Titanium Tetrachloride

Document History
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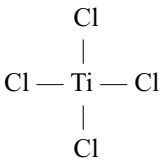
I. IDENTIFICATION

Chemical Name: Titanium Tetrachloride ($TiC1_4$)
Synonyms: Titanium Chloride
CAS Number: 7550-45-0
Molecular Formula: ($TiC1_4$)
Structural Formula:



II. CHEMICAL AND PHYSICAL PROPERTIES[1]

Physical State and Appearance: Colorless to light yellow liquid
Odor Description: Irritating; sharp; acidic
Molecular Weight: 189.73
Density: 1.726
Conversion Factors: 1 ppm = 7.75 mg/m^3
1 mg/rn^3 = 0.129 ppm
Boiling Point: 136°C (276.8°F) at 760 mmHg
Melting Point: -0.24°C (-11.2°F) at 760 mmHg
Vapor Density (Air = 1): 6.54
Vapor Pressure: 12 mmHg at 25°C (77°F)
Saturated Vapor Concentration: 16,300 ppm at 25°C (77°F)
Flash Point: Will not flash
Flammability Limits: Will not burn
Autoignition Temperature: Will not ignite
Solubility: Soluble in water, alcohol, and dilute hydrochloric acid.
Stability: Not stable in the presence of moisture.
Reactivity and Incompatibilities: ($TiC1_4$) hydrolyzes rapidly in air to form a dense white cloud of titanium oxychloride and hydrochloric acid.

III. USES

Polymerization catalyst; intermediate in the production of titanium metal and titanium pigments; mordant in the textile industry; used in the manufacture of iridescent glass and artificial pearls; used in dyeing leather and in smoke screens.

IV. ANIMAL TOXICITY DATA

A. Acute Toxicity

1. *Oral Toxicity*

A single oral dose of 464 mg/kg was lethal to 100% of the rats tested.[2]

2. *Eye Toxicity*

One drop of liquid $TiCl_4$ applied for 10 seconds with subsequent copious washing with water caused a suppurative conjunctivitis darkening of the cornea. An aqueous solution caused hyperemia of the conjunctiva.[3] Rats develop corneal opacity when exposed to fumes.[4]

3. *Skin Absorption*

Rabbits: LD_{50} = 3160 mg/kg[2]

4. *Skin Irritation*

Guinea pigs: Severely irritating[3]

Rabbits: Liquid not irritating, whereas an aqueous solution causes burns[3]

5. *Skin Sensitization*

No data available.

6. *Inhalation Toxicity*

Acute inhalation data are given on the next page:

TABLE I

Species	Test	Results
Rat	4-hr ALC*	110 mg/m^3 [6]
	4-hr LC_{50}	460 mg/rn^3 [7]
	2-hr LC_{50}	1100 mg/rn^3 [7]
	1-hr LC_{50}	1300 mg/rn^3 [7]
	30-min LC_{50}	3000 mg/rn^3 [7]
	10-min RD_{50}	2430 mg/rn^3 [8]
Mouse	2-hr ALC	600 mg/rn^3 [9]

* ALC = approximate lethal concentration

In rats, deaths occurred during exposure and up to 1 week post-exposure. Pulmonary edema was the most likely cause of death. Necropsy revealed inflammation of the eye and respiratory tract.

7. Intraperitoneal Toxicity

No data available.

8. Intravenous Toxicity

No data available.

B. Subacute Toxicity

No data available.

C. Subchronic Toxicity

Groups of 25 male rats were exposed to $TiC1_4$ atmospheric products at concentrations of 0, 5, or 40 mg/m^3 6 hr/day 5 thy/week for 4 weeks. Two rats died during exposure to 40 mg/rn^3, apparently of respiratory failure. The remaining rats survived the exposures but exhibited a slight depression in weight gain. Rats exposed to 10 mg/m^3 or 40 mg/m^3 exhibited acute inflammation of the respiratory tract at the termination of exposures. Signs of repair with the development of fibrotic collagenization were noted up to one year post-exposure. The only evidence of toxicity in rats exposed to 5 mg/m^3 was a slight increase in the lung-to-body weight ratio.[14]

Four dogs were exposed to $TiCl_4$ fumes 6 hr/day 5 days/week for a total of 45 exposures. The atmospheric concentration of titanium ranged from 12 mg/m^3 to 133 mg/m^3 and averaged 66 mg/m^3 (as titanium; this is equivalent to 261 mg/m^3 $TiCl_4$). The volatile HC1 concentration averaged 6.8 ppm. The dogs showed no subjective disturbances except a tendency to gag and expel small amounts of mucus during exposure. The lungs showed minute foci containing particles of titanium in monocytes. These foci contained masses of necrotic cells and were associated with the proliferation of connective tissue cells. The data suggest that the damage is repairable only by scar tissue formation, which would result in reduced pulmonary capacity and increased susceptibility to infection.[5]

D. Chronic Toxicity/Carcinogenicity

Groups of 100 male and 100 female rats were exposed to 0, 0.1, 1.0, or 10 mg/m^3 of $TiC1_4$ 6 hr/day 5 days/week for 2 years. No clinical or pathological effects other than mild rhinitis were noted in rats exposed to 0.1 mg/m^3. In rats exposed to 1.0 mg/m^3, the incidence of rhinitis and tracheitis was increased, and minute particle-laden macrophages were present in the lung. Also a slight Type II pneumocyte hyperplasia was noted in alveoli. These reactions are common in fume/dust studies and they are completely reversible on cessation of exposure; therefore, 1.0 mg/rn^3 was identified as a no observable adverse effect level (NOAEL). At 10 mg/m^3, extrapulmonary particle laden macrophages were found in the tracheo-bronchial lymph nodes, liver, and spleen. A higher incidence of macrophages was found in the alveoli; however, mixed-cell reactions were not seen. Also, a non-statistically significant incidence of an unusual lesion identified as a "well-differentiated, cystic keratinizing squamous carcinomas" was observed. These lesions have been found in other "particle/dust" studies and a meeting of experimental pathologists from throughout the world has reviewed these lesions and agreed that they are not tumors but should be classified as cysts.[16]

The incidences of rhinitis, tracheitis, f-macrophage infiltration, granuloma, bronchio-alveolar adenoma, and cysts are given below.

TABLE II

Selected Incidence Data for Rats Exposed to TiCL for 2 Years

Dose (mg/m^3):	0		0.1		1		10	
Group:	M	F	M	F	M	F	M	M
No. in group:	79	77	77	75	78	79	75	75
Lesion:								
Rhinitis	25	18	47	46	41	33	48	38
Tracheitis	2	—	8	13	35	29	31	3
Foamy Macrophage infiltration	14	8	8	3	10	13	49	61
Granuloma	7	2	3	1	4	2	13	19
Bronchio-alveolar adenoma	2	—	—	—	1	—	1	1
Cysts	—	—	—	—	—	—	2	3

The incidence of the lesions in the respiratory tract represents rather minor effects in rats exposed to 10 mg/m^3 for 2 years. These effects clearly indicate $TiC1_4$, to be more irritating than a nuisance dust, but no other significant lesions were noted.

E. Reproductive/Developmental Toxicity

No data available.

F. Genotoxicity

$TiCl_4$ was most mutagenic in *Bacillus subtilis*[10,11] and was negative in the CHO/HGPRT bioassay.[12]

G. Metabolism/Pharmacokinetics Following an acute inhalation study in rats, the titanium concentration in the blood was 10 µg/g. After 24 hr, the concentration was 0.5 µg/g. More titanium was in the feces than in the urine. After exposure, the concentration of titanium in the lung was 28 µg/g, which decreased to 15 µg/g within 6 days post-exposure.[13]

V. HUMAN USE AND EXPERIENCE

Severe localized skin burns might result because of the intense exothermic reaction between $TiCl_4$ and water. Three cases of severe chemical burns and nine cases of less severe bums were produced by liquid $TiC1_4$.[17]

Corneal damage was reported in 5 people who were severely exposed to fumes of $TiCl_4$. In one fatal case, the victim exhibited severe conjunctivitis with extensive destruction of corneal tissue. The cause of death was reported to be the effects on the respiratory tract.[18]

No evidence of progressive or cumulative changes in the lungs of 10 workers exposed intermittently to "low-level concentrations" of $TiCl_4$ fumes was determined as evidenced by X-ray and pulmonary function studies.[17]

Workers exposed for a short time to 15–20 mg/rn^3 experienced no irritation.[19]

A study of 969 workers who had been exposed to undetermined concentrations of $TiC1_4$ showed no increase in lung cancer mortality. Evidence based on a number of factors did not show a causal relationship between $TiC1_4$ exposure and lung cancer risk.[20]

VI. RATIONALE

The 4-hr approximate lethal concentration (ALC) of titanium tetrachloride in rats is 110 mg/m^3, and the 10-min RD_{50} in mice is 2430 mg/m^3. The skin LD_{50} in rabbits is 3160 mg/kg, and it is severely irritating to the skin of guinea pigs. In humid air, or as an aqueous solution, $TiCl_4$ will burn the skin of rabbits. Rats exposed to $TiC1_4$ fumes develop eye opacity.

In a 28-day study, 5 mg/rn^3 was considered a NOAEL, whereas exposure to 10 rng/m^3 or 40 mg/m^3 resulted in acute inflammation of the respiratory tract, which produced scar tissue during recovery periods up to 1-year post-exposure.

In dogs exposed to an average of 66 mg/rn^3 Ti (261 mg/m^3 $TiC1_4$) from $TiC1_4$ aerosol in humid air showed no adverse effects. Microscopic examination of the respiratory tract revealed necrotic foci containing particulate titanium and a proliferation of connective tissue cells.

Rats exposed to 10 mg/rn^3 $TiCl_4$ for two years developed a few well-differentiated keratinizing cysts in the alveolar duct region. Also, at 10 mg/rn^3, rhinitis and tracheitis were noted and particulate-ladened macrophages were found in alveoli and in tracheobronchial lymph nodes. The incidences of foamy macrophages and granulomas were increased. At 0.1 mg/m^3 and 1.0 mg/m^3, occasional rhinitis and tracheitis were observed. No evidence of progressive or cumulative lung damage has been noted in humans, and no evidence of an increase in cancer mortality has been found in $TiCl_4$ workers.

Based on a NOAEL of 1.0 rng/rn^3 and minimal effects at 10 mg/m^3 in rats exposed 6 hr/day 5 days/week for 2 years, an OEL of 500 [µg/m^3 (0.5 mg/rn^3) should provide adequate worker protection. Since the RD_{50} of $TiCl_4$ is 2430 mg/m^3, 500 µg/m^3 should be well below thresholds of irritation.

VII. RECOMMENDED OEL

8-hr time-weighted average: 500 p. µ/m^3 (0.5 mg/m^3). The concentration is determined by measuring titanium and calculating the equivalent $TiC1_4$ based on the total titanium present.

VIII. REFERENCES

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