Safety Data Sheet

Ethionine

Division of Safety
National Institutes
of Health

WARNING!

THIS COMPOUND IS ABSORBED THROUGH THE INTESTINAL TRACT AND TRANSPLACENTALLY. IT IS TOXIC, CARCINOGENIC, AND TERATOGENIC. 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 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 WATER TO DISSOLVE COMPOUND. WASH DOWN AREA WITH SOAP AND WATER. DISPOSE OF WASTE SOLUTIONS AND MATERIALS APPROPRIATELY.

A. Background

Ethionine is a white crystalline solid. It is acutely toxic to animals (target organs are pancreas and liver) and probably to humans. It is not mutagenic but is teratogenic in chicks. Its action is that of an antagonist to the natural amino acid, methionine. It has no commercial use.

B. Chemical and Physical Data

1. Chemical Abstract No.: 67-21-0 (DL form); 13073-35-3 (L form)

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This data sheet is provided by the Division of Safety, NIH, to accompany the *NIH Guidelines for the Laboratory Use of Chemical Carcinogens.* The information included in this document is believed to be current and accurate, but no warranty is expressed or implied.

2. Synonyms:

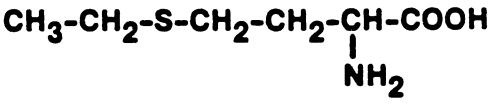
   2-Amino-4-(ethylthio)butyric acid

   α-Amino-γ-(ethylmercapto)butyric acid

   S-Ethyl homocysteine

   DL-Homocysteine, S-ethyl- (9CI)

3. Molecular formula: $C_6H_{13}NO_2S$

   structure: 

   weight: 162.25

4. Density: No data.

5. Absorption spectroscopy: No analytically useful absorption.

6. Volatility: No data; for practical purposes, ethionine is nonvolatile.

7. Solubility: Very soluble in water and ethanol; insoluble in nonpolar solvents.

8. Description, appearance: White crystalline solid.

9. Boiling point: No data.

   Melting point: 257-260°C with decomposition for the DL form; 272-274°C for the L form. Sublimes at 133°C at 0.3 mm Hg.

10. Stability: No data, but probably very high.

11. Chemical reactivity: Undergoes the usual reactions of aliphatic amines, carboxylic acids, and sulfur-containing amino acids. Not easily decomposed by acids, alkalis, or oxidants.

12. Flash point: No data.

13. Autoignition temperature: No data.

14. Explosive limits in air: No data.

Fire, Explosion, and Reactivity Hazard Data

1. Ethionine 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. Ethionine does not require nonspark equipment.

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 ethionine.

1. Chemical inactivation: No validated method reported.

2. Decontamination: Turn off equipment that could be affected by ethionine or the materials used for cleanup. If more than 10 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 water, followed by soap and water. Animal cages should be washed with water.

3. Disposal: No waste streams containing ethionine shall be disposed of in sinks or general refuse. Surplus ethionine or chemical waste streams contaminated with ethionine 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 ethionine 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 ethionine shall be disinfected by heat using a standard autoclave treatment and packaged for incineration, as above. Burnable waste (e.g., absorbent bench top liners) minimally contaminated with ethionine 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 ethionine shall be handled in accordance with the NIH radioactive waste disposal system.

4. Storage: Store in screw-capped bottles or vials with Teflon cap liners.

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: This may be carried out using either an α-amino acid reagent (ninhydrin) or a thioether detecting agent (reaction with iodine, catalyzed by sodium azide). In the presence of other amino acids, this should be preceded by separation by paper chromatography (Fink et al., 1963).

Biological Effects (Animal and Human)

1. Absorption: Ethionine is absorbed readily from the gastrointestinal tract (in which there is also partial metabolism). There are no data on other routes of administration except that ethionine crosses the placental barrier from pregnant mother to embryo in the rat.

2. Distribution: Very few data. Following oral administration to rats, radioactivity due to L-(1-^{14}C ethyl) ethionine is found after 8 hours in the liver, plasma, kidney, small intestine, and red blood cells (in order of decreasing concentration) (Brada et al., 1975).

3. Metabolism and excretion: There are three pathways of ethionine metabolism: (a) oxidation to the sulfoxide and subsequent acetylation; (b) activation into S-adenosylethionine; and (c) oxidation of the ethyl group to CO_2. Urinary metabolite composition in rats depends on dosage: 1-2 mg/kg yields only L-acetylethionine sulfoxide, while 10 mg/kg yields, in addition, ethionine sulfoxide, unchanged ethionine, and S-adenosylethionine (Brada and Bulba, 1977). Radioactivity due to orally or intraperitoneally administered labeled ethionine is also found as CO_2 in the expired air. After oral dosage, there is also some fecal excretion of unabsorbed ethionine.

4. Toxic effects: There are no data on LD50s of ethionine in animals. Dogs given 75-100 mg/kg DL-ethionine intraperitoneally died, while those given 50 mg/kg or less survived with liver disease symptoms (Molokhia et al., 1971). The chief target organs of ethionine toxicity in animals are the pancreas (destruction of the exocrine portion) and liver (fatty infiltration). These effects are consistent with a mode of toxic action as a methionine antagonist (Lombardi, 1976). The mechanism appears to be ethylation of hepatic protein, RNA, and, to a smaller extent, DNA through the intermediate S-adenosylethionine (Levine and Tarver, 1951). Very low chronic doses of ethionine to rats results in irreversible testicular lesions.

5. Carcinogenic effects: Primary hepatomas are produced in rats after treatment with ethionine.

6. Mutagenic and teratogenic effects: Ethionine is not an active mutagen in the direct or induced Ames test; it is teratogenic in rats and chicks.

G. 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 water. Induce vomiting.

3. Inhalation: Remove victim promptly to clean air. Administer rescue breathing if necessary.

4. Refer to physician.

H. References

Brada, Z., and S. Bulba. 1977. Regulation of DL-ethionine metabolism in rats in vivo. Fed Proc 36:1074.

Brada, Z., S. Bulba, and J. Cohen. 1975. The metabolism of ethionine in rats. Cancer Res 35:2674-2683.

Fink, K., R.E. Cline, and R.M. Fink. 1963. Paper chromatography of several classes of compounds: Correlated Rf values in a variety of solvent systems. Anal Chem 35:389-398.

Levine, M., and H. Tarver. 1951. Studies on ethionine. J Biol Chem 192:835-850.

Lombardi, B. 1976. Influence of dietary factors on the pancreatotoxicity of ethionine. Am J Pathol 84:633-645.

Molokhia, F.A., R.B. Ponn, P.J. Asimacopoulos, H.S. Sise, and J.C. Norman. 1971. DL-ethionine-induced clotting-factor deficiencies in the dog with survival. Surgery 69:741-747.