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Monochlorobenzene

Guideline

The maximum acceptable concentration (MAC) for monochlorobenzene in drinking water is 0.08 mg/L (80 μg/L); the aesthetic objective (AO) is ≤0.03 mg/L (≤30 μg/L).

Identity, Use and Sources in the Environment

Monochlorobenzene (MCB), a chlorinated aromatic compound with a molecular weight of 112.6, exists as a colourless liquid at room temperature. It has a relatively high vapour pressure (1165 Pa at 25°C), is relatively insoluble in water (295 mg/L) and has an octanol–water partition coefficient of 955.[1]

Monochlorobenzene is not manufactured in Canada, but several tonnes are imported each year from the United States for use mainly as a solvent for adhesives. Because of its volatility, it is likely that most of the MCB emitted during production and use is released to the atmosphere.

Exposure

Only limited data are available on the concentrations of MCB in Canadian drinking water supplies. Monochlorobenzene was detected in 16 of 90 potable water samples taken at 30 treatment facilities across Canada. Mean concentrations were less than 1 μg/L, and the maximum value recorded was 5 μg/L.[2] Because of its volatility, there is also potential for exposure in the home to airborne MCB released from tap water.

There are no data available on the MCB content of food. In air, MCB was detected in 43 of 46 samples in Montreal and 83 of 100 samples in Toronto; mean concentrations were less than 0.4 $\mu g/m^3$, and the maximum value recorded was 2.2 $\mu g/m^3$.[3] Although the available data are sparse, it is likely that the intake of MCB from air is considerably greater than that from food or drinking water; for suckling infants, mothers' milk may also be an important source of exposure.

Analytical Methods and Treatment Technology

Monochlorobenzene is detected by a purge and trap gas chromatographic procedure.[4] The practical quantitation limit (based on the ability of laboratories to measure MCB within reasonable limits of precision and accuracy) is 5 μg/L.[4,5]

It is unlikely that MCB levels are reduced significantly during conventional drinking water treatment processes. There is, in fact, some evidence that chlorination produces chlorobenzenes by reaction of chlorine with organic material in the raw water supply; for example, Otson and co-workers observed that the frequency of detection of MCB at 30 Canadian water treatment facilities was less for raw water than for drinking water samples (3 and 16%, respectively).[2]

Removal of volatile organic compounds by packed tower aeration and granular activated carbon adsorption has been estimated to be 90 to 99% effective, and it is likely that MCB concentrations below 1 μg/L can be achieved in Canadian drinking water supplies using these methods.[4]

Health Effects

Monochlorobenzene is readily absorbed through the lungs and gastrointestinal tract. It is likely, given its lipophilic nature, that MCB is also absorbed through the skin; however, quantitative data on uptake are not available for any of these routes of exposure. Once absorbed, MCB is rapidly distributed to many tissues; concentrations are greatest in fatty tissue. Monochlorobenzene is primarily metabolized by oxidative reactions involving the mixed-function oxidase enzymes to ortho-, meta- or para-chlorophenols. The chlorophenols can conjugate with glutathione, glucuronic acid or sulphate and be excreted in the urine. Intermediates of the metabolism of MCB, possibly arene oxides and the chlorophenols, can bind to cellular proteins; binding of these metabolites appears to be correlated with necrotic pathological changes in the kidney and liver of rodents.[6]

There have been isolated reports in the literature of neurotoxicity in individuals exposed to high concentrations of MCB in air.[6] However, most of the information on the toxicity of this compound has been obtained by animal bioassays.

Acute exposure to MCB causes sensory irritation of the respiratory system, narcosis, central nervous system depression and respiratory paralysis; systemic effects of acute toxic doses include damage to the liver and kidney and effects on bile duct–pancreatic flow.[6,7] In 14-day repeated-dose gavage studies in F344/N rats (125 to 2000 mg/kg bw per day in corn oil) and B6C3F$_1$ mice (30 to 500 mg/kg bw per day in corn oil), prostration, reduced response to stimuli and death of all animals in the high-dose groups of rats (≥1000 mg/kg bw per day) were observed; however, there were no noteworthy histopathological effects at necropsy. In the mice, there were no clinical signs of toxicity, compound-related deaths or histopathological effects in any of the dose groups.[8,9]

Several subchronic toxicity studies of the effects of inhalation and ingestion of MCB have been conducted.[8,10–13] The most recent and well-documented of these studies have been those completed under the auspices of the National Toxicology Program (NTP), in which F344/N rats and B6C3F$_1$ mice (10 of each sex per group) were administered MCB at 0 to 750 mg/kg bw per day in corn oil by gavage, five days per week for 13 weeks. The no-observed-adverse-effect level (NOAEL) in both species was 125 mg/kg bw per day; the lowest-observed-adverse-effect level (LOAEL) was 250 mg/kg bw per day.[9] Effects at this dose included reduced survival in both sexes of mice and reduction of gain in body weight in male rats and mice. At higher doses (≥500 mg/kg bw per day), there was an increase in liver porphyrin and serum hepatic enzymes in female rats, porphyrinuria in both sexes of rats and female mice and lymphoid or myeloid depletion of the thymus, spleen or bone marrow in both species. In both rats and mice, there were also dose-related increases in histopathological lesions in the liver (hepatocellular degeneration and necrosis) and kidney (degeneration and focal necrosis of the proximal renal tubules).

The carcinogenicity of MCB has also been investigated in an NTP bioassay.[8] Doses of 0, 60 or 120 mg/kg bw were administered daily by gavage in corn oil, five days per week for 103 weeks, to groups of 50 male and 50 female F344/N rats and 50 female B6C3F$_1$ mice. Doses administered to male mice of the same strain on the same schedule were 0, 30 or 60 mg/kg bw. There was no convincing evidence in this study of compound-related toxicity in either rats or mice. Evidence for mild hepatocellular necrosis in rats was equivocal, and, although there was a significant decrease in the survival of male rats in the high-dose group (120 mg/kg bw per day), the absence of marked toxic lesions did not support a causal relationship with MCB administration.

There was, however, a significant increase in hepatic neoplastic nodules in the high-dose group of male rats (120 mg/kg bw per day). The increase was significant in comparison with both concurrent vehicle and pooled controls, and there was a marginally significant dose–response trend (2/50, 4/49 and 8/49 at 0, 60 and 120 mg/kg bw per day, respectively). However, there were no hepatocellular carcinomas in exposed male rats, and analysis of combined data on neoplastic nodules and hepatocellular carcinomas reduced the significance of the observed increase in tumour incidence. No other significant increases in tumour incidence were observed in either rats or mice. It was concluded that the NTP study provided *some* evidence of carcinogenicity in male F344/N rats, but *no* evidence of carcinogenicity in either female F344/N rats or B6C3F$_1$ mice of either sex.

Available data indicate that MCB has little mutagenic potential; it has, however, induced chromosomal aberrations in plants and bacteria. Clastogenic potential has not been observed in mammalian systems.[6,7] There was no evidence that MCB was teratogenic in rats or rabbits in the one relevant study conducted to date;[14] MCB did, however, induce slight delays in foetal skeletal development, but only at dose levels that were toxic to the mothers.

Classification and Assessment

Based on the increased incidence of hepatic neoplastic nodules in F344/N male rats observed in the NTP carcinogenesis bioassay,[9] MCB has been classified in Group IIIB — possibly carcinogenic to man (inadequate evidence in man, limited evidence in animals).

For compounds classified in Group IIIB, the maximum acceptable concentration (MAC) is derived on the basis of division of the NOAEL or LOAEL in an animal species by an uncertainty factor that takes into account the equivocal evidence of carcinogenicity. For MCB, the acceptable daily intake (ADI) is derived as follows:

$$\text{ADI} = \frac{125 \text{ mg/kg bw per day} \times 5}{10\,000 \times 7} \cong 0.0089 \text{ mg/kg bw per day}$$

where:

- 125 mg/kg bw per day is the NOAEL in two species (rats and mice) in the most recent and well-documented subchronic study[9]
- 5/7 is the conversion of five days per week of dosing to seven days per week
- 10 000 is the uncertainty factor (×10 for interspecies variation; ×10 for intraspecies variation; ×10 for less-than-chronic study; and ×10 for equivocal evidence of carcinogenicity).

Rationale

Because MCB is classified in Group IIIB, the MAC for MCB in drinking water is derived from the ADI as follows:

$$\text{MAC} = \frac{0.0089 \text{ mg/kg bw per day} \times 70 \text{ kg} \times 0.20}{1.5 \text{ L/d}} \cong 0.08 \text{ mg/L}$$

where:

- 0.0089 mg/kg bw per day is the ADI, as derived above
- 70 kg is the average body weight of an adult
- 0.20 is the proportion of total intake assumed to be ingested in drinking water (available data were inadequate for estimation of this value)
- 1.5 L/d is the average daily consumption of drinking water for an adult.

The aesthetic objective (AO) for MCB in water is ≤30 µg/L, based on the threshold odour value.[15]

References

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