortality occurred during exposure during the 14-day recovery period. Under these experimental conditions, lead oxide dust is not a Class B Poison* by the inhalation route" (21).

- "Ten rats were exposed to a time-weighted average atmospheric concentration of 4.38 mg/l lead oxide dust for a single one-hour head only exposure. One rat was sacrificed five days post-exposure because of a non-compound related injury. Under these experimental conditions, this sample of lead oxide dust (200 ppm organolead content) is not a Class B Poison" (22).

6. Injection

- LD50 (rat, intraperitoneal) = 630 mg/kg (7).

- LD50 (rat, intraperitoneal) = 430 mg/kg (8).

- Following intravenous injection of lead oxide into rats, lead was found in femoral bone tissue (6).

B. Extended Studies

1. Oral

- Lead oxide as a 10% suspension in peanut oil was administered to six male rats 5x/week/2 weeks. Three test rats and three control rats were killed four hours and 14 days following the last dose. The results are:

*Hazardous Material Regulations of the Department of Transportation, Agent R. M. Graziano's Tariff No. 31, March 31, 1977

Dose mg/kg	No. of Doses	Mortality	Toxic Signs	Pathologic Changes
1000	10	0/6	First Week: severe weight loss, weakness, chewing and pawing motions after dosing, salivation Second Week: severe weight loss, weakness, emaciation, incoordination, chewing and pawing motions after dosing Recovery Period: although rate of weight gain slightly greater than that of controls, final average weight 110 grams less; slightly emaciated for 1 week	After 10th Dose: bilateral dilatation of tubules of inner cortex of kidney; absence of perinuclear vacuolation of liver cells 14 Days After 10th Dose: histologic changes in kidney still present; kidney very large; liver essentially normal

"Lead monoxide induced signs of severe cumulative oral toxicity when administered to rats. The animals lost weight during the dosing period, became emaciated and exhibited signs of central nervous system stimulation. Histologic examination of tissues revealed severe damage to the kidneys, which was not ameliorated in 14 days, and transient cellular changes in the liver" (23).

- The toxicity of three poisons, lead oxide, lead acetate and arsenic oxide, was investigated in white mice given the poison in feed every day for 30 days. The survival time of the animals fed lead oxide was significantly longer than the others (11).

- Broilers fed lead oxide in the diet at concentrations as high as 80 ppm for 7 weeks showed the highest concentration of lead accumulation in the bones (12).

2. Inhalation

- The lungs of rats which inhaled 200 $\mu g/m^3$ for 14 days showed damage to the alveolar macrophages and type I pneumocytes. Ultrastructural changes included changes in the structures of the mitochondria and endoplasmic reticulum (24).

- Workers dismantling an elevated train network were exposed to high levels of lead oxide fumes. The average concentration for 32 burner workers was 4.36 mg/m^3 while the mean was 0.23 mg/m^3 for non-burner workers. Some observations were:

	Burner Workers	Non-Burner Workers
Blood Lead	44-110 µg/100g	24-75 µg/100g
Average Hematocrit	41.4%	44.0%
Free Erythrocyte Protoporphyrin	1134 µg/dl	714 µg/dl
Mean Peroneal Motor-Nerve Conduction Velocity	43.2 m/s	49.0 m/s

Burners also experienced nausea, abdominal discomfort, mood change and irritability, sleeplessness, fatigue, headache and numbness and tingling of the extremities (25).

- Exposure of rats to lead oxide at 2.4 µg for 78 days decreased the activity of cholinesterase and levels of Hb and protein sulfhydryl groups in the blood. Also observed were increases in reticulocyte count, decrease in the ascorbic acid content of lungs, liver, spleen and central nervous system. A high accumulation of lead was found in adrenal glands, bones, spleen, liver and lungs. Lead affected the activity of the central nervous system (16).

- "Nearly continuous exposure of monkeys and rats to airborne particulate lead oxide for 1 year increased Pb levels of the blood to 28 µg/100 ml in rats and 17 µg/100 ml in monkeys. These maximum levels were reached after the first few months of exposure and did not increase after that. Pb levels rose to 2-3 µg/g in soft tissue and up to .006 µg/g in bone. Delta-aminolevulinic

acid dehydrase of erythrocytes was decreased by approximately 70% in rats, however there was no alteration in the excretion of heme precursors. There did not appear to be any change in blood chem. or hematol. nor were there any gross, microscopic, or ultrastructural pathologic changes" (13,14).

- "Inhalation of 150 µg lead oxide/m^3 for 4 days caused ultrastructural damage to the lung paranchyma of rats and significantly decreased the activity of lung benzopyrene hydroxylase. A similar treatment for 14 days increased the labeling of pneumocyte I cells by 3H-labeled thymidine, but pneomocyte type II cells were unaffected. Exposure of rats to titanium dioxide dust followed by inhalation of 82-168 µg lead oxide/m^3 significantly increased the retention of dust in the lung. These results indicate that the primary site of toxic action of Pb in lung is the reticular membrane and that low concentration of Pb can cause localized damage in the lung" (15).

C. Intratracheal Instillation

- After 10 weekly intratracheal instillations of 1 mg of lead oxide in combination with benzo[a]pyrene (1 mg) hamsters exhibited typical epithelial proliferation, ademoma and adenocarcinoma of the lungs. "Similar administration of lead oxide or benzo[a]pyrene alone produced only alveolar hyperplasia and metaplasia. No tumorous changes were found in control groups. Thus lead oxide exhibited a cocarcinogenic effect with benzo[a] pyrene in the lungs. The induced tumors generally appeared in the peripheral areas of the lungs, indicating bronchioloalveolar origin" (9).

- In a forty day study the intratracheal administration of moderate doses of lead oxide to rats resulted in a significant increase in the number of recoverable pulmonary alveolar macrophages. Thus lead oxide shows low order of toxicity to alveolar macrophages (10).

D. Mutagenic Potential

- To investigate the correlation between chromosomal damage and occupational exposure to lead, chromosomal analyses and biochemical tests were performed on workers in a lead-oxide factory, where all subjects were found to have a significantly elevated blood lead level (74.7 microg/100 ml vs normal value of 14.9 microg/100 ml). Blood lymphocyte cultures showed an increased proportion of mitoses with secondary chromosomal aberrations in the workers exposed to lead-oxide, compared with a control group of healthy blood donors. The percentage of abnormal mitoses rose with an increasing delta-aminolevulinic-acid excretion in the urine. In addition to chromosomal breaks there were also nonspecific changes such as spiralizing defects, chromosomal adhesions and pulverization. The proportion of tetraploid mitoses and the mitoses index were slightly increased over those in the control group (26).

- The lead concentration in blood and aberrations of chromosomes were detected in workers exposed to lead in the manufacture of lead oxide. The lead concentration was 30-75 µg/100 ml in exposed workers as compared to 15-35 µg/100 ml in controls. A significant increase of chromatid and chromosome aberrations occurred in exposed workers (28).

E. Carcinogenic Potential

A study performed by State University of New York began in June 1974 was completed in December 1977. The project summary follows:

- Male Syrian Golden hamsters were exposed to lead monoxide and platinum dioxide by intratracheal instillation once a week for 16 weeks. Each metal compound was administered alone and in combination with benzo[a]pyrene in saline suspension. Benzo[a]pyrene, alone and in combination with Fe_2O_3, a potent inducer of pulmonary neoplasia, was also given to obtain positive controls. Animals were maintained for their lifetimes. At death, gross and histopathologic examinations were performed.

These metals are being evaluated for their potential carcinogenicity in the induction of neoplasia, particularly of the respiratory tract, in conjunction with benzo[a]pyrene. More than 80% of the animals have been autopsied and data are presently being accumulated on pathologic alterations. A final report is expected in March 1978 (27).

RELATED INFORMATION

CA 79: 88057p Cytotoxocity of lead. Beck, E. G.; Manojlovic, N.; Fischer, A. B. (Med. Inst. Lufthyg. Silikoseforsch., Univ. Duesseldorf, Duesseldorf, Ger.). *Proc., Int. Symp., Environ. Health Aspects Lead* 1972 (Pub. 1973), 451–62 (Ger). Comm. Eur. Communities. Cent. Inform. Doc.: Luxembourg. Luxembourg. *Lead* [7439-92-1] and airborne dusts were toxic to line L cells, as shown by inhibitions of division and disturbance of cell permeability and intermediary metab.; the reprodn. of human fetal connective tissue cells was also impaired. Guinea pig alveolar macrophages showed both rapid lysis of the cell and slower bullate vacuolation in response to Pb. The vacuolation was produced by both Pb and airborne dust and was comparable in alveolar macrophages, line L cells, and human fetal connective tissue cells. Treatment of *lead oxide* [1317-36-8] and airborne Pb with *calcium ethylenediaminetetraacetate* [64-03-9] chelator decreased their toxicity. PbO, *lead bromide* [10031-22-8], and *lead acetate* [301-04-2] after aq. extn., or their aq. exts., had a toxic effect which varied according to the type of compd. Thus, atm. Pb may be a pathogenic factor in a multi-causal etiol. of various illnesses.

CA 81: 29036z Effect of low lead concentration on human body. Saito, Kazuo; Sato, Toshio; Sato, Yuji; Niizuma, Kozo (Sch. Med., Hokkaido Univ., Sapporo, Japan). *Ind. Health* 1973, 11(3), 85–93 (Eng). Microhematocrit, sp. gr. of blood, Pb concn. in whole blood, and δ-amino- levulinic acid dehydrase activity (ALAD) in erythrocytes were measured in 203 policemen on patrol by car and 19 workers exposed to PbO dust in a ceramic factory, and the blood Pb levels and ALAD activity correlated with the Pb concn. in the working atm. The Pb level in blood for the workers and the policemen were 14.3–31.2 and 2.0–31.1 μg/100ml, resp., and the mean ALAD activities were 0.96 and 1.23, resp. In policemen with < 15 μg Pb/100 ml there was no significant decrease of ALAD activity and no correlation.

K. Aparajithna

CA 76: 108111y **Comparative biological activity of metal oxides at the level of their threshold doses introduced singly.** Rabotnikova, L. V. (Med. Inst., Perm, USSR). *Gig. Tr. Prof. Zabol.* 1971, 15(8), 33–6 (Russ). The exptl. found THRESHOLD DOSES for 24 different toxic METAL OXIDES, administered in a single injection to white mice, showed close correlation with the officially admissible max. concns. An equation for the calcn. of an approx. max. concn. for a given metal oxide on the basis of its threshold dose is recommended. The threshold doses were detd. by testing changes in blood, summation–threshold index of the nervous system, and total body, liver, kidney, and spleen wts.

CA 66: 84266q Toxicity of metal oxides and its correlation with various physico-chemical properties and the normal content of the element in the body. L. V. Rabotnikova. *Vop. Obshch. Chastn. Prom. Toksikol., Leningrad* 1965, 52–5(Russ). LD_{50} values were detd. for 23 metal oxides on i.p. injection to mice. The correlation coeffs. between LD_{50} and sp. gr. of the oxide, the m.p., the normal potential of the element, the primary ionization potential, and the at. wt. were detd. A correlation was found between log LD_{50} of the oxides and the log of the permissible concns. and normal content of the element in the body. For several oxides, permissible concn. deviated toward a higher toxicity not corresponding to LD_{50} (e.g., PbO, PbO_2, BeO, Cr_2O_3, Co_2O_3). For these compds., addnl. factors must be taken into account in calcn. of permissible concn. For quick detn. of LD_{50} of oxide compds. it can be calcd. from the correlation with the oxide m.p. From *Ref. Zh., Biol. Khim.* 1966, Abstr. No. 22F1786.
MVRL

CA 84: 84: 160211g **Growth inhibition by mercury, arsenic, and lead of crops.** Shimagami, Hideo; Izawa, Kiyomi (Tokyo Fert. Feed Insp. Off., Tokyo, Japan). *Hiken Kaiho* 1975, 28(4), 15–34 (Japan). The toxicity of Hg [as $Hg(OAc)_2$ [1600-27-7], HgO, $HgCl_2$, *MeHgCl* [115-09-3]], As [as $NaAsO_2$, Na_2HAsO_4, $Ca_3(AsO_3)_2$, $Ca_3(AsO_4)_2$] and Pb [as $Pb(OAc)_2$ [301-04-2], PbO] to crops was studied under various environmental conditions. Pb at concns. as high as 1500–2000 ppm was nontoxic to rice, Chinese cabbages, and small turnips. Hg was highly toxic to dry field crops, whereas As was highly toxic to paddy field crops. Hg was more toxic to rice grown in alluvial soil than in trass, and HgO was more toxic than $Hg(OAc)_2$. By contrast, soils and chem. forms did not significantly affect the toxicity of Hg to Chinese cabbages. $NaAsO_3$ was more toxic than $Ca_3(AsO_4)_2$ to paddy rice, whereas no such relation was obsd. in dry field rice. $NaAsO_3$ was also more toxic than $Ca_3(AsO_4)_2$ to Chinese cabbages. The toxicity of As in various soils decreased in the order: sandy soil > alluvial soil > black soil > red clay.

CA 79: 88056n **Pulmonary resorption of lead dusts.** Schlipkoeter, H. W.; Pott, F. (Med. Inst. Lufthyg. Silikoseforsch., Univ. Duesseldorf, Duesseldorf, Ger.). *Proc., Int. Symp., Environ. Health Aspects Lead* 1972 (Pub. 1973), 403–13 (Ger). Comm. Eur. Communities, Cent. Inform. Doc.: Luxembourg, Luxembourg. The percentage of pulmonary and enteral resorption of *lead oxide* [1317-36-8] or *lead bromide* [10031-22-8] in rats was measured by the amt. of Pb deposited in the bones and the decrease of *δ-aminolevulinic acid dehydrase* [9036-37-7] activity by Pb. Pb administered intratracheally gave the same results as i.v. administration of the same Pb dose. Orally administered Pb showed only 5–10% resorption. Pb compds. were apparently absorbed very rapidly and almost completely when in the lung, but in the intestine the resorption was only 5–10% due to the poor solv. conditions.

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