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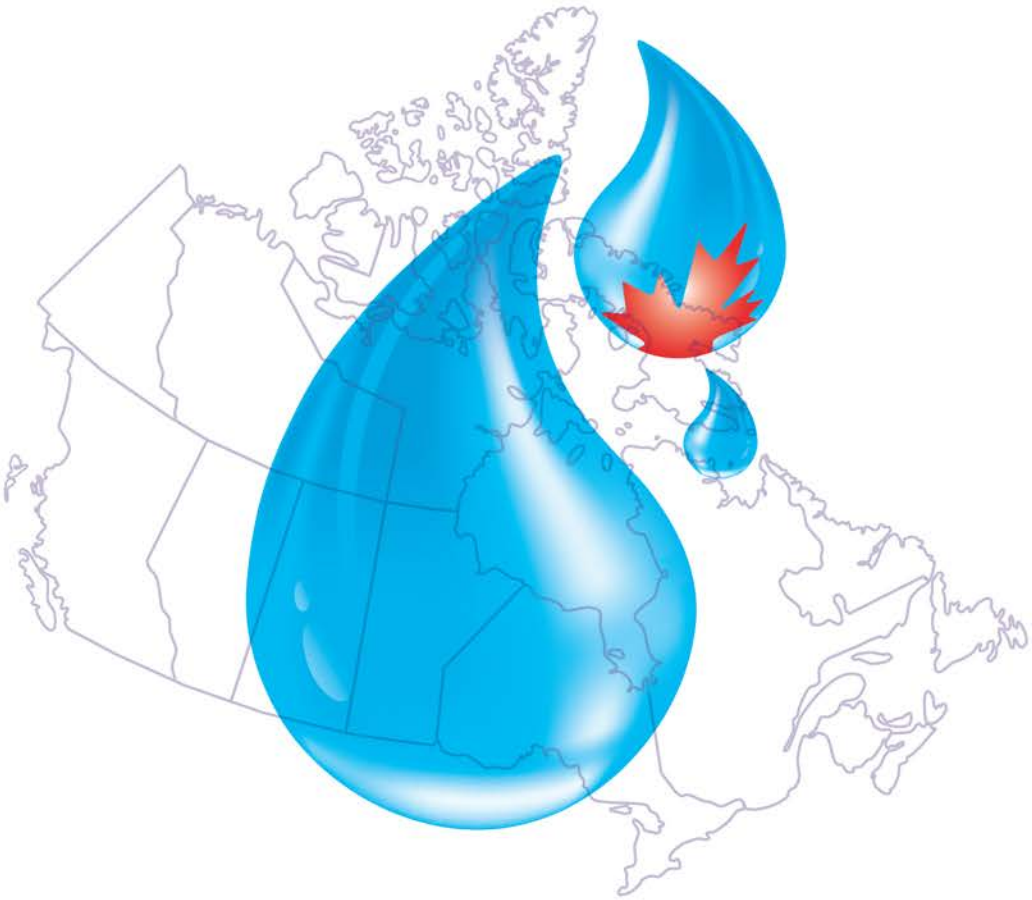
Guidelines for Canadian Drinking Water Quality

Guideline Technical Document

Metolachlor



Canada

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Metolachlor

Guideline

The maximum acceptable concentration (MAC) for metolachlor in drinking water is 0.05 mg/L (50 µg/L).

Identity, Use and Sources in the Environment

Metolachlor ($C_{15}H_{22}ClNO_2$) is a chloracetanilide herbicide used in Canada primarily for the control of grasses in corn, beans, soybeans and other crops, and it is often applied in combination with broadleaf herbicides. More than 1 000 000 kg are used annually in Canada.[1]

The solubility of metolachlor in water is 530 mg/L at 20°C; its vapour pressure at 20°C is 1.7×10^{-3} Pa.[2] Reported log octanol–water partition coefficients range from 3.04 to 4.72,[3] indicating that metolachlor has some potential for bioaccumulation.

Metolachlor is readily adsorbed onto organic matter in soil; little leaching occurs in soils with high organic content. Leaching is also inhibited by high clay content of the soil.[4] Biodegradation results in the oxidation of the acetyl group to form an oxalic acid derivative; the biodegradation half-life in soil is about six to 10 weeks.[3] Metolachlor will not accumulate in soil following repeated annual applications.[4]

Exposure

Metolachlor was detected (detection limit 0.02 mg/L) in 21 of 440 surface water samples in three Ontario river basins surveyed from 1981 to 1985, where annual use was greater than 300 000 kg, based on data from 1983 (detection limit 0.02 µg/L). Annual means of the detected concentrations in each area ranged from 0.7 to 4.1 µg/L.[5] During a survey in southern Ontario conducted in 1985, 15% of 351 private wells suspected of being contaminated with alachlor had detectable metolachlor concentrations (detection limit 0.1 µg/L).[6] Metolachlor was detected in 125 of 917 samples from municipal and private water supplies in the Atlantic region (1985 to 1986), Quebec (1984 to 1985), Ontario (1979 to 1986) and Alberta (1986) (detection limits ranged from 0.1 to 1.0 µg/L). The maximum concentration of metolachlor in a water supply was 1800 µg/L, obtained from a site in Ontario.[6]

The theoretical maximum daily intake of metolachlor in food is 0.026 mg, based on the residue tolerance limits established by the Food Directorate of the Department of National Health and Welfare.[7] No information on actual levels found in foods was identified. In residue trials (application rate unspecified), the mean concentration in a variety of consumer vegetables was 0.046 mg/kg; the maximum residue detected was 0.08 mg/kg in potatoes.[7]

Analytical Methods and Treatment Technology

Metolachlor in water can be determined by extraction with chloroform, separation by gas–liquid chromatography and measurement by electrolytic conductivity detector, nitrogen mode (detection limit 0.02 µg/L).[5] An alternative method involves extraction with dichloromethane, separation by gas chromatography and measurement by nitrogen–phosphorus detector (estimated detection limit 0.1 to 2.0 µg/L).[8]

Treatment with granular activated carbon is reported to be 99.5% effective in the removal of metolachlor from wastewater with an initial average concentration of 16.4 mg/L.[9]

Health Effects

Metolachlor is readily absorbed from the gastrointestinal tract. In rats, 70 to 90% of single oral doses of 28.6 or 52.4 mg/kg bw of ^{14}C-labelled metolachlor was found to be excreted as metabolites within 48 hours. Metolachlor is metabolized via *d*echlorination, O-methylation, N-dealkylation and side-chain oxidation. Urinary metabolites in the rat include 2-ethyl-6-methylhydroxyacetanilide (MET-002) and N-(2-ethyl-6-methylphenyl)-N-(hydroxyacetyl)-DL-alanine (MET-004); metabolites identified in the faeces are 2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-hydroxy-1-methylethyl) (MET-003) and MET-004.

No unchanged parent compound was isolated in the urine or faeces of rats administered oral doses of approximately 31 mg/kg bw.[10,11]

No information on the oral toxicity of metolachlor in humans was identified. Other than isolated reports of skin allergies, information on the toxicity of metolachlor in humans has not been identified.

Groups of 60 or 70 CD-Crl:CD(SD) BR rats were fed dietary concentrations of metolachlor of 0, 30, 300 or 3000 ppm (equivalent to doses of 0, 1.5, 15 or 150 mg/kg bw per day) for two years. Mean body weights of females in the highest dose group were depressed from two weeks after the beginning of treatment until cessation; this difference was significant for 26 of the 59 measurement intervals. Reduced food consumption was also noted in this group of rats. No significant differences in gross pathology, mortality, organ weights or relative organ weights among groups were reported. Males consuming diets containing 300 and 3000 ppm metolachlor had atrophied testes, along with degeneration of the tubular epithelium. An increased incidence of eosinophilic foci was observed in the livers in both sexes in the 3000 ppm group. No dose-related differences were noted in clinical pathology except for a decrease in glutamic–oxaloacetic transaminase activity in high dose males at 12 months. An increased incidence of proliferative hepatic lesions (combined neoplastic nodules/carcinomas) was reported in females consuming 3000 ppm metolachlor. Six of the 60 animals in this dose group had neoplastic nodules, and seven had unspecified liver tumours (incidence in controls not reported).[12] In later amendments to this report, an increase was reported in the incidence of nasal cavity tumours (two adenocarcinomas and one fibrosarcoma) in male rats in the 3000 ppm dose group (none reported in other groups).[7] The no-observed-adverse-effect level (NOAEL) in this study is considered to be 30 ppm, or 1.5 mg/kg bw per day.[8]

In a validated study conducted by Industrial Bio-Test Laboratories, albino Charles River rats (number per group and sex not specified) were fed metolachlor in the diet for two years at concentrations of 0, 30, 300, 1000 or 3000 ppm (equivalent to doses of 0, 1.5, 15, 50 or 150 mg/kg bw per day). Females in the high dose group had decreased body weight gain and increased relative kidney and thyroid weights. Spleen weight was decreased in males consuming 300 ppm and in both males and females consuming 1000 ppm. There was a dose-related increase in the incidence of hepatocellular hypertrophy in male rats. Two of the 60 females in the high dose group had hepatocellular carcinomas, compared with none in the other groups (the incidence of this lesion based on historical data is less than 1%). There was also an increase in the incidence of cystic cholangioma in the female rats consuming 3000 ppm metolachlor (10% vs. 3.3 to 3.7% in each of the other groups).[13] The NOAEL for non-neoplastic effects was considered by the consultation group of the World Health Organization to be 300 ppm, or 15 mg/kg bw per day.[7]

Metolachlor does not induce genetic mutations in bacterial and mammalian cells. It does not induce unscheduled DNA synthesis in rat hepatocyte and human fibroblast cultures or nuclear anomalies and dominant lethal mutations in mice.[7]

In a three-generation reproductive study conducted by Industrial Bio-Test Laboratories and reviewed by the World Health Organization,[7] no adverse effects were observed in albino rats fed dietary concentrations of 0, 30, 300 or 1000 ppm metolachlor (approximately equivalent to doses of 0, 1.8, 18 and 60 mg/kg bw per day, respectively) in terms of mortality, fertility indices, fecundity or parturition, number of live, dead or total pups, and pup survival or body weight. In a two-generation study in Charles River CD rats (15 males and 30 females per group), dietary doses of metolachlor of 0, 30, 300 or 3000 ppm were administered. Based on time-weighted-average analysis of the diet, the actual concentrations of metolachlor administered to the animals were 0, 32, 294 and 959 ppm, which were considered to be equivalent to doses of 0, 1.6, 14.7 and 48 mg/kg bw per day, respectively.[8] No effects were reported on mating, gestation, lactation and female and male fertility indices in either generation. Pup weights were significantly reduced in the F_{1a} and F_{2a} generations in the high dose group, and food consumption was significantly reduced in F_1 females at 30 ppm and above.[14]

No foetotoxic or developmental effects were observed in pregnant rats (25 per dose group) administered oral doses of metolachlor of 0, 60, 180 or 360 mg/kg bw per day during days 6 to 15 of gestation.[15] No foetotoxic or teratogenic effects were reported in New Zealand white rabbits administered doses of 0, 36, 120 or 360 mg/kg bw per day of metolachlor suspended in 0.75% hydroxymethyl-cellulose on days 6 to 18 of gestation, although signs of maternal toxicity were observed at dose levels of 120 mg/kg bw per day and greater.[16]

Rationale

The negligible daily intake (NDI) of metolachlor has been determined by the Food Directorate of the Department of National Health and Welfare as follows:

$$\text{NDI} = \frac{1.5 \text{ mg/kg bw per day}}{300} = 0.005 \text{ mg/kg bw per day}$$

where:

- 1.5 mg/kg bw per day is the NOAEL in the two- year study in rats[12]
- 300 is the uncertainty factor.

Based on the above NDI, the maximum acceptable concentration (MAC) for metolachlor in drinking water is derived as follows:

$$\text{MAC} = \frac{0.005 \text{ mg/kg bw per day} \times 70 \text{ kg bw} \times 0.20}{1.5 \text{ L/d}} \approx 0.05 \text{ mg/L}$$

where:

- 0.005 mg/kg bw per day is the NDI established by the Food Directorate
- 70 kg bw is the average body weight of an adult
- 0.20 is the proportion of daily intake of metolachlor attributed to drinking water
- 1.5 L/d is the average daily consumption of drinking water by an adult.

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