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Minireview

Genotoxicity of disinfection byproducts and disinfected waters: A review of recent literature

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ABSTRACT

The presence of water disinfection byproducts (DBPs) in tap water, resulting from disinfection processes involving chlorination or chloramination, increases the mutagenicity of the water and may pose adverse health effects. The topic was reviewed by DeMarini and coworkers in 2007. Here, we review research on the genotoxicity of DBPs published since that time. Studies, primarily using the *Salmonella* mutagenicity assay, have continued to show that chlorination or chloramination of source waters results in finished, tap, or swimming pool/spa water that is more mutagenic than the original source water. The genotoxic potencies of DBPs in both bacterial and mammalian cells generally rank as iodinated > brominated > chlorinated. Several DBPs are genotoxic *in vivo* in plants as well as in animals such as the worm *Caenorhabditis elegans* and the zebrafish *Danio rerio*. Studies primarily using the comet assay in mammalian cells have identified several non-regulated DBPs as genotoxic. However, the comet assay detects DNA damage that is generally repaired by the cells; thus, genotoxicity data more relevant to persistent mutations, such as chromosomal or gene mutations, are needed for these DBPs. Recent molecular epidemiology has indicated that activation of brominated trihalomethanes by the enzyme GSTT1 and the lack of metabolism of haloacetic acids by a variant of enzyme GSTZ1 are likely causative mechanisms for bladder cancer associated with exposure to chlorinated water. Further studies, especially *in vivo*, are needed to determine the ability of various DBPs, especially unregulated ones, to induce both gene as well as chromosomal mutations. Such investigations, along with additional molecular epidemiology studies, are required for a comprehensive understanding of the genotoxic and carcinogenic risks associated with DBP exposure.

1. Introduction

The implementation of disinfection procedures in public water sources is undoubtedly one of the most important health advances of modern times. In this way, many of the effects associated with waterborne infectious diseases have been significantly reduced, although they persist in many regions worldwide [1]. However, chemical disinfectants react with organic matter and inorganic ions present in source waters, forming new chemical species, water disinfection byproducts (DBPs). In the past 40 years, several studies have examined potential health risks posed by these compounds. Epidemiological evidence links exposure to DBPs to increased risk of bladder cancer and reproductive effects [2,3].

An important milestone in our knowledge on the toxic, genotoxic, and carcinogenic effects of DBPs is the extensive review carried out in 2007 by DeMarini and colleagues [4]. Our present aim is to review subsequently published data. The studies have been classified according to whether they were obtained using *in vitro* or *in vivo* (including some human biomonitoring studies) approaches. In addition, studies have also been divided between those using water samples containing DBPs mixtures, which reflect the actual exposure scenario, and those using individual DBPs, to identify the most hazardous chemicals.

2. DBP classification

DBPs were first identified and associated with water disinfection processes in the 1970s [5,6]. By 2000, many of the currently known DBPs had been identified [7,8]. Nevertheless, In the past decade, the analysis of diverse water sources and the implementation of modern analysis techniques such as high-resolution mass spectrometry have led to the identification of several new chemical species [9–11]. To date, the number of reported DBPs is more than 600 [4]. Table 1 summarizes the main classes of known DBPs as well as the range of concentrations found in disinfected waters. As observed, they belong to many chemical

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Table 1
Main groups of DBPs and their levels of occurrence.
Occurrence data taken from [4,38,77–81].

Disinfection by-products	Occurrence (μg/L)
HALONITROMETHANES	0.1–5
Chloronitromethane, Dichloronitromethane, Trichloronitromethane (Chloropicrin), Bromonitromethane, Dibromonitromethane, Tribromonitromethane (Bromopicrin), Bromochloronitromethane, Bromodichloronitromethane, Dibromochloronitromethane	
HALOACETIC ACIDS AND OTHER HALOACIDS	1–2600
Chloroacetic acid, Dichloroacetic acid, Trichloroacetic acid. Bromoacetic acid, Dibromoacetic acid, Tribromoacetic acid, Iodoacetic acid, Diiodoacetic acid, Triiodoacetic acid, Bromochloroacetic acid, Bromodichloroacetic acid, Bromoiodoacetic acid, Dibromochloroacetic acid, Chlorodibromoacetic acid	
TRIHALOMETHANES	0.05–380
Chloroform, Bromoform, Dibromochloromethane, Bromodichloromethane, Dichloroiodomethane, Bromochloroiodomethane, Dibromoiodomethane, Chlorodiiodomethane, Bromodiiodomethane, Iodoform, Dichloromethane, Bromochloromethane, Chlorodibromomethane, Dibromomethane	
OXYHALIDES	0.2–1100
Bromate (0.2 − 25.1), Chlorate (up to 190), Chlorite (up to 1100)	
HALOFURANONES	0.08–0.85
MX, Red-MX, Ox-MX, EMX, ZMX, Mucochloric acid, BMX-1, BMX-2, BMX-3, BEMX-1, BEMX-2, BEMX-3	MX (0.08–0.85),
HALOACETONITRILES	0.5–219
Chloroacetonitrile, Dichloroacetonitrile, Trichloroacetonitrile, Bromoacetonitrile, Dibromoacetonitrile, Tribromoacetonitrile, Bromochloroacetonitrile, Bromodichloroacetonitrile, Dibromochloroacetonitrile, Iodoacetonitrile	
HALOKETONES	10–60
Chloroacetones	
HALOAMIDES	Up to 9.4
Chloroacetamide, Dichloroacetamide, Trichloroacetamide, Bromoacetamide, Dibromoacetamide, Tribromoacetamide, Bromochloroacetamide, Bromoiodoacetamide, Bromodichloracetamide, Dibromochloroacetamide, Iodoacetamide, Diiodoacetamide, Chloroiodoacetamide	
HALOAMINES & OTHER AMINES	1–1180
Chloramines, Nitrosamines (NDMA), Heterocyclic amines	
ALDEHYDES	0.4–497
Formaldehyde, Acetaldehyde, Chloroacetaldehyde, Dichloroacetaldehyde, Bromochloroacetaldehyde, Trichloroacetaldehyde (chloral hydrate), Tribromoacetaldehyde	Formaldehyde (up to 13.7)
Other DBPs	
Quinones, Cyanogen halides, Chlorophenols, Aldoketoacids, Carboxylic acids, Haloacetates, Halopyrroles, Others	

families.

3. Formation of DBPs

The presence and abundance of each DBP depends on the disinfectant used, its concentration, and on the spectrum of organic and halogenated molecules present in the source water. The physicochemical characteristics of treated waters also influence the formation of DBPs. Additional variables to be taken into consideration are the contact time and the characteristics of the distribution network. Factors modulating the formation of DBPs are summarized in Table 2.

Chlorine is the most commonly used disinfectant, and the relationship between chlorine dose and the amount of organic matter in the treated water is the determining factor behind the by-products that will form. The use of chlorine has been linked to the formation of trihalomethanes (THMs), haloacetic acids (HAAs), halonitromethanes (HNMs), haloacetonitriles, chloramines, chlorophenols, the so-called "mutagen X" (MX), and bromate and chloral hydrate, among others. The use of other disinfectants has also been associated with formation of different DBP classes. The use of chlorine dioxide (ClO_2) is associated with the formation of chlorite, chlorate, and chloride. The use of ozone is related to formation of bromate, formaldehyde, other aldehydes, peroxides, and brominated methane; chloramination procedures may lead to formation of dichloramines, trichloramines, cyanogen chloride, and chloral hydrate [12].

In addition to the disinfectant used, the molecules initially found in the water also influence the DBP species formed. The concentration of organic matter is directly correlated to the concentration of DBPs found in disinfected waters. The presence of aromatic molecules in particular seems to increase the formation of DBPs [13]. Recently, the presence in raw waters of anthropogenic organic compounds such as pharmaceuticals, hormones, pesticides, textile dyes, UV filters, and fuels has led the scientific community to ponder their potential risks. Even though their levels in potable water do not pose a health concern *per se*, there are concerns regarding the formation of potentially hazardous DBPs during the disinfection process. For instance, analgesics such as

Table 2
Factors affecting DBP formation.
Data taken from [8,82–84].

Factors	Effects
Organic matter in water	*DBP formation is proportional to the concentration of NOM*
	Aromatic NOM increases the formation of halogenated DBPs
Ion presence in water	*Bromide presence determines the formation of brominated DBPs*
Water pH	*A basic pH favors the formation of THMs*
	Acidic pH can favor the formation of HAAs
Water temperature	*Higher temperatures demand the use of higher disinfectant doses*
Disinfectant employed	*Chlorine: THMs, HAAs, HNMs, haloacetonitriles, chloramines, chlorophenols, MX, bromate and chloral hydrate*
	Chlorine dioxide: chlorite, chlorate and chloride
	Ozonation: bromate, formaldehyde, other aldehydes, hydrogen peroxides and brominated methanes
	Chloramination: dichloramines, trichloramines, cyanogen chloride and chloral hydrate
Contact time	*Residual chlorine in distribution systems favors the formation of HAAs over THMs*