

Carbofuran

Guideline

The maximum acceptable concentration (MAC) for carbofuran in drinking water is 0.09 mg/L (90 µg/L).

Identity, Use and Sources in the Environment

Carbofuran (C₁₂H₁₅NO₃) is a carbamate insecticide and nematocide used for the control of a variety of soil-dwelling and foliar-feeding pests on many fruit and vegetable crops. Between 100 000 and 500 000 kg are used annually in Canada.¹ Carbofuran has a vapour pressure of 2.7×10^{-3} Pa at 33°C; its solubility in water is 700 mg/L at 25°C.² Its log octanol–water partition coefficient is reported to range from 1.60 to 2.32;³ therefore, carbofuran is not likely to bioaccumulate significantly.

Carbofuran is degraded in soil by hydrolysis, microbial action and, to a lesser extent, photo-decomposition. Its persistence is dependent upon pH, soil type, temperature, moisture content and the microbial population.⁴ Degradation products in soil include carbofuran phenol, 3-hydroxycarbofuran and 3-ketocarbofuran; field studies have indicated a half-life of 26 to 110 days in soil.⁵ Carbofuran may leach significantly, although leaching may not occur in highly organic soils.⁵

Carbofuran is degraded in water by hydrolysis, microbial decomposition and photolysis.⁴ Hydrolysis half-lives in water at 25°C of 690, 8.2 and 1.0 weeks have been reported for pH levels of 6.0, 7.0 and 8.0, respectively.⁵

Exposure

Carbofuran was detected only once (at 3.0 µg/L) in 678 samples from surveys of Canadian municipal and private water supplies conducted from 1971 to 1986 (detection limits ranged from 0.01 to 2.0 µg/L).⁶ It was not detected in 60 samples from 38 sites in the Prairies from 1974 to 1975 (detection limit 1.0 µg/L).⁶ It was also not found in 314 samples from three Ontario river

basins from 1981 to 1985 (detection limit 1.0 µg/L), even though annual use in these areas was in the range of 15 000 to 20 000 kg.⁷

The theoretical maximum daily intake of carbofuran from food is 0.16 mg/d, based on the residue tolerance limits set by the Food Directorate of the Department of National Health and Welfare.⁸ Actual intake is probably much lower; the average daily intake for a 70-kg adult from food is estimated to be 0.14 µg/d, based on a U.S. market basket survey.⁹

Analytical Methods and Treatment Technology

The concentration of carbofuran in water may be determined by separation by high-performance liquid chromatography, hydrolysis with sodium hydroxide, reaction of the resulting methylamine with o-phthalaldehyde and fluorescence detection of the derivative (detection limit 0.9 µg/L).² The concentration of carbofuran may also be quantified by acidification of the sample, extraction with dichloromethane and separation by gas chromatography with a nitrogen–phosphorus detector (detection limit 0.1 µg/L).¹⁰

Carbofuran may be effectively removed from drinking water by activated carbon adsorption; removal of 99.9% of an initial concentration of 2250 mg/L has been reported for a full-scale treatment plant. Based on data on the removal of other pesticides, reverse osmosis is expected to be effective in removing carbofuran. Oxidation by ozone and ozone/ultraviolet removes 99.9% of 49 mg/L of another carbamate pesticide; similar results are expected for carbofuran.²

Health Effects

Carbofuran is rapidly and completely absorbed by the gastrointestinal tract. It is quickly metabolized by hydrolysis, oxidation and conjugation; the major metabolites include 3-hydroxycarbofuran, 3-ketocarbofuran, carbofuran phenol, 3-hydroxycarbofuran phenol and 3-ketocarbofuran phenol. The main route of excretion is in the urine as conjugates of glutathione.¹¹

Half-lives for elimination of carbofuran and 3-hydroxycarbofuran in the rat of 29 and 64 minutes have been reported.¹²

Carbofuran is an acetylcholinesterase inhibitor. In a human volunteer study, groups of two subjects ingested single doses of 0.05, 0.10 or 0.25 mg/kg bw. There were no effects at the lowest dose, whereas subjects ingesting 0.10 mg/kg bw experienced headaches and lightheadedness. At the highest dose level, symptoms of acetylcholinesterase depression were reported, including salivation, diaphoresis, abdominal pain, drowsiness, dizziness, anxiety and vomiting. The no-observed-adverse-effect level (NOAEL) was considered to be 0.05 mg/kg bw.¹³

Groups of 180 rats (90 male and 90 female per group) were fed carbofuran at concentrations of 0, 10, 20 or 100 mg/kg diet for two years. No differences were reported in clinical chemistry, haematology, urinalysis or ophthalmological examinations, except for a significant depression in plasma, red blood cell and brain cholinesterase in rats of both sexes exposed to the highest dose level. Growth was significantly depressed in rats fed carbofuran at 100 mg/kg diet. No significant change in cholinesterase activity was observed in rats consuming food containing 20 mg/kg carbofuran. The NOAEL was considered to be 20 mg/kg diet, equivalent to 1.0 mg/kg bw per day.¹⁴

In a similar study, Charles River CD-1 mice (100 male and 100 females per group) were fed diets containing 0, 20, 125 or 500 mg/kg carbofuran for two years. Examinations at six-month intervals revealed a slight decrease in growth and food consumption in the highest dose group during the first year. There was a higher incidence of localized hair loss and reddening of the ears, often followed by scabbing or sloughing of portions of the ear, in treated mice. Brain cholinesterase activity was significantly depressed in both the 125 and 500 mg/kg diet groups. No other differences were observed in terms of haematological, clinical chemistry or urinalysis parameters. The NOAEL for cholinesterase depression in mice was reported to be 20 mg/kg diet, or 2.5 mg/kg bw per day.¹⁴

Beagle dogs were administered carbofuran doses of 0.25, 0.50 or 12.5 mg/kg bw per day in the diet for one year. At 12.5 mg/kg bw per day, there was a marked depression of plasma and erythrocyte cholinesterase levels in both males and females; testicular degeneration and some aspermia in males and uterine hyperplasia and hydrometria in females were also observed. No significant adverse effects were observed at the two lowest dose levels. The NOAEL in dogs was considered to be 0.50 mg/kg bw per day.¹⁵

Carbofuran was not carcinogenic or tumorigenic in the two-year studies in rats and mice, based on both gross and microscopic examinations.¹⁴ Several negative

results and one positive result for mutagenicity have been obtained from Ames bacterial tests. Carbofuran was not mutagenic in several other organisms in *in vitro* tests, although positive results were reported in Chinese hamster ovary cells (CHO V79) without metabolic activation.²

In a three-generation study in rats consuming diets containing carbofuran at concentrations of 20 or 100 mg/kg, no effects on fertility, gestation, lactation or viability were reported. However, there was a significant reduction of growth—as evidenced by differences in food consumption and body weight—through the three generations at the 100 mg/kg level but not at the 20 mg/kg level.¹⁴ Carbofuran was not teratogenic in rats administered daily doses of 0, 0.1, 0.3 or 1.0 mg/kg bw per day, although signs of maternal toxicity were noted in the two highest dose groups.¹⁶ No teratogenic effects were noted in rabbits administered 0.2, 0.6 or 2.0 mg/kg bw per day of carbofuran, although dams in the two highest dose groups had symptoms of cholinesterase depression.¹⁷

Rationale

The acceptable daily intake (ADI) of carbofuran has been derived by the Food and Agriculture Organization (FAO) and the World Health Organization (WHO)¹⁴ as follows:

$$\text{ADI} = \frac{1.0 \text{ mg/kg bw per day}}{100} = 0.01 \text{ mg/kg bw per day}$$

where:

- 1.0 mg/kg bw per day is considered to be the NOAEL for cholinesterase inhibition and growth suppression in a two-year study in rats¹⁴
- 100 is the uncertainty factor.

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

$$\text{MAC} = \frac{0.01 \text{ mg/kg bw per day} \times 70 \text{ kg bw} \times 0.20}{1.5 \text{ L/d}} \approx 0.09 \text{ mg/L}$$

where:

- 0.01 mg/kg bw per day is the ADI established by the FAO/WHO
- 70 kg bw is the average body weight of an adult
- 0.20 is the proportion of daily intake of carbofuran allocated to drinking water
- 1.5 L/d is the average daily consumption of drinking water by an adult.

References

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