SAFETY DATA SHEET

Updated on 26/09/2024

1. Material Identification

Product Name : Fumaric acid
Catalog Number : io-2427
CAS Number : 110-17-8
Identified uses : Laboratory chemicals, manufacture of chemical compounds
Company : Ionz

>> R&D Use only

2. Hazards Identification

GHS Classification:

Flammable liquid (category 2)
Acute toxicity, oral (Category 3)
Acute toxicity, dermal (Category 3)
Acute toxicity, inhalation (Category 3)
Specific target organ toxicity, single exposure (Category 1)

Pictogram(s)

GHS Hazard Statements

>> H290 (47.4%): May be corrosive to metals [Warning Corrosive to Metals]

>> H314 (48.7%): Causes severe skin burns and eye damage [Danger Skin corrosion/irritation]

>> H318 (40.4%): Causes serious eye damage [Danger Serious eye damage/eye irritation]

>> H319 (50%): Causes serious eye irritation [Warning Serious eye damage/eye irritation]

Precautionary Statement Codes

>> P234, P260, P264, P264+P265, P280, P301+P330+P331, P302+P361+P354, P304+P340, P305+P351+P338, P305+P354+P338, P316, P317, P321, P337+P317, P363, P390, P405, P406, and P501

Note

>> Pictograms displayed are for > 99.9% (3252 of 3254) of reports that indicate hazard statements. This chemical does not meet GHS hazard criteria for < 0.1% (2 of 3254) of reports.

EPA Safer Chemical:

EPA labels products so that consumers can easily choose ones that are safer for people and the environment. When consumers see the Safer Choice label on a product, they can be confident that the ingredients have been through a rigorous EPA review. The label means that EPA scientists have evaluated every ingredient in the product to ensure it meets Safer Choice's stringent criteria. When people use Safer Choice products, they are protecting their families and the environment by making safer chemical choices.

EPA Safer Chemical

>> Chemical: Fumaric acid

>> Green circle - The chemical has been verified to be of low concern based on experimental and modeled data.

Health Hazards:

>> Inhalation of dust may cause respiratory irritation. Compound is non-toxic when ingested. Prolonged contact with eyes or skin may cause irritation. (USCG, 1999)

>> Special Hazards of Combustion Products: Irritating fumes of maleic anhydride may form in fires.

>> Behavior in Fire: Dust presents explosion hazard; knock down dust with water fog. (USCG, 1999)

>> Combustible. Gives off irritating or toxic fumes (or gases) in a fire. Finely dispersed particles form explosive mixtures in air.

3. Composition/Information On Ingredients

Chemical name : Fumaric acid
CAS Number : 110-17-8
Molecular Formula : C4H4O4
Molecular Weight : 116.0700 g/mol

4. First Aid Measures

First Aid:

>> EYES: First check the victim for contact lenses and remove if present. Flush victim's eyes with water or normal saline solution for 20 to 30 minutes while simultaneously calling a hospital or poison control center. Do not put any ointments, oils, or medication in the victim's eyes without specific instructions from a physician. IMMEDIATELY transport the victim after flushing eyes to a hospital even if no symptoms (such as redness or irritation) develop.

>> SKIN: IMMEDIATELY flood affected skin with water while removing and isolating all contaminated clothing. Gently wash all affected skin areas thoroughly with soap and water. If symptoms such as redness or irritation develop, IMMEDIATELY call a physician and be prepared to transport the victim to a hospital for treatment.

>> INHALATION: IMMEDIATELY leave the contaminated area; take deep breaths of fresh air. If symptoms (such as wheezing, coughing, shortness of breath, or burning in the mouth, throat, or chest) develop, call a physician and be prepared to transport the victim to a hospital. Provide proper respiratory protection to rescuers entering an unknown atmosphere. Whenever possible, Self-Contained Breathing Apparatus (SCBA) should be used; if not available, use a level of protection greater than or equal to that advised under Protective Clothing.

>> INGESTION: DO NOT INDUCE VOMITING. If the victim is conscious and not convulsing, give 1 or 2 glasses of water to dilute the chemical and IMMEDIATELY call a hospital or poison control center. Be prepared to transport the victim to a hospital if advised by a physician. If the victim is convulsing or unconscious, do not give anything by mouth, ensure that the victim's airway is open and lay the victim on his/her side with the head lower than the body. DO NOT INDUCE VOMITING. IMMEDIATELY transport the victim to a hospital. (NTP, 1992)

First Aid Measures

Inhalation First Aid

>> Fresh air, rest.

Skin First Aid

>> Rinse skin with plenty of water or shower.

Eye First Aid

>> First rinse with plenty of water for several minutes (remove contact lenses if easily possible), then refer for medical attention.

Ingestion First Aid

>> Rinse mouth.

5. Fire Fighting Measures

>> Use water spray, dry powder, foam, carbon dioxide.

6. Accidental Release Measures

Spillage Disposal:

Methods for containment and safety measures to protect workers dealing with a spillage of this chemical.

>> Personal protection: particulate filter respirator adapted to the airborne concentration of the substance. Do NOT let this chemical enter the environment. Sweep spilled substance into covered containers. If appropriate, moisten first to prevent dusting. Then store and dispose of according to local regulations.

7. Handling And Storage

Safe Storage:

>> Separated from oxidizing materials.

Storage Conditions:

>> The bulk material should be stored in a well-closed container in a cool, dry place.

8. Exposure Control/ Personal Protection

Inhalation Risk:

>> A nuisance-causing concentration of airborne particles can be reached quickly when dispersed.

Effects of Short Term Exposure:

>> The substance is irritating to the eyes.

Acceptable Daily Intakes:

An estimate of the amount of a chemical in food or drinking water that can be consumed daily over a lifetime without presenting an appreciable risk to health. It is usually expressed as milligrams of the substance per kilogram of body weight per day and applies to chemicals such as food additives, pesticide residues and veterinary drugs.

>> JECFA: ADI: Not specified. No safety concern when used at current levels of intake as a flavoring agent.

Fire Prevention

>> NO open flames. Prevent deposition of dust. Closed system, dust explosion-proof electrical equipment and lighting.

Inhalation Prevention

>> Use local exhaust or breathing protection.

Skin Prevention

>> Protective gloves.

Eye Prevention

>> Wear safety goggles.

Ingestion Prevention

>> Do not eat, drink, or smoke during work.

9. Physical And Chemical Properties

Molecular Weight:

>> 116.07

Exact Mass:

>> 116.01095860

Physical Description:

>> Fumaric acid appears as a colorless crystalline solid. The primary hazard is the threat to the environment. Immediate steps should be taken to limit spread to the environment. Combustible, though may be difficult to ignite. Used to make paints and plastics, in food processing and preservation, and for other uses.

>> ODOURLESS COLOURLESS CRYSTALLINE POWDER.

Color/Form:

>> Needles, monoclinic prisms or leaflets from water

Odor:

>> Odorless

Taste:

The sensation of flavor perceived in the mouth and throat on contact with a substance.

>> Fruit acid

Boiling Point:

>> 329 °F at 1.7 mmHg ; sublimes (NTP, 1992)

Melting Point:

>> 572 to 576 °F (NTP, 1992)

Flash Point:

>> 273 °C (open cup)

>> 273 °C

Solubility:

>> less than 1 mg/mL at 72 °F (NTP, 1992)

>> Solubility in water, g/100ml at 25 °C: 0.63 (poor)

Density:

>> 1.635 at 68 °F (USCG, 1999) - Denser than water; will sink

>> Density (at 20 °C): 1.64 g/cm³

Vapor Pressure:

>> 0.000154 [mmHg]

LogP:

>> 0.46 (estimated)

Stability/Shelf Life:

>> Fumaric acid is stable although it is subject to degradation by both aerobic and anaerobic microorganisms. When heated in sealed vessels with water at 150 - 170 °C it forms DL-malic acid.

Autoignition Temperature:

>> 1364 °F (USCG, 1999)

>> 375 °C (powder)

Heat of Combustion:

>> -4,970 Btu/lb = 2,760 cal/g = -116X10+5 J/kg

pH:

pH is an expression of hydrogen ion concentration in water. Specifically, pH is the negative logarithm of hydrogen ion (H+) concentration (mol/L) in an aqueous solution. The term is used to indicate basicity or acidity of a solution on a scale of 0 to 14, with pH 7 being neutral.

>> 3,0-3,2 (0,05 % solution at 25 °C)

Ionization Efficiency:

The ratio of the number of ions formed to the number of electrons or photons used in an ionization process.

Ionization mode

>> Negative

logIE

>> -1.08

pH

>> 10.5

Instrument

>> Thermo LTQ

Ion source

>> Electrospray ionization

Additive

>> ammonia (10nM)

Organic modifier

>> MeCN (80%)

Reference

>> DOI:10.1016/j.aca.2018.05.072

Dissociation Constants:

pKa

>> 3.03 (at 18 °C)

>> pKa1 = 3.03; pKa2 = 4.44 at 18 °C

Collision Cross Section:

Collision cross section (CCS) represents the effective area for the interaction between an individual ion and the neutral gas through which it is traveling (e.g., in ion mobility spectrometry (IMS) experiments). It quantifies the probability of a collision taking place between two or more particles.

>> 133.58 Å² [M+Na]+ [CCS Type: DT; Method: stepped-field]

10. Stability And Reactivity

>> Slightly soluble in water.

11. Toxicological Information

Toxicity Summary:

>> Acute Toxicity: Fumarate is also an endogenous electrophile and reacts spontaneously with cysteine residues in proteins by a Michael addition reaction to form S-(2-succinyl) cysteine, a process termed succination. Lachrymators such as fumarate are thought to act by attacking sulfhydryl functional groups in enzymes. One of the most probable protein targets is the TRPA1 ion channel that is expressed in sensory nerves (trigeminal nerve) of the eyes, nose, mouth and lungs. Chronic Toxicity: Fumarate is increasingly being identified as an oncometabolite. Fumarase or fumarate hydratase (FH) is a tumor suppressor, whose mutation is associated with the development of leiomyomata, renal cysts, and tumors. Loss of FH enzymatic activity results in accumulation of intracellular fumarate which has been proposed to act as a competitive inhibitor of 2-oxoglutarate-dependent oxygenases including the hypoxia-inducible factor (HIF) hydroxylases, thus activating oncogenic HIF pathways. Mitochondrial dysfunction is also associated with FH deficiency. Fumarate hydratase-deficient cells and tumors have been shown to accumulate fumarate to very high levels with

multiple consequences including the activation of oncogenic pathways (A15199). Fumarate (and succinate) inhibit the activity or function of other members of the 2-oxoglutarate-dependent oxygenase superfamily, including histone demethylase enzymes (HDMs) and the TET family of 5-methlycytosine (5mC) hydroxylases which are critical in epigenetic regulation of gene expression.. Fumarate accumulation may also affect cytosolic pathways by inhibiting the reactions involved in the biosynthesis of arginine and purine. More recently it has been found that fumarate promotes p65 phosphorylation and p65 accumulation at the HIF-1α promoter through non-canonical signaling via the upstream Tank Binding Kinase 1 (TBK1). Fumarate is also an endogenous electrophile and reacts spontaneously with cysteine residues in proteins by a Michael addition reaction to form S-(2-succinyl) cysteine, a process termed succination. Accumulation of cellular fumarate has been shown to correlate directly with an increase in succinated proteins. Targets for succination include the glycolytic enzyme glyceraldehyde-3-phosphate dehydrogenase, adiponectin, cytoskeletal proteins, and endoplasmic reticulum chaperone proteins. Furthermore, evidence suggests that succination of these proteins in cells may impair their functions.

Carcinogen Classification:

This section provides the International Agency for Research on Cancer (IARC) Carcinogenic Classification and related monograph links. In the IARC Carcinogenic classification, chemicals are categorized into four groups: Group 1 (carcinogenic to humans), Group 2A (probably carcinogenic to humans), Group 2B (possibly carcinogenic to humans), and Group 3 (not classifiable as to its carcinogenicity to humans).

>> Not listed by IARC. Has been implicated in oncogenesis (A15088, A15092).

Health Effects:

>> Acute exposure to fumaric acid can cause skin redness (skin contact), cough or sore throat (inhalation), abdominal cramps, nausea and diarrhea (ingestion). Chronically high levels of fumaric acid are associated with at least 3 inborn errors of metabolism including: 2-Ketoglutarate dehydrogenase complex deficiency, Fumarase deficiency and Pyruvate carboxylase deficiency. Fumarase deficiency causes encephalopathy, severe mental retardation, unusual facial features, brain malformation, and epileptic seizures. High intracellular fumaric acid levels are associated with the development of renal cancer, leiomyomata, renal cysts, and tumors.

Exposure Routes:

>> Endogenous, ingestion, contact (skin and eyes)

Inhalation Exposure

>> Cough. Sore throat.

Skin Exposure

>> Redness.

Eye Exposure

>> Redness. Pain.

>> Acute exposure to fumaric acid can cause eye and skin irritation, cough or sore throat (inhalation), abdominal cramps, nausea and diarrhea (ingestion).

Adverse Effects:

An adverse effect is an undesired harmful effect resulting from a medical treatment or other intervention.

>> Dermatotoxin - Skin burns.

Treatment:

Treatment when exposed to toxin

>> Acute exposure: EYES: irrigate opened eyes for several minutes under running water. INGESTION: do not induce vomiting. Rinse mouth with water (never give anything by mouth to an unconscious person). Seek immediate medical advice. SKIN: should be treated immediately by rinsing the affected parts in cold running water for at least 15 minutes, followed by thorough washing with soap and water. If necessary, the person should shower and change contaminated clothing and shoes, and then must seek medical attention. Chronic Exposure: There is no treatment for fumarase deficiencies. Only palliative care is possible. For cancers caused by intracellular fumarate excess, there are a wide variety of cancer treatments including drugs and surgery.

Interactions:

>> The inhibitory effect of fumaric acid (FA) on hepatocarcinogenesis was examined in mice fed thioacetamide (TAA). A group of male ICR mice was fed TAA at a level of 0.035% in the diet for 40 weeks and then fed a basal diet for 48 weeks. Hepatic tumors developed in 11 of the 24 animals of this group and they were diagnosed as hepatocellular carcinomas. However, cirrhotic lesions and the enlargement of hepatocyte nucleoli were not as marked in mice as in previous findings in rats fed TAA. The effect of FA on the carcinogenesis was examined in a group of mice fed this compound at a level of 1% in a basal diet after ingestion of TAA. The inhibitory effect of FA on TAA carcinogenesis was so marked that no hepatic carcinomas were found in any of the 15 animals fed FA in combination with TAA.

Antidote and Emergency Treatment:

>> Immediate first aid: Ensure that adequate decontamination has been carried out. If patient is not breathing, start artificial respiration, preferably with a demand-valve resuscitator, bag-valve-mask device, or pocket mask, as trained. Perform CPR as necessary. Immediately flush contaminated eyes with gently flowing water. Do not induce vomiting. If vomiting occurs, lean patient forward or place on left side (head-down position, if possible) to maintain an open airway and prevent aspiration. Keep patient quiet and maintain normal body temperature. Obtain medical attention. /Organic acids and related compounds/

Human Toxicity Excerpts:

>> /HUMAN EXPOSURE STUDIES/ In humans, no changes in the blood and urine parameters or in liver function were found after administration of 8 mg fumaric acid/kg bw/day for one year.

Non-Human Toxicity Excerpts:

>> /LABORATORY ANIMALS: Acute Exposure/ Guinea pig maximization test: not sensitizing

Non-Human Toxicity Values:

>> LD50 Mouse ip 100 mg/kg

12. Ecological Information

ICSC Environmental Data:

>> The substance is harmful to aquatic organisms.

Sediment/Soil Concentrations:

Concentrations of this compound in sediment/soil.

>> SEDIMENT: Bog sediments collected in the foothills of the Sierra Nevada Mountains contained fumaric acid levels of 4.76 mg/kg(1).

13. Disposal Considerations

Spillage Disposal

>> Personal protection: particulate filter respirator adapted to the airborne concentration of the substance. Do NOT let this chemical enter the environment. Sweep spilled substance into covered containers. If appropriate, moisten first to prevent dusting. Then store and dispose of according to local regulations.

Disposal Methods

>> SRP: Criteria for land treatment or burial (sanitary landfill) disposal practices are subject to significant revision. Prior to implementing land disposal of waste residue (including waste sludge), consult with environmental regulatory agencies for guidance on acceptable disposal practices.

>> SRP: Expired or waste pharmaceuticals shall carefully take into consideration applicable DEA, EPA, and FDA regulations. It is not appropriate to dispose by flushing the pharmaceutical down the toilet or discarding to trash. If possible return the pharmaceutical to the manufacturer for proper disposal being careful to properly label and securely package the material. Alternatively, the waste pharmaceutical shall be labeled, securely packaged and transported by a state licensed medical waste contractor to dispose by burial in a licensed hazardous or toxic waste landfill or incinerator.

>> SRP: At the time of review, regulatory criteria for small quantity disposal are subject to significant revision, however, household quantities of waste pharmaceuticals may be managed as follows: Mix with wet cat litter or coffee grounds, double bag in plastic, discard in trash.

>> Observe all federal, state, and local environmental regulations. Contact a licensed professional waste disposal service to dispose of this material. Dissolve or mix the material with a combustible solvent and burn in a chemical incinerator equipped with an afterburner and scrubber.

14. Transport Information

DOT

Fumaric acid

Reportable Quantity of 5000 lb or 2270 kg

IATA

Fumaric acid

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15. Regulatory Information

Clean Water Act Requirements:

The Clean Water Act (CWA) of 1972 establishes the basic structure for regulating discharges of pollutants into the waters of the United States and regulating quality standards for surface waters. Under CWA, the U.S. Environmental Protection Agency (EPA) developed the Toxic Pollutant List (40 CFR Part 401.15) and the Priority Pollutant List (40 CFR Part 423, Appendix A). These lists are to be used by EPA and States to develop the Effluent Guidelines regulations and ensure water quality criteria and standards.

>> Fumaric acid is designated as a hazardous substance under section 311(b)(2)(A) of the Federal Water Pollution Control Act and further regulated by the Clean Water Act Amendments of 1977 and 1978. These regulations apply to discharges of this substance. This designation includes any isomers and hydrates, as well as any solutions and mixtures containing this substance.

Regulatory Information

The Australian Inventory of Industrial Chemicals

>> Chemical: 2-Butenedioic acid (2Z)-, homopolymer

The Australian Inventory of Industrial Chemicals

>> Chemical: 2-Butenedioic acid, (E)-

REACH Registered Substance

>> Status: Active Update: 21-02-2023 https://echa.europa.eu/registration-dossier/-/registered-dossier/15099

>> Status: Active Update: 14-12-2022 https://echa.europa.eu/registration-dossier/-/registered-dossier/25887

>> Status: Active Update: 15-06-2011 https://echa.europa.eu/registration-dossier/-/registered-dossier/6159

New Zealand EPA Inventory of Chemical Status

>> Fumaric acid: Does not have an individual approval but may be used under an appropriate group standard

New Zealand EPA Inventory of Chemical Status

>> 2-Butenedioic acid (2Z)-, homopolymer: Does not have an individual approval but may be used under an appropriate group standard

16. Other Information

Toxic Combustion Products:

Toxic products (e.g., gases and vapors) produced from the combustion of this chemical.

>> Irritating fumes of maleic anhydride may form in fires.

Other Safety Information

Chemical Assessment

>> IMAP assessments - 2-Butenedioic acid, (E)-: Human health tier I assessment

>> IMAP assessments - 2-Butenedioic acid, (E)-: Environment tier I assessment

Chemical Assessment

>> IMAP assessments - 2-Butenedioic acid, (Z)-, homopolymer: Human health tier I assessment

"The information provided is believed to be accurate but is not comprehensive and should be used as a reference. It reflects our current knowledge and is intended for safety guidance related to the product. This document does not constitute a warranty of the product's properties. Ionz is not responsible for any damages resulting from handling or contact with the product incorrectly."