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Evaluation of N-acetylcysteine and glutathione as quenching agents for the analysis of halogenated disinfection by-products

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ABSTRACT

Disinfection by-products (DBPs), formed from the reactions of disinfectants with natural organic matter and halides in drinking water, were considered to be cytotoxic and genotoxic, and might trigger various cancers. The relatively low concentration of DBPs in finished water (low μg/L or even ng/L levels) and the interference from water matrix inhibited *in situ* determination of DBPs. Moreover, the further formation and degradation of DBPs by disinfectants during the holding time (several hours to several days) from sample collection to analysis could adversely affect the determination of DBPs. To obtain accurate, precise and reliable data of DBP occurrence and formation, robust and reliable sample preservation is indispensable. However, the commonly used quenching agents (e.g., sodium sulfite, sodium thiosulfate, and ascorbic acid) for sample preservation can decompose reactive DBPs by reductive dehalogenation. This study evaluated the performance of N-acetylcysteine (NAC) and glutathione (GSH) as quenching agents for the analysis of halogenated DBPs by investigating the stoichiometry of the disinfectant-quenching agent reaction, the formation of DBPs during chlor(am)ination of NAC or GSH, and the effects of NAC or GSH on the stability of 18 individual DBPs and total organic halogen (TOX). Based on the results of this study, NAC and GSH were considered to be ideal quenching agents for the analysis of most DBPs and TOX, except halonitromethanes.

Introduction

The chlorination and chloramination of drinking water remain the most commonly used methods to inactivate pathogenic microorganisms during drinking water treatment. Moreover, the addition of disinfectants is used to provide residual disinfectants in drinking water distribution system for the prevention of microorganisms regrowth in finished water (Richardson et al., 2007; Liu et al., 2017; Dong et al., 2021).

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However, the reactions of disinfectants with natural organic matter, anthropogenic contaminants and inorganic halides also produced unwanted disinfection by-products (DBPs) (Richardson et al., 2007; Pan and Zhang, 2013; Zhou et al., 2014; Ding et al., 2019a). Research into DBPs is worth of attention, since epidemiology studies have discovered the association between potential health risk and exposure to DBPs (Richardson et al., 2007; Stalter et al., 2016; Wagner and Plewa, 2017).

To investigate the occurrence, formation, and mitigation of DBPs, robust and sensitive analysis techniques and sample handing procedures are indispensable (Ding and Chu, 2017). The relatively low concentration of DBPs in finished water (low μg/L or even ng/L levels) and the interference from water matrix inhibit *in situ* determination of DBPs (Bond et al., 2011; Huang et al., 2017). Therefore, samples are firstly transported from sampling site to laboratory before analysis by gas chromatography (GC) and liquid chromatography (LC) based analytical instruments. However, the further formation of DBPs during the holding time (several hours to several days) from sample collection to analysis could lead to an overestimation of actual DBP concentration (Wang et al., 2016). Moreover, DBPs also undergo hydrolysis and chlor(am)ination degradation between water sample collection and analysis (Chen, 2011; Kristiana et al., 2014; Ding et al., 2018a). Fig. S1 presents the transformation pathway of CX_3R-type DBPs (X = H, Cl, Br or I, R = functional group) in the absence and presence of chlor(am)ines. It has been reported that CX_3R-type DBPs including haloacetic acids (HAAs), haloacetaldehydes (HALs), haloketones (HKs), haloacetonitriles (HANs), halonitromethanes (HNMs), and haloacetamides (HAMs) underwent base catalyzed hydrolysis with a half-life ranging from several hours to several ten days at pH 7.0 (Glezer et al., 1999; Nikolaou et al., 2001; Zhang and Minear, 2002; Na and Olson, 2004; Koudjonou and LeBel, 2006; Joo and Mitch, 2007; Chen, 2011; Ding et al., 2018a; Xiao et al., 2020). The presence of chlorine or chloramines further accelerated the degradation of DBPs (particular for HANs, HAMs, and HALs), and the half-lives of above-mentioned DBPs even decreased to several minutes (Na and Olson, 2004; Joo and Mitch, 2007; Yu and Reckhow, 2015; Ma et al., 2016; Ding et al., 2018a). Reciprocal transformation among CX_3R-type DBPs by chlorine and chloramines affect the precise and accurate of determination.

Owing to the above two reasons, the use of an appropriate quenching agent is critical to prevent further formation of additional DBPs and degradation of existing DBPs by chlorine and chloramines during the holding time (Gong et al., 2016; Ding and Chu, 2017). Particularly, intensified disinfection amid COVID-19 pandemic was considered to result in high disinfectant residual in natural water and reclaimed wastewater, and might in turn lead to high dosage of quenching agents for sample preservation (Chu et al., 2021). However, commonly used quenching agents (e.g., sodium sulfite, sodium thiosulfate, ascorbic acid [AC], and ammonium chloride) can also decompose several reactive DBPs by reductive dehalogenation (Croue and Reckhow, 1989; Kristiana et al., 2014; Ding et al., 2018b). For example, HALs, HKs, HNMs, HANs, and HAMs were reduced to half of initial concentrations after several hours exposure to sodium sulfite (sufficient to quench 3.0–4.0 mg/L chlorine), and bromine- or iodine-containing DBPs were even more susceptible (Croue and Reckhow, 1989; Kristiana et al., 2014; Ding et al., 2018a). The destruction of cyanogen chloride by sodium thiosulfate, sodium sulfite and sodium metabisulfite was primarily attributable to the chemical reduction pathway with second-order rate constants of 0.6 $(mol/L)^{-1}sec^{-1}$, 3.5 $(mol/L)^{-1}sec^{-1}$, and 5.4 $(mol/L)^{-1}sec^{-1}$, respectively (Shang et al., 2005). A study conducted by Kristiana et al. (2014) investigated the impact of five quenching agents (sodium sulfite, sodium arsenite, sodium borohydride, AC, and ammonium chloride) on the stability of several groups of CX_3R-type DBPs, and demonstrated that there was no ideal quenching agent suitable for the determination of all groups of CX_3R-type DBPs. Moreover, it should be noted that the above-mentioned CX_3R-type DBPs only accounted for ~ 30.0% of total organic halogen (TOX) on a weight basis (Krasner et al., 2006). Liu and Zhang (2013) demonstrated that sodium arsenite, a weaker reductant, caused negative interferences in the TOX measurement. On the one hand, the competitive adsorption onto activated carbon between halogenated DBPs and the excessive sodium arsenite existed during initial quenching period ($\leq$ 10.0 min), on the other hand, the decomposition of easily-reduced halogenated DBPs took place after long quenching time ($>$ 60.0 min). However, the effects of commonly used quenching agents (sodium sulfite, sodium thiosulfate, and AC) on the decreases of TOX remain unknown.

Our recent study found that reduced sulfur compounds (RSCs), including *N*-acetylcysteine (NAC), glutathione (GSH), and glutathiol (GSSG), readily reacted with chlorine and chloramines, and the formation of CX_3R-type DBPs could be neglected when the molar ratio of RSCs to chlor(am)ines were $<$ 5 (Ding et al., 2019b). The much higher reactivity of chlorine and chloramines toward reduced sulfur groups in RSCs protected other functional groups (e.g., alkyl, amine, and amide), which were responsible for the formation of CX_3R-type DBPs (Shah and Mitch, 2012; Dong et al., 2019). Previous study has demonstrated that the second order rate constants for the reaction of Cl_2 with GSH are higher than 1.0×10^7 $(mol/L)^{-1}sec^{-1}$ over the pH ranges of 5.0–9.0, which is even slightly higher compared to ascorbic acid (6.0×10^6 $(mol/L)^{-1}sec^{-1}$ at pH 7.0) (Folkes et al., 1995). Later studies demonstrated that various thiol-containing compounds could be easily oxidized by chlorine or chloramines within a few milliseconds (Armesto et al., 2000; Brace, 2000; Deborde and von Gunten, 2008). This has stimulated us to evaluate the performances of RSCs as quenching agents for the analysis of halogenated DBPs. The objective of this study was therefore to investigate the stoichiometry of disinfectant-quenching agent (NAC and GSH) reaction; the formation of CX_3R-type DBPs during chlor(am)ination of NAC and GSH; and the stability of CX_3R-type DBPs and TOX in the presence of NAC and GSH.

1. Materials and methods

1.1. *Materials*

The characteristics, sources, and purity of 18 DBP standards were shown in Appendix A Table S1. NAC (98.0%), GSH (98.0%), sodium sulfite (98.0%), sodium thiosulfate (99.0%),

AC (99.0%), Methyl–*tert*–butyl ether (MTBE, 99.0%), anhydrous sodium sulfate (99.0%), humic acid, sodium hypochlorite (active Cl_2 = 6.0%–14.0%) were all purchased from Aladdin Industrial Inc. (Shanghai, China). Sodium hypochlorite stock solution was prepared by diluting with ultrapure water to approximate concentration (8.0 g/L as Cl_2) and preserved in an aluminum foil-covered glass bottle at 4 °C. Preformed chloramine solution was prepared freshly by slowly adding 50.0 mL of sodium hypochlorite stock solution into 50.0 mL of ammonium chloride solution, which was adjusted to pH 8.5 with hydrochloric acid and sodium hydroxide over 30.0 min of reaction, at a hypochlorite to ammonia molar ratio of 1:1.2. Before use, the free chlorine and total chlorine concentrations in preformed chloramine solution were calibrated and the proportion of free chlorine to total chlorine should be lower than 5.0%. The residual chemical reagents, which were of at least analytical grade and used as received without further purification, were all obtained from Sinopharm Chemical Reagent Co., Ltd. (Shanghai, China). All solutions were prepared using ultrapure water produced by a Millipore Milli-Q Gradient water purification system (18 MΩ•cm, Billerica, USA).

YSP water was collected from filtered water of YSP drinking water treatment plant, which was located at Shanghai, China, in December 2020. HP river water and TH lake water were collected from Yangtze River delta in 2021. All water samples were immediately transported to a laboratory at Tongji University (Shanghai, China) and preserved at 4 °C before use. The characteristics of four water samples were shown in Appendix A Table S2.

1.2. *Experimental procedures*

The reaction of NAC or GSH with disinfectant under pH 7.0 (20.0 mmol/L phosphate buffer) in the dark at 25.0 ± 0.5 °C were conducted in 250.0 mL brown glass bottles to investigate the stoichiometry of disinfectant-quenching agent reaction and the formation of CX_3R-type DBPs. To investigate the effects of NAC and GSH on the stability of 18 DBPs including trichloromethane (TCM), bromodichloromethane (BDCM), dibromochloromethane (DBCM), tribromomethane (TBM), dichloroacetic acid (DCAA), bromochloroacetic acid (BCAA), dibromoacetic acid (DBAA), trichloroacetic acid (TCAA), dichloroacetaldehyde (DCAL), trichloroacetaldehyde (TCAL), 1,1,1- trichloropropanone (1,1,1-TCP), dichloroacetonitrile (DCAN), dibromoacetonitrile (DBAN), trichloroacetonitrile (TCAN), dichloronitromethane (DCNM), trichloronitromethane (TCNM), dichloroacetamide (DCAM), and trichloroacetamide (TCAM), predetermined volume of individual DBPs was introduced into 1.0 L of a 20.0 mmol/L phosphate buffer solution (pH = 7.0) to obtain an initial DBP concentration of 50.0 μg/L at the beginning of each experiment, and then 500.0 μL of quenching agents (40.0 mmol/L) or ultrapure water was added to initiate reaction in the dark at 25.0 ± 0.5 °C. At pre-determined contact times, 20.0 mL aliquots of samples were taken to analyze DBP concentration. The observed rate constants (k_h and k_{obs}) of specific DBP degradation in the absence and presence of quenching agents were determined based on Eq. (1). To compare the effects of different quenching agents on TOX determination, the reactions of water samples with disinfectants (8.0 mg/L) were conducted in 4.0 L brown glass bottles in the dark at 25.0 ± 0.5 °C. The total chlorine residuals in the water samples were consumed to < 0.1 mg/L as Cl_2 after specific reaction periods (24 - 36 hr). Then, 200.0 mL aliquots of samples were taken and dosed with different quenching agents to achieve an initial concentration of 20.0 mmol/L of quenching agents. After specific reaction periods, 100.0 mL aliquots of samples were taken to determine TOX concentration. All experiments were carried out at least in duplicates and the error bars in figures represented the standard deviation.

$$\frac{d[C]}{dt} = -k_{obs} \times [C] \quad (1)$$

1.3. *Analytical methods*

Dissolved organic carbon (DOC) was determined with a Shimadzu TOC analyzer (TOC-VCPH, Kyoto, Japan). Absorbance at 254 nm was measured using a HACH DR6000 UV–vis spectrophotometer (Loveland, USA). Free chlorine and total chlorine concentrations were determined by a portable colorimeter (HACH Pocket Colorimeter TM^{II}, Loveland, USA) with DPD free chlorine reagent and total chlorine reagent (HACH, Loveland, USA). For the analysis of trihalomethanes (THMs), HALs, HKs, HANs, HNMs, or HAMs, 10.0 mL aliquot of sample was immediately liquid-liquid extracted by adding 2.0 mL of MTBE and 3.0 g of anhydrous sodium sulfate, and was then shaken for 5.0 min using a multi-tube vortex mixer (DMT-2500, Shanghai, China) at 2300 r/min. After 5.0 min settling, 1.0 mL of MTBE extract was withdrawn into a 1.5 mL vial for determination. 1.0 μL of MTBE extract was separated via a splitless injector onto a GC column (RTX-5MS, 30.0 m × 0.25 mm ID, 0.25 μm film thickness) and measured using a gas chromatograph with electron capture detector (GC/ECD, QP2010plus, Shimadzu Corporation, Kyoto, Japan). For the analysis of HAAs, 20.0 mL aliquot of sample was firstly acidified with 1.0 mL of sulfuric acid (95.0%–98.0%) to achieve pH < 0.5, and then was immediately liquid-liquid extracted by adding 4.0 mL of MTBE and 6.0 g of anhydrous sodium sulfate. After 5.0 min shaking at 2300 r/min and 5.0 min settling, 2.0 mL of extract was withdrawn and derivatized using 1.0 mL of 10.0% sulfuric acid in methanol (V/V) for 2.0 hr at 50.0 °C. Afterwards, cold mixtures were neutralized with 4.0 mL of a saturated sodium bicarbonate solution. 1.0 μL of MTBE extract was separated via a splitless injector onto a GC column (RTX-5MS, 30.0 m × 0.25 mm ID, 0.25 μm film thickness) and analyzed by a GC coupled with mass spectrometry (GC/MS, QP2020, Shimadzu Corporation, Kyoto, Japan). Details of the analytical methods (including GC columns, oven temperature programmes, etc.) for 18 CX_3R-type DBPs are summarized in Table S3. TOX was analyzed using an Analytikjena MultiX® 2500 total organic halogen analyzer (Jena, Germany) with the Standard Method 5320B (APHA, AWWA, WEF et al., 1995).

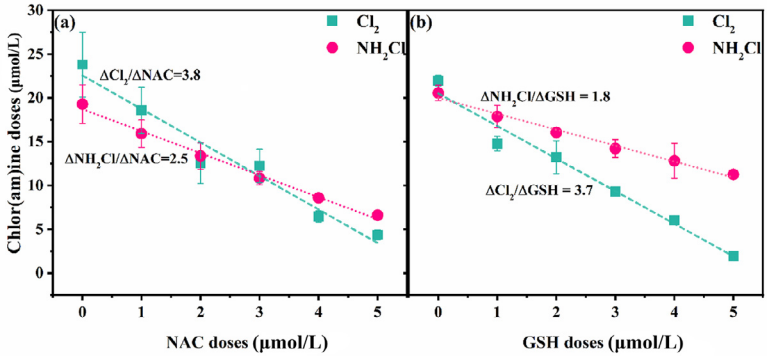

Fig. 1 – Stoichiometry of disinfectant-quenching agent reaction (reaction conditions: initial chlorine or monochloramine dose = 20.0 μmol/L, pH = 7.0, and reaction time = 10.0 min).

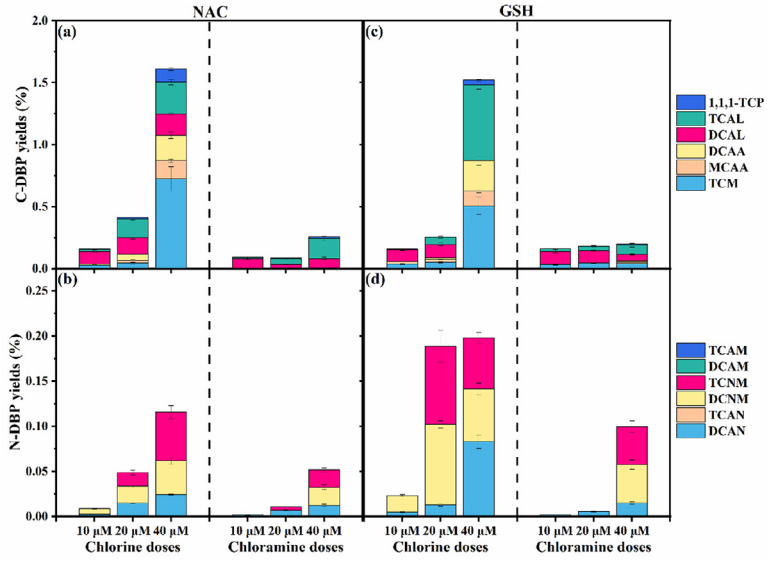

Fig. 2 – Formation of CX_3R-type DBPs during chlor(am)ination of NAC (a and b) and GSH (c and d) under following reaction conditions: NAC or GSH dose = 20.0 μmol/L, pH = 7.0 ± 0.2, temperature = 25.0 ± 0.5 °C, and time = 24.0 ± 0.5 hr.

2. Results and discussion

2.1. *Stoichiometry of disinfectant-quenching agent reaction*

The stoichiometry of the disinfectant-quenching agent reaction was determined by measuring the residual disinfectant with the addition of various quenching agent ranging from 0 μmol/L to 5.0 μmol/L at pH 7.0 after 10.0 min reaction. As shown in Fig. 1, the residual disinfectant decreased with the increases of NAC or GSH doses. A complete consumption of Cl_2 using NAC and GSH were observed with a Cl_2 : quenching agent ratio of 3.8 and 3.7 (slope of straight line in Fig. 1a and Fig. 1b), respectively, whereas the stoichiometry of NAC and GSH to NH_2Cl was 2.5 and 1.8 (slope of straight line in Fig. 1a and Fig. 1b), respectively. Stoichiometry of Cl_2-quenching agent reaction was consistent with a previous study which indicated that the stoichiometry of Cl_2 with NAC or GSH was 4 (Prütz, 1996). The lower stoichiometry of NH_2Cl with NAC or GSH than that of Cl_2 may be attributed to the weaker oxidizability (Deborde and von Gunten, 2008). According to previous studies, the sulfhydryl group (RSH) and amino group (R-NH_2) in NAC and GSH were the first and second reactive site for electrophilic attack by Cl_2 or NH_2Cl, respectively (Thomas et al., 1983; Folkes et al., 1995; Prütz, 1996). During chlor(am)ination of NAC or GSH, the sulfhydryl group was firstly transformed to sulfenyl chloride group (RSCl) via electrophilic substitution, which was further hydrolyzed to sulfenic acid (RSOH) as the initial products (Appendix A Fig. S2) (Deborde and von Gunten, 2008). Then RSOH can undergo quick hydrolysis and oxidation to yield the corresponding sulfinic acids (RSO_2H) and sulfonic acid (RSO_3H). Both chlorination and chloramination could achieve above reaction process (Thomas et al., 1983; Prütz, 1996). However, the reactivity of Cl_2 to amine group was several orders of magnitude higher than that of NH_2Cl (Deborde and von Gunten, 2008; Yu and Reckhow, 2017), for which the stoichiometry of NH_2Cl with NAC or GSH was lower than that of Cl_2.

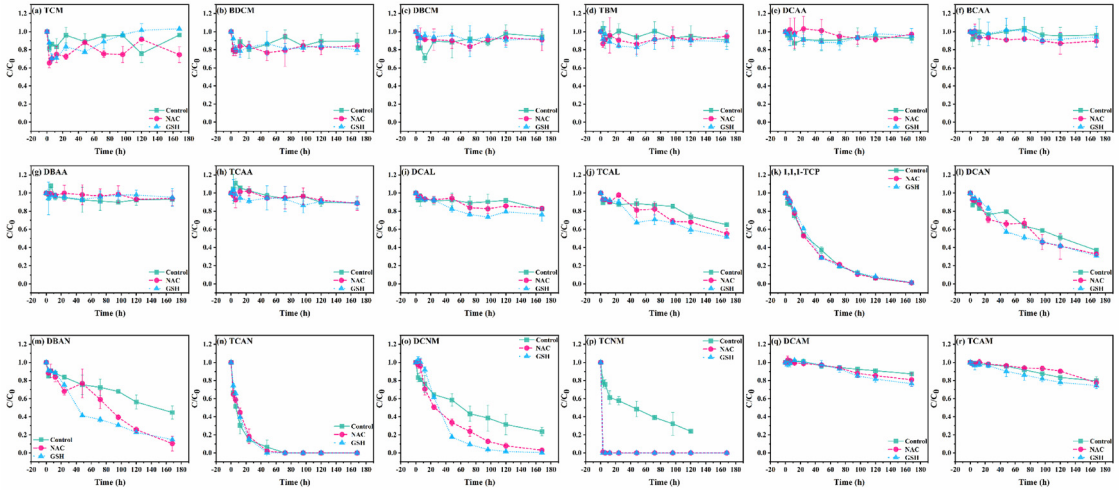

Fig. 3 – The stability of 18 CX_3R-type DBPs in the absence and presence of NAC or GSH (reaction conditions: initial DBP concentration = 50.0 μg/L, NAC or GSH concentration = 20.0 μmol/L, pH = 7.0, and temperature = 25.0 ± 0.5 °C).

2.2. *Formation of CX_3R-type DBPs during chlor(am)ination of NAC and GSH*

Fig. 2 shows the effect of disinfectant dose on the formation of CX_3R-type DBPs during chlor(am)ination of NAC and GSH. The aggregate carbonaceous DBP (C-DBP) yields (sum of TCM, monochloroacetic acid [MCAA], DCAA, DCAL, TCAL, and 1,1,1-TCP) from the chlorination of NAC and GSH increased from 0.16% ± 0.02% to 1.61% ± 0.18% and from 0.16% ± 0.01% to 1.52% ± 0.16% as the ratio of chlorine to NAC or GSH increased from 0.5 to 2.0. It should be noted that the increases of aggregate C-DBP yields were disproportionate with the increases of chlorine doses, and the aggregate C-DBP yields at lower chlorine doses (10.0 μmol/L and 20.0 μmol/L) were far lower than that at higher chlorine doses (40.0 μmol/L). Compared with chlorination, chloramination of NAC and GSH under same reaction condition produced less C-DBPs with the yields in the ranges of 0.09% ± 0.01% - 0.26% ± 0.03% and 0.16% ± 0.02% - 0.20% ± 0.03%, respectively. The aggregate C-DBP yields slightly increased with the increases of monochloramine dose. Aggregate nitrogenous DBP (N-DBP) yields (sum of DCAN, TCAN, DCNM, TCNM, DCAM, and TCAM) from chlor(am)ination of NAC and GSH under different disinfectant doses were far lower than aggregate C-DBP yields, which was consistent with our previous study (Ding et al., 2019b). When the molar ratio of chlor(am)ine to NAC or GSH was 0.5, the formation of N-DBP could be ignored. Although aggregate N-DBP yields from the chlor(am)ination of NAC and GSH increased with the increases of chlor(am)ine doses, the highest aggregate N-DBP yield was lower than 0.20%. According to above analysis, the formation of CX_3R-type DBPs during chlor(am)ination of NAC and GSH could be neglected when the molar ratio of chlor(am)ine to NAC or GSH was lower than 0.5, and free chlorine and monochloramine could be completely quenched under this condition.

2.3. *Stability of CX_3R-type DBPs in the presence and absence of NAC or GSH*

The stability of 18 CX_3R-type DBPs in the absence and presence of NAC or GSH was depicted in Fig. 3. The decreases of four THMs (TCM, BDCM, DBCM, and TBM), four HAAs (DCAA, BCAA, DBAA, and TCAA) and DCAL in the absence of NAC or GSH over 168 hr could be neglected (nearly less than 10.0%). Previous studies have demonstrated that the hydrolysis rate constants for these THMs and HAAs at pH 7.0 ranged from 2.3×10^{-8} hr^{-1} to 1.3×10^{-5} hr^{-1}, and the half-lives were longer than one year (Zhang and Minear, 2002; Chen, 2011). According to quantitative structure–activity relationship, the hydrolysis rate constant of DCAL at pH 7.0 was predicted to be 2.0×10^{-6} hr^{-1} (Chen, 2011). For this reason, the degradation kinetics of THMs, HAAs and DCAL in the absence and presence of NAC or GSH within 168 hr were not determined in this study. The stability analysis (Fig. 3a–i) showed that there were no significant differences in the concentrations of THMs, HAAs, and DCAL in the non-quenched sample, NAC-quenched sample, and GSH-quenched sample. Therefore, both NAC and GSH were suitable to quench disinfectant before the analysis of THMs, HAAs and DCAL.

TCAL, DCAN, DBAN, DCAM, and TCAM slightly underwent hydrolysis with pseudo-first order observed rate constants (k_{obs}) of 1.9×10^{-3} hr^{-1}, 5.2×10^{-3} hr^{-1}, 4.1×10^{-3} hr^{-1}, 0.9×10^{-3} hr^{-1}, and 1.4×10^{-3} hr^{-1}, respectively. The determined hydrolysis rate constants (k_h) of TCAL, DCAN, DBAN, DCAM, and TCAM were similar to previous studies (Table 1) (Glezer et al., 1999; Koudjonou and LeBel, 2006; Chen, 2011; Yu and Reckhow, 2015; Ding et al., 2018a). Owing to the typical time scale of sample holding process (e.g., 3 days), the concentrations of DBP species with k_h at 10^{-3} hr^{-1} level will reduce by around 20.0%. Thus, samples for the determination of TCAL, DCAN, DBAN, DCAM, and TCAM should be immediately analyzed to abate negative interference from hydrolysis.

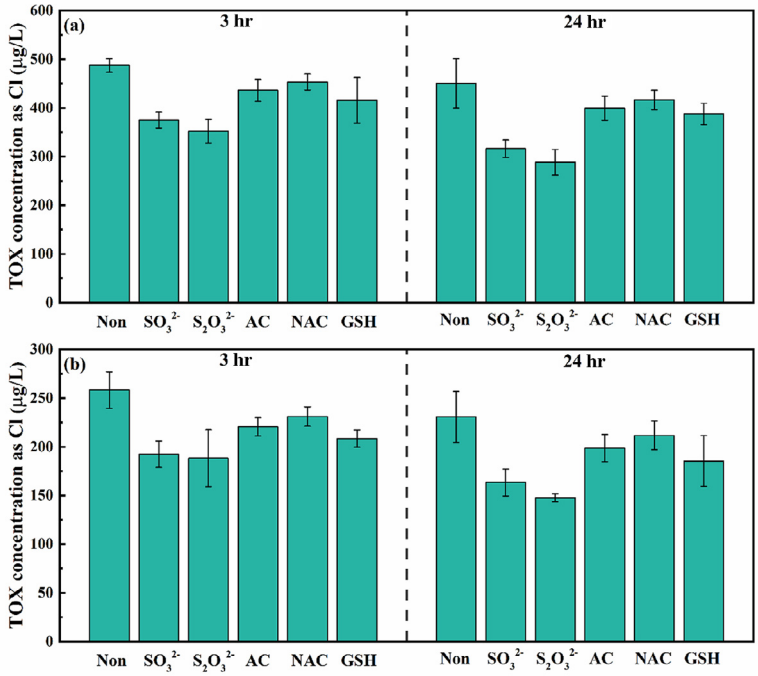

Fig. 4 – The decreases of TOX for chlorinated (a) and chloraminated (b) YSP filtered water in the absence and presence of quenching agent (reaction conditions: quenching agent concentration = 20.0 μmol/L, pH = 7.0, and temperature = 25.0 ± 0.5 °C).

Table 1 – The stability of the CX_3R-type DBPs in the absence and presence of NAC or GSH.

DBP species	k_h (Non-quenched)	k_h in ref	k_{obs} (NAC-quenched)	k_{obs} (GSH-quenched)
TCM	-	2.3×10^{-8} hr^{-1}	-	-
BDCM	-	4.3×10^{-7} hr^{-1}	-	-
DBCM	-	1.1×10^{-7} hr^{-1}	-	-
TBM	-	1.3×10^{-8} hr^{-1}	-	-
DCAA	-	$< 10^{-8}$ hr^{-1} (Predicted) [a]	-	-
BCAA	-	$< 10^{-8}$ hr^{-1} (Predicted) [a]	-	-
DBAA	-	$< 10^{-8}$ hr^{-1} (Predicted) [a]	-	-
TCAA	-	1.3×10^{-5} hr^{-1}	-	-
DCAL		2.0×10^{-6} hr^{-1} (Predicted) [a]	-	
TCAL	1.9×10^{-3} hr^{-1}	2.1×10^{-4} hr^{-1}	3.3×10^{-3} hr^{-1}	3.8×10^{-3} hr^{-1}
1,1,1-TCP	2.4×10^{-2} hr^{-1}	1.8×10^{-1} hr^{-1}; 6.4×10^{-3} hr^{-1}	2.4×10^{-2} hr^{-1}	2.4×10^{-2} hr^{-1}
DCAN	5.2×10^{-3} hr^{-1}	1.4×10^{-2} hr^{-1}; 2.3×10^{-3} hr^{-1}	6.5×10^{-3} hr^{-1}	7.1×10^{-3} hr^{-1}
DBAN	4.1×10^{-3} hr^{-1}	3.5×10^{-3} hr^{-1}; 4.0×10^{-3} hr^{-1}; 8.2×10^{-4} hr^{-1}	1.2×10^{-2} hr^{-1}	1.2×10^{-2} hr^{-1}
TCAN	7.9×10^{-2} hr^{-1}	5.4×10^{-1} hr^{-1}; 6.3×10^{-2} hr^{-1}; 1.3×10^{-2} hr^{-1}	6.6×10^{-2} hr^{-1}	7.7×10^{-2} hr^{-1}
DCNM	8.1×10^{-3} hr^{-1}	-	2.1×10^{-2} hr^{-1}	3.5×10^{-2} hr^{-1}
TCNM	1.0×10^{-2} hr^{-1}	-	1.7 hr^{-1}	3.3 hr^{-1}
DCAM	9.0×10^{-4} hr^{-1}	9.0×10^{-4} hr^{-1}	1.4×10^{-3} hr^{-1}	1.7×10^{-3} hr^{-1}
TCAM	1.4×10^{-3} hr^{-1}	9.0×10^{-4} hr^{-1}	1.2×10^{-3} hr^{-1}	1.8×10^{-3} hr^{-1}

[a] The hydrolysis rate constants for DCAA, BCAA, DBAA, and DCAL were adapted from Chen (2011).

The presence of NAC or GSH (20.0 μmol/L) slightly accelerated the destruction of TCAL, DCAN, DCAM, and TCAM, which was observed by comparing the difference between k_h and k_{obs}. The addition of NAC or GSH (20.0 μmol/L) as quenching agents slightly increased the decomposition of DBAN by ~2 folds with k_{obs} of 1.2×10^{-2} hr^{-1}. In general, the leaving tendency of the halogen in alkyl halides decreased in the following order: bromo– >> chloro–, which was attributed to the longer bond length and the lower dissociation energy of the bromine (Croue and Reckhow, 1989; Ding et al., 2018b). Although NAC or GSH promoted the reduction of TCAL, DCAN, DBAN, DCAM, and TCAM, the reductive dehalogenation rates of these DBPs by NAC or GSH were comparable to their k_h (Table 1). Moreover, it should be noted that the dose of NAC or GSH (20.0 μmol/L), which was sufficient to quench 80.0 μmol/L (5.6 mg/L) Cl_2, was in high excess. If the quenching agent dose was 100.0%–120.0% of the stoichiometric amount of the chlorine residual in a water sample, the molar ratios of dosed NAC/GSH to disinfec-

tant were generally lower than 0.5. Moreover, in general, the disinfectant residual in finished water is lower than 1.0 mg/L (15.0 μmol/L), for which the dosage of NAC/GSH for dechlorination is lower than 7.5 μmol/L. Accordingly, the reductive dehalogenation rates of these DBPs during water sample preservation may become lower and even could be ignored. Thus, NAC and GSH can be used to quench residual disinfectant before the analysis of above-mentioned DBPs.

Fig. 3k and n illustrate that 1,1,1-TCP and TCAN are immediately hydrolyzed, resulting in their quick loss within several hours under pH 7.0. The k_h values of 1,1,1-TCP and TCAN were 2.4×10^{-2} hr^{-1} and 7.9×10^{-2} hr^{-1}, respectively (Table 1), which were approximate to previously determined values (Glezer et al., 1999; Nikolaou et al., 2001; Chun et al., 2005; Yu and Reckhow, 2015). Based on the chemical kinetic calculation result, the half-lives of 1,1,1-TCP and TCAN were 28.9 hr and 8.8 hr, respectively, for which the determined concentrations of 1,1,1-TCP and TCAN in finished water and distribution system water were relatively lower than those of other CX_3R-type DBPs (Krasner et al., 2006; Bond et al., 2011). Unlike sodium sulfite and sodium thiosulfate (Croue and Reckhow, 1989; Shang et al., 2005; Kristiana et al., 2014), the impact of NAC or GSH (20.0 μmol/L) on 1,1,1-TCP and TCAN stabilities could be neglected by comparing the differences between k_h and k_{obs} (Table 1). As a result, the addition of NAC and GSH as quenching agents were suitable for the measurement of 1,1,1-TCP and TCAN. Notably, the determination of 1,1,1-TCP and TCAN should be conducted as quickly as possible to avoid the hydrolysis.

The decomposition of DCNM and TCNM in the absence and presence of NAC or GSH were observed in Fig. 3o and p. In the absence of NAC or GSH, DCNM and TCNM slightly underwent hydrolysis with k_h of 8.1×10^{-3} hr^{-1} and 1.2×10^{-2} hr^{-1}, respectively, indicating that HNMs should be analyzed as quickly as possible. The dramatic reductions of DCNM and TCNM were observed in the presence of NAC and GSH. The k_{obs} of DCNM decomposition in samples quenched with NAC and GSH increased by 1.6 folds and 3.3 folds to 2.1×10^{-2} hr^{-1} and 3.5×10^{-2} hr^{-1}, respectively. TCNM completely disappeared after 3 hr in the presence of 20.0 μmol/L NAC or GSH, which was also observed when TCNM was decomposed by sodium sulfite, sodium thiosulfate, and AC (Croue and Reckhow, 1989; Kristiana et al., 2014). The evolution of TCNM by NAC and GSH was further investigated by shortening the reaction time. As shown in Appeendix A Fig. S3, TCNM was readily reduced to DCNM by NAC and GSH within 120.0 min and the k_{obs} of TCNM degradation by NAC and GSH were 1.7 hr^{-1} and 3.3 hr^{-1}, respectively, which were lower than that by sodium sulfite (4.1 hr^{-1}) (Croue and Reckhow, 1989). The sum of DCNM and TCNM decreased with the increase of reaction time, indicating the further dehalogenation of DCNM. Compared with other CX_3R-type DBPs, the stability of DCNM and TCNM was significantly affected by NAC and GSH. This phenomenon can be explained by the fact that the higher electron-withdrawing ability of nitro group (bound to carbon atom of the CX_3- group) than other functional groups (e.g., hydrogen, carboxyl, aldehyde, nitrile, and amide group) makes the carbon atom of the CX_3- group more electrophilic, thus increasing SN2 reaction rate (Ding et al., 2018b). Similar to sodium sulfite, sodium thiosulfate and AC (Croue and Reckhow, 1989; Liew et al., 2012; Kristiana et al., 2014), the rapid degradation of TCNM by NAC or GSH limits their use in the analysis of TCNM. Alternatively, the samples should be analyzed immediately without the addition of any quenching agent.

2.4. *Effects of various quenching agents on the determination of TOX*

Effects of various quenching agents (e.g., NAC, GSH, sodium sulfite, sodium thiosulfate, and AC) on the determination of TOX were also investigated. The selection of 3 hr and 24 hr as quenching time was corresponding to that in laboratory and practical sampling, respectively. The addition of a relatively high amount of quenching agents was to amplify the TOX variation. Chlorination and chloramination of YSP filtered water produced 463.2 ± 32.7 μg/L and 255.3 ± 31.1 μg/L of TOX as Cl before quenching. The variation of TOX in non-quenched samples after 3 hr of reaction time could be neglected (< 5.0%), which was consistent with a previous study (Liu and Zhang, 2013). As reaction time increased to 24 hr, TOX in both chlorinated and chloraminated samples slightly decreased to 450.3 ± 50.9 μg/L and 230.6 ± 26.1 μg/L as Cl, respectively. This phenomenon reflected that most of halogenated DBPs were not decomposed over 24 hr. Compared with non-quenched samples, TOX decreased by 23.1% and 27.8% to 374.7 ± 16.3 μg/L and 351.8 ± 24.4 μg/L when chlorinated samples were quenched with sodium sulfite and sodium thiosulfate for 3 hr. After the addition of sodium sulfite and sodium thiosulfate, TOX in chloraminated samples decreased by 25.5% and 27.1% to 192.3 ± 13.6 μg/L and 188.1 ± 29.3 μg/L. As the quenching time increased to 24 hr, the continuous decreases of TOX in samples quenched with sodium sulfite and sodium thiosulfate were observed, indicating that quenching with overdosed sodium sulfite and sodium thiosulfate would exert substantially negative impacts on TOX determination. The decreases of TOX in samples quenched with AC, NAC, and GSH over 3 hr were relatively low, ranging from 7.0% to 19.3%. With the increases of quenching time to 24 hr, the reduction of TOX in samples quenched with AC (12.0%), NAC (8.0%), and GSH (13.0%–19.0%) was lower than those quenched with sodium sulfite (30.0%) and sodium thiosulfate (36.0%). Moreover, the effect of water matrix on the performances of various quenching agents for TOX determination was also compared. As shown in Appendix A Fig. S4, similar results were observed in four chlorinated samples. In general, the negative impact of five quenching agents on TOX determination decreased in the following order: sodium thiosulfate > sodium sulfite > GSH ≥ AC ≥ NAC. Accordingly, NAC and GSH are suitable for the analysis of TOX as quenching agents.

3. Conclusions

This study evaluated the performances of NAC and GSH as quenching agents in the analysis of seven classes of CX_3R-type DBPs and TOX. The reactivity of sulfhydryl group in NAC and GSH toward chlorine and chloramine were several orders of magnitude higher than other functional groups, for which the sulfhydryl group was the first reactive site for electrophilic attack by Cl_2 or NH_2Cl. The stoichiometry of Cl_2 to NAC and

GSH over 10.0 min was 3.8 and 3.7, respectively, whereas the stoichiometry of NH_2Cl to NAC and GSH was lower compared to Cl_2, which was attributed to the weaker reactivity of NH_2Cl to amine group. Formation of CX_3R-type DBPs during chlor(am)ination of NAC and GSH did not adversely affect the analysis of CX_3R-type DBPs when the molar ratio of Cl_2 or NH_2Cl to NAC or GSH was lower than 0.5, and Cl_2 and NH_2Cl could be completely quenched under this condition. Although NAC or GSH significantly destructed HNMs, the use of NAC or GSH as quenching agents had no/little effects on the stability of THMs, HAAs, HALs, HKs, HANs, and HAMs. 1,1,1-TCP, TCAN, and TCNM should be analyzed as soon as possible since they were shown to be quickly hydrolyzed. The negative impact of five quenching agents on TOX determination decreased in the following order: sodium thiosulfate > sodium sulfite > GSH ≥ AC ≥ NAC. According to the results of this study, NAC and GSH were considered to be ideal quenching agents for the analysis of THMs, HAAs, HALs, HKs, HANs, HAMs, and TOX. HNMs should be analyzed immediately without the addition of any quenching agent.

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Appendix A Supplementary data

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jes.2022.01.033.

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