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Vinyl Chloride

Guideline

The maximum acceptable concentration (MAC) for vinyl chloride in drinking water is 0.002 mg/L (2 µg/L).

Identity, Use and Sources in the Environment

Vinyl chloride is a colourless, flammable, explosive gas with a vapour pressure of 2530 mmHg at 20°C and a boiling point of −13.4°C. It is slightly soluble in water (1.1 g/L at 28°C) but highly soluble in fats and organic solvents. It polymerizes in light and in the presence of a catalyst. On combustion, it degrades to hydrogen chloride, carbon dioxide and traces of phosgene. It has a pleasant, ether-like odour at low concentrations.[1]

In 1982, 86% of the Canadian production of vinyl chloride was used to manufacture polyvinyl chloride (PVC), 4% was used to manufacture 1,1,1-trichloroethane and 10% was exported.[2] PVC is used in electrical wire, insulation and cables, industrial and household equipment, medical supplies, food packaging materials, building and construction products and piping. In addition, PVC is used as a raw material in the paper, glass, rubber and automotive industries. Vinyl chloride and PVC copolymers are distributed and processed in a variety of forms, such as dry resins, plastisol, organosol and latex.[3] Concentrations of vinyl chloride monomer in PVC were reduced drastically between 1973 and 1975 and range from 1 to 10 ppm.[4]

Vinyl chloride is a synthetic chemical with no known natural sources. It is now used with stringent methods for containment and recovery. Releases to the environment will be limited to areas where vinyl chloride is produced and used and to leaching of the entrapped monomer from PVC pipe. Its presence in the aquatic environment is primarily a result of industrial discharges from chemical and latex manufacturing plants.[1] Vinyl chloride is also formed from trichloroethylene and perchloroethylene in groundwater.[5]

The low boiling point, high vapour pressure and low water solubility of vinyl chloride indicate that any vinyl chloride released to surface water will migrate rapidly to air, where it will be photodegraded in a few hours. Vinyl chloride that is released to the ground does not adsorb onto soil; any that does not evaporate migrates readily to groundwater, where it is expected to remain for months to years. The half-life of 1 ppm vinyl chloride monomer in open water at a 1-m depth is estimated to be 26 minutes, and 90% is lost by evaporation within 96 minutes.[6] Under aerobic conditions, vinyl chloride in samples taken from a shallow aquifer (groundwater) was readily degraded, with more than 99% being degraded after 108 days and approximately 65% being mineralized to carbon dioxide.[7] Vinyl chloride does not bioaccumulate in animals or food chains.

Exposure

In a national survey of 30 Canadian water treatment facilities conducted in 1979, vinyl chloride was detected at <1 µg/L in one sample each of treated and raw water collected in the months of November and December but was not present in August and September samples.[8] It was also detected in U.S. drinking water at concentrations up to 10 µg/L.[1]

In recent years, PVC pipes have been used for conveying potable water. The World Health Organization[9] has concluded that the occurrence of vinyl chloride in potable water is primarily associated with the use of PVC water pipes manufactured with incompletely polymerized vinyl chloride monomer. Drinking water that ran through recently installed PVC pipes contained vinyl chloride at 1.4 µg/L, whereas water that passed through nine-year-old pipes contained vinyl chloride at 0.03 to 0.06 µg/L.[10] A number of product standards exist that specify the quality of PVC water pipes in order to limit the quantity of free monomer present. The Canadian Standards Association's standard for all plastic pipes was revised in 1990 and includes a leaching test for vinyl chloride from pipes; the maximum allowable leaching of vinyl chloride in water from pipes is 0.002 mg/L.[11] If pipes of this quality are used, only very low concentrations of vinyl chloride monomer are likely to be present in drinking water.

Samples of wastewaters from seven areas in the United States having vinyl chloride and/or PVC manufacturing plants were reported to have vinyl chloride levels ranging from 0.05 to 20 mg/L.[9]

There is very little information on concentrations of vinyl chloride in food. The leaching of vinyl chloride monomer from wet food packaging materials is low; however, the monomer is soluble in alcohols and mineral oil. Canadian Food and Drug Regulations prohibit the sale of any food packaged in materials that leach detectable residues of vinyl chloride monomer,[12] as determined by an analytical method with a detection limit of 50 µg/kg.[13] A recent estimate of vinyl chloride intake via food and drinks is 0.1 µg/day.[9,14]

Air in rural/remote and urban/suburban areas of the United States usually contains undetectable amounts of vinyl chloride,[15,16] and the average daily intake of vinyl chloride by inhalation in rural/remote and urban/suburban areas has therefore been estimated to be essentially zero. A level of less than 0.013 µg/m^3 (5 ppt) has been suggested for rural air.[17] The average vinyl chloride concentration in air near polymerization plants in the United States was reported by the U.S. Environmental Protection Agency in 1976 as 44 µg/m^3.[4] In Alberta, 24-hour average concentrations of vinyl chloride at the perimeter of a vinyl chloride plant from 1979 to 1984 were: 12.9 µg/m^3 (5 ppb) 86 to 98% of the time; 12.9 to 23.2 µg/m^3 (5 to 9 ppb) 0.3 to 4.9% of the time; 25.8 to 77.4 µg/m^3 (10 to 30 ppb) 0.1 to 6.5% of the time; and 77.4 µg/m^3 (30 ppb) 0.3 to 2.4% of the time.[18]

The general public may therefore be exposed to small amounts of vinyl chloride from inhalation of ambient air in urban areas, typically in the order of 5 µg/day per person,[4] with higher amounts in the vicinity of vinyl chloride and PVC plants. Vinyl chloride has been detected in tobacco smoke (5.6 to 28 ng/cigarette)[1] and occasionally in the interior of new cars (824 to 3120 µg/m^3).[16]

Analytical Methods and Treatment Technology

Vinyl chloride in drinking water is analysed by a purge and trap gas chromatographic procedure[16] followed by mass spectrometry. This method is applicable to the measurement of vinyl chloride over a concentration range of 0.06 to 1500 µg/L. The detection limit is 0.3 µg/L, and the practical quantitation limit (PQL) is estimated to be 2 µg/L.[19]

There is little information available on the effectiveness of conventional water treatment processes for the removal of vinyl chloride from raw water. Its volatility and relatively high Henry's law constant (approximately 1.2 atm•m^3/mol at 10°C)[16] suggest aeration as a potential removal technique.[20] Removals of up to 99% were achieved using a pilot packed tower aerator. In similar studies, vinyl chloride was removed from groundwater using a spray aerator system with a total volatile organic contaminant concentration of 100 to 200 µg/L. Air stripping techniques have also been recommended.[21,22] Granular activated carbon adsorption techniques have been less successful than aeration in removing vinyl chloride from water, as the capacity of activated charcoal to adsorb vinyl chloride is limited.

Toxicokinetics

No published data on the toxicokinetics of vinyl chloride in humans have been found. In animals, vinyl chloride is readily absorbed via all routes of exposure and rapidly distributed throughout the body. Following gastric intubation of 10 mL of aqueous solutions containing 2.26 to 2.82 mg/mL vinyl chloride (total dose 22.6 to 28.2 mg/animal) in male Wistar rats, peak blood concentrations (6 to >40 µg/mL) were found in less than 10 minutes.[23] Vinyl chloride is quickly cleared from the body, through either metabolism or excretion of the parent compound.[1] In an experiment in which rats were given single oral doses (by gavage) of 0.05, 1 or 100 mg/kg bw of ^{14}C-labelled vinyl chloride dissolved in corn oil, the percentage of the dose expired within 72 hours as unchanged vinyl chloride was 1.4%, 2.1% and 67%, respectively; excretion in urine was 59%, 68% and 11%, respectively; and the $^{14}CO_2$ in expired air accounted for 9%, 13% and 2.5%, respectively. The liver was found to retain the maximum percentage of activity at all dose levels, three to five times the percentage found in muscle, lungs or fat.[24]

The major metabolic pathway for vinyl chloride occurs through mixed function oxidase systems involving cytochrome P-450, and its two major metabolites are chloroethylene oxide and chloroacetaldehyde. Both metabolites are excreted in urine. Metabolism and excretion occur through saturable processes.[24,25] When rats were exposed to vinyl chloride at below 100 ppm (260 mg/m^3) for five hours, 69% of the absorbed dose was excreted as metabolites within 24 hours in urine. An additional 1.7% was found in the urine 24 to 48 hours later.[26] The half-life for urinary excretion in rats was about four hours. As much as 12% of the dose was excreted unchanged through exhalation during the 72 hours after exposure of the rats to 1000 ppm of the chemical in air for six hours, whereas less than 2% was exhaled after exposure to 10 ppm. With the increase in dose via inhalation or ingestion, the proportion exhaled increased and that excreted in the urine and faeces decreased. The proportion retained in the carcass also decreased.[24]

The fate of vinyl chloride in the rat appears to be dose dependent.[27] This is primarily due to the non-linear kinetics of the metabolic pathway for vinyl chloride,

which is saturated at high doses following either single oral administration or inhalation exposure. Vinyl chloride must be metabolized to produce carcinogenicity, as carcinogenicity is a function of the amount of the active metabolites produced rather than the chemical itself.[14]

Health Effects

Vinyl chloride is a narcotic agent, and loss of consciousness can occur from exposure to high concentrations (25 000 mg/m^3). Acute exposure to high concentrations in air also causes central nervous system depression in humans, with symptoms of dizziness, light-headedness, nausea, headache, irritability, poor memory, tingling sensations, weight loss, irritation of the respiratory tract and chronic bronchitis.[1]

Chronic inhalation exposure to lower levels (levels not specified) of vinyl chloride has been found to cause degenerative bone changes in workers.[28] Other chronic effects include Raynaud's syndrome, circulatory disturbances in the extremities, thrombocytopenia, dermatitis, scleroderma-like skin changes, lytic lesions of the terminal phalanges in hands and feet and pseudo clubbing of the fingers (acro-osteolysis), thyroid insufficiency, damage to liver, spleen and lungs, as well as functional disturbances of the central nervous system.[1,4]

Administration of vinyl chloride monomer dissolved in soyabean oil by gavage to groups of Wistar rats (30/group) at doses of 0, 30, 100 or 300 mg/kg bw per day six days per week for 13 weeks did not result in adverse effects at the 30 mg/kg bw level. A dose-related increase in relative liver weight was observed at the two highest dose levels, but the increase was statistically significant only at 300 mg/kg bw.[29] Inhalation exposure of guinea pigs, rats, rabbits and dogs to 50 ppm (130 mg/m^3), 100 ppm or 200 ppm vinyl chloride seven hours per day, five days per week for 26 weeks did not induce any adverse effects at 50 ppm as observed by appearance, growth, haematology, liver weight and mortality; however, rats exposed to 100 ppm (260 mg/m^3) had increased liver weights, one of the most sensitive indicators of hepatotoxity.[30]

Sufficient evidence has accumulated in recent years to implicate vinyl chloride as a human and animal carcinogen. The first experimental data on the carcinogenic effects of vinyl chloride in rats were published in 1971,[31] and the first four cases of liver cancer in workers employed by a vinyl chloride plant were reported in 1974.[32] Several comprehensive reviews and evaluations of existing studies have been published.[1,4,14,16,33,34] A number of studies have associated occupational exposure to vinyl chloride with cancers of the liver, brain and possibly other sites. All studies refer to inhalation exposure, and positive findings come from industrial populations exposed to high concentrations of vinyl chloride. Most of the studies of workers exposed to vinyl chloride have focused on cases of angiosarcoma of the liver, a type of cancer that occurs infrequently in the general population. Because of its rare occurrence, a causal relationship between exposure to vinyl chloride and the development of this tumour is now commonly accepted. Tumours of the respiratory tract, digestive system, cardiovascular system and other sites have also been reported, but increased incidences were observed in very few studies.

A number of recent epidemiological studies have confirmed the association between occupational exposure to vinyl chloride and cancer of the liver, both angiosarcoma and nonangiosarcoma.[35–37] Pirastu and colleagues[35] conducted a mortality study on 5946 vinyl chloride and PVC workers from nine Italian plants. Analysis of the data (death certificates, clinical and pathological information) confirmed the carcinogenic action of vinyl chloride on the liver (14 liver cancers) but not on the other suggested target organs (i.e., lung, lymphopoietic tissues, brain). In a seven-year follow-up of a French prospective cohort study of 1100 exposed and 1100 unexposed subjects, three cases of angiosarcoma of liver and 14 cases of Raynaud's disease were found among the exposed group and one case of Raynaud's disease among non-exposed subjects. The diseases of the respiratory system did not differ between the two groups (relative risk [RR] = 1.1; 95% confidence interval [CI] = 0.7 to 1.8).[36]

An update of an industry-wide epidemiological study of 10 173 men (1942 to 1982) who were exposed to vinyl chloride for at least one year prior to 1973 at 37 plants in the United States was carried out by Wong *et al.*[37] Analyses by length of exposure, latency, age at first exposure, calender year of first exposure and type of products were performed. The study confirmed that workers exposed to vinyl chloride experience a significant mortality excess for angiosarcoma (15 deaths), cancer of the liver and biliary tract (standardized mortality ratio [SMR] = 641) and cancer of the brain and central nervous system (23 deaths compared with 12.8 expected; SMR = 180). However, half of the cases of brain cancer came from two plants that were manufacturing only PVC. Only the cancer of the liver showed increasing trends by length of exposure and by latency period since first exposure and decreasing trends by age at first exposure. The study did not find any excess in respiratory cancer or lymphatic and haematopoietic cancer.

The International Agency for Research on Cancer (IARC) coordinated a multicountry (Italy, Norway, Sweden and the United Kingdom) cohort study with 14 351 individuals from 19 factories to investigate the dose–response relationship between liver cancer and

exposure to vinyl chloride and to assess the cancer risks for sites other than liver. A nearly threefold increase in liver cancer was reported on the basis of 24 observed deaths and 8.4 expected (SMR = 286; 95% CI = 186 to 425). The excess from liver cancer was clearly associated with the elapsed time since the first exposure, duration of employment and quantitative exposures. No statistically significant excess of mortality was reported for the cancers at sites other than the liver due to exposure to vinyl chloride.[38]

In the 1970s, IARC concluded that vinyl chloride could be associated with hepatocellular carcinoma, brain tumours, lung tumours and malignancies of lymphatic and haematopoietic tissues,[1] but this position may change based on recent studies.[38] The European Chemical Industry Ecology and Toxicology Centre (ECETOC)[4] pointed out that there is insufficient evidence to establish any relationship between exposure to vinyl chloride and an increased incidence of cancers of brain, lung and lymphatic or haematopoietic tissue. Similarly, Doll[34] stated that evidence of a hazard of any type of cancer other than the liver has not been found except for the possibility of a small increased risk of lung cancer when exposure was very heavy.

Vinyl chloride is a versatile carcinogen that induces neoplasms at multiple sites in several species of animals when administered by inhalation or orally. In the rat, mouse and hamster, it has induced hepatic haemangiosarcoma, Zymbal gland tumours, nephroblastoma, pulmonary and mammary gland tumours and forestomach papillomas. The minimum dose at which compound-related tumours were induced by inhalation (four hours per day, five days per week) was 10 ppm (26 mg/m^3) for 52 weeks for rats, 50 ppm for 30 weeks for mice and 500 ppm for 30 weeks for hamsters.[39] When vinyl chloride in PVC powder was administered orally to rats, the minimum effective dose of vinyl chloride (causing liver tumours) was 1.7 mg/kg bw per day.[40]

The most comprehensive carcinogenesis bioassays relevant to the assessment of risk associated with the ingestion of vinyl chloride are those of Maltoni *et al.*,[39] Feron *et al.*[41] and Til *et al.*[40,42] Groups of 40 male and 40 female (80/group) 13-week-old Sprague-Dawley rats received gastric intubations of 0, 3.33, 16.65 or 50 mg/kg bw per day of vinyl chloride dissolved in olive oil, four to five times per week for 52 weeks. At 136 weeks, 17 liver angiosarcomas (eight in males and nine in females) were found in the 50 mg/kg bw per day group; 10 liver angiosarcomas (four in males and six in females) occurred in rats administered the 16.65 mg/kg bw per day dose. No hepatic angiosarcomas were observed in low-dose and control rats. No dose–response relationship was observed in the induction of other tumours in these animals. Two nephroblastomas (one in each sex), one Zymbal gland tumour and one thymic and one intraabdominal angiosarcoma were observed in the highest dose group, and two Zymbal gland carcinomas (one in each sex) and three nephroblastomas (two in males and one in females) were observed in rats administered 16.65 mg/kg bw per day.[39] In a second experiment, vinyl chloride doses of 0.003, 0.3 or 1.0 mg/kg bw per day were administered to 10-week-old rats (75/sex/group) five days per week for 59 weeks, followed by an extended observation period. At 136 weeks, hepatic angiosarcomas were found in 1/74 males and 2/75 females administered 1.0 mg/kg bw per day and in 1/73 females administered 0.3 mg/kg bw per day. No exposure-related liver or kidney tumours were observed in low-dose or control animals.[39]

The carcinogenicity of vinyl chloride monomer administered by the oral route was investigated by incorporating vinyl chloride monomer in PVC powder and then mixing the PVC powder in the rat diet.[41] Groups of 60 to 80 Wistar rats of each sex were fed 0, 1.7, 5.0 or 14.1 mg/kg bw vinyl chloride in the diet four hours per day, seven days per week. As a positive control, vinyl chloride dissolved in soyabean oil (300 mg/kg bw) was also administered by gavage daily. The experiment was terminated when about 75% of the control rats were dead (135 weeks for males and 144 weeks for females). Hepatic angiosarcomas were observed in males (27/55, 27/59, 6/56) and females (2/59, 9/57, 29/54) in the three highest dose groups (5.0, 14.1, 300 mg/kg bw per day), respectively, but not in the low-dose group or controls. Males at the 5.0 and 14.1 mg/kg bw per day doses developed three times more angiosarcomas than females. Liver cell tumours and an increased incidence of foci of cellular alteration were observed at the lowest level (1.7 mg/kg bw per day). In a second study carried out at the same laboratory and using the same protocol,[40,42] oral vinyl chloride doses of 0.017, 0.17 and 1.7 mg/kg bw per day were administered. An increased incidence of liver nodules was the only neoplastic response in rats administered 0.17 mg/kg bw per day, but both hepatocellular carcinomas (3/sex) and hepatic angiosarcomas (1/49 males, 2/49 females) were observed at the highest dose (1.7 mg/kg bw per day), although in small numbers. No angiosarcomas of the liver were observed at the 1.7 mg/kg bw per day level in the original study.[41]

The only carcinogenic bioassay in which vinyl chloride has been administered in drinking water to rats is the unpublished work of Evans *et al.* (1978, cited in ref. 4). Groups of male and female (150/group) Wistar rats received vinyl chloride at concentrations of 0, 2.5, 25 or 250 ppm (equivalent to daily intakes of approximately 0, 0.12, 1.2 or 12 mg/kg bw per day for males and 0, 0.22, 2.2 or 22 mg/kg bw per day for females) for up to 152 weeks, except for males and females of the

highest dose group, which received the dose for 115 and 101 weeks, respectively. In rats receiving the highest dose, there was a significantly higher incidence of liver angiosarcomas (8/50 males, 8/49 females) and hepatomas (3/50 males, 3/49 females). Only one of 47 males developed hepatic angiosarcomas in the 25 ppm dose group. There was no dose–response relationship in the development of kidney and brain tumours in these animals.

Vinyl chloride is mutagenic in a wide range of test systems.[4,33,43] The mutagenicity of vinyl chloride is substantially increased in most systems by the addition of S-9 metabolic activating systems from rat, mouse and human liver. Pre-induction of the metabolic activating systems (e.g., with phenobarbital, 3-methylcholanthrene or Aroclor 1254) substantially increases the mutagenicity of vinyl chloride, indicating that metabolites are responsible for its mutagenic activity.[1,4] Studies in workers indicate an association between vinyl chloride exposure and the occurrence of chromosomal aberrations.[44] An increase in sister chromatid exchange and micronuclei in peripheral blood lymphocytes as well as inhibited cell kinetics were observed in 52 workers exposed to vinyl chloride in the plastic industry compared with a nonexposed group.[45]

No adverse reproductive effects were reported in workers exposed to vinyl chloride,[46] although an increase in total birth malformations in populations employed in the vinyl chloride industry has been suggested by a few investigators.[47,48] An association between parental occupational exposure to vinyl chloride and foetal loss has also been suggested,[47,49] but exposures were not measured. Theriault *et al.*[48] investigated the incidence of birth defects for infants born between 1966 and 1979 to residents of Shawinigan, a Canadian town where a vinyl chloride polymerization plant has been in operation since 1943. The incidence of birth defects (observed 159 vs. expected 107) was significantly greater in Shawinigan than in any or all of the matched control towns with no potential exposure to vinyl chloride. The incidence rate peaked in March and was lowest in September, which corresponded to variation in atmospheric levels of vinyl chloride at the time of the first three months of pregnancy (vinyl chloride monomer was not detected in air samples taken between December and February). No such variations were observed in the control communities. However, there was no excess of stillbirths in Shawinigan. As several other industries emitted pollutants into the atmosphere in Shawinigan, these observations remain inconclusive.

No significant embryotoxic, foetotoxic or teratogenic effects were observed in groups of pregnant CF-mice, Sprague-Dawley rats or New Zealand white rabbits exposed seven hours per day via inhalation to vinyl chloride at doses of 50 or 500 ppm on days 6 to 15 of gestation (mice) or doses of 500 or 2500 ppm on days 6 to 15 (rats) or days 6 to 18 (rabbits) of gestation.[50] Maternal toxicity, such as higher death rate, decreased food consumption and increased liver weight, was observed in mice and rats exposed to 500 ppm and 2500 ppm, respectively. Foetal effects consisted of delayed skeletal development in mice and an increase in the incidence of dilated ureter in rats following a maternally toxic exposure.[50]

Classification and Assessment

Vinyl chloride is a well-known human and animal carcinogen. It has, therefore, been classified in Group I (carcinogenic to humans). Epidemiological data are insufficient to serve as a basis for quantitative estimation of cancer risks associated with exposure to low levels of vinyl chloride; the relevant studies do not contain adequate information on degree of exposure. Cancer risks have, therefore, been estimated on the results of the most relevant studies in rats.[40–42] These results are supported by the studies of Maltoni *et al.*[39] in rats and by the only study (Evans *et al.*, unpublished, 1978, cited in ref. 4) in which administration was by the route of interest, i.e., drinking water. There was, however, insufficient information provided in a published account of this study to use in the assessment of risk.

Incorporating a surface area correction and using the model free extrapolation method, one can calculate that the unit lifetime cancer risk associated with the ingestion of 1 µg/L vinyl chloride in drinking water ranges from 5.6×10^{-6} to 5.8×10^{-7} (based on hepatocellular angiosarcomas in female rats). The estimated concentrations in drinking water corresponding to lifetime risks of 10^{-5}, 10^{-6} and 10^{-7} for these same tumour types based on the model described above are as follows*:

Lifetime risk	Concentrations in drinking water (µg/L)
10^{-5}	1.8 – 17
10^{-6}	0.18 – 1.7
10^{-7}	0.018 – 0.17

Rationale

Because vinyl chloride is classified in Group I (carcinogenic to humans), the 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.

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

A MAC of 0.002 mg/L (2 µg/L) was established, therefore, on the basis of the following considerations:

(1) The estimated unit lifetime cancer risks associated with the ingestion of 1 µg/L vinyl chloride in drinking water range from 5.6×10^{-6} to 5.8×10^{-7} (based on hepatocellular angiosarcomas in female rats). Therefore, the estimated lifetime cancer risk associated with the ingestion of drinking water containing 2 µg/L vinyl chloride (i.e., 1.12×10^{-5} to 1.16×10^{-6}) is within a range that is considered to be "essentially negligible."

(2) The PQL (based on the ability of laboratories to measure vinyl chloride within reasonable limits of precision and accuracy) is 2 µg/L.

(3) Existing product standards, which specify the quality of PVC water pipes to limit the amount of free vinyl chloride monomer present, prevent any excessive leaching of vinyl chloride from the pipes. Available data indicate that vinyl chloride concentrations in water are not reduced significantly during conventional drinking water treatment processes. However, concentrations of vinyl chloride below 2 µg/L can be achieved by packed tower aeration, considered to be the best available treatment technology.

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