

Safety Data Sheet

Uracil mustard

Division of Safety
National Institutes
of Health



WARNING!

THIS COMPOUND IS ABSORBED THROUGH THE INTESTINAL TRACT. IT IS TOXIC, CARCINOGENIC, MUTAGENIC, AND TERATOGENIC. IT MAY IRRITATE TISSUES. AVOID FORMATION AND BREATHING OF AEROSOLS.

LABORATORY OPERATIONS SHOULD BE CONDUCTED IN A FUME HOOD, GLOVE BOX, OR VENTILATED CABINET.

AVOID SKIN CONTACT: IF EXPOSED, WASH WITH SOAP AND WATER.

FOR EYE EXPOSURE, IRRIGATE IMMEDIATELY WITH LARGE AMOUNTS OF WATER. FOR INGESTION, DRINK PLENTY OF MILK OR WATER. INDUCE VOMITING. FOR INHALATION, REMOVE VICTIM PROMPTLY TO CLEAN AIR. ADMINISTER RESCUE BREATHING IF NECESSARY. REFER TO PHYSICIAN.

IN CASE OF LABORATORY SPILL, WEAR PROTECTIVE CLOTHING DURING CLEANUP. AVOID SKIN CONTACT OR BREATHING OF AEROSOLS. USE ACETONE TO DISSOLVE COMPOUND. WASH DOWN AREA WITH SOAP AND WATER. DISPOSE OF WASTE SOLUTIONS AND MATERIALS APPROPRIATELY

A. Background

Uracil mustard is a white crystalline solid. It is toxic to humans and rodents, highly irritating to skin and eyes, carcinogenic in laboratory animals, mutagenic in the Ames test, and teratogenic in rats. Its mode of action is that of an alkylating agent. Uracil mustard has been used as an antineoplastic agent in the treatment of conditions associated with proliferation of white blood cells and in immunosuppressive therapy.

B. Chemical and Physical Data

1. Chemical Abstract No.: 66-75-1

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Synonyms:

Aminouracil mustard

5-[Bis(2-chloroethyl)amino]uracil

5-N,N-Bis(2-chloroethyl)aminouracil

Demethyldopan, Desmethyldopan

5-[di-(beta-Chloroethyl)amino]uracil

2,6-di-Hydroxy-5-bis(2-chloroethyl)aminopyrimidine

Nordopan

2,4(1H,3H)Pyrimidinedione, 5-[bis(2-chloroethyl)amino]- (9CI)

Uramustine

Molecular

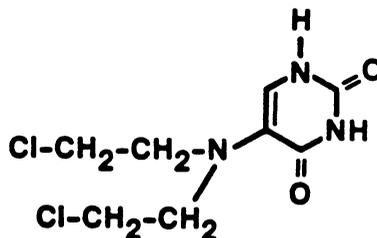
formula:



weight:

252.1

structure:



Density: No data.

Absorption spectroscopy: UV (0.01N H₂SO₄ in 95% ethanol): λ (log ϵ) = 257 (4.76); IR and Raman spectra are described by Grasselli and Ritchey (1975).

Volatility: No data.

Solubility: Very slightly soluble in water; slightly soluble in methanol and acetone (2 mg/ml); soluble in dimethylacetamide and a 5% aqueous solution of dimethylacetamide.

Description, appearance, and odor: Cream-white crystalline odorless powder.

Boiling point: No data.

Melting point: 200°C (with decomposition).

Stability: Unstable in water and acid solutions.

Chemical reactivity: As an alkylating agent, uracil mustard reacts with proteins and a variety of nucleophilic compounds, including water, acids, and alkalies, by replacement of one or both chlorine atoms.

12. Flash point: No data.
13. Autoignition temperature: No data.
14. Explosive limits in air: No data.

Fire, Explosion, and Reactivity Hazard Data

1. Uracil mustard does not require special fire-fighting procedures or equipment and does not present unusual fire and explosion hazards.
2. No conditions contributing to instability are known to exist.
3. No incompatibilities are known.
4. No hazardous decomposition products have been identified.
5. Uracil mustard does not require nonspark equipment. When handled in flammable solvents, the precautions required for such solvents apply.

Operational Procedures

The NIH Guidelines for the Laboratory Use of Chemical Carcinogens describe operational practices to be followed when potentially carcinogenic chemicals are used in NIH laboratories. The Guidelines should be consulted to identify the proper use conditions required and specific controls to be implemented during normal and complex operations or manipulations involving uracil mustard.

1. Chemical inactivation: No validated method reported.
2. Decontamination: Turn off equipment that could be affected by uracil mustard or the materials used for cleanup. If more than 1 g has been spilled or if there is any uncertainty regarding the procedures to be followed for decontamination, call the NIH Fire Department (dial 116) for assistance. Wash surfaces with copious quantities of water. Glassware should be rinsed (in a hood) with alcohol, followed by soap and water. Animal cages should be washed with water.
3. Disposal: No waste streams containing uracil mustard shall be disposed of in sinks or general refuse. Surplus uracil mustard or chemical waste streams contaminated with uracil mustard shall be handled as hazardous chemical waste and disposed of in accordance with the NIH chemical waste disposal system. Nonchemical waste (e.g., animal carcasses and bedding) containing uracil mustard shall be handled and packaged for incineration in accordance with the NIH medical-pathological waste disposal system. Potentially infectious waste (e.g., tissue cultures) containing uracil mustard shall be disinfected by heat using a standard auto-

clave treatment and packaged for incineration, as above. Burnable waste (e.g., absorbent bench top liners) minimally contaminated with uracil mustard shall be handled as potentially infectious waste and packaged for incineration, as above. Absorbent materials (e.g., associated with spill cleanup) grossly contaminated shall be handled in accordance with the chemical waste disposal system. Radioactive waste containing uracil mustard shall be handled in accordance with the NIH radioactive waste disposal system.

4. Storage: Store in sealed ampoules or in amber screw-capped bottles or vials with Teflon cap liners. Solutions of uracil mustard may be stored in bottles or vials with a silicone septum having a Teflon liner and sampled with needle and syringe. Avoid unnecessary exposure to light.

Monitoring and Measurement Procedures Including Direct Field Measurements and Sampling for Subsequent Laboratory Analysis

1. Sampling: No specific methods have been reported.
2. Separation and analysis: Extraction procedures from blood and tissues have been described (Petering and Van Giessen, 1963; Klatt et al., 1960). Colorimetric determination of the blue reaction product of uracil mustard with 4-(p-nitrobenzyl)pyridine has been applied to blood and other biological materials (Petering and Van Giessen, 1963; Klatt et al., 1960). The reported detection limit in blood is 5 µg/ml. This method is not specific for uracil mustard but is positive with many alkylating agents unless preceded by TLC.

Biological Effects (Animal and Human)

1. Absorption: Absorbed from the gastrointestinal tract and by parenteral administration. While uracil mustard is a severe irritant of skin and eyes, it is not known whether it is absorbed via these routes to produce systemic effects.
2. Distribution: Very few data. Radioactivity due to intraperitoneally administered ¹⁴C-uracil mustard is incorporated chiefly into nuclear RNA of many tissues with smaller amounts in DNA and proteins.
3. Metabolism and excretion: No data.
4. Toxic effects: The acute oral or intraperitoneal LD50s in mice and rats are in the range of 2.2 to 4.4 mg/kg. In humans, low dosages produce nausea and vomiting; when the total approaches 1 mg/kg, cumulative damage to bone marrow may be irreversible. Other toxic effects of the 1-2 mg/day therapeutic dose include alopecia, skin reactions, and central nervous system manifestations of nervousness, irritability, and depression.

5. Carcinogenic effects: Mice and rats dosed intraperitoneally with uracil mustard develop tumors of the lungs, ovaries, and mammary glands; lymphomas; and peritoneal sarcomas. Tumors of the liver and pancreas are rarer (Weisburger et al., 1975).
6. Mutagenic and teratogenic effects: Uracil mustard is an active mutagen in the Ames test and is teratogenic in rats.

Emergency Treatment

1. Skin and eye exposure: For skin exposure, remove contaminated clothing and wash skin with soap and water. For eye exposure, irrigate immediately with copious quantities of running water for at least 15 minutes.
2. Ingestion: Drink plenty of milk or water. Induce vomiting.
3. Inhalation: Remove victim promptly to clean air. Administer rescue breathing if necessary.
4. Refer to physician. Observe for delayed vesicant effects. Consider ophthalmological consultation.

References

- Grasselli, J.G., and W.M. Ritchey, eds. 1975. Atlas of Spectral Data and Physical Constants for Organic Compounds. CRC Press, Cleveland, OH.
- Klatt, O., A.C. Griffin, and J.S. Stehlin. 1960. Method for determination of phenylalanine mustard and related alkylating agents in blood. Proc Soc Exp Biol Med 104:629-631.
- Petering, H.G., and G.J. Van Giessen. 1963. Colorimetric method for determination of uracil mustard and related alkylating agents. J Pharm Sci 52:1159-1162.
- Weisburger, J.H., D.P. Griswold, J.D. Prejean, A.E. Casey, H.B. Wood, and E.K. Weisburger. 1975. The carcinogenic properties of some of the principal drugs used in clinical cancer chemotherapy. Recent Results Cancer Res 52:1-7.