Ozone disinfection of drinking water – why the current limit for bromate is safe

MSc. Inês Simões, MSc. Roman Gyssels and Dr. Jaak Ryckeboer (EurO$_3$zon[1]ivzw); Dr. Jörg Mielcke (Xylem Services GmbH, WEDECO); Dr. Matthias Rothe (ProMinent GmbH); Dr. Matthias Hoffmann (BWT Wassertechnik GmbH); Mr. Bernhard Paolini (SUEZ Ozonia), Chairman of EurO3zon ivzw.

Abstract

Ozone is a highly effective oxidant and has a strong ability to inactivate a wide range of pathogens, including viruses. The treatment, incl. disinfection, of drinking water and wastewater with ozone is associated with the formation of disinfection by-products (DBP). Among the possible DBPs, bromate (BrO_3^-) is of increased concern because it is considered a potential carcinogenic to humans. The limit concentration established assumes, with the present risk calculations, that there might be some risk for human health. However, it is approved to consider technical and analytical feasibilities when implementing new limit concentrations. A lower limit concentration may have some impact on the use of ozone in disinfection or oxidation processes, which would trigger further sincere and undesirable consequences.

In this paper, EurO$_3$zon ivzw addresses recent proposals to alter the bromate limit concentration in drinking water.

Keywords: Ozone; Disinfection by-products; Bromate; Drinking water; Human health; Risk assessment

Bromate toxicity assessment

The classification of bromate in category 1B for carcinogenicity, meaning that it is *"presumed to have carcinogenic potential for humans"*, is largely based on animal evidence [1]. In fact, there is a lack of epidemiological studies on noncarcinogenic or carcinogenic effects of bromate exposure in humans. The available scientific literature shows that species differ substantially in their sensitivity to bromate, and the target tissues also depend on the animal species and the results of various toxicology tests are inconsistent.

Humans can be exposed to bromate via drinking water, because it may be formed if water treated with ozone contains bromide (Br-). The current bromate limit concentration in drinking water is 10 µg/L [2]. The limited knowledge on the effect of small concentrations of bromate in human health may concern health authorities.

Risk estimation based on toxicity studies in mammals

Several authors have studied the effects of oral exposure to bromate via drinking water on rats, mice, and hamsters. Carcinogenic effects were mainly observed in kidneys, testes and thyroid gland. Typically, bromate concentrations used in the studies ranged between 5 and 800 mg/L (in drinking water).

In 2005, the World Health Organization (WHO) has estimated cancer risks based on low-dose linear extrapolation, starting from the results of one study from 1998 [3,4]. The upper-bound estimate of the cancer potency for bromate is 0.19 mg/kg of body weight per day and the concentrations in drinking water associated with upper-bound excess lifetime cancer risks of 10^{-4}, 10^{-5} and 10^{-6} are 20, 2 and 0.2 µg/L, respectively.

Because of lacking information on the mode of carcinogenic action of bromate, a Tolerable Daily Intake (TDI) was also calculated based on a No Observable Effect Level (NOEL) for the formation of renal cell tumors in rats at 1.3 mg/kg of body weight per day. The calculation of a TDI for humans is based on a non-linear approach, and the obtained value is 1 µg/kg of body weight. This derivation considers an uncertainty factor of 1000, that comprises two 10-fold factors for each intra- and interspecies variation and 10 for possible carcinogenicity [5]. Using this value, and assuming a 60-kg person, drinking 2 litres of water per day and an allocation factor of 20% of the TDI to drinking water, a value of 6 µg/L is obtained for bromate concentration in drinking water.

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The WHO considered that, due to analytical and technological limitations, the health-based value of 2 µg/L (related to the upper-bound excess lifetime cancer risk of 10^{-5}) should be raised to 10 µg/L. This provisional value is deemed to be associated with an upper-bound excess lifetime cancer risk of 5×10^{-5}.

Since then, the guidelines have been revised by WHO and other entities, and authorities worldwide maintain the same limit of 10 µg/L, including the EU Directive on drinking water quality published in 2020 [2].

Recent studies on bromate toxicity

The present guidelines for bromate limit concentrations are based on high-dose studies in experimental animals performed 20 or more years ago.

A more recent (2015) thorough evaluation and toxicological assessment of bromate was done with ICR mice and Wistar rats, based on acute and cumulative toxicity test, Ames test, bone marrow cell micronucleus test, sperm aberration test and 30-day animal oral toxicity study (including body weight, vital organ weight, food intake, haematology, and blood biochemistry) [6]. The acute oral toxicity LD_{50} dosage of potassium bromate found was 215 mg/kg in rats and 464 mg/kg in mice, and it did not differ by gender. The cumulative toxicity of bromate is not obvious because increasing its cumulative dose (up to 5.3 times the LD_{50}) did not induce animal death during the 20-days test period. The results of the Ames test indicated that bromate had no mutagenic effect on the *Salmonella* strains (TA98 and TA100). In this study, it was also demonstrated that bromate had no bone marrow toxicity in mice, and that it did not cause sperm shape abnormality when administered orally. For a systematic estimation of the toxicity of bromate, a 30-day feeding study was conducted, with dose levels based on the standards for drinking water. During the 30-days study in rats, no abnormal behaviors, physical signs of toxicity, nor mortalities were observed. The clinical blood biochemistry analysis showed that albumin, creatinine, total cholesterol, triglycerides, and glucose levels increased with bromate ingestion. After the 30-days testing period, no significant changes in the color, shape and size of liver, kidney, spleen, stomach, heart, lung, duodenum, gonads, and brain were observed, and bromate did not affect the organ weight and the organ-to-body weight ratios either. Regarding hematology, however, it was noted that white blood cell counts in rats significantly decreased with the increase of bromate concentration, with a more notorious effect in male animals. The authors regarded this as the most sensitive indicator of the bromate toxicity and suggest to further investigate the underlying mechanisms.

Absorption and degradation of bromate upon ingestion were analyzed by administering orally doses of bromate ranging from 0.077 to 3.8 mg/kg body weight [7]. The plasma concentrations of bromate were reduced to one third of their peak after 60 minutes. In the same study, it was also observed that, probably, there is endogenous formation of bromate. The plasma half-life following oral administration was estimated as 37 min, and the major product of bromate degradation was bromide ion. The rapid reduction of bromate was confirmed by the observation of a rapid increase in plasma bromide 10 min after oral administration of bromate. The results indicated that, at low doses (i.e., $\leq$ 0.077 mg/kg), gastric and plasma degradation seemed to be a significant barrier to absorption of orally administered bromate.

Dutch bromate limit concentration in drinking water

Very recently (2021), the National Institute for Public Health and the Environment (RIVM) of The Netherlands published a report on the risk limits for bromate in surface waters. A Dutch limit of 1 µg/L is set as the maximum concentration for bromate in drinking water, with the exception that a maximum limit of 5 µg/L is allowed in case bromate is formed during the disinfection process of drinking water (as 90 percentile value, with a maximum of 10 µg/L). The report proposes to set a more stringent limit of 1 µg/L for bromate in surface waters at drinking water intake points. However, the RIVM does not advise to lower the bromate limit for drinking water, currently set at 1 µg/L and 5 µg/L in case of disinfection.

Future regulations based on new data

The Water Research Foundation (WRF) has prepared a report of a project to investigate the mode of action of bromate-induced carcinogenesis, based on molecular toxicology studies [8]. The obtained data constitutes adequate evidence that bromate acts primarily through non-genotoxic mechanisms. Therefore, the risk of bromate-induced cancer can be addressed by establishing a non-zero Maximum Contaminant Level Goal (MCLG) rather than by low-dose linear extrapolation.

Additionally, the results also suggest that human risk assessment should consider the lesser sensitivity of humans compared to rats. The authors conclude that the rationale for lowering the bromate Maximum Contaminant Level (MCL) below 10 µg/L (that corresponds to a TDI of 1.67 µg/kg of body weight) should be removed, and further restrictions on the use of ozone as drinking water disinfectant should be prevented.

Conclusion

Health authorities, such as the WHO, in future revisions of drinking water quality standards, should develop appropriate toxicology-based limits for bromate. For decades, guideline values for bromate were derived through linear extrapolation, considering, by default, that the carcinogenic effects develop from genotoxic events. However, the most recent scientific information brings a better understanding on the mode of action of bromate and endorses the non-genotoxic mechanisms.

Consequently, linear extrapolation (that leads to a maximum contaminant level goal of zero) for risk estimation is no longer required. If the cancer arises from non-genotoxic effects, a non-zero limit must be adopted by establishing a point of departure (i.e., NOAEL, LOAEL) and applying uncertainty factors.

Despite the existence of proposals to lower the limit for bromate concentration in drinking water, there is evidence now that the current level of 10 µg/L is safe.

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