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Formation and control of disinfection byproducts and toxicity during reclaimed water chlorination: A review

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ABSTRACT

Chlorination is essential to the safety of reclaimed water; however, this process leads to concern regarding the formation of disinfection byproducts (DBPs) and toxicity. This study reviewed the formation and control strategies for DBPs and toxicity in reclaimed water during chlorination. Both regulated and emerging DBPs have been frequently detected in reclaimed water during chlorination at a higher level than those in drinking water, indicating they pose a greater risk to humans. Luminescent bacteria and *Daphnia magna* acute toxicity, anti-estrogenic activity and cytotoxicity generally increased after chlorination because of the formation of DBPs. Genotoxicity by *umu*-test and estrogenic activity were decreased after chlorination because of destruction of toxic chemicals. During chlorination, water quality significantly impacted changes in toxicity. Ammonium tended to attenuate toxicity changes by reacting with chlorine to form chloramine, while bromide tended to aggravate toxicity changes by forming hypobromous acid. During pretreatment by ozonation and coagulation, disinfection byproduct formation potential (DBPFP) and toxicity formation potential (TFP) occasionally increase, which is accompanied by DOC removal; thus, the decrease of DOC was limited to indicate the decrease of DBPFP and TFP. It is more important to eliminate the key fraction of precursors such as hydrophobic acid and hydrophilic neutrals. During chlorination, toxicities can increase with the increasing chlorine dose and contact time. To control the excessive toxicity formation, a relatively low chlorine dose and short contact time were required. Quenching chlorine residual with reductive reagents also effectively abated the formation of toxic compounds.

Contents

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Introduction

The multiple pressures of climate change, population growth, urbanization and industrialization have led to declining availability of fresh water resources (Bagatin et al., 2014; Sun et al., 2016). According to the WRG (2009), the world is likely to be confronted with a 40% water deficit if current trends continue. Accordingly, reclaimed water has become an essential alternative water resource to address the ever-increasing demand for water resources worldwide (Tortajada and Nam Ong, 2016; Fatta-Kassinos et al., 2016) and is now extensively used for industry, agriculture, landscaping, and even potable reuse (Asano et al., 2007). Given its stable quantity, developed wastewater treatment technologies, and economic and social benefits, reclaimed water is likely to play a critical role in future water resources.

Because it contains a variety of pathogens, reclaimed water needs to be disinfected to minimize the health risk it poses to humans (Li et al., 2013). Despite the development of many alternative disinfectants, including chloramines, chlorine dioxide, ozone, and UV, disinfection with chlorine is still the technology most extensively utilized to ensure the safety of reclaimed water (US EPA, 2004). In addition to being applied at the end of treatment to inactivate pathogens, chlorination is widely used to provide residual chlorine in distribution systems to control the regrowth of microorganisms, as well as to destroy biofilms during backflushing of biological activated carbon and reverse osmosis system.

Although it inactivates pathogens, the extensive use of chlorination has led to concern regarding the formation of disinfection byproducts (DBPs) (Chu et al., 2016a). During chlorination, chlorine reacts with precursors, primarily dissolved organic matter (DOM), to form various DBPs (Richardson, 2011). Most identified individual DBPs and the mixture of DBPs (such as the total organic halogen; TOX) have been shown to be cytotoxic, genotoxic and carcinogenic (Richardson et al., 2007). Given the potential ecological and health risks that might be posed by DBPs, researchers have focused on the precursors, formation, speciation, toxicity, and identification of DBPs for years (Chu et al., 2016b, 2016c; Krasner et al., 2006; Plewa et al., 2004a; Wu et al., 2016). DBPs in drinking water have been studied and reviewed in detail because of their potential for direct contact and ingestion by humans; however, it is harder to study DBPs in chlorinated reclaimed water because of the diversity and complexity of water quality and precursors. The concentration, reactivity, and composition of DOM, which are precursors of DBPs, in reclaimed water are significantly different from those in drinking water (Chang et al., 2001; Hu et al., 2016; Hudson et al., 2007), which inevitably leads to the formation of different DBPs in varying concentrations and subsequent harmful effects (Sirivedhin and Gray, 2005). However, the formation of DBPs in chlorinated reclaimed water needs to be further explored.

Toxicity studies have been conducted to understand the risk posed by chlorinated water, but because most of these have investigated individual DBPs, our understanding is limited regarding real-world mixtures of DBPs in chlorinated water. Thus, many investigators have evaluated comprehensive bio-toxicity (Bayo et al., 2009; Patterson et al., 1995; Rice et al., 2008; Watson et al., 2012; Yang et al., 2014). For years, different bioassay methods with subject organisms of different levels have been developed to evaluate toxicity (Jeong et al., 2012; Narotsky et al., 2012; Patterson et al., 1995; Rice et al., 2008; Simmons et al., 2002, 2004). Assays typically and widely applied to evaluate the safety of reclaimed water include those of acute toxicity, such as the luminescent bacteria test and *Daphnia magna* test; evaluation of genotoxicity by the *umu*-test, which measures the degree of repair of the injured DNA of *Salmonella typhimurium* TA1535/pSK1002 caused by genotoxic substances (Wang et al., 2007a, 2007b; Wu et al., 2010); those that investigate endocrine disruption, such as estrogenic activity and anti-estrogenic activity, which measure the β-galactosidase induced and inhibited by estrogenic and anti-estrogenic chemicals, respectively, in yeast cells with the rat estrogen receptor ERα and the coactivator TIF2 (Wu et al., 2009; Tang et al., 2014a, 2014b); and tests of cytotoxicity, which measure the viability of mammalian cells or human cells under the stress of xenobiotics (Plewa et al., 2004a; Yang et al., 2015). These methods have been widely adopted to assess the toxicity of reclaimed water, and they are all helpful indicators for controlling water safety from different perspectives.

Notably, significant changes in toxicity have been observed in reclaimed water after chlorination, and different bioassay methods have exhibited different trends (Wang et al., 2007a, 2007b). Accordingly, elucidating the changes in different toxicity is of importance to reveal the potential risk during reclaimed water chlorination. Moreover, changes in toxicity would be obviously impacted by water quality, especially for reclaimed water, which frequently shows large variations in water quality. In some cases, complex wastewater sources and improper treatment cause reclaimed water to be vulnerable to high ammonia and high bromide concentrations (Tang, 2014; Tang et al., 2014a; Wu et al., 2010). Thus, the impact of ammonia and bromide on the formation of toxic materials is not negligible.

In most cases, formation of DBPs and toxicity increase in reclaimed water after chlorination; therefore, strategies are required to minimize this risk (Blatchley et al., 1997). Pretreatment for removing DOM from reclaimed water is expected to be an effective approach since DOM is the major precursor. A number of pretreatments have been widely applied before chlorination during wastewater reclamation to eliminate DOM, including coagulation, ozonation, and adsorption (Tang, 2014; Tang et al., 2014b). Different technologies exhibited various performance and preferential removal of different components, leading to the different removal of DBPs and toxicities (Liu et al., 2016; Zhang et al., 2013). Furthermore, each component in the DOM makes a different potential contribution to the formation of DBPs and toxicity during chlorination (Han et al., 2015; Zhang et al., 2009, 2010). Therefore, identification and elimination of the key components in DOM is conductive to precisely minimizing the risk. Moreover, the operation conditions for chlorination would influence the DBPs and toxicity formation. It is ideal to inactivate pathogens while generating as few DBPs as possible. It is thusly necessary to take operation conditions into account during treatment.

This paper reviewed the formation and control of DBPs and toxicities during reclaimed water chlorination. Levels of DBPs, including regulated trihalomethanes (THMs) and haloacetic acids (HAAs), emerging nitrogenous DBPs, and TOX were summarized. Changes in toxicity of reclaimed water during chlorination based on the luminescent bacteria acute toxicity, *D. magna* test, *umu*-test, estrogenic activity, anti-estrogenic activity, and cytotoxicity have been investigated and the impact of ammonia and bromide on their formation was given. The control strategies for DBPs and toxicity formation, including pretreatments such as coagulation and ozonation, operation conditions and post treatment, were summarized.

1. Data collection and quality control

Data in this paper were collected from literature on DBPs and toxicities of reclaimed water over the last 15 years. The term "reclaimed water" in this paper refers to the generalized treated wastewater, including secondary effluent and tertiary effluent of wastewater treatment plant. The water quality in the reviewed literature was analyzed within 24 hr after sampling. The experiment for DBPs and toxicity determination also conducted within 24 hr after sampling. In the reviewed literature, each analysis was conducted by duplicate or triplicate.

2. Formation of DBPs during reclaimed water chlorination

The collected statistics of DBP levels found in reclaimed water during chlorination are shown in Fig. 1. Different kinds of DBPs, including regulated DBPs, emerging DBPs and TOX were given. The median values of four THMs, chloroform (TCM), bromodichloromethane (BDCM), dibromochloromethane (DBCM) and bromoform (TBM), were 12.50, 14.98, 23.77 and 4.10 μg/L, respectively, which were in line with a survey about the DBP levels in WWTPs effluent in the United States (THM4 ranging from 11 to 92 μg/L) (Krasner et al., 2009). The mean values of the four THMs were 64.86, 22.21, 22.50 and 9.00 μg/L, respectively. The mean level was reportedly 38 μg/L for THM4 (four THMs in total) in drinking water (McGuire et al., 2003), indicating that the THM concentrations in reclaimed water were much higher than those in drinking water. The median values of the five regulated HAAs, chloroacetic acid (MCAA), dichloroacetic acid (DCAA), trichloroacetic acid (TCAA), bromoacetic acid (MBAA), and dibromoacetic acid (DBAA), were 10.2, 8.2, 4.6, 4.2, and 0.8 μg/L and the mean values were 12.8, 21.8, 14.7, 4.9, and 4.7 μg/L, respectively. The mean value of HAA5 (five HAAs in total) in drinking water was reportedly 23 μg/L (McGuire et al., 2003), indicating that reclaimed water also forms more HAAs during chlorination. Evaluation of bromo-chloro-HAAs, such as bromochloroacetic acid (BCAA) and bromodichloroacetic acid (BDCAA), revealed that the formed concentrations were comparable to HAA5 during chlorination (Fig. 1). Although chlorination tended not to generate iodinated DBPs since chlorine oxidizes iodide to iodate (Bichsel and Von Gunten, 2000; Plewa et al.,

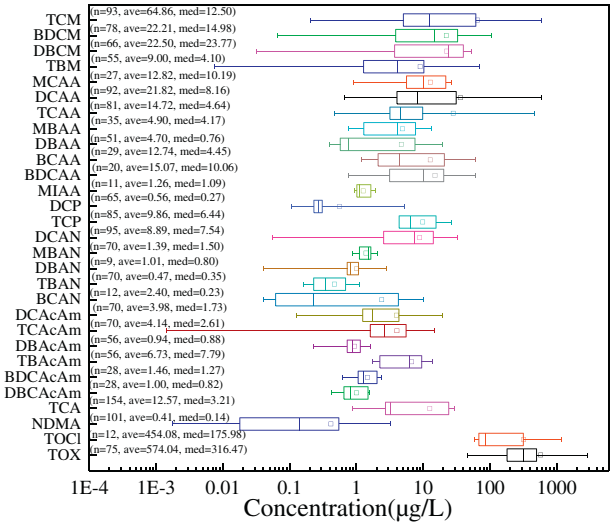

Fig. 1 – Levels of disinfection byproducts (DBPs) found in reclaimed water during chlorination. The two whiskers in the box chart represent the 5th and 95th percentiles. The three lines in the box chart represent the 25th, 50th, and 75th percentiles. (The literature containing the original data for composing the figure was listed in Appendix A Text S1.).

2004a, 2004b), iodoacetic acid was also found at the μg/L level during reclaimed water chlorination.

Different classes of emerging DBPs were also found in reclaimed water. Haloketones, such as 1,1-dichloropropanone (DCP) and 1,1,1-trichloropropanone (TCP), were found in chlorinated reclaimed water with medians of 0.27 and 6.44 μg/L, respectively. The levels of TCP were higher than those of DCP, which was consistent with the levels in drinking water (McGuire et al., 2003). Haloacetonitriles, including dichloroacetonitrile (DCAN), bromoacetonitrile (MBAN), dibromoacetonitrile (DBAN), tribromoacetonitrile (TBAN), and bromochloroacetonitrile (BCAN), were found at low μg/L levels, and DCAN was the most prevalent species. Levels of haloacetamides, such as dichloroacetamide (DCAcAm), trichloroacetamide (TCAcAm), dibromoacetamide (DBAcAm), tribromoacetamide (TBAcAm), bromodichloroacetamide (BDCAcAm), and dibromochloroacetamide (DBCAcAm), were also found at low μg/L levels. Notably, chlorohydrate (TCA) and *N*-nitrosodimethylamine (NDMA), which are both rather genotoxic and carcinogenic DBPs, were found in reclaimed water at higher levels (with medians of 3.2 μg/L and 10 ng/L, respectively) than drinking water (Richardson et al., 2007). The levels of total organic chlorine (TOCl) and TOX were also summarized in Fig. 1. The median values of these compounds were 176.0 and 316.5 μg/L, respectively, which were also higher than the median levels reported in drinking water from a U.S. Nationwide DBP Study of 12 drinking water plants that focused on locations with higher dissolved organic carbon (DOC) and bromide (Krasner et al., 2006).

In general, different classes of DBPs in reclaimed water were found at higher levels during chlorination than in drinking water. Therefore, the risk brought by DBPs in reclaimed water requires a great deal of attention. While the data on reclaimed water is limited by a smaller number of studies relative to huge amount of data from the U.S. Information Collection Rule (McGuire et al., 2003), it does appear to show higher levels of DBPs formed.

3. Changes of toxicity during chlorination

3.1. *Changes in toxicity*

Despite the formation of DBPs during reclaimed water chlorination being widely studied, it is not possible to detect every byproduct present because of limitations in sample preparation, analytical methods and the cost of manpower and material resources. Therefore, the potential ecological and health risk induced by chlorination cannot be estimated by single or only a few identified DBPs. However, bio-toxicity tests can provide direct assessment of different biological effects of chlorinated reclaimed water.

The luminescent bacteria test is widely used to represent the acute toxicity in both chlorinated effluents of wastewater treatment plants and batch studies (Watson et al., 2012; Wei et al., 2006; Wang et al., 2007a). In this test, the effects of treated water samples are quantified based on the decrease of luminescence intensity of test bacteria. Wei et al. (2006) studied changes in the luminescent bacteria toxicity of wastewater during the reclamation process, including activated sludge, coagulation and microfiltration, founding that the toxicity decreased significantly unless there was a pre-chlorination step before coagulation, sedimentation or a subsequent disinfection with chlorine. As shown in Fig. 2a, the relative toxicity (defined as the ratio of toxicity after chlorination over the toxicity before chlorination) increased significantly after chlorination, generally to 2 to 3 times the original toxicity. This indicates the formation of toxic byproducts during chlorination since the residual chlorine was diminished or not detected before the bioassays. The toxicity values estimated in these studies ranged widely from 1 to 18 times because of the different chlorine dosage and contact times, as discussed later in this review.

D. magna is a small plankton crustacean that is sensitive to water quality; therefore, it has been a common subject organism of ecotoxicology research. The mortality, reproduction and movement inhibition of *D. magna* can be used to assess the acute toxicity of WWTP effluent before and after chlorination. In this paper, toxicity by mortality of *D. magna* was reviewed. Fig. 2b presents the opposite trends in estimated toxicity values according to different reports. As shown in the figure, 78% of these values increased, while the others had a decreasing trend. Blatchley et al. (1997) claimed that wastewater did not elicit a substantial toxicological response before or after chlorination. In contrast, an increase in *D. magna* toxicity was detected in other studies (Kontana et al., 2009; Cao et al., 2009). Notably, a mortality of 100% was frequently detected, despite variations in chlorine dosage and contact time. Moreover, the 48 hr mortality of neonates was still 70%, even when the chlorinated water was diluted by 4 times (Cao et al., 2009).

Genotoxicity focuses on the DNA and/or chromosome damage induced by exogenous chemicals. Methods of measuring short-term genotoxicity, such as the *umu*-test, are helpful in monitoring the genotoxicity of DBPs and the presence of unknown genotoxic chemicals in wastewater (Wu et al., 2010; Wang et al., 2007b). The *umu*-test determines genotoxicity by measuring the β-galactosidase activity, which correlates to the extent of DNA lesions (ISO, 2000), was reviewed in this paper. Although the evaluation method is highly standardized, the effects of chlorination on genotoxicity of wastewater are more complex than for other bioassays. As shown in Fig. 2c, genotoxicity increased and decreased by 45% and 55%, respectively. Moreover, the genotoxicity was reduced by more than a half during chlorination in about 35% of water samples. The toxicity values could be less than 20% of the original water samples (Wu et al., 2010), or up to 2–4 times higher after chlorination in other studies (Wei et al., 2012; Wang et al., 2007b). These findings suggest that variations in genotoxicity may be related to water quality.

Endocrine disrupting chemicals (EDCs) have raised a great deal of concern due to their ability to disturb the endocrine systems of humans and animals (Schilirò et al., 2009). The estrogenic/anti-estrogenic chemicals in wastewater mimic or antagonize the actions of steroid hormones, which has been reported to affect the reproduction and development of animals (Wu et al., 2009). Oxidation processes, including chlorination, are promising options for controlling the estrogens in water treatment (Lee et al., 2008). Unlike estrogenic chemicals, the estrogenic activity measured by *in vitro* bioassays

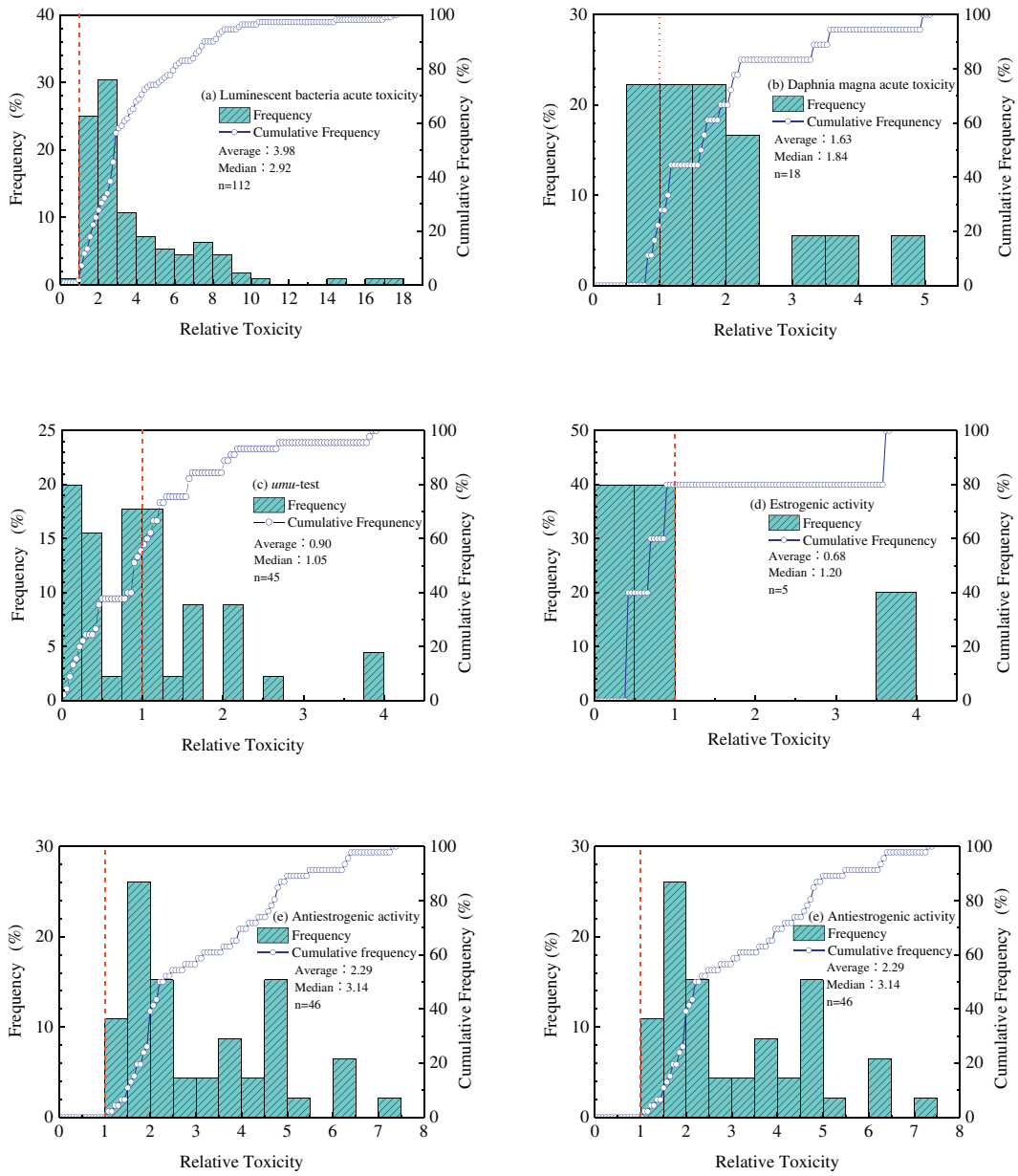

Fig. 2 – Cumulative distribution of different toxicities after reclaimed water chlorination. The relative toxicity refers to the ratio of toxicity after chlorination over toxicity before chlorination. The dash line represents the original toxicity of unchlorinated reclaimed water. (a) Luminescent bacteria acute toxicity; (b) *D. magna* acute toxicity measured by mortality; (c) genotoxicity measured by the *umu*-test; (d) estrogenic activity; (e) anti-estrogenic activity; (f) cytotoxicity. (The literature containing the original data for composing the figure was listed in Appendix A Text S2.)

during wastewater chlorination have not been thoroughly investigated. As shown in Fig. 2d, the estrogenic activity decreased on most occasions. The level of estrogenic activity generally decreased to 40%–90% of the original wastewater (Wu et al., 2009; Schilirò et al., 2009; Zeng et al., 2016), which indicated that the estrogenic chemicals were reduced by chlorine to produce products with less estrogenic activity. However, Watson et al. (2012) reported both increases and decreases in the same WWTP effluent on different occasions, and an increase of almost 4 times was detected in another sample after chlorination. It is possible that a mixture of industrial estrogen mimics, natural estrogens, and anti-estrogens present in the estimated samples at trace concentrations caused the mixed results.

In contrast to estrogenic chemicals, anti-estrogenic chemicals have a de-feminization effect and have been shown to disrupt the estrous cycles and affect the fertility of female animals. Considering the wide detection in wastewater and reclaimed water, anti-estrogenic activity is worth studying as an important endocrine disruption effect (Wu et al., 2014). It is obvious that chlorination increased the anti-estrogenic activity by 1 to 7.5 times that of the original water (Fig. 2e), which might result from the formation of anti-estrogenic DBPs. Furthermore, aromatic amino acids and humic/fulvic

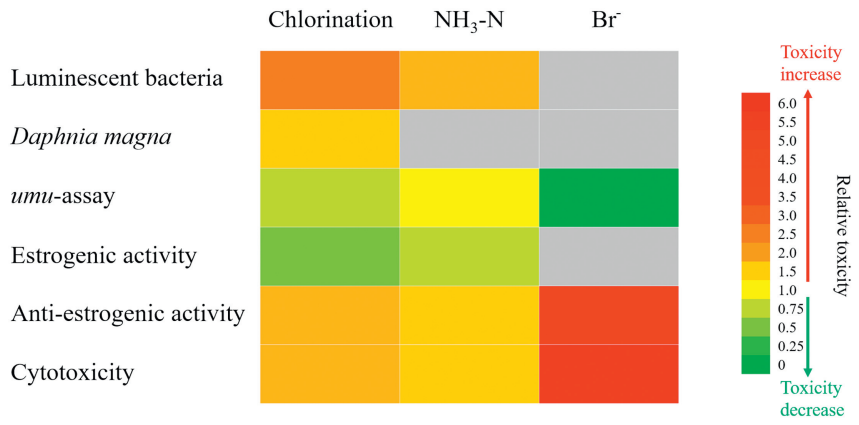

Fig. 3 – Variations in toxicities after chlorination and the influence of NH_3-N and Br^-. Plotted are the medians of ratios (%) calculated from the toxicity after chlorination over toxicity before chlorination. A ratio > 100% represents an increase of toxicity, while a ratio < 100% represents a reduction. Gray blocks indicate unavailable values. (The literature containing the original data for composing the figure was listed in Appendix A Text S2.)

acids have been identified as important precursors of anti-estrogenic byproducts (Wu et al., 2009; Tang et al., 2014a, 2014b).

When compared with bioassays of bacteria or lower animals, cytotoxicity assays, which evaluate the toxic effects using mammalian cells, provide a more valuable reference to human health risks. *In vitro* testing systems such as 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT), neutral red uptake and adenosine triphosphate assays can be utilized to estimate cell viability during evaluation of cytotoxicity. However, the MTT signal was observed to be increased by DOMs from secondary effluents, indicating that it might not be a suitable method for analysis of wastewater (Yang et al., 2015). The cytotoxicity level increased from 1 to 6 times in most cases (Fig. 2f), and the frequency seems to distribute equably here. Fukushima et al. (2014) reported an increase in cytotoxicity after chlorination of active sludge effluents with occasional decreases in S-MBR. These findings imply that the water qualities could affect variations in cytotoxicity.

3.2. *Influence of water quality on toxicity*

As discussed in Section 3.1, the toxicity varied among water samples, indicating that water quality had notable impact on these values. The effects of NH_3-N and bromide on different toxicities are shown in Fig. 3. As the NH_3-N levels increased, the luminescent acute toxicity, anti-estrogenic activity, and cytotoxicity of chlorinated water decreased obviously (Wang et al., 2007a; Tang et al., 2014a, 2014b; Yang, 2016). This reduction might have been caused by the reaction of ammonia nitrogen with free chlorine to form combined chlorine (chloramine), which is less reactive and therefore produces fewer toxic byproducts than free chlorine. However, in the case of genotoxicity and estrogenic activity, NH_3-N tended to inhibit the decrease in toxicity during chlorination since fewer toxic chemicals were removed (Wu et al., 2014). Moreover, the formation of chloramine led to N-DBPs generation, which caused an increase in genotoxicity (Wang et al., 2007a, 2007b).

The bromide in wastewater promotes a significant decrease in the genotoxicity, even when there are high NH_3-N concentrations (Fig. 3). This is primarily attributed to the removal of some of the genotoxic compounds during chlorination, despite the formation of brominated DBPs, which are more genotoxic than chlorinated DBPs. Therefore, the enhanced genotoxicity reduction suggests that the hypobromous acid formed during chlorination destroyed more genotoxic compounds than free chlorine and chloramines (Wu et al., 2010). However, the anti-estrogenic activity and cytotoxicity were found to be higher in the presence of bromide as a result of the brominated DBP formation (Wu et al., 2014; Yang, 2016).

In conclusion, ammonia tended to attenuate toxicity changes by reacting with chlorine to form chloramine. For toxicities that increased after chlorination, ammonia tended to attenuate the increase because it formed fewer DBPs. However, for the toxicities that decreased after chlorination, ammonia tended to weaken the decrease, and even increase the toxicity because of the weak oxidizability of chloramine and the formation of nitrogenous DBPs. Conversely, bromide tended to aggravate changes in toxicity by forming hypobromous acid during chlorination, which increased the anti-estrogenic activity and cytotoxicity by forming more toxic brominated DBPs and decreased the genotoxicity *via* its higher oxidizability to destroy genotoxic compounds. It could also be inferred that, during chlorination, changes in luminescent acute toxicity, anti-estrogenic activity and cytotoxicity were more dependent on the formation of toxic byproducts, while variations in genotoxicity and estrogenic activity were mainly influenced by the removal of toxic chemicals from wastewater.

4. Control of DBPs and toxicities

4.1. *Control of precursors by pretreatment*

4.1.1. *Relationship between DOC removal and DBPs control*

DOM is the major precursor for DBPs, and DOC is the most comprehensive parameter that is most commonly used to

characterize the concentration of DOM. Removing DOM from reclaimed water before chlorination is expected to be an effective method of controlling DBP formation. Assessing the formation potential (FP) of DBPs and toxicity after pretreatment helps us understand the performance of different pretreatment. During wastewater reclamation, different advanced treatments, including coagulation, ozonation, adsorption and soil aquifer treatment (SAT) exhibited a wide range of performance for eliminating DOC (Fig. 4a and b). In general, the removal of DOC increased with increased reagent dose and prolonged retention time (Liu et al., 2016; Zhang et al., 2013). While consistent DOC removal was observed under different treatments, the elimination of DBPFP and TFP differed greatly.

Coagulation resulted in DOC removal of 2%–85% (Fig. 4a and b), while THMFP, HAAFP and TFP of zebra embryo developmental toxicity were reduced by 45%–86%, 3%–61% and 39%–64%, respectively, indicating coagulation efficiently removed the precursors for THMs, HAAs and zebra embryo developmental toxicity to some degree. However, NDMAFP increased in most cases after coagulation. This might have been because coagulation preferentially removed the precursors that consumed chlorine, but were responsible for little NDMAFP (Park et al., 2015). Dissolved organic nitrogen (DON) containing amine was found to be an important precursor for NDMA, while coagulation limited the removal of DON (Hu et al., 2016). Therefore, the organic materials remaining after coagulation had high potential to form NDMA; thus, increased NDMAFP was observed after coagulation. Furthermore, some coagulants containing dimethylamine could also contribute to the formation of NDMA, increasing the levels of NDMAFP (Park et al., 2009). Moreover, as the DOC was reduced by 3%–38%, anti-estrogenic activity formation potential (AEAFP) showed varied removal (from –94% to 42%) after coagulation, indicating coagulation was inefficient for removal of precursors of AEAFP. The organic materials consuming chlorine removed during coagulation might not be the precursors for AEAFP, thus causing the chlorine to transform the precursors to anti-estrogenic byproducts on a large scale (Tang et al., 2013).

Ozonation is another process that is widely adopted during wastewater reclamation. As a strong oxidant, ozone tends to react with unsaturated bonds in DOM and transform them into small molecules, even directly mineralizing a portion of DOM, thus leading to the diminution of DOC (Tang et al., 2014a, 2014b). As shown in Fig. 4a and b, DOC was reduced by 2% to 42% during ozonation. However, ozonation was limited to reduce THMFP and HAAFP in some cases (Fig. 4a). The maximum removal of THMFP was 21%, while in more cases ozonation increased the THMFP and HAAFP. The maximum enhancement of HAAFP even approached 100% after ozonation. The enhanced DBPFP could be explained by the transformation of DOM, of which the products after ozonation might have greater potential to form THMs and HAAs (Cao et al., 2009). Evaluation of FP revealed that both AEAFP and zebra embryo TFP were reduced after ozonation (Fig. 4b). The maximum FP reduction of anti-estrogenic activity and zebra embryo toxicity were 53% and 64%, respectively, indicating that the toxicity precursors were degraded effectively during ozonation. Other treatments, including SAT and activated carbon adsorption, were also efficient at eliminating DOC, and both showed good DBPFP removal (Fig. 4a).

In conclusion, as shown in Fig. 4a and b, each pretreatment was efficient at DOC removal to some extent, while the FP removal of DBPs and toxicities varied greatly. In some cases, the DOC removal was even accompanied by increased DBPs and toxicities. Moreover, the DBPFP or TFP removal showed poor correlation with DOC removal. Therefore, it is difficult to infer the reduction of DBPFP or TFP through DOC removal. Thus, simply controlling DOC is limited to some extent and

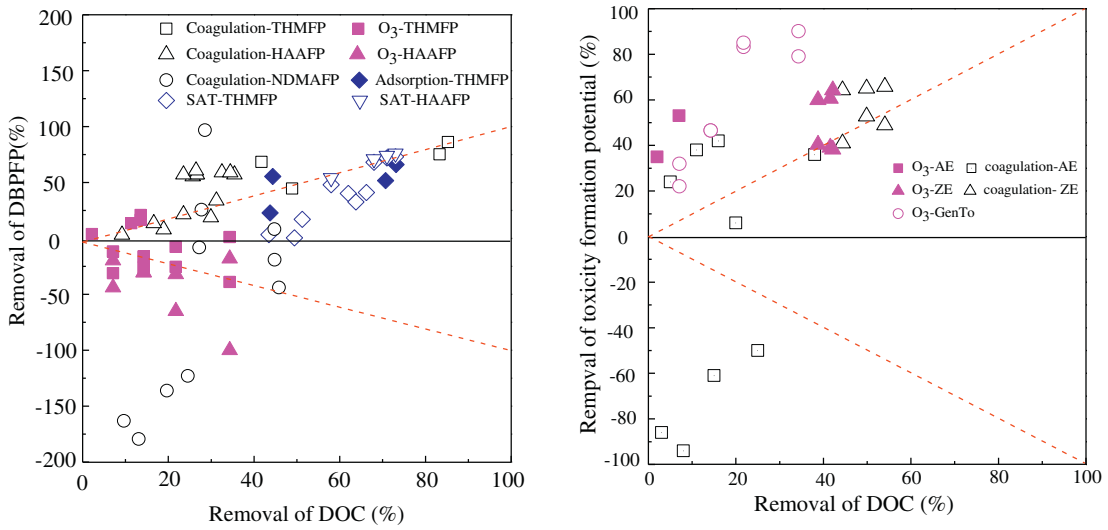

Fig. 4 – Relationship between dissolved organic carbon (DOC) removal and (a) disinfection byproduct formation potential (DBPFP) removal; (b) toxicity formation potential (TFP) removal. AE: anti-estrogenic activity; ZE: zebra embryo toxicity; GenTo: genotoxicity by *umu*-test. The dash line in Fig. 4a and b represent that the DOC removal equals to the DBPFP of TFP removal. (The literature containing the original data for composing the figure was listed in Appendix A Text S3.).

the key precursor fraction in DOM needs to be identified and eliminated before chlorination.

4.1.2. Key precursor fractions associated with DBPs and toxicities formation

Table 1 shows the contribution (percentages) of different fractions in DOM to DBPFP and TFP. Different studies have shown results with large variations, thus leading to relatively large deviations. Nevertheless, we could still identify an overall trend. The hydrophobic acids (HOA) fraction and hydrophilic acids (HIA) fraction were responsible for the most THM4 formation, accounting for 38.5% and 29.0%, respectively. The hydrophilic substances (HIS), especially HIA and hydrophilic neutrals (HIN), formed the most HAA5. Moreover, the HIN fraction was the predominant precursor for nitrogenous DBPs, including DCAN, DCAcAm, and TCAcAm, of which the HIN fraction contributed 41%, 48%, and 60% of the formation, respectively. Evaluation of toxicity revealed that the prevalent precursor fraction for anti-estrogenic activity was HOA, which accounted for 45.0% of the AEAFP during chlorination. Both HOA and HIS were important for the contribution to genotoxicity, accounting for 30.5% and 41.0% of the composition of genotoxic chemicals after chlorination, respectively. Evaluation of the luminescent bacteria acute toxicity indicated that HOA, hydrophobic bases (HOB), hydrophobic neutrals (HON), and HIS contributed equally, with each fraction accounting for around 25% of the TFP after chlorination.

Although the key precursor fractions for different DBPFP and TFP varied, HOA and HIN were the most important fractions (Table 1). HOA was responsible for the formation of most DBPs after chlorination because of the high level of humic acid with unsaturated bonds, which served as important precursors (Zhang et al., 2009). The DON was considered the major precursor for nitrogenous DBPs, which was the main constituent in HIN (Hu et al., 2016). This explained why the HIN formed the large portion of nitrogenous DBPs. Thus, different fractions in DOM made widely different contributions to DBPFP and TFP; therefore, focusing on the elimination of key fractions would achieve a better performance in DBPs and toxicities removal.

4.2. Optimization of chlorination

4.2.1. Effect of chlorine dose on toxicity changes

Chlorine dose obviously impacts the formation of DBPs and toxicities. Fig. 5 shows the changes in luminescent bacteria toxicity, genotoxicity, anti-estrogenic activity and cytotoxicity under different chlorine doses. Each toxicity exhibited an increase with increasing chlorine dose, except for the genotoxicity under low ammonia conditions. For luminescent bacteria acute toxicity, changes in dispersal were observed after chlorination because of variations in water quality. In some cases, rapid increases in acute toxicity were observed under low chlorine dose. Acute toxicity could reach 8.2 times the original acute toxicity with the addition of 5 mg/L chlorine, and a relative acute toxicity of 9.3 times was detected with the addition of 10 mg/L chlorine (Fig. 5a). However, the relative toxicity was only 2.5 times under 50 mg/L chlorine in some cases. Despite the relative dispersion of toxicity, the increase in acute toxicity changes with increasing chlorine dose was easy to identify. Similarly, the increase in anti-estrogenic activity and cytotoxicity was positively related to the chlorine dose as well (Fig. 5c and d).

The change in genotoxicity (*umu*-test) after chlorination was influenced by the ammonium concentration (Fig. 5b). As mentioned in Section 3, chlorination decreased the genotoxicity

Table 1 – Contribution of different fractions in DOM to DBPFP and TFP in reclaimed water.

		Contribution of different fractions in DOM (%)							Reference
		HOA	HOB	HON	HIA	HIB	HIN	HIS [a]	
Disinfection byproducts formation potential	THM4	38.5 ± 21.3 [b] (*n* = 6) [c]	8.8 ± 12.5 (*n* = 6)	14.5 ± 6.2 (*n* = 6)	29.0 ± 26.2 (*n* = 3)	2.0 ± 3.5 (*n* = 3)	15.0 ± 3.6 (n = 3)	30.7 ± 16.3 (n = 3)	(Han et al., 2015; Zhang et al., 2009, 2010, 2011)
	HAA5	16.0 ± 13.3 (*n* = 4)	12.5 ± 12.0 (*n* = 4)	15.0 ± 12.7 (*n* = 4)	24.3 ± 21.4 (*n* = 3)	4.7 ± 8.1 (*n* = 3)	20.3 ± 5.5 (*n* = 3)	79	(Wang et al., 2007a, 2007b; Zhang et al., 2009, 2010, 2011)
	DCAN	22	2	5	9	22	41	/	(Huang et al., 2016)
	DCAcAm	26	0	4	11	12	48	/	
	TCAcAm	18	0	0	10	12	60	/	
Toxicity formation potential	Anti-estrogenic activity	45.0 ± 14.4 (*n* = 3)	4.3 ± 4.5 (*n* = 3)	20.3 ± 20.5 (*n* = 3)	11.5 ± 4.9 (*n* = 2)	4.0 ± 0.0 (*n* = 2)	−3.0 ± 14.0 (*n* = 2)	37	(Tang, 2014; Wu et al., 2010)
	Genotoxicity	30.5 ± 7.4 (*n* = 6)	21.5 ± 25.9 (*n* = 6)	7.2 ± 7.4 (*n* = 6)	/	/	/	41.0 ± 25.5 (*n* = 6)	(Wang et al., 2007a, 2007b; Wu et al., 2010)
	Luminescent bacteria	22	27	27	0	0	23	/	(Zhang et al., 2010)

The literature containing the original data for composing the figure was listed in Text S4. DOM: dissolved organic matter; DBPFP: disinfection byproduct formation potential; TFP: toxicity formation potential; HOA: hydrophobic acid; HOB: hydrophobic base; HON: hydrophobic neutral; HIS: hydrophilic substance; HIA: hydrophilic acid; HIN: hydrophilic neutral; HIB: hydrophilic base.

[a] Some researches fractionated the DOM into HOA, HOB, HON, and HIS, while some researches further fractionated the HIS into HIA, HIB, and HIN. Both the two approaches were discussed in this work.

[b] The results were presented as mean value ± standard deviation.

[c] The *n* in the brackets represents the sample number, otherwise there was one sample.

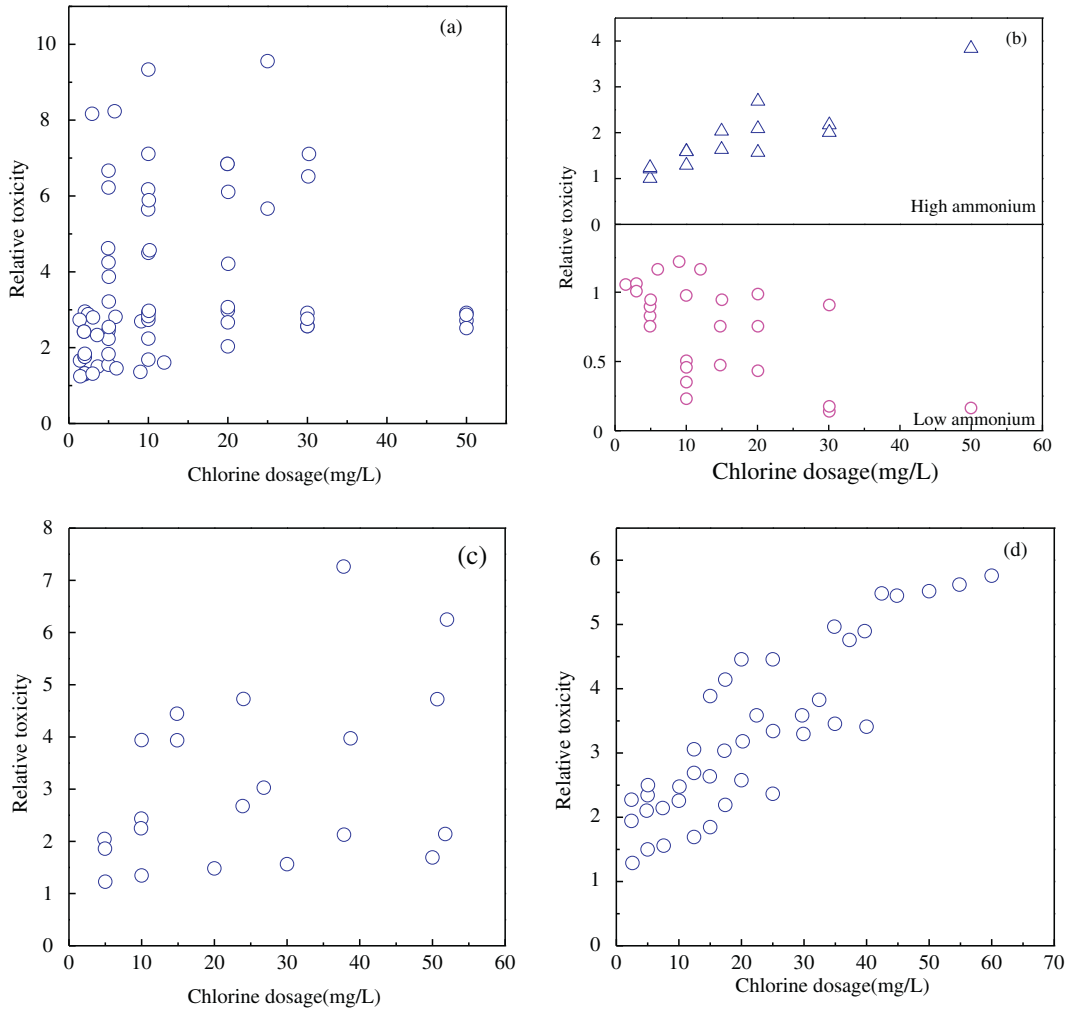

Fig. 5 – Changes in toxicity under different chlorine dose: (a) luminescent bacteria acute toxicity; (b) genotoxicity (*umu* test, high ammonium: NH_3-N > 20 mg/L; low ammonium: NH_3-N < 20 mg/L); (c) anti-estrogenic activity; (d) cytotoxicity (relative toxicity represents the toxicity after chlorination over the toxicity before chlorination). (The literature containing the original data for composing the figure was listed in Appendix A Text S5.).

under low ammonium conditions. The degree of attenuation was also accompanied by increasing chlorine dose. However, in the presence of high ammonium concentration, chlorination reduced the genotoxicity of reclaimed water. This might have occurred because the formation of chloramine led to the generation of nitrogenous DBPs and iodinated DBPs (Wang et al., 2007a, 2007b), which were reported to be much more genotoxic (Richardson et al., 2007). Under high ammonium concentrations, increased genotoxicity was observed with increasing chlorine doses, which might be attributed to the sustained increase of N-DBPs or I-DBPs.

4.2.2. Effect of contact time on toxicity changes

The influence of chlorine contact time on toxicity is shown in Fig. 6. In general, different toxicities followed the same trend, increasing with increased contact time. Moreover, luminescent bacteria acute toxicity increased dramatically within a short time. The maximum 9.6 times relative toxicity was reached within 10 min of chlorination. Combining the substantial elevation under the low chlorine dose, luminescent bacteria toxicity was susceptible to chlorine to reach a higher level. Cytotoxicity increased with chlorination duration as well, reaching the maximum around 48 hr (Du et al., 2017). Anti-estrogenic activity also increased with increased contact time, despite the limited augmentation. The maximum relative toxicity of 1.7 times was reached after 72 hr of contact time, indicating that anti-estrogenic activity was relatively insensitive to contact time compared to others. The increased toxicities could be explained by the growth of DBP formation because many DBPs, including HAAs and DCAN, were reported to keep forming within 72 hr of chlorination (Lu et al., 2009; Yang et al., 2007). Although some DBPs, such as 1,1,1-trichloro-2-propanone, could hydrolyze within a few hours, such DBPs might generate other products to exhibit toxicities (Lu et al., 2009).

Based on the discussion above, toxicities increased with the increasing chlorine dose and contact time in most cases. Under conditions in which pathogen inactivation was achieved,

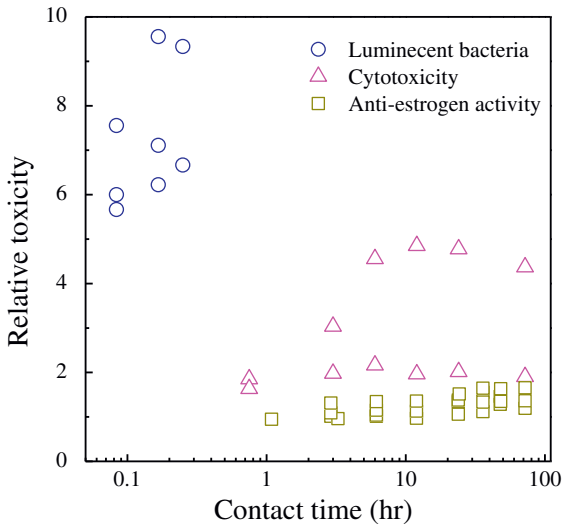

Fig. 6 – Changes in toxicity with increasing chlorine contact time. (The literature containing the original data for composing the figure was listed in Appendix A Text S6.).

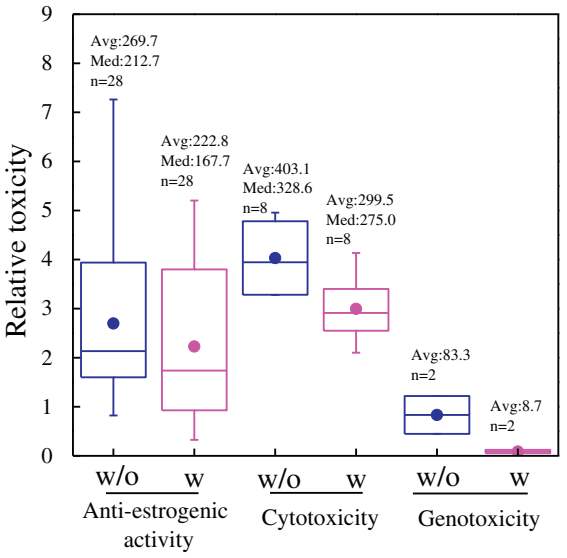

Fig. 7 – Decreases in toxicities after quenching with reductive reagents including sodium thiosulfate, sodium sulfite and ascorbic acid. Relative toxicity represents the toxicity after chlorination over the toxicity before chlorination. w: with quenching; w/o: without quenching. The two whiskers in the box chart represent the 5th and 95th percentiles. The three lines in the box chart represent the 25th, 50th, and 75th percentiles. (The literature containing the original data for composing the figure was listed in Appendix A Text S7.).

a relatively low chlorine dose and short contact time were required to protect the water quality from formation of excessive toxicity.

4.3. *Quenching residual chlorine*

Quenching residual chlorine is a widely used process after chlorination to protect aquatic organisms from residual chlorine. Reductive reagents, such as sodium sulfite, sodium thiosulfate, sodium arsenite and ascorbic acid, were widely used as quenching agents (Deng et al., 2014; Zhai and Zhang, 2009). At the same time, the lower DBP formation was frequently observed after quenching with reductive agents. THM formation and HAN formation decreased by 4% and 14%, respectively, after quenching with sodium sulfite (Wang et al., 2016). In addition, both TOCl and total organic bromine (TOBr) were attenuated after quenching with arsenite (Liu and Zhang, 2013). Thus, quenching with reductive agents might be an effective way to decrease the formation of toxicity in response to chlorination.

Changes in toxicities, including anti-estrogenic activity, cytotoxicity and genotoxicity, after quenching with reductive agents are shown in Fig. 7. All toxicities decreased with quenching. The medians of the anti-estrogenic activity before and after quenching were 2.1 times and 1.7 times higher relative to unchlorinated reclaimed water, respectively, demonstrating that quenching could substantially reduce the formation of anti-estrogenic activity. Similarly, the median relative cytotoxicity without quenching was 3.3 times, while the median after quenching was reduced to 2.8 times. The maximum reduction of relative toxicity was observed for genotoxicity. The median relative toxicity of 83.3% was found without quenching, while after quenching the relative genotoxicity was only 8.7%.

The attenuated toxicity might have occurred because the quenching agents stopped further reactions between chlorine and organic materials. Another possible explanation is that the reductive agents tended to destroy or transform the formed DBPs. Studies have demonstrated that TOX was decomposed through dehalogenation when quenching with arsenite and sulfite (Croue and Reckhow, 1989; Zhai and Zhang, 2009). Some DBPs, such as TCAN and chloropicrin, also transformed into HAAs with no C-X break but caused decreased toxicities (Croue and Reckhow, 1989; Plewa et al., 2004a, 2004b). Thus, quenching with reductive agents appears to be an ideal method of controlling the formation of DBPs and toxicity.

5. Conclusions

This paper reviewed the formation of DBPs and toxicities in reclaimed water during chlorination. Levels of different kinds of DBPs formed after chlorination were given. The distribution frequency of changes in toxicity after chlorination and factors impacting the toxicities were discussed. Moreover, the control strategies for DBPs and toxicities, including pretreatment, chlorination conditions, and post-treatment, were put forward. The main conclusions are summarized below:

(1) Different kinds of DBPs were frequently detected in reclaimed water during chlorination. Regulated DBPs, emerging DBPs and nitrogenous DBPs were present at higher levels than those reported in drinking water. Accordingly, the risk posed by DBPs in reclaimed water requires a great deal of attention.

(2) Various changes in toxicities were observed after chlorination. In general, luminescent bacteria and *D. magna* acute toxicity, anti-estrogenic activity and cytotoxicity were increased after chlorination because of the formation of DBPs. The genotoxicity determined by the *umu*-test and estrogenic activity were decreased after chlorination because of the destruction of toxic chemicals.
(3) The ammonia tended to attenuate toxicity changes by reacting with chlorine to form chloramine. Conversely, the bromide tended to aggravate changes in toxicity by forming hypobromous acid during chlorination, which increased the anti-estrogenic activity and cytotoxicity by forming more toxic brominated DBPs and decreased the genotoxicity due to the higher oxidizability.
(4) During pretreatments such as ozone and coagulation, despite the efficient removal of DOC, the DBPFP and TFP increased in some cases. Thus, DOC removal was limited to indicate the DBPFP and TFP removal. Therefore, it is important to focus on eliminating the key fractions of DOM, such as HOA and HIN.
(5) Within the critical range, both toxicities increased with increasing chlorine dose and contact time. When pathogen inactivation was achieved, a relatively low chlorine dose and short contact time were required to protect the reclaimed water from the formation of excessive toxicity. Additionally, quenching chlorine residual with reductive agents effectively abated the formation of toxicity. Therefore, it is feasible to remove the toxicity by quenching with reductive agents after chlorination.

Future works should focus on developing the comprehensive bio-toxicity assay to characterize the risk of reclaimed water which is more closed to human health and optimizing the advanced treatment before chlorination which is better at precursor removal.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.jes.2017.01.013.

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