

Impact of Addition of Halogens to the α -Carbon of Acetic Acids on Mutagenicity and Developmental Toxicity Endpoints

Raghuraman Venkatapathy
ORISE post-doctoral research scientist
NCEA, Cincinnati
(513) 569-7077
venkatapathy.raghuraman@epa.gov

Authors: Raghuraman Venkatapathy, Robert M. Bruce, and Chandrika J. Moudgal

Key Words: disinfection byproducts, haloacetic acids, mutagenicity, developmental toxicity, quantitative structure-toxicity relationships (QSTRs)

Chlorine-containing chemicals, such as chlorine gas, chlorine dioxide, and monochloramine, have been used as disinfectants in drinking water systems to eliminate microbial contaminants. However, the chlorine in the disinfectants and other halides water, such as bromide, react with humic acids and other natural organic matter to form halogenated disinfection byproducts (DBPs) such as trihalomethanes (THMs), halogenated acetic acids (HAAs), and halogenated acetonitriles (HANs). Various studies in the literature have shown that animal exposure to DBPs may cause developmental, reproductive, neurotoxic, and mutagenic/carcinogenic side effects. The DBPs for which toxicity data are available in the literature mostly include chlorinated chemicals such as chloroform, bromodichloromethane, dichloroacetic acid, and trichloroacetic acid. However, experimental toxicity data are not available for a majority of DBPs, such as their brominated or iodinated analogs. In addition, where toxicity data are available, there is lack of information on mechanisms of toxicity for those DBPs. This paucity of toxicological data can be circumvented by the use of Quantitative Structure-Toxicity Relationships (QSTRs). The objective of this research is to (a) predict the mutagenicity and developmental toxicity of all possible HAAs and (b) determine the reason or mechanism behind the mutagenic and developmental toxicity potential of the HAAs using a commercial QSTR model, TOPKAT. Although fluorinated DBPs are generally not found in drinking water systems, they have been included in this study for comparison purposes. Ames mutagenicity and developmental toxicity potential predictions for the 34 possible HAAs using TOPKAT indicated that a majority of mono- and dihalogenated acetic acids were mutagenic, while most trihalogenated acetic acids were nonmutagenic. In the case of developmental toxicity potential, all mono- and trihalogenated acetic acids were predicted as developmental toxicants, while dihalogenated acetic acids were predicted as nontoxic. The impact of the α -carbon and the degree of halogenation of the acetic acids were ascertained by comparing the contributions of the 1- and 2-atom fragments in the HAAs toward the toxicity potential for the two endpoints. In the case of developmental toxicity potential, the presence of a $>CHX$ fragment in a given chemical seemed to inhibit developmental toxicity, while the presence of $-CH_2X$ or $-CX_3$ seemed to promote developmental toxicity. Results of the QSAR analysis seem to indicate that the mutagenicity of the HAAs seems to be dependent on their ability to undergo electrophilic reactions with specific fragments in the DNA or form hydrogen bonds with hydrogen-bonding donor sites at the DNA, thereby suggesting that an electron-donating ability is essential for a chemical to be mutagenic.