Liter-Equivalence Extrapolation for Four Trihalomethanes (THMs): What Drink Would It Take to Get the Same Internal Dose?

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Due to their presence in water as volatile disinfection byproducts (DBPs), THMs pose a potential health risk from exposure via oral, dermal and inhalation routes. Environmental exposure studies demonstrate that dermal and inhalation exposure to water containing THMs during showering or bathing results in more THMs delivered to systemic circulation than oral exposure. Using a physiologically-based pharmacokinetic (PBPK) model, we conducted a liter-equivalence analysis (Leq). We determined the concentration in one liter of water consumed orally needed to achieve the same internal dose as from a 10-minute shower for chloroform (TCM), bromodichloromethane (BDCM), dibromochloromethane (DBCM), and bromoform (TBM). Model structure and physiological parameters are the same as our published adult human BDCM model (Kenyon et al., 2016). Because human chemical-specific metabolism parameters are not available for all four THMs, rat metabolism parameters obtained from the literature were used to avoid confounding of comparisons across the chemicals. We simulated showering for 10 minutes with water containing 8.2, 12.2, 13.5, and 8.7 µg /L for TCM, BDCM, DBCM and TBM, respectively. These are measured drinking water concentrations from an area with predominantly brominated THMs (Gulf coast TX, Lynberg et al., 2001). Two measures of internal dose, area under curve in venous blood (AUCv) and amount of specific THM metabolized in liver (AML) were evaluated. For AUCv, the oral Leq concentrations for the showering scenario were 20.9, 38.5, 43.8, and 29.9 µg/L for TCM, BDCM, DBCM and TBM, respectively. For AML, the oral Leq concentrations for the showering scenario were 1.3, 1.9, 1.9, and 1.4 µg/L for AML for TCM, BDCM, DBCM and TBM, respectively. These results demonstrate that dermal and inhalation exposure routes contribute significantly to internal doses of THMs reaching the systemic circulation (AUCv). In sum, consideration of the contribution of multiple routes of exposure to internal dosimetry should decrease uncertainty in dose-response characterizations of water-borne THMs. (This abstract does not reflect U.S. EPA Agency policy.)