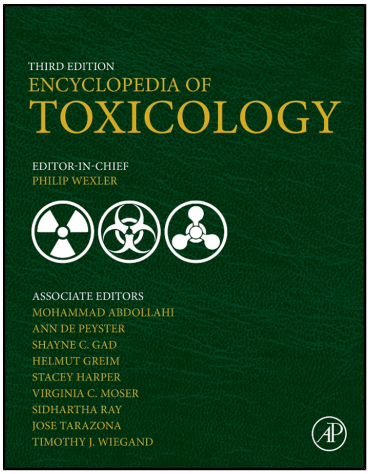

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Pyridine

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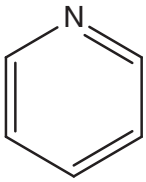
- Name: Pyridine
- Chemical Abstracts Service Registry Number: 110-86-1
- Synonyms: Azabenzene, Azine, Tritisan, NCI-C55301, RCRA Waste Number U196
- Chemical/Pharmaceutical/Other Class: Aromatic heterocyclic amine
- Molecular Formula: C_5H_5N
- Molecular Mass: 79.1 g mol^{-1}
- Appearance and Odor: Colorless or yellow liquid with a penetrating, sickening odor
- Chemical Structure:



Occurrence

Pyridine is found in nature in the leaves and roots of *Atropa belladonna* and among the volatile components of black tea and in its leaves and roots. Occupational occurrence of pyridine may exist during its production by synthesis or by treatment and distillation of crude coal tar, during the processing of oil shale, and at coke-oven works. It may also be emitted as a breakdown product of 4-methylpropylpyridine used as a binder catalyst in the molding process of iron foundry. Environmental occurrence of pyridine exists during its production and use as a solvent and intermediates in the synthesis of drugs, insecticides, and herbicides, and as a by-product of coal gasification. Pyridine is a component in the basic fraction of oil-shale retort waters. It has also been isolated in the volatile components from cooked beef (sukiyaki) in Japan, fried chicken in the United States, fried bacon, Beaufort cheese, black tea aroma, and coffee aroma, and it has been detected as a component of tobacco and marijuana smoke.

Uses

Pyridine is used directly in the denaturation of alcohol and as a solvent in paint and rubber preparation. It is also used in research laboratories for functions such as extraction of plant hormones. About 50% of pyridine produced is used as an intermediate in making various insecticides and herbicides for agricultural applications while 20% goes into the production of piperidine, which has a significant industrial application for the production of dipiperidinyl dithiuram tetrasulfide, used as a rubber vulcanization accelerator. Pyridine has also been used as an intermediate in the preparation of drugs such as antihistamines, steroids, sulfa-type and other antibacterial agents, as well as intermediate in the preparation of dyes, water repellents, and polycarbonate resins. Further, it is also used as a flavoring agent in food preparation.

Exposure Routes and Pathways

Pyridine can affect the body if it is inhaled, comes in contact with the eyes or skin, or is swallowed or digested.

Toxicokinetics

Pyridine is absorbed through the gastrointestinal tract, through the skin, and by inhalation where part of it is excreted in the urine unchanged and a smaller portion is methylated at the N position forming the urinary metabolite *N*-methylpyridinium hydroxide. Elimination of pyridine is biphasic in nature, the first phase being more prolonged for pyridine and β-picoline than for α- or γ-picoline. It may also undergo oxygenation by liver microsomes (i.e., cytochrome P450) in the presence of NADPH (nicotinamide adenine dinucleotide phosphate) and oxygen.

Acute and Short-Term Toxicity (or Exposure)

Animal

Fish toxicity includes 26 000 µg l^{-1} 96 h LC_{50} (mortality) for common, mirror, colored, carp (*Cyprinus carpio*), 1430 mg l^{-1} 24 h EC_{100} (abundance) invertebrate toxicity for water flea (*Daphnia magna*), algal toxicity of 280 000 µg l^{-1} 48 h (population growth) for green algae (*Scenedesmus pannonicus*), and 10 000 µg l^{-1} 96 h (abnormality) for clawed toad (*Xenopus laevis*). For rabbits, dermal LD_{50} values are 1121 mg kg^{-1}, and for guinea pigs, 1 g kg^{-1}. Intravenous LD_{50} values for dogs are 880 mg kg^{-1} and for mice 420 mg kg^{-1}. An intraperitoneal injection LD_{50} of 1200 mg kg^{-1} was reported for mice. Acute LD_{50} values for subcutaneously administered pyridine in rats have been reported as 1000 and 866 mg kg^{-1}. Oral LD_{50} values are 4 g kg^{-1} for guinea pigs, 1500 mg kg^{-1} for mice, and 891 mg kg^{-1} for rats. The LC_{Lo} (inhalation) in rats is 4000 ppm per 4 h.

Human

Inhalation of pyridine can cause nausea, vomiting, headache, and dizziness. Dermal exposure can lead to irritation,

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photosensitization, and contact dermatitis. Ingestion of approximately 500 mg kg^{-1} bw pyridine can cause nausea, dizziness, abdominal pain, and lung congestion, followed by death after 43 h. Acute pyridine intoxication generally affects the central nervous system with symptoms of dizziness, headache, nausea, anorexia, abdominal pain, and pulmonary congestion. High dose can lead to lethality.

Chronic Toxicity (or Exposure)

Animal

Mortality rates for rats that received subcutaneous injections of pyridine two times weekly for a year at levels up to 100 mg kg^{-1} day^{-1} were comparable to mortality rates of controls. Pyridine was hepatotoxic in Fischer 344 and Wistar rats and can cause an increase in granular casts and renal tubule hyaline degeneration in male Fischer 344 rats. Inhalation can cause necrotic damage of the nasal epithelium. It is also known as an inducer of CYP2E1 in the liver and kidney in rats and rabbits. Evidence of anemia was present in Fischer 344 rats after water consumption of 1000 ppm pyridine for 13 weeks. Further, exposure to pyridine (500 or 1000 ppm) increased alanine aminotransferase and sorbitol dehydrogenase activities and the incidence of centrilobular degeneration, hypertrophy, chronic inflammation, and pigmentation in the liver of all rats. In Fischer 344 rats, the incidence of renal tubule hyperplasia was increased in males exposed to 400 ppm pyridine in drinking water for 103–104 weeks compared with controls. Hematopoietic cell proliferation in the spleen and follicular cell hyperplasia in the thyroid gland were noted in B6C3F1 mice treated with drinking water with up to 1000 ppm pyridine for 104–105 weeks. In mice, pyridine also increased incidences of hepatocellular carcinomas and hepatoblastomas.

Human

Inhalation of pyridine vapors at 125 ppm for 4 h per day for 1 or 2 weeks can result in headache, dizziness, insomnia, nausea, and anorexia. Inhalation, ingestion, or prolonged skin contact can lead to systemic toxicity, with symptoms including pulmonary edema, central nervous system depression, nervousness, vertigo, agitation, fatigue, insomnia, peripheral neuritis, and weakness, and in severe cases coma and respiratory depression. There are not enough data to make an assessment whether pyridine can cause cancer or mutations. Chronic exposures may cause some kidney and liver changes as systemic effects. The most important effect of pyridine inhalation is chronic poisoning involving the liver, kidneys, and bone marrow. Mild symptoms of central nervous system injury have also been reported following chronic exposure to 6–12 ppm. Repeated ingestion of low levels may result in cirrhosis of the liver. Administration of 1.8–2.5 ml day^{-1} for 2 months produced severe liver and kidney injuries. It is an allergen and exposure may result in sensitization.

In Vitro Toxicity Data

Pyridine did not induce mutations in *Salmonella typhimurium*, in *Escherichia coli*, or in mouse lymphoma cells. Negative results were also obtained in chromosomal aberration and sister chromatid exchange assays in Chinese hamster studies. Pyridine induced aneuploidy in *Saccharomyces cerevisiae*, when tested without metabolic activation only. It also induced chromosomal malsegregation and increased nondisjunction in *Drosophila melanogaster* females. In another study, it is nongenotoxic in B6C3F1 mouse liver using the unscheduled DNA synthesis endpoint.

Clinical Management

Patients should be removed from exposure sites, including contaminated clothing and personal effects. Soiled clothing should then be placed in a double bag and sealed in a container labeled as biohazard. Any adherent liquid from the patient should then be gently blotted away. Contaminated hair and skin should be washed with copious amounts of water (preferably warm) and soap for at least 10–15 min. Decontaminate open wounds first and avoid contamination of unexposed skin. One should also pay attention to skinfolds, axillae, ears, fingernails, genital areas, and feet.

For ocular exposure, contact lenses should be removed if necessary and immediately irrigate the affected eye thoroughly with water or 0.9% saline for at least 10–15 min. Patients with corneal damage or those whose symptoms do not resolve rapidly should be referred for urgent ophthalmological assessment.

In case of inhalation and ingestion, patients should be ensured a clear airway and adequate ventilation. Oxygen should also be provided to symptomatic patients. If the patient has clinical features of bronchospasm, treat conventionally with nebulized bronchodilators and steroids. One should also apply other supportive measures as indicated by the patient's clinical condition. For ingestion, one should monitor the patient's blood pressure and pulse. Moreover, if the victim is conscious and not convulsing, one or two glasses of water should be given to dilute the chemical and a hospital or poison control center should be called immediately. The patient may also be administered with activated charcoal, taking note that large doses could act as a heart poison.

Environmental Fate

If released to water, pyridine minimization is expected to occur by volatilization to air and by biodegradation. If released on land, pyridine will leach into the ground and biodegrade. In general, pyridine is biodegradable and not considered a threat to the environment.

Exposure Standards and Guidelines

Pyridine has a time-weighted average of 1 ppm threshold limit value and no short-term exposure limit as proposed by the American Conference of Governmental Industrial Hygienists.

See also: Federal Insecticide, Fungicide, and Rodenticide Act, US; Heterocyclic Amines.

Further Reading

Harper, B.L., Ramanujam, V.M., Gad-El-Karim, M.M., Legator, M.S., 1984. The influence of simple aromatics on benzene clastogenicity. Mutat. Res. 128, 105–114.

National Toxicology Program (NTP), 2000. Toxicology and Carcinogenesis Studies of Pyridine (CAS No. 110-86-1) in F344/N Rats, Wistar Rats and B6C3F1 Mice(Drinking Water Studies). NTP Technical Report Series No. 470. NIH Publication No. 97-3960. US Department of Health and Human Services, Research Triangle Park, NC.

Santodonato, J., Bosch, S., Meylan, W., Becker, J., Neal, M., 1985. In: Corporation, S.R. (Ed.), Monograph on Human Exposure to Chemicals in the Workplace: Pyridine. National Cancer Institute, Division of Cancer Etiology, Bethesda, MD; Syracuse, NY.

Relevant Websites

http://www.hpa.org.uk – Health Protection Agency. Pyridine incident management. 2010

http://www.safe.nite.go.jp – Incorporated Administrative Agency National Institute of Technology and Evaluation. Summary of initial risk assessment report: Pyridine.

http://www.atsdr.cdc.gov – Agency for Toxic Substances and Disease Registry. Toxicological Profile for Pyridine.