Assessment of genotoxic and carcinogenic potential of long-term exposure to monohaloacetic acids

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Water disinfection has been one of the biggest sanitary achievements of the past century, dramatically improving our public health status. However, a large and increasing number of chemical species, globally named water disinfection by-products (DBPs), are formed during the sanitation process. Consistent evidence has proven that exposure to DBPs increases the risk of bladder and colon cancer. This risk has been associated to some DBPs, which concentrations have been regulated by different public health agencies. However, compounds that belong to non-regulated classes still present a possible hazard, as their harmful potential still has to be tested.

Haloacetic acids are one of the most abundant classes of DBPs. Among them, monohaloacetic acids (chloroacetic acid (CAA), bromoacetic acid (BAA), and iodoacetic acid (IAA)), have been shown to present the highest cytotoxic and genotoxic effect when compared to their polyhaloacetic counterparts in short-term *in vitro* studies. Nevertheless, acute, high concentration treatments do not present a realistic outline of carcinogenicity induction. The aim of our study was to analyze the effect of these chemicals in an *in vitro* system that better emulates a real exposure scenario. Using this experimental approach, a cell line (UROtsa) derived from the main target of DBPs carcinogenicity -the bladder- was exposed to a long-term (8-10 weeks) treatment of low concentrations of all three compounds. Preliminary results confirm that all three compounds presented citotoxicity at 24 hours, showing an IC50 of 776±63 μM for CAA, 11,4±1 μM for BAA and 2,7±0,5 μM for IAA. Based on these results, two non-cytotoxic concentrations were chosen for each chemical: 10 μM and 100 μM for CAA, 0.005 μM and 0.05 μM for BAA and 0.1 μM and 0.01 μM for IAA, respectively. Preliminary data showed that 24 hours of treatment had no effect over cell proliferation or DNA genotoxic and oxidative damage at these concentrations. The acquisition of different *in vitro* cancer-like features, such as alterations in cellular morphology and proliferation, will be monitored throughout the whole exposure time. Other carcinogenic biomarkers analyzed will be genomic and oxidative DNA damage, assessed by Comet assay; chromosomal damage measured by the micronucleus test; matrix metalloproteinases activity, measured by zymography; and colony formation and promotion, tested by soft-agar assay.