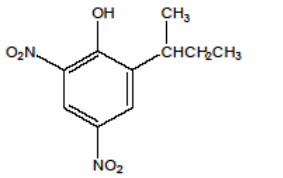
Hazard Data Book for Chemical Substances

No.	2001-15	Cabinet Order No.	3-828 (Chemical Substance Control Law) 1-339 (Law for PRTR and Promotion of Chemical Management)	CAS Registry No.	88-85-7

Chemical Name	2-(1-Methylpropyl)-4,6-dinitrophenol Synonyms: Dinoseb, DNBP, Premerge, 2,4-Dinitro-6-(1-methylpropyl)phenol	Structural Formula	
Chemical Formula	$C_{10}H_{12}N_2O_5$	Molecular Weight	240.24

Products on the market (Typical example) [1)]

Purity: >98%

Impurity: 4-(1-Methylpropyl)-2,6-dinitrophenol

Additives/Stabilizers: No

1. Physical-Chemical Properties

Appearance: Orange-yellow solid [2)]

Melting point: 38-42℃[2)]

Boiling point: 332℃

Flash point: 177℃[3)]

Ignition point: No reference given

Explosion limit: No reference given

Specific gravity: d_4^{45} 0.1.2647[2)]

Vapor density: 8.28 (Air = 1)

Vapor pressure: 0.007 Pa (5.3×10-5mmHg) (20℃)[4)]

Partition coefficient: log Pow ; 3.09 (measured)[5)], 3.67 (calculated)[6)]

Hydrolyzability: No chemical bonds hydrolyzed

Dissociation constant: pKa = 4.62[2)]

Spectrum: Major MS fragment

m/z 211 (base peak, 1.0) 、163 (0.42) 、147 (0.12)7)

Adsorption/Desorption properties: Soil sorption coefficient Koc; 124[2)]

Viscosity range: No reference given

Solubility: 2-(1-Methylpropyl)-4,6-dinitrophenol/water; 25.8 mg/L[5)]

Easily mixed with organic solvents, such as ethyl ether, toluene, xylene[2)]

Conversion factor: 1ppm = 10.0 mg/m^3

(Air, 20℃) 1mg/m^3= 0.100 ppm

2. Source/Exposure level

Produced amounts, etc.: 604 tons (FY1998) (Production: 0 ton, Import: 604 tons)[8)]

Emission/Exposure volume: No reference given

Utilization: Additives for resin[1)]

3. Environmental Fate

1) Biodegradability

Aerobic conditions

No report

Anaerobic conditions

No report

Abiotic conditions

Reactivity to OH^- radical

The rate constant is 4.03 x 10^{-12} cm^3/molecule·sec (25℃) in tropospheric air[9)].

If a concentration of OH radical is 5 x 10^{-5} ～ 1 x 10^{-6} molecules/cm^3, the half-life of this chemical substance is estimated to be 2-4 days.

Photolysis in water

There is a report that the photolysis half-life of this chemical substance is 14-18 days in epipelagic water.

Biodegradability in soil

There is a report that the half-life is 30 days in soil.

2) Degree of concentration

Low-concentration [5)] (Chemical Substance Control Law)

Lipid content		Test period
4.1%		6 weeks
	Test concentration	Concentration rate
1st section	10 mg/L	< 0.3-1.0
2nd section	1 mg/L	< 2.5

3) Environmental distribution/Monitoring data

No report

4. Ecological toxicity

System	Species name	LC_{50} (mg/L) Exposure time	EC50 (mg/L) (Exposure time) :Environmental impact index	Toxicity category*[12)]
Alga	*Chlorella pyrenoidosa*[13)] (Chlorella)		0.001 (24 hours) : Growth inhibition	Equivalent to acute category 1 (Exposure time

				differs.)
Crustacean	*Daphnia magna*[13] (Water flea)		0.24 (48 hours) : Immobilization inhibition	Equivalent to acute category 1
Fish	*Pinephales promelas*[13] (Fathead minnow)	0.088 (96 hours)		Equivalent to acute category 1
	Ictalurus punctatus[13] (Channel catfish)	0.028 (96 hours)		<Other than recommended species >
	Oncorhynchus clarki[13] (Cutthroat trout)	0.041 (96 hours)		<Other than recommended species >

*Category based on OECD classification criteria.

5. Toxicity data on mammals

1) Acute toxicity

	Mouse	Rat	Rabbit	Guinea pig
Oral LD_{50}	16 mg/kg	25 mg/kg	—	20 mg/kg
Inhalational LC_{50}	—	—	—	—
Dermal LD_{50}	—	80 mg/kg	80 mg/kg	—
Intraperitoneal LD_{50}	10 mg/kg	—	—	—
Subcutaneous LD_{50}	—	20 mg/kg	—	—

In an administration of 750 and 1,000 mg/kg body weight to rats (route of administration unknown), petit mal epileptiform activity was expressed in rat electroencephalograms (EEGs) in the 750 mg/kg group in particular.[2]

2) Irritant/corrosive property

Strong irritability has been expressed in tests where 50μg is administered to the eyes of rabbit[3] [14]

3) Sensitization properties

None in particular

4) Toxicity on repeat administration

(1) Oral administration

In a 5-13 day feeding, laboratory animals fed laboratory chow containing 0.05% of this chemical substance, expressed acute debility, slight effect on the kidneys and liver, and death was also observed.[2]

In a 153-day administration of 2.5 to 25 mg/kg body weight of this chemical substance to rats, death was observed in groups of more than 15 mg/kg of rats. In addition, growth inhibition was observed in all rats.[3]

This substance had no effect on rats fed laboratory chow during a 6-month feeding containing 0.01% of this chemical substance, or in a 90-day administration to dogs given at a dose of 4 mg/kg/day.

5) Mutagenicity /genotoxicity

Test method		Test condition	Result*
in vitro	Reversion test	*E. coli* WP2*uvr*A: < 1000μg/mL[15)]	−
	DNA repair test	*B. subtilis rec*: > approx. 1000μg/mL[15)]	+
		*S. typhimurium uvr*B *rec*: > approx. 1000μg/mL[15)]	+
	Unscheduled DNA synthesis test	Human lung cell line WI-38: < approx. 1000μg/mL[15)]	−
in vivo	Sex-linked recessive lethal test	Drosophila: < 10 mg/kg[15)]	−

* −:negative, +: positive

6) Carcinogenicity

In a 100-week feeding with CD-1 mice given doses of 1, 3 and 10 mg/kg/day of this chemical substance, a significant increase in incidence rates of liver adenoma in female mice fed more than 3 mg/kg/day was seen. In addition, an increase in incidence of carcinoma was observed in some mice. However, it was concluded that it was not caused by the administration of this substance due to the small number of cases.[16)]

No increase in carcinoma incidence was observed in an 18-month feeding of C3H/Anf x C57BL/6 F1 hybrid mice and AKR x C57BL/6 F1 hybrid mice (1-week-old) that were fed laboratory chow containing 0.0007% of this chemical substance, after a 3-week oral administration of 2.15 mg/kg/day of this chemical substance.[16)]

It was reported that there was no carcinogenicity in a 104-week feeding trial with rats given doses of 1, 3 and10 mg/kg/day of this chemical substance.[16)]

7) Reproductive/developmental toxicity

(1) Oral administration

Malformations (details unknown) of the musculoskeletal system were observed on administration of 26 mg/kg/day of this chemical substance to mice on day 8 of gestation.[3)]

Toxicity (details unknown) was observed in mothers and fetuses on administration of 5 mg/kg/day of this chemical substance to rats during the gestational period (details unknown).[3)]

Inhibition of weight gain in mothers as well as microphthalmia in fetuses was observed in a 9-day feeding with rats given 0.02% of this chemical substance on day 6 through day 14 of gestation.[2)]

In a feeding with male Sherman rats fed laboratory chow containing 0.0075, 0.015, 0.0225, and 0.03% of this chemical substance, differentiation abnormality was observed in 90% of sperm of the epididymides after 20 days. In addition, amorphous sperm and a reduction in the number of sperm were observed after 30 days. On histological examination, changes to sperm, spermatocyte and spermatogonia in the testes were observed after 20 and 30 days, and a critical effect to the spermatogonia were observed after 50 days. Reproductive inhibition was observed at 0.0225 and 0.03% of this chemical substance, but abnormality of sexual behavior, such as copulation, was not observed at these dosages. Almost no recovery of these symptoms was seen 16 weeks after administration. At 0.015%, changes such as a reduction in number and abnormality in the sperm of the epididymides were observed, but no abnormality in fertility function was observed. No abnormalities were observed at 0.0075%.[2)]

In a three-generation reproductive study with rats fed laboratory chow containing 1, 3, and 10 mg/kg/day of this chemical

substance for 29 weeks, an inhibition of weight gain was observed in each generation at the premating period, and although no effect on birth weight of F_1, F_2 or F_3 was observed, an inhibition of weight gain during the lactation period was detected.

6. Effects on human

1) Acute effect

An increase in oxygen consumption, body temperature, respiratory rate, and heart rate occurs rapidly with acute toxicity. This chemical substance has a corrosive property, and a thick liquid solution causes the corrosion of the mucosa of the mouth, throat, esophagus and gastrointestinal tract. This substance stimulates and inhibits the cerebrum or lower brain center directly, and brings on necrotic lesions in the renal tubules. In fatal cases involving acute toxicity, death can occur within 24 hours, with the cause of death being respiratory and circulatory disorder.[2)]

2) Chronic effect

Although hidrosis, dry mouth, fatigue, anxiety, flush and frequent urination have been reported as chronic effects, a feeling of happiness and vigor have also been reported.[2)] This chemical substance is toxic to the liver, kidney and nervous system. In addition, progressive changes are observed in liver parenchyma and renal tubules, and an increase in albuminuria, thick urine, hematurea and blood urea nitrogen (BUN) is reported. Rapid postmortem rigidity is observed in fatal cases.[2)]

3) Carcinogenicity[17), 18), 19)]

Organization	Category	Standard
EPA (1999)	Group D	A substance not being classifiable as to human carcinogenicity
EU	-	This substance has not been evaluated for human carcinogenicity as of 2000.
NTP		This substance has not been evaluated for human carcinogenicity as of 2000.
IARC	-	This substance has not been evaluated for human carcinogenicity as of 2000.
ACGIH	-	This substance has not been evaluated for human carcinogenicity as of 2000.
Japan Society for Occupational Health	-	This substance has not been evaluated for human carcinogenicity as of 2000.

There are no reports of human carcinogenicity.

4) Threshold limit [18), 19)]

Organization	Threshold limit	Transdermal absorption property
ACGIH (2000)	No record	-
Japan Society for Occupational Health (2000)	No record	-

7. In vivo fate

Most nitrophenol types are easily absorbed by the gastrointestinal tract or skin. If absorbed, these substances are also

absorbed by the lungs and attach to protein in blood.

In rats and rabbits, 2-(2-hydroxy-1-methylpropyl)-4,6-dinitrophenol, 2-methyl-2-(2-hydroxy-3,5-dinitrophenyl) propionic acid, 2-amino-6-(1-methylpropyl)-4-nitrophenol and glucuronate conjugates are detected in the urine. In addition, butanoic acid, 2-sec-buthyl-4-nitro-6-aminophenol, 2-sec-butyl-4-acetamido-6-aminophenol and 2-(3,5-dinitro-2-hydroxyphenyl)-2-methylpropanoic acid are also detected.[2),3)]

One thought is that this chemical substance is reduced to a primary amine in liver enzymatically. Another is that it involves a route such as oxidation of lateral chains.[2)]

In the case of oral administration of this substance in rats, approx. 25% of the dose is excreted in the feces. In the case of mice, approx. 20% of the dose is excreted in the urine, and approx. 30% in the feces. However, in the case of intraperitoneal administration in mice, approx. 40% of the dose is excreted in the feces. This shows that this substance is excreted in the intestinal tract after first being absorbed.[3)]

8. Classification (OECD classification criteria)

Category	Classification*[12)]
Acute toxicity	Category 2 (Based on data of oral and inhalation administration)
Aquatic ecotoxicity	Acute category 1 (Based on the data of crustacean and fish)

* This classification is used if the data of this research is applied. This is not final.

Classification of acute toxicity: Based on the classification category of acute toxicity in OECD, classified to use the value of the route indicating stronger toxicity.

Classification of aquatic ecotoxicity: Based on the classification category of aquatic ecotoxicity in OECD, classified to use the value of aquatic species indicating strongest toxicity.

9. Overall evaluation

1) Summary of hazardous properties

This chemical substance has a transdermal absorption property and a corrosion property. In acute toxicity, this substance has an effect on the central nervous system and can cause death due to respiratory and circulatory disorders. It can also cause necrotic lesions in the renal tubules of the kidney. In chronic toxicity, symptoms such as hidrosis, dry mouth, and fatigue are observed, and this substance is toxic to the liver, kidney and nervous system. It has been reported that there is an effect on the liver and kidney in laboratory animals. There have been some positive reports for mutagenicity tests, but there is no evidence regarding carcinogenicity. In reproductive/developmental toxicity, this substance has an effect on the formation of sperm and induces a reduction in fertility. Moreover, there are reports of teratogenicity.

If this substance is released into the environment, its concentration property in the hydrosphere is low. In the atmosphere, from the reactivity to the OH radical the half-life of this chemical substance is estimated to be several days. There is no monitoring data from the Ministry of the Environment. The acute toxicity to aquatic species is very strong.

2) Indicated items

(1) This chemical substance has an effect on an entire body by transdermal absorption.

(2) This chemical substance has a corrosion property.

(3) This chemical substance has an effect on the central nervous system and causes toxicity to the liver and kidney.

(4) This chemical substance has an effect on the formation of sperm in laboratory animals.

(5) Acute toxicity to aquatic species is very strong.
(6) This chemical substance is specified in the "Class I PRTR Chemicals" of the "Law for PRTR and Promotion of Chemical Management" (PRTR Law), the management of emission allowance is needed.

Documented in July 2003

Reference

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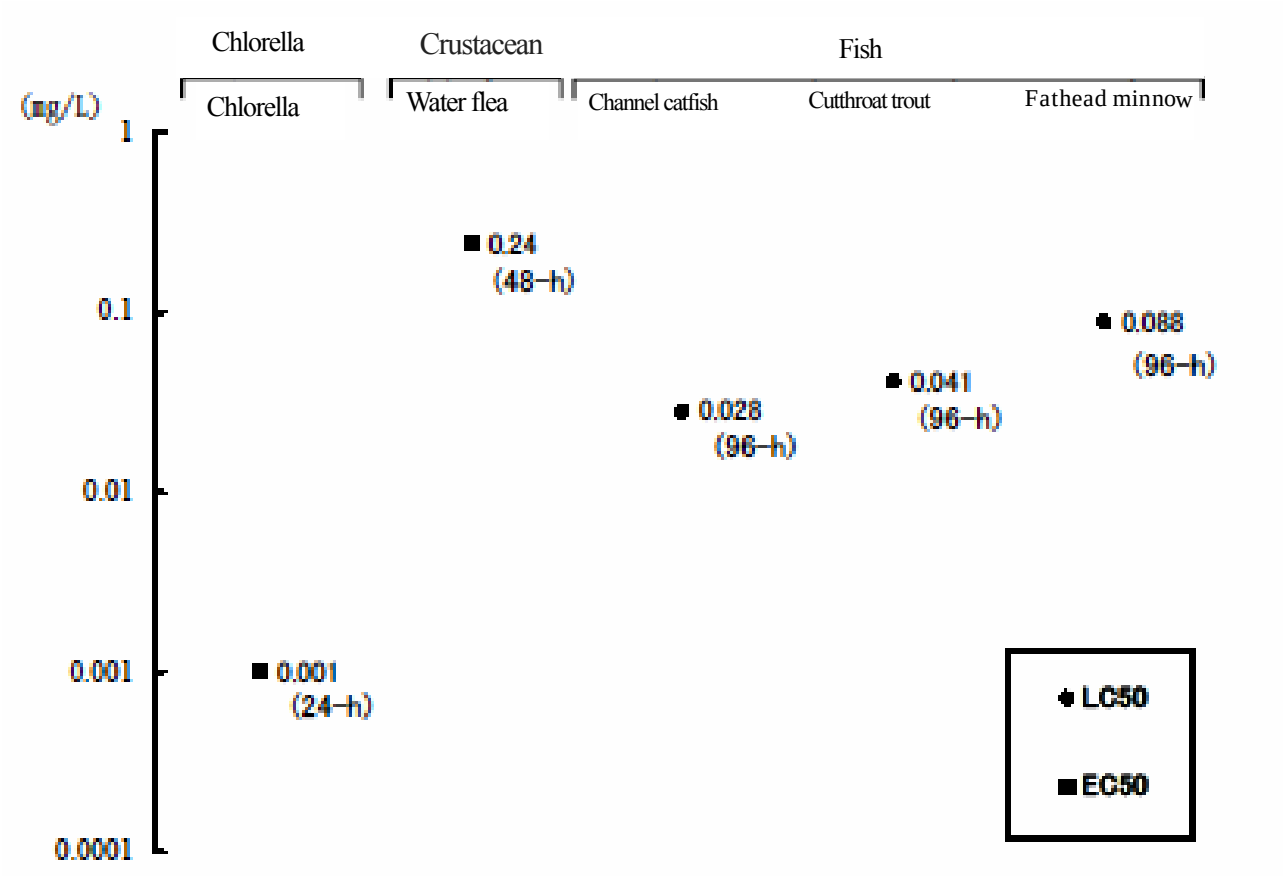
2) Hazardous Substances Data Bank (HSDB), U.S. National Library of Medicine (1998).
3) Sharat Gangolli, The Dictionary of Substances and their Effects, 2nd. Ed., The Royal Society of Chemistry (1999).
4) IPCS, International Chemical Safety Cards (1995).
5) "Data Book on Safety Checks for Existing and New Chemical Substances under the PRTR Law, Supervised by the Chemical Products Safety Division, MITI, Edited by the Chemicals Inspection & Testing Institute (CITI)", Japan Chemical Industry Ecology-Toxicology & Information Center (JETOC) (1992).
6) KowWin, Syracuse Research Compounds.
7) NIST Library of 54K Compounds.
8) Survey on Produced and Imported Amounts of Chemical Substances (FY1998), MITI
9) AOPWIN ver1.86 (Syracuse Research Corporation).
10) US EPA, Drinking Water Health Advisory, Pesticides Chelsea, MI, Lewis Publ Inc p.324-5 (1989).
11) Gustafson DI, Environ Toxicol Chem, 8, 339-57 (1989).
12) OECD, Harmonised Integrated Classification System for Human Health and Environmental Hazards of Chemical Substances and Mixtures. OECD Series on Testing and Assessment No. 33 (2001).
13) AQUIRE (US EPA, ECOTOX Database System).
14) Registry of Toxic Effects of Chemical Substances (RTECS), US NIOSH (1998).
15) Neil E. Garrett, Evaluation of the genetic activity profiles of 65 pesticides, Mutation Research., 168, 301-325 (1986).
16) Integrated Risk Information System (IRIS), U.S. Environmental Protection Agency (1998)
17) JETOC, Classification of Carcinogenic Chemicals and the Criteria, List of the Carcinogenic Chemicals, 4th Edition (1999).
18) ACGIH, Booklet of the Threshold Limit Values and Biological Exposure Indices (2000).
19) Recommendation of Occupational Exposure Limits, Journal of Occupational Health, 42, 130-154 (2000).

Additional reference

1) Figure on ecotoxicity
2) Figure on toxicity to mammals

Figure on ecotoxicity



Reference_

1) AQUIRE (US EPA, ECOTOX Database System)

Figure on toxicity to mammals (Oral administration)

Toxicity on repeat administration	Carcinogenicity		Reproductive/developmental toxicity		
Rat	Mouse	Rat	Mouse	Rat	Mouse
153 d	3 w + 18 month	104 w	1 d		three-generation reproductive study