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Chlorination and chloramination of tetracycline antibiotics: Disinfection by-products formation and influential factors

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ABSTRACT

Formation of disinfection by-products (DBPs) from chlorination and chloramination of tetracycline antibiotics (TCs) was comprehensively investigated. It was demonstrated that a connection existed between the transformation of TCs and the formation of chloroform ($CHCl_3$), carbon tetrachloride (CCl_4), dichloroacetonitrile (DCAN) and dichloroacetone (DCAce). Factors evaluated included chlorine (Cl_2) and chloramine(NH_2Cl) dosage, reaction time, solution pH and disinfection modes. Increased Cl_2/NH_2Cl dosage and reaction time improved the formation of $CHCl_3$ and DCAce. Formation of DCAN followed an increasing and then decreasing pattern with increasing Cl_2 dosage and prolonged reaction time. pH affected DBPs formation differently, with $CHCl_3$ and DCAN decreasing in chlorination, and having maximum concentrations at pH 7 in chloramination. The total concentrations of DBPs obeyed the following order: chlorination > chloramination > pre-chlorination (0.5 h) > pre-chlorination (1 h) > pre-chlorination (2 h).

1. Introduction

Tetracycline antibiotics (TCs) are a family of broad-spectrum antibiotics. Since the first member, chlortetracycline (CTC), was developed in 1947 (Duggar, 1948), other natural TCs were soon isolated for clinical use, including tetracycline (TC) and oxytetracycline (OTC). Then some semisynthetic TCs were generated by modifying naturally occurring TCs and synthetizing novel compounds within the tetracycline family. Two of the more common semisynthetic TCs are doxycycline (DC) and minocycline (MC). The favorable antimicrobial properties of TCs led to their extensive use in human and veterinary medicine to treat bacterial infections and promote animal growth (De Liguoro et al., 2003; Kordick et al., 1997; Kumar et al., 2005; Sarmah et al., 2006). The usage of TCs was approximately 16.268 t in the UK in 2000 (Sarmah et al., 2006). The United States produced as high as 3000 t of TCs in 2003 for farm animals (Arikan et al., 2007; Bao et al., 2009). In China, TCs are also one of the most widely used antibiotics. The widespread and long-term usage of TCs resulted in the emergence of drug resistance in almost all bacteria genera (Adam, 2002; Boxall et al., 2003; Sarmah et al., 2006).

In 1980s, Watts et al. (1983) first reported the presence of TC in river water samples. Since then, TCs have been frequently detected in surface water (Li et al., 2008; Lin and Tsai, 2009; Spongberg et al., 2011; Wei et al., 2011). As an antibiotic used against various bacterial infections, TC was measured in many US and Canadian sites with concentrations up to 300 ng/L (Kolpin et al., 2004; Miao et al., 2004). Kolpin et al. (2002) reported that maximum concentrations of CTC, OTC and TC in US surface waters were 690 ng/L, 340 ng/L and 110 ng/L, respectively. Even higher concentrations (i.e., 72.9 μg/L for OTC, and 10.3 μg/L for TC) were recorded by Wei et al. (2011) in Chinese surface waters.

The frequent detection of TC residues and related microbial resistance in the environment poses threats to the human health and ecosystem. While many studies highlighted the occurrence of TCs in the environment, little attention has been paid to their behaviors in a drinking water treatment process. As conventional drinking treatment processes (i.e., coagulation, sedimentation and filtration) can poorly remove pharmaceuticals in water (Stackelberg et al., 2007), it is well-known that disinfection by chlorination or chloramination is a final step for drinking water treatment. Wang et al. (2011) reported that the oxidation kinetics of TCs by chlorine (Cl_2) are rapid with large apparent second-order rate constants of 1.12×10^4–$1.78\times10^6\ M^{-1}\ s^{-1}$ at pH 7. Wan et al. (2013) also observed the chloramination of TC exhibited pseudo-first-order kinetics with the rate constants (k_{obs}) ranging from 0.0082 to 0.041 min^{-1} at pH of 6–8.

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Disinfection by-products (DBPs) are concomitant problem of water disinfection, attracting considerable attention in the recent years (Hebert et al., 2010; Krasner et al., 2006; Sadiq and Rodriguez, 2004). They are generally formed by the reaction of disinfectants with natural organic matter (Hong et al., 2013; Lin and Wang, 2011), but it cannot be ignored that contaminants with activated benzene rings or other functional groups that can react with oxidants (i.e., Cl_2 and NH_2Cl) are potential DBPs precursors (Duirk et al., 2011; Richardson, 2009; Shen and Andrews, 2011b). Shen and Andrews (2011a) reported that controlled laboratory reactions of TC with chlorine and chloramine were able to form corresponding nitrosamines. And 25 nM TC showed 0.8–1.2 percent molar conversions in both Milli-Q and tap water, which decreased slightly with increasing initial tetracycline concentration.

Although the trace level of TCs in surface water may not account for the majority of DBPs precursors during the disinfection process, the huge use of TCs makes it a potential risk to human health. The overall objectives of this research were (1) to demonstrate a connection between the transformation of TCs and the formation of DBPs during Cl_2 and NH_2Cl disinfection, (2) to evaluate the factors affecting DBPs formation, including Cl_2 and NH_2Cl dosage, reaction time, solution pH and disinfection modes.

2. Materials and methods

2.1. Chemicals

All chemicals were at least of analytical grade except as noted. TC ($\geq$98.0 percent), OTC ($\geq$95.0 percent), and CTC ($\geq$97.0 percent) were obtained from Sigma-Aldrich (USA). DC ($\geq$98.0 percent) was purchased from Aladdin Chemistry Co., Ltd. (Shanghai, China). Chloroform ($CHCl_3$), carbon tetrachloride (CCl_4), dichloroacetonitrile (DCAN) and dichloroacetone (DCAce) were purchased from Sigma-Aldrich (USA). Sodium hypochlorite (NaOCl) solution (available chlorine 4.00–4.99 percent) was purchased from Sigma-Aldrich (USA). Analytical grade reagents including ammonium chloride (NH_4Cl), ammonium acetate, NaH_2PO_4, Na_2HPO_4, NaOH, Na_2CO_3, $NaHCO_3$, CH_3COOH and HCl were purchased from Sinopharm Chemical Reagent Co., Ltd. (Shanghai, China) without further purification. All chemical solutions were prepared using ultrapure water produced from a Milli-Q water purification system (Millipore, USA). Methyl tert-butyl ether (MTBE) was obtained from J.T. Baker (USA).

2.2. Experimental procedures

NH_2Cl solutions were freshly generated by adding NaOCl solution gently into a stirred NH_4Cl solution with the Cl:N molar ratio of at least 1:1.2 to prevent breakpoint chlorination due to local excess of OCl^-, and pH was kept at around ten to avoid the disproportionation of NH_2Cl to $NHCl_2$ (Mitch and Sedlak, 2002).

Chlorination experiments were carried out using sealed 45 mL amber glass bottles at controlled temperature (25 $\pm$ 0.5 °C) in dark. The concentrations of TCs were 0.025 mM and appropriate Cl_2 or NH_2Cl was added to the TCs solutions at a desired molar ratio of 1, 5, 15, and 25. The pH range of the reactions was controlled from 5 to 9, which were buffered with 10 mM acetate (for pH 5), 10 mM phosphate (for pH 6–7) and 10 mM carbonate (for pH 8–9) solutions, and pH values were adjusted with small volumes of 0.01, 0.1, or 1 M HCl and/or NaOH. In all experiments, the initial and final pH difference was less than 0.1. For comparison, five chorination/chloramination disinfection modes, including chlorination (Mode I), chloramination (Mode II), and pre-chlorination for 0.5 h (Mode III), 1 h (Mode IV) and 2 h (Mode V) before NH_4Cl addition were also investigated.

Prior to DBPs analysis, the residual Cl_2 was quenched by NH_4Cl (20 mM) with a double normality of the initial added Cl_2 normality to avoid the interaction with formed DBPs.

2.3. Analytical methods

Cl_2 and NH_2Cl concentration were quantitatively determined by the N,N-dethyl-p-phenylenediamine (DPD) colorimetric method (APHA et al., 1998). pH was measured using a pH-meter (module PHS-3B, Shanghai LEICI Analysis Instrument Factory, China).

The concentrations of DBPs including $CHCl_3$, CCl_4, DCAN and DCAce were measured based on USEPA method of 551.1 (U.S.EPA, 1995). Samples were extracted by MTBE, and then analyzed by a GC-ECD (GC-2010, Shimadzu, Japan). The column was a fused silica capillary (HP-5, 30 m $\times$ 0.25 mm inner diameter with 0.25 μm film thickness, J&W, USA). All the tests were conducted at least in duplicate. The relative standard deviations (RSD) for different batches were normally < ten percent.

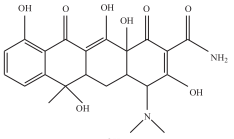
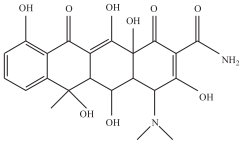
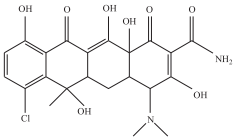
3. Results and discussion

3.1. Chlorination and chloramination of TCs

Four kinds of TCs (Table 1), including TC, OTC, CTC and DC, were selected in this study to evaluate the impact of structural variation for the chlorination and chloramination. As shown in Table 1, TCs molecules contain connected ring systems with several electron-rich moieties that are likely to be susceptible to attacks by oxidants like Cl_2 and NH_2Cl.

$CHCl_3$ was stable in the presence of Cl_2 and was the final product during the chlorination of many compounds (Lopez et al., 2001). As shown in Fig. 1, $CHCl_3$ was the major volatile degradation product during both chlorination and chloramination of all tested TCs. The maximum concentration of $CHCl_3$ was 0.452 μM (molar yield as 1.81 percent) by chlorination of TCs, which was 1.6 times higher than that during chloramination (0.281 μM, molar yield as 1.12 percent). The concentrations of CCl_4 were low and

Table 1
Structures and properties of TCs investigated in this study.

Compounds	Formula	Molecular weight	Molecular structure
TC	$C_{22}H_{24}N_2O_8$	480.90	
OTC	$C_{22}H_{24}N_2O_9$	496.89	
CTC	$C_{22}H_{23}ClN_2O_8$	515.34	
DC	$C_{22}H_{24}N_2O_8$	480.90