United States
Environmental Protection
Agency

Office of Health and
Environmental Assessment
Washington DC 20460

Research and Development

EPA/600/S8-83/031F Aug. 1989

EPA

Project Summary

Health Assessment Document for Vinylidene Chloride

The Office of Health and Environmental Assessment has prepared this health assessment to serve as a "source document"for EPA use. The health assessment document was originally developed for use by the Office of Air Quality Planning and Standards to support decision-making regarding possible regulation of vinylidene chloride as a hazardous air pollutant. However, the scope of this document has since been expanded to address multimedia aspects.

In the development of the assessment document, the scientific literature has been inventoried, key studies have been evaluated and summary/conclusions have been prepared so that the chemical's toxicity and related characteristics are qualitatively identified. Observed effect levels and other measures of dose-response relationships are discussed, where appropriate, so that the nature of the adverse health responses are placed in perspective with observed environmental levels.

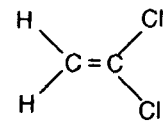
Any information regarding sources, emissions, ambient air concentrations, and public exposure has been included only to give the reader a preliminary indication of the potential presence of this substance in the ambient air. While the available information is presented as accurately as possible, it is acknowledged to be limited and dependent in many instances on assumption rather that specific data. This information is not intended, nor should it be used, to support any conclusions regarding risks to public health.

This Project Summary was developed by EPA's Environmental Criteria and Assessment Office, Research Triangle Park, NC, to announce key findings of the research project that is fully documented in a separate report of the same title (see Project Report ordering information at back).

Introduction

Vinylidene chloride is a highly reactive, flammable, clear, colorless liquid that, in the presence of air, can form complex peroxides in the absence of chemical inhibitors. The peroxides are violently explosive, and formaldehyde, phosgene, and hydrochloric acid are produced as decomposition products. Vinylidene chloride has a boiling point of 31.6°C at 760 mm Hg and a vapor pressure of 600 mm Hg at 25°C. The solubility of vinylidene chloride in water is 2250 mg/l at 25°C, and the density of the liquid is 1.2132 g/cm^3 (20°C). Vinylidene chloride vapor is 3.34 times as dense as air.

Synonyms for vinylidene chloride are 1,1-dichloroethene, 1,1-DCE, and 1,1-dichloroethylene. Vinylidene chloride has a molecular weight of 96.95 and a molecular formula of $C_2H_2Cl_2$. The structural formula is given below.



Vinylidene chloride monomer production capacity in the United States is approximately 178 million pounds per year. Virtually all of the vinylidene chloride produced is used in the production of copolymers with vinyl chloride or acrylonitrile. A small percentage (4%) of vinylidene chloride is used as chemical intermediates.

Sampling and Analytical Methods

The two primary methods that have been used in recent years for the sampling and analysis of vinylidene chloride in ambient air are the freeze-trap method and the sorption onto Tenax-GC method with subsequent analysis of the desorbed vinylidene chloride by high resolution gas chromatography with either flame ionization, electron capture, electrical conductivity, or mass spectrometric detectors. Both the freeze-trap and Tenax-GC methods of sample collection have some disadvantages. For example, the freeze-trap method using liquid oxygen is a cumbersome method both for sample collection and transportation, and the Tenax-GC method may suffer from serious problems of artifact formation.

The two methods commonly used for the analysis of vinylidene chloride in grab aqueous samples are the static head-space method and the dynamic purge-trap method. However, for aqueous samples containing very low levels of vinylidene chloride (e.g., potable water), the dynamic purge-trap method is more suitable than the static head-space method because of the higher sensitivity of the former. Although gas chromatography with either flame ionization, electron capture, electrical conductivity or mass spectrometric detectors has been used for the final quantification of vinylidene chloride by both methods, the electrical conductivity detector is preferable to other detectors because of its greater sensitivity and selectivity The mass spectrometric method is usually used as a confirmatory technique.

Vinylidene chloride in soil samples has been analyzed by solvent extraction in sealed vials with subsequent quantification by gas chromatography—flame ionization detector (GC-FID), and using mass spectrometry as the confirmatory technique. The analysis of vinylidene chloride in food wrapping materials, foods, and biological tissues has been performed either by the static head-space method or by the dynamic purge-trap method in a manner similar to that employed for aqueous samples.

Sources in the Environment

Due to its high volatility, vinylidene chloride is lost to the atmosphere during industrial manufacture of the monomer and polymer, and during storage and handling. The total emission of vinylidene chloride to all media from these facilities has been estimated to be 1,300,400 pounds per year. Moreover, vinylidene chloride originally in aqueous solution is likely to contribute to air contamination as a result of its high volatility from water.

Under atmospheric smog conditions, the half-life of vinylidene chloride in air has been determined to be 5 to 12 hours. In the absence of smog conditions, vinylidene chloride may persist in the atmosphere with a half-life of approximately 2 days. Volatilization from aquatic media is probably the most significant fate-determining process for vinylidene chloride, although the role of biodegradation still remains uncertain. The half-lives of volatilization of vinylidene chloride from pond, river, and lake water have been estimated to be 6.1 days, 1.2 days, and 4.2 days, respectively. The fate of vinylidene chloride in soils has not been evaluated with certainty However, it has been concluded from the limited data that both volatilization and leaching may play significant roles in determining the fate of this chemical in soils.

The median ambient air level of vinylidene chloride in urban/suburban areas of the U.S. was estimated to be 5 ppt (20 ng/m^3). However, the median concentration value is substantially higher, 2182 ppt (8.66 µg/m^3) for ambient air in the vicinity of point sources of emission. The estimated daily vinylidene chloride intake from ambient air in urban/suburban areas through inhalation is 0.4 µg. However, the daily inhalation exposure from ambient air may be as high as 0.17 mg in the immediate vicinity of point sources. Vinylidene chloride has been detected in approximately 3% of the total drinking water supplies in the U.S. at an estimated mean concentration of 0.3 µg/l and a concentration range of 0.2 to 0.5 µg/l. For the majority of the U.S. population, the daily exposure to vinylidene chloride from ingestion of drinking water has been estimated to be less than 0.6 µg, although the maximum daily exposure in certain communities could exceed 1 µg. Because of the paucity of data, no estimate of the dietary intake of vinylidene chloride in the U.S. can be made at the present time.

Biological Effects on Aquatic Organisms

Vinylidene chloride is acutely toxic to aquatic animals at exposure concentrations in the milligrams per liter range. The lowest concentration reported to be acutely toxic to an aquatic organism is 2.4 mg/l. Reported acute and subchronic LC_{50} values ranged between 11.6 and 250 mg/l for aquatic animals. Vinylidene chloride was not acutely toxic to aquatic algae at concentrations of 712 to 798 mg/l. Vinylidene chloride was, however, toxic to yeast. No information was found concerning the toxicity of vinylidene chloride to domestic animals and non-aquatic wildlife.

Biological Effects in Animals and Man

Vinylidene chloride is readily absorbed by mammals following oral or inhalation exposure. Vinylidene chloride is metabolized in the liver with a number of possible reactive intermediates, including an epoxide, being formed. These reactive intermediate metabolites can react with macromolecules; this is a characteristic of many chemical carcinogens. The metabolites of vinylidene chloride produce toxic lesions in the liver and kidneys, with inhibitors of metabolism providing protection from vinylidene chloride toxicity. The heptatotoxic effect can be extensive and histological effects can be noted within 2 hours after the onset of exposure. The acute hepatotoxicity of vinylidene chloride was shown to be greater than that of any other chloroethylene. The liver and kidneys remain the target organs for toxic effects regardless of the route of administration (administration vehicle may influence vinylidene chloride metabolism and therefore affect the extent of toxicity) or whether acute, subacute, or chronic exposure occurs.

Vinylidene chloride has been described as a possible weak teratogen in a study using rats and mice. In this study, the experimental levels of vinylidene chloride were toxic to the dams, confounding the interpretation of the results. It was clear however, that exposure of pregnant rats and mice to high levels of vinylidene chloride could cause fetotoxicity and adversely affect the outcome of pregnancy. Another study reported no teratogenic effect in rats or rabbits inhaling up to 160 ppm vinylidene chloride for 7 hours per day or in rats given drinking water containing 200 ppm vinylidene chloride. Embryo and maternal toxicity were observed among rats inhaling 80 or 160 ppm vinylidene chloride and rabbits inhaling 160 ppm. At exposures causing little or no maternal toxicity (20 ppm in rats, 80 ppm in rabbits), there was no effect on embryo or fetal development. The effect of vinylidene chloride on reproduction and fetal and neonatal development of rats was tested in a three generation study with six litter groups being produced. Hepat

cellular fatty changes were observed in ats ingesting 50, 100 or 200 ppm vinylidene chloride.

A large number of studies indicate that vinylidene chloride is mutagenic to bacteria and that this activity is largely dependent on microsomal activation. Vinylidene chloride was reported to produce positive results for gene reversion and conversion in yeast, which was also dependent on metabolic activation, and was positive in Tradescantia. In mammalian systems, vinylidene chloride failed to induce gene mutations in V79 cells at two separate loci, failed to induce cromosomal aberrations in mouse bone marrow in vivo, and failed to induce dominant lethals in either mice or rats. Vinylidene chloride was found to alkylate the DNA of mice exposed through inhalation and may have caused unscheduled DNA synthesis in the kidneys of similarly exposed mice.

Analysis of the data relating to the potential of vinylidene chloride to behave as a human germ-cell mutagen indicates that based on the criteria established in the Agency's Proposed Guidelines for Mutagenicity Risk Assessment, the evidence at the present time is classified as limited. This designation indicates that there are insufficient data on either mutagenicity or interaction with germ cells to classify the evidence as either sufficient or suggestive of potential germ-cell mutagenicity. However, available data also do not permit the classification of vinylidene chloride as a non-germ-cell mutagen.

Based on the limited evidence from animal studies, supporting evidence from mutagenicity studies, and related biochemical and toxicity considerations, it is recommended that vinylidene chloride be considered a "possible" carcinogen for humans.

A total of 18 chronic studies in animals were evaluated for evidence of carcinogenicity The exposure regimes for these studies were as follows. 11 were inhalation, 4 were gavage, 1 was drinking water, 1 was subcutaneous injection, and 1 was skin application. Evidence for carcinogenicity was found in Swiss mice exposed to vinylidene chloride by inhalation, 4 hours daily for 12 months. A statistically significant increase of kidney adenocarcinomas, a rare tumor type, was observed in male mice. Statistically significant increases in mammary carcinomas and pulmonary adenomas were observed in mice of both sexes, although the importance of these findings is uncertain because no clear dose-response relationship was evident. Vinylidene chloride has also been shown to be a tumor initiator in mouse skin. the remaining 16 animal studies have negative (assuming non-treatment related increases are also negative) findings for carcinogenicity; however, these negative findings may be partially explained by study characteristics such as, less than lifetime dosing, below maximum tolerated dose levels, and single dose studies, which individually or in combination, reduce the sensitivity of detecting a carcinogenic response While the number of studies are many, the inadequacy of test conditions demonstrates the need for additional testing to elucidate the potential for human carcinogenicity. The mutagenic activity of vinylidene chloride, its chemical structure, its activity as a tumor initiator in mouse skin, and the ability of metabolites to react with DNA, signal that the animal evidence should not be lightly dismissed.

There is only one epidemiologic study for vinylidene chloride While the study concluded that a carcinogenic effect could not be attributed to vinylidene chloride, limiting characteristics made it inadequate to evaluate the carcinogenic potential.

The carcinogenicity evidence has been evaluated using the EPA's Proposed Guidelines for Carcinogen Risk Assessment as well as the International Agency for Research for Cancer (IARC) criteria for assessing weight of evidence. Using the EPA criteria, the weight of evidence is such that the animal data for carcinogenicity is limited and the epidemiologic data is inadequate The overall ranking of the weight of evidence is Group C meaning that the substance is a "possible" carcinogen for humans. Using the IARC weight-of-evidence criteria, the animal and epidemiologic data have the same ranking as in the EPA classification, limited and inadequate; however, the overall ranking is considered to be Group 3. An IARC Group 3 classification means that while the evidence may range from limited to inadequate, the overall conclusion is that the data are "inadequate" to assess the human carcinogenic potential. The Agency believes that its ranking criteria are more instructive for public health impact analysis. The Group C (possible carcinogen) classification given to vinylidene chloride is one of five that could be assigned to a substance. The five classifications are: human carcinogen, probable human carcinogen, possible human carcinogen, not classified (inadequate evidence for assessing carcinogenicity), and no evidence of carcinogenicity for humans.

Although vinylidene chloride has only limited carcinogenicity evidence, an upper-bound estimate of incremental cancer risk can be estimated from the kidney adenocarcinoma data in male mice. The development of this risk estimate is for the purpose of evaluating the "what-if" question: If vinylidene chloride is carcinogenic in humans, what is the possible magnitude of the public health impact? Any use of the risk estimates should include a recognition of the weight-of-evidence likelihood for the carcinogenicity of vinylidene chloride in humans The upper-bound incremental cancer risk is calculated to be 1.16×10^{-3} for 1 µg/kg body weight/day for a continuous lifetime exposure to vinylidene chloride under the presumption that vinylidene chloride is carcinogenic in humans. The upper-bound nature of this estimate is such that the true risk is not likely to exceed this value and may be lower. Expressed in terms of relative potency, vinylidene chloride ranks in the third quartile among the 54 suspect or known human carcinogens evaluated by EPA's Carcinogen Assessment Group.

This Project Summary was prepared by staff of the Environmental Criteria and Assessment Office, Research Triangle Park, NC 27711.

The complete report, entitled "Health Assessment Document for Vinylidene Chloride," (Order No. PB 86-100 641/AS; Cost: $36.95, subject to change) will be available only from:

National Technical Information Service
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EPA/600/S8-83/031F