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1,2-Dichloroethane

Guideline

The interim maximum acceptable concentration (IMAC) for 1,2-dichloroethane in drinking water is 0.005 mg/L (5 μg/L).

Identity, Use and Sources in the Environment

1,2-Dichloroethane (ethylene dichloride) is a clear, colourless, oily liquid with a chloroform-like odour and a boiling point of 83.5°C. Its vapour pressure ranges from 5.33 to 14.0 kPa over the temperature range 10 to 30°C. 1,2-Dichloroethane is miscible with most organic solvents and is appreciably soluble in water, with a solubility ranging from 8700 to 9200 mg/L over the temperature range 0 to 25°C. It has a log octanol–water partition coefficient of 1.48.[1]

1,2-Dichloroethane has been reported to be one of the most widely used chemicals in the world.[2] Annual usage in the Great Lakes Basin has been estimated at 900 million kilograms.[3] Canadian production in 1984 was 680 million kilograms, of which 180 million kilograms were exported and 500 million kilograms were consumed domestically.[4]

Almost all of the domestic 1,2-dichloroethane is used as a chemical intermediate in the preparation of vinyl chloride. About 1% is used as a solvent and as a lead scavenger in leaded gasoline formulations.[4] This use has decreased over the past few years and will continue to decrease as the use of lead in fuels drops.[5] 1,2-Dichloroethane enters the environment through atmospheric emissions, waste effluents to waterways and land disposal of liquid and solid wastes.[6] Because of its high volatility, 1,2-dichloroethane that is released to land and water can be expected to be transferred predominantly to the atmosphere. About 1 to 1.7% of total U.S. yearly production was estimated to be released to the environment as emissions.[6]

Exposure

1,2-Dichloroethane was detected frequently in treated drinking water and raw water samples taken from 30 treatment facilities across Canada in 1979.[7] Mean concentrations in treated water were between 4 and 5 μg/L during August and September and less than 1 μg/L in November and December. The overall mean of 31 positive determinations was 3.2 μg/L. Maximum concentrations of 30 and 11 μg/L were found during August and September and during November and December, respectively. 1,2-Dichloroethane was detected at trace levels (0.34 to 0.38 μg/L) in one municipal water supply in Quebec during February 1986, but it was not detected in a later survey, during August 1986, of 18 Quebec municipalities.[8] It was also undetected in 1985 and 1986 surveys of 40 municipalities in the four Maritime provinces,[9,10] in a 1984 survey of seven municipalities in the Niagara River area[11] and in the 1978 to 1985 surveys of 29 municipal water supplies in Alberta.[12] The average daily intake* from drinking water containing 1,2-dichloroethane was estimated to be 0.069 μg/kg bw, based on the mean of 3.2 μg/L observed in the Otson study.[7]

Few data are available on concentrations of 1,2-dichloroethane in foods. Concentrations ranging from 2 to 23 μg/g were found in 11 of 17 different spice oleoresins that had been subjected to solvent extraction with 1,2-dichloroethane.[13] Residues of 1,2-dichloroethane in grain products arising from its use as a grain fumigant are expected to be negligible, as this use was suspended in Canada in 1984. The human intake from food sources was estimated to be negligible.[6]

No Canadian data are available on ambient air concentrations of 1,2-dichloroethane. A review of recent reports revealed that U.S. ambient air concentrations ranged from 0.062 to 6.20 ppb (0.25 to 25 $\mu g/m^3$) with an intermediate value of 0.62 ppb (2.5 $\mu g/m^3$).[6] Based on these concentrations, the estimated average daily human intake of 1,2-dichloroethane from ambient air is

* This estimate was based on an adult body weight of 70 kg and average daily drinking water consumption of 1.5 L.

0.71 µg/kg bw, with a range of 0.07 to 7.14 µg/kg bw*. Atmospheric concentrations near production facilities were in the order of 10 ppb (40 µg/m^3), and those near end-use facilities ranged from 0.69 to 0.99 ppb (2.8 to 4.0 µg/m^3).[6]

Inhalation would therefore appear to be the primary route of exposure to 1,2-dichloroethane, with 0.71 µg/kg bw or 91% of an estimated total daily intake of 0.78 µg/kg bw derived from this source. The contribution from food is negligible,[6] and estimated intake from drinking water is 0.07 µg/kg bw or 9% of the total.

Analytical Methods and Treatment Technology

The analysis of 1,2-dichloroethane in water at concentrations as low as 0.10 µg/L is possible using the purge and trap method and gas/liquid chromatography instrumentation equipped with a halogen-specific detector.[6] The practical quantitation limit (PQL) (based on the ability of laboratories to measure 1,2-dichloroethane within reasonable limits of precision and accuracy) is 5 µg/L.[14]

The removal efficiency of volatile organic compounds by packed tower aeration and granular activated carbon adsorption for chlorinated aliphatic hydrocarbons has been estimated to be 90 to 93%.[14] It would appear that, using advanced technology, a reduction in the concentration of 1,2-dichloroethane in drinking water to less than 1 µg/L would be feasible.

Health Effects

Animal studies with 1,2-dichloroethane have shown that it is rapidly and extensively absorbed via the lungs.[15] Uptake from the gastrointestinal tract was efficient and rapid,[15] although both the rate and extent were vehicle-dependent,[16] peak values for the blood levels being 5 times higher for solutions in water than for solutions in oil. Dermal absorption was shown to be significant in rats, with an absorption rate of 479 nmol/min per square centimetre.[17]

1,2-Dichloroethane was rapidly distributed to all body tissues.[15] As expected from its properties as a general anaesthetic in man, it readily crossed the blood–brain barrier. It was also efficiently transferred to the foetus of the rat.[18]

There was good evidence to show that the metabolism of 1,2-dichloroethane proceeded via two principal pathways. One involved a saturable microsomal (P-450-mediated) oxidation, leading to the formation of 2-chloroacetaldehyde, the putative 1-chloroso-2-chloroethane and, ultimately, glutathione conjugates. A second pathway involved a cytosolic glutathione-dependent pathway leading to glutathione conjugates, such as S-(2-chloroethyl glutathione).[19,20] These metabolites were believed to be involved in covalent binding with DNA, although other metabolites, conjugates and intermediates were also formed.[19,20]

The elimination of 1,2-dichloroethane followed a two- or three-compartment mathematical model after administration by various routes and was dose-dependent.[15,16,21] Material balance studies, following oral and inhalation dosing, have shown that metabolism was the primary elimination mechanism.[15] After the administration of an oral dose of 150 mg/kg bw to rats, 29% was excreted unchanged in exhaled air, 5% was metabolized to carbon dioxide and 60% appeared in the urine as metabolites. After an inhalation exposure to 150 ppm (600 mg/m^3) for six hours, rats were estimated to have received a total dose of 50 mg/kg bw. Of this dose, 2% was excreted unchanged in air, 7% was metabolized to carbon dioxide and more than 84% was recovered as urinary metabolites.

No epidemiological studies on human health effects induced by 1,2-dichloroethane have been published. The characteristic symptoms of poisoning by chlorinated aliphatic hydrocarbons have been reported in acute and chronic occupational exposures to inhaled 1,2-dichloroethane. Nausea, headache, gastrointestinal disturbances, vomiting, rapid and weak pulse, progressive cyanosis, dyspnoea, loss of consciousness and, ultimately, death have been documented.[6] Deaths have also been reported after ingestion of 1,2-dichloroethane, and the acute lethal dose in humans has been estimated to be between 8 and 200 mL (143 to 3571 mg/kg bw).[6]

Acute exposure studies in animals showed that the severity of effects was dependent on the duration and level of exposure to 1,2-dichloroethane. For rats exposed for five to eight hours via inhalation, adverse effects were not elicited at 200 ppm (800 mg/m^3). The first signs of intoxication appeared at a concentration of 300 ppm (1200 mg/m^3) and mortality at about 600 ppm (2400 mg/m^3).[22,23] The acute lethal oral dose in rats was reported to be 680 mg/kg bw.[24] In male and female CD-1 mice, the acute lethal oral doses were 489 and 413 mg/kg bw, respectively.[25] The LD_{50} for skin exposures in rabbits was estimated to be between 2.8 and 4.9 g/kg bw.[6]

In a subchronic study, 15 rats of each sex, eight guinea pigs of each sex, one female and two male rabbits and two male monkeys were exposed to 1,2-dichloroethane vapour at concentrations of 400 and 100 ppm (1600 and 400 mg/m^3) for 7 h/d, five days per week for six months. In addition, a further 15 rats of each sex and eight guinea pigs of each sex were exposed to 200 ppm (800 mg/m^3) for 30 and 36 weeks, respectively.[22] No adverse effects were observed in any

* This estimate was based on a 70-kg man breathing 20 m^3 of air per day.

of the four species exposed to 100 ppm. At the 200 ppm level, no adverse effects were seen in rats, but slight parenchymatous degeneration of the liver, with some vacuolization, was seen in guinea pigs. Severe effects, including hepatotoxicity and death, were observed in rats and guinea pigs exposed at the 400 ppm level.

Chronic studies with 1,2-dichloroethane in animals have been limited to those that were primarily designed as cancer bioassays. There have been two principal studies, one in which both sexes of rats and mice were dosed by gavage with solutions in corn oil[26] and the other in which the same species were exposed by the inhalation route.[27]

In the National Cancer Institute study,[28] the maximum tolerated dose (MTD) and one-half the MTD, determined from preliminary studies, were administered by gavage on five consecutive days per week to 50 Osborne-Mendel rats of each sex, beginning at eight weeks of age, and to 50 B6C3F_1 mice, starting at five weeks of age. In addition, 20 animals were given no treatment, and 20 animals were dosed with the vehicle alone for each dose and sex group. Early signs of toxicity in both species indicated that the selected MTDs were inappropriate and necessitated several changes in the administered dosages during the 78 weeks of the study. Thus, the time-weighted average doses received by the male and female rats were 97 and 47 mg/kg bw (MTD and one-half the MTD). For male mice, the doses were 195 and 97 mg/kg bw, and for female mice, 299 and 149 mg/kg bw.

Multiple tumours were induced in both species. A statistically significant increase ($P < 0.05$) in the incidence of squamous cell carcinomas of the forestomach, hemangiosarcomas of the circulatory system and fibromas of the subcutaneous tissue occurred in male rats. There was also a statistically significant increase in the incidence of adenocarcinomas of the mammary gland and hemangiosarcomas of the circulatory system in female rats. Tumours were also observed at other sites, including the spleen, liver, adrenal glands, pancreas, large intestine, subcutaneous tissue and abdominal cavity.

In B6C3F_1 mice, there was a statistically significant increase in incidences of hepatocellular carcinomas and alveolar/bronchiolar adenomas in male mice. In female mice, there was a statistically significant increase in incidences of alveolar/bronchiolar adenomas, mammary carcinomas and endometrial tumours.

Supportive evidence for the National Cancer Institute study was available from a pulmonary tumour bioassay[29] in which mice were dosed intraperitoneally with 1,2-dichloroethane in tricaprylin and from a skin application study in mice.[30] Both of these studies showed that 1,2-dichloroethane could induce a significant increase in tumours at sites (e.g., lung and stomach) remote from the point of application.

No evidence of carcinogenicity was found in a recent lifetime inhalation study in which Sprague-Dawley rats and Swiss mice were exposed to concentrations of 1,2-dichloroethane that ranged from 5 to 150 ppm (20 to 600 mg/m^3).[27] Nor was there any evidence of carcinogenicity from an earlier subchronic study in which Wistar rats were exposed to 200 ppm (800 mg/m^3) 7 h/d, five days per week for six months.[22] The apparent discrepancies between inhalation and other routes of exposure in oncogenicity studies have led to considerable discussion.[15,31] Among other factors it was considered that the delivered dose in the inhalation studies was lower than that received by the animals in the oral dosing study and was probably too low to elicit a statistically significant tumour response in the number of animals used.

A recent review has concluded that 1,2-dichloroethane causes gene mutations in bacteria, plants, *Drosophila* and Chinese hamster ovary cells.[32] The results of reproductive and teratogenicity testing have indicated that 1,2-dichloroethane has little potential for producing adverse reproductive effects or for adversely affecting the developing foetus unless the exposure is high enough to produce maternal toxicity.[6,33]

Classification and Assessment

1,2-Dichloroethane is classified in Group II — probably carcinogenic to man (sufficient evidence in animals, inadequate evidence in man) — on the basis that it has been shown to be carcinogenic in both sexes of two animal species. Incorporating a surface area correction and using the robust linear extrapolation model, one can calculate the unit lifetime risk associated with the ingestion of 1 µg/L 1,2-dichloroethane in drinking water to be 1.6×10^{-6} (based on hemangiosarcomas in the circulatory system of male Osborne-Mendel rats)*.[26] These tumours were selected because they represented the most sensitive response and occurred at locations remote from the site of contact with the agent. The estimated concentrations in drinking water corresponding to lifetime risks of 10^{-5}, 10^{-6} and 10^{-7} for the same tumour type based on the model described above are 6.2, 0.62 and 0.062 µg/L.

* Average adult body weight = 70 kg; average daily intake of drinking water = 1.5 L.

Rationale

Because 1,2-dichloroethane is classified as a probable human carcinogen in Group II, the maximum acceptable concentration (MAC) is derived based on consideration of available practicable treatment technology and estimated lifetime cancer risks. Because the MAC must also be measurable by available analytical methods, the PQL is also taken into consideration in its derivation.

An interim MAC (IMAC) of 0.005 mg/L (5 µg/L) for 1,2-dichloroethane was established, therefore, on the basis of the following considerations:

(1) The estimated unit lifetime risk associated with the ingestion of 1 µg/L 1,2-dichloroethane in drinking water is 1.6×10^{-6} (based on hemangiosarcomas in male rats). Therefore, the estimated lifetime risk associated with the ingestion of drinking water containing 5 µg/L 1,2-dichloroethane is 8×10^{-6}. The MAC is considered interim because intake in drinking water is approximately 9% of the total intake, and the estimated total risk from all sources therefore will exceed 1×10^{-5}, which is above the maximum value in the range considered "essentially negligible."

(2) It is unlikely that 1,2-dichloroethane concentrations are reduced significantly during conventional water treatment processes. However, it is possible to achieve concentrations below 1 µg/L using packed tower aeration or granular activated carbon adsorption.

(3) The PQL (based on the ability of laboratories to measure 1,2-dichloroethane within reasonable limits of precision and accuracy) is 5 µg/L.

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