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Boron

Guideline

The interim maximum acceptable concentration (IMAC) for boron in drinking water is 5 mg/L (5000 µg/L).

Identity, Use and Sources in the Environment

Boron is ubiquitous in the environment, occurring naturally in over 80 minerals and constituting 0.001% of the Earth's crust.[1] Although sedimentary rocks contain more boron than igneous rocks, the element is most commonly found in granitic rocks and pegmatites. Volcanic emissions release boric acid (orthoboric acid, $B(OH)_3$) and boron trifluoride (BF_3). Consequently, concentrations of boron in water in volcanic regions are high. Ocean water also contains boric acid; evaporation of seawater from closed basins is a commercial source of boron.[2]

Boron compounds, most notably boric acid and sodium borate (borax, $Na_2B_4O_7.10H_2O$), are used in the preparation of disinfectants and drugs, in the manufacture of borosilicate glass, as components of enamels, as antioxidants for soldering, and in the cosmetics, leather, textile, paint and wood-processing industries. Borax and boric acid are used in Canada as insecticides; borax is also used as an antimicrobial agent. Borax is used extensively as a cleaning compound.

Boron is an essential element for plant growth and is applied directly to the soil as a plant fertilizer. Sodium borate and boric acid are used as fungistatic agents on vegetables, fruits and trees.[3]

The boron content of soils ranges from 0.002 to 0.1 mg/g dry weight;[4] it is highly mobile in this medium and is easily leached. Factors influencing boron adsorption to soil include soil pH, texture, organic matter, cation exchange capacity, moisture and temperature.[5]

Exposure

The predominant form of boron in water is boric acid.[6] The concentration of boron in seawater ranges from 4 to 5 mg/L.[7,8] Boron levels in Canadian coastal waters are reported to range between 3.7 and 4.3 mg/L,[9] and estuarine waters are generally rich in boron.[10] Levels in well water have been reported to be more variable and often higher than those in surface waters,[11] most likely owing to erosion from natural sources.[12]

Median concentrations of boron in surface water determined by colorimetric analyses were well below 0.5 mg/L (overall mean 0.16 mg/L) at over 90% of locations in the National Water Quality Data Bank; concentrations at a few stations exceeded 2.0 mg/L. Single values ranged from not detectable (detection limit 0.02 mg/L) to 2.9 mg/L, with provincial median values ranging from 0.01 mg/L for British Columbia to 0.15 mg/L for Manitoba and Saskatchewan.[13]

Average boron concentrations in 3842 samples of treated and distributed water in 51 Ontario communities surveyed from 1987 to early 1989 ranged from 0.042 to 235 µg/L. The maximum boron concentration in a water sample was 570 µg/L. Boron concentrations were less than or equal to 100 µg/L in more than 97% of the total water samples analysed in 36 of the 51 communities.[14] In approximately 83% of the 803 municipal systems surveyed in Quebec in 1988, boron concentrations were less than 0.5 mg/L; at one site, however, the concentration was ">3 mg/L."[15] Boron concentrations were less than 0.02 mg/L in 84% of 38 municipal supplies surveyed (one sample was analysed from each site) in Newfoundland and Labrador in 1989.[16]

The presence of boron in the atmosphere has been attributed to sea spray (sea salt aerosol degassing), volcanic activity, accumulation in dust and industrial emission of boron oxide, boric acid and sodium or other metal borates in the form of particulate matter or aerosol.[1] Fly ash from coal combustion also contributes to the boron content of air.[17] Boron concentrations of 1.7×10^{-4} mg/m^3 have been reported in the air over the oceans.[18] No data on boron concentrations in air in Canada were found.

Few data are available on the boron content of food. Boron accumulates in plants,[19] with concentrations in legumes being highest (0.025 to 0.05 mg/g dry weight), followed by those in fruits and vegetables (0.005 to 0.02 mg/g) and cereals and grains (0.001 to 0.005 mg/g). Concentrations in the fresh edible portion of berries and citrus fruits ranged from 0.0003 to 0.0024 mg/g.[20]

Animal tissues and organs contain between 0.05 and 0.6 μg/g fresh weight; levels in bone tend to be much higher.[21] Cow's milk normally contains 0.5 to 1.0 mg/L, but levels vary depending upon the boron intake of the cow.[20] Limited available data indicate that the boron content of beverages varies considerably;[22] wines may contain up to 8.5 μg/g.[21]

Owing to the lack of available data on boron levels in Canadian foodstuffs, it is difficult to estimate daily intake in the diet. Using the Canadian Food Consumption Patterns Report[23] and limited data on boron content of common foods as determined in a survey of hospital diets,[24] dietary intake of a Canadian adult between 20 and 40 years of age is estimated to range from 1 to 3 mg of boron. The higher value would result from intake of a diet rich in boron-containing vegetables. This estimate for Canadians compares reasonably well with that estimated for the U.S. population,[25] based on analysis of a 4200-calorie diet consumed by adolescent boys, which included water used for cooking and drinking (2.1 to 4.3 mg/d). These figures are also similar to the mean boron intake of 2.819 ± 1.554 mg/d estimated on the basis of an English total diet study.[26]

Based on a daily water consumption of 1.5 L and the maximum boron content of 0.57 mg/L measured in drinking water in the Ontario survey,[14] the maximum daily intake of boron in Canadian drinking water is estimated to be 0.86 mg. Because average drinking water concentrations at most sites in the survey were much lower than 0.57 mg/L, daily consumption of boron in drinking water is likely to be less than 0.86 mg.

Even at the maximum levels measured in marine air, intake of boron through inhalation is likely to be negligible compared with that ingested in food and water.

The mean total daily boron intake of Canadians is therefore estimated to range from 1 to 4 mg, with food being the principal source.

Analytical Methods and Treatment Technology

Boron in water can be determined by several methods, including the curcumin method, consisting of acidification and evaporation in the presence of curcumin to produce rosocyanine, which is taken up with ethanol and compared photometrically with standards, and the carmine method, which involves combination with carmine or carminic acid in sulphuric acid followed by photometric measurement. The curcumin method is recommended for water with boron concentrations between 0.1 and 1.0 mg/L, whereas the carmine method is optimum for determination of boron levels in the range of 1 to 10 mg/L.[27] Other analytical methods include spectrophotometric determination with 1,1′-dianthrimide (for boron levels in the 0.01 to 0.2 mg/L range) or azomethine-H, or by volumetric determination following distillation (optimum for waters that contain more than 0.2 mg/L boron and that are coloured or contain non-filterable turbidity).[28]

Little boron is removed from water by conventional treatment technologies.[29] Adsorption methods using both magnesium oxide and ion exchange processes have been reported to be 85 to 90% effective in removing boron from drinking water supplies (initial concentrations 4 to 7 mg/L).[30]

Health Effects

In the past, boron has been considered to be non-essential for animals. However, a recent study that indicated a narrow range of levels in human blood[31] and deprivation studies in rats[32,33] suggest that boron might indeed be an essential element. Boron meets some of the criteria for essentiality, but it has not been possible to establish that its deficiency reproducibly impairs a biological function from optimal to suboptimal.[34] Experiments in animals indicate that boron may indirectly influence calcium, phosphorus, magnesium and cholecalciferol metabolism.[32]

The effect of boron on major mineral metabolism and its potential role as an inhibitor of osteoporosis in humans have been investigated. Boron reduced urinary excretion of calcium and magnesium in 12 post-menopausal women consuming a diet low in boron (0.25 mg/d) for 119 days, followed by a diet supplemented by 3.0 mg/d for 48 days; this reduction was more marked when dietary magnesium was low. Boron supplementation also increased serum-β-oestradiol and testosterone levels.[35]

Boron compounds are rapidly and completely absorbed from the gastrointestinal tract,[36] through mucous membranes and through damaged or abraded skin. Boron concentrations in the liver, kidney, brain and blood of rats increased steadily during the first nine days of exposure to drinking water containing 100 ppm sodium borate, with peak concentrations occurring in the kidney. Levels in the kidney, liver and brain gradually returned to normal by the end of the 21-day exposure period, whereas concentrations in blood continued to rise up to day 21.[37] Boron does not accumulate in normal tissues but may concentrate in malignant brain tumours.[38] In human tissues, the

following mean boron concentrations have been reported (μg/g wet weight): kidney, 0.6; lung, 0.6; lymph nodes, 0.6; blood, 0.4; liver, 0.2; muscle, 0.1; testes, 0.09; and brain, 0.06.[39]

Boron is eliminated from the body mainly by the kidney, with minor amounts being excreted in faeces, sweat and saliva;[40] it is also excreted in cow's milk.[41] About half of the boron absorbed by man is excreted during the first 24 hours after intravenous administration of 562 to 611 mg of boric acid;[40] more than 92% elimination has been reported to occur within 96 hours of ingestion of 750 mg of boric acid in water or up to 50 mg in a water-emulsifying ointment by human volunteers.[42]

A number of acute poisonings in man from boric acid or borax have been reported following ingestion, parenteral injection, lavage of serous cavities, enemas and application of dressings, powders or ointments to large areas of burned or abraded skin.[20] Symptoms of acute boron poisoning include nausea, vomiting, diarrhoea, headache, skin rashes, desquamation and evidence of central nervous system stimulation followed by depression.[3] In severe cases, death usually results in five days as a result of circulatory collapse and shock.[43] The acute lethal dose of boric acid has been estimated to be 15 to 20 g for adults, 5 to 6 g for infants and 1 to 3 g for newborns.[36,44] Children, the elderly and individuals with kidney problems are most susceptible to the acute toxic effects of boron.

Krasovskii *et al*.[45] examined the sexual function of men (determined by questionnaire) living in areas with varying concentrations of boron in water supplies ("0.015, 0.05 or 0.3 mg/kg"). It was reported that there was a tendency towards a reduction of function in men consuming water with a boron content of "0.3 mg/kg." However, the validity of the results could not be assessed owing to the lack of information included in the published account of the study.

In studies conducted by Weir and Fisher,[46] groups of five young male and five female beagle dogs were fed diets containing borax or boric acid at concentrations of 17.5, 175 or 1750 ppm as boron equivalent for 90 days. Appearance, behaviour, elimination, body weights and food consumption were normal in animals in all dose groups; there was, however, one death in the highest dose group. There were no adverse effects at 175 ppm boron (as borax or boric acid), whereas both borax and boric acid at levels of 1750 ppm boron caused severe testicular atrophy in males.

In a separate study, four male and four female beagle dogs were exposed to concentrations of boron, as borax or boric acid, of 0, 58, 117 and 350 ppm for two years, or 1170 ppm for 38 weeks. No differences in appearance, behaviour, appetite, elimination, body weight, food consumption, organ weights or haematological and biochemical parameters between the control animals and dogs exposed to either borax or boric acid at 350 ppm boron or less were observed. The only adverse effects noted were testicular changes (spermatogenic arrest and atrophy of the seminiferous epithelium of the tubules) in males exposed to the highest dose of either compound (1170 ppm). The no-observed-adverse-effect level (NOAEL) was considered to be 350 ppm boron,[46] equivalent to a boron concentration of 8.75 mg/kg bw per day.[1]

The same researchers[46] conducted a study in which 10 male and 10 female albino Sprague-Dawley rats ingested borax or boric acid in the diet at levels of 52.5, 175, 525, 1750 or 5250 ppm as boron equivalent for 90 days. There were no obvious adverse effects in rats consuming 525 ppm or less, whereas growth and "food utilization efficiency" were significantly reduced at the two highest dose levels. However, partial atrophy of the testes was reported in four males consuming 525 ppm boron as borax and in one rat ingesting 525 ppm as boric acid. Complete atrophy of the testes was observed in all males exposed to 1750 ppm boron as either borax or boric acid. In an additional study, 35 male and 35 female weanling Sprague-Dawley rats received dietary doses of 117, 350 or 1170 ppm boron equivalent as borax or boric acid for two years. Animals in the two lowest dose groups appeared normal in appearance and behaviour; no histological alterations were observed. Rats ingesting 1170 ppm had coarse hair coats, scaly tails, hunched position, swelling and desquamation of the pads of the paws, abnormally long toenails, shrunken scrotum in males, inflamed eyelids and a bloody discharge of the eyes. Atrophy of the testes and seminiferous epithelium was observed in all males receiving 1170 ppm at 6, 12 and 24 months; decreased tubular size in the testes was also noted. The NOAEL was considered to be 350 ppm boron[46] (equivalent to 17.5 mg/kg bw per day).[1]

In another more limited study,[47] weanling male Long-Evans rats (15 per dose group) were exposed to drinking water containing 0, 150 or 300 mg/L boron as borax and a basal diet containing 54 μg/g boron for 70 days. Total daily intake of boron in this study has been calculated to be 23.7 and 47.4 mg/kg bw per day for the 150 and 300 mg/L dose groups, respectively.[1] Growth was suppressed by 7.8 and 19.8% in the 150 and 300 mg/L groups, respectively. Rats consuming water containing 300 mg/L boron had long toenails, atrophic scrotal sacs and coarse pelages. A significant decrease was reported in the weights of testes, seminal vesicles, spleen and right femur in both the 150 and 300 mg/L dose groups. The number of rats with spermatozoa present in the 300 mg/L dose group (3 out of 15) was significantly lower than that in the low dose or control groups (actual numbers were not specified). Plasma

triglyceride, plasma protein, haematocrit and percent fat in bone were all lower in the high dose group than in the controls. The lowest-observed-adverse-effect level (LOAEL) in this study is considered to be 150 mg/L (23.7 mg/kg bw per day); however, it is not possible to determine from the published account of the study whether the tissues were examined histologically.

In a study by Lee *et al*., groups of 18 male Sprague-Dawley rats were administered 500, 1000 or 2000 ppm boron as borax in the diet for 30 and 60 days; estimated intakes for the three dose groups were 12.5, 25 and 50 mg/kg bw per day.[48] By 30 days, there was a reduction of spermatocytes, spermatids and mature spermatozoa in the two highest dose groups. At 60 days, near or complete germinal aplasia was observed in these two dose groups, and testicular and epididymal weights were significantly decreased. Boron accumulation in testes appeared to increase with both dose and duration of exposure.

In a limited study in which 54 Swiss mice of the Charles River CD strain were exposed for life to drinking water containing 5 ppm boron as sodium metaborate, there were no effects on body weight gain, incidence of tumours (based upon gross examination of tumours at death) or longevity.[49]

In a carcinogenesis bioassay conducted under the auspices of the National Toxicology Program (NTP),[50] groups of 50 male and 50 female $B6C3F_1$ mice were fed diets containing 2500 or 5000 ppm boric acid for two years. Survival was reduced in both groups of treated males; it should be noted, however, that five males in the high dose group accidentally drowned. A dose- related decrease in body weight gain was observed in both male and female mice, and the incidence of testicular atrophy and interstitial cell hyperplasia was increased in males in the high dose group. No compound-related increase in the incidence of tumours was reported. It was concluded that, under the conditions of this study, boric acid was not carcinogenic in mice. The sensitivity of this study may have been reduced, however, by the decreased survival of treated males.

The NTP[50] also evaluated the chronic feeding study in Sprague-Dawley rats conducted by Weir and Fisher[46] and concluded that this study provided adequate data for a lack of carcinogenic effect of boric acid in rats. In a limited bioassay in which 2% boric acid suspended in the gum tragacanth was administered intravaginally twice weekly for 50 weeks, there was no definite evidence of carcinogenicity in the genital tract of female mice.[51]

In a series of genotoxicity tests conducted by the NTP,[50] boric acid was not mutagenic in prokaryotic and eukaryotic cells. It did not induce sister chromatid exchange or chromosomal aberrations in Chinese hamster ovary cells. No evidence of mutagenic activity of borax or boric acid was found in *Salmonella typhimurium* preincubation tests.[38]

In serial mating studies involving five rats from each dosage group in the experiment by Lee *et al*.,[48] pregnancy rate, litter size and appearance were normal for unexposed virgin females mated with male rats exposed to 500 ppm boron. Pregnancy rates were reduced for females mated with male rats exposed to 1000 or 2000 ppm boron for either 30 or 60 days. Males administered 1000 and 2000 ppm were infertile; fertility in the 1000 ppm dose group returned to normal four weeks after cessation of exposure, whereas males in the 2000 ppm dose group remained infertile 32 weeks after treatment was discontinued. Infertility was apparently due to germ cell depletion.

Weir and Fisher[46] conducted a three-generation reproductive study on Sprague-Dawley rats fed diets with borax or boric acid at levels of 117, 350 or 1170 ppm boron. No adverse effects on reproduction were observed at the 117 or 350 ppm levels, whereas all rats fed diets of 1170 ppm boron were sterile.

Classification and Assessment

As there was no evidence of carcinogenicity in adequate bioassays in two species (rats and mice),[46,50] boron has been classified in Group IVC—probably not carcinogenic to man. The recommended value, based solely on health considerations, therefore is derived on the basis of division of NOAELs or LOAELs by an uncertainty factor.

Available data from several studies in mice, dogs and two strains of rats [46–48,50] indicate that exposure to boron causes testicular atrophy and spermatogenic arrest in males, resulting in infertility. The lowest reported NOAEL was that observed in dogs in the study by Weir and Fisher,[46] in which ingestion of 1170 ppm boron in the diet for 38 weeks resulted in testicular degeneration (NOAEL in animals exposed for two years was 8.75 mg/kg bw per day). Total daily intake may have been higher, however, as the boron content of the basal diet was not specified. The NOAELs in one chronic,[46] two subchronic[46,48] and two reproductive studies[46,48] in Sprague-Dawley rats were similar.

In the study in which boron was administered for the greatest proportion of the life span of the test animal (i.e., two years in rats), the NOAEL for adverse testicular effects was 350 ppm (considered to be equivalent to 17.5 mg/kg bw per day) following administration of borax and boric acid in the diet.[46] Although there was one study in which boron was administered to Long-Evans rats in a more appropriate vehicle (i.e., drinking water),[47] the period of exposure was short (70 days), and no NOAEL was determined. It should be noted, however, that the LOAEL in this

study[47] was only slightly greater than the NOAEL in the two-year study in rats, indicating that the dose–response curve may be steep in this dose range. Thus, the acceptable daily intake (ADI) is derived as follows:

$$\text{ADI} = \frac{17.5 \text{ mg/kg bw per day}}{500} = 0.035 \text{ mg/kg bw per day}$$

where:
- 17.5 mg/kg bw per day is the NOAEL for testicular atrophy and spermatogenic arrest obtained in a two-year study in rats[46]
- 500 is the uncertainty factor (10 for intraspecies variation; 10 for interspecies variation; and 5 for the steepness of the dose–response curve).

Based on the above ADI, the recommended value, based solely on health considerations, of boron in drinking water is derived as follows:

$$\frac{0.035 \text{ mg/kg bw per day} \quad 70 \text{ kg bw} \quad 0.20}{1.5 \text{ L/d}} \approx 0.3 \text{ mg/L}$$

where:
- 0.035 mg/kg bw per day is the ADI, as derived above
- 70 kg bw is the average body weight of an adult
- 0.20 is the proportion of total daily intake of boron allocated to drinking water (available data are insufficient to estimate this proportion)
- 1.5 L/d is the average daily consumption of drinking water for an adult.

However, an ADI based on the lowest reported NOAEL for adverse testicular effects of 8.75 mg/kg bw per day, which was obtained in the study in dogs by Weir and Fisher[46] (actual intake may have been higher, as the boron content of the basal diet was not specified), is considered to be more appropriate. This NOAEL is approximately twofold more than the NOAEL reported in a 90-day study in dogs conducted by the same investigators; however, this may be attributed principally to the rather large (e.g., 10-fold) variation between doses in the shorter-term study. Thus, the ADI is derived as follows:

$$\text{ADI} = \frac{8.75 \text{ mg/kg bw per day}}{500} = 0.0175 \text{ mg/kg bw per day}$$

where:
- 8.75 mg/kg bw per day is the NOAEL for testicular atrophy and spermatogenesis obtained in a two-year study in dogs[46]
- 500 is the uncertainty factor (10 for interspecies variation; 10 for intraspecies variation; and 5 for limitations of the critical study [i.e., small number of experimental animals exposed for a small proportion of their life span]).

Based on the above ADI, the recommended value, based solely on health considerations, of boron in drinking water is calculated as follows:

$$\frac{0.0175 \text{ mg/kg bw per day} \quad 70 \text{ kg bw} \quad 0.20}{1.5 \text{ L/d}} \approx 0.2 \text{ mg/L}$$

where:
- 0.0175 mg/kg bw per day is the ADI, as determined above
- 70 kg bw is the average body weight of an adult
- 0.20 is the proportion of total daily intake of boron allocated to drinking water (insufficient data are available to estimate this proportion)
- 1.5 L/d is the average daily consumption of drinking water for an adult.

Thus, the values derived on the basis of the two-year studies in rats and dogs are similar. However, in the establishment of a maximum acceptable concentration (MAC), available practicable treatment technology and analytical methods are also taken into consideration. Available practicable treatment technology is inadequate to reduce boron concentrations in Canadian drinking water supplies to less than 5 mg/L; on this basis, an interim maximum acceptable concentration (IMAC) of 5 mg/L has been established. This IMAC will be reviewed periodically in light of new data.

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