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Systematic screening and identification of the chlorinated transformation products of aromatic pharmaceuticals and personal care products using high-resolution mass spectrometry

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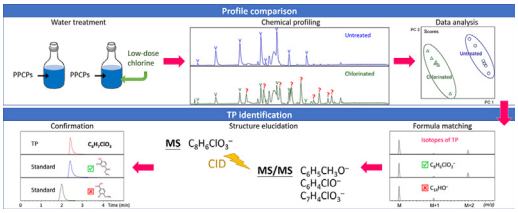
HIGHLIGHTS

- TPs of ten aromatic PPCPs were simultaneously studied.
- Compound profiles of the chlorinated and untreated water were compared.
- HRMS and library searching determined the molecular formulae of unknowns.
- LC and collision-induced dissociation facilitated structure elucidation.
- Low-dose chlorine transformed nine aromatic PPCPs into chlorinated derivatives.

GRAPHICAL ABSTRACT



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ABSTRACT

Pharmaceuticals and personal care products (PPCPs) are an emerging concern because of the large amount of PPCPs that is discharged and its potential ecological effects on the aquatic environment. Chlorination has proven efficient for removing some aromatic PPCPs from wastewater, but the formation of by-products has not been thoroughly investigated partly because of analytical difficulties. This study developed a method for systematically screening and identifying the transformation products (TPs) of multiple aromatic PPCPs through high-resolution mass spectrometry (HRMS). We spiked an environmentally relevant concentration (5000 ng/L) of three anti-inflammatory drugs, four parabens, bisphenol A, oxybenzone, and triclosan in the Milli-Q water and water containing natural organic matter (NOM). Low-dose chlorination (0.2–0.7 mg/L) was performed. We compared the chemical profiles of the chlorinated and untreated water and selected the ions to be identified based on the results of *t*-test and the ratio of signal intensities. Compound matching and isotopic pattern comparison were applied to characterising the molecular formulae of TPs. The fragmentation of the PPCPs and TPs was used in elucidating the structures of the TPs. The confirmation of TPs was achieved by comparing the retention time and fragment patterns of TPs with the isomer standards. In the chlorinated water, the aromatic PPCPs were substantially removed, except for the anti-inflammatory drugs (removal rates −5.2%–26%). Even with moderate chlorine dosages, all of the aromatic PPCPs, except for acetylsalicylic acid, were transformed into chlorinated derivatives in the Milli-Q water, and so were some PPCPs in the NOM-added water. The results of structure elucidation and compound confirmation as well as the increases in log K_{ow} suggested that chlorination could transform aromatic PPCPs into more persistent, bioaccumulative, and toxic TPs. The presence of these TPs in the effluents where the PPCPs are removed through chlorination may pose increased risks to aquatic organisms.

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1. Introduction

Emerging contaminants (ECs) are substances that have entered the environment in a considerable amount, potentially causing adverse ecological effects, but have not been regularly monitored (U.S. Geological Survey, 2016). Among the long list of ECs, pharmaceuticals and personal care products (PPCPs) are a principal contributor to pollution in rivers receiving municipal wastewater. Despite the ubiquity of wastewater treatment plants, PPCPs are frequently detected in surface waters (Pal et al., 2014).

Studies on the removal of PPCPs through wastewater treatment processes have presented various findings. In general, conventional processes, including primary and secondary treatments, can remove 30–70% of PPCPs (Afonso-Olivares et al., 2017; Lonappan et al., 2016). Physicochemical treatments are responsible for removing the compounds adsorbed onto particulate matter, whereas biological treatments remove polar pharmaceuticals (Ahmed et al., 2017; Baalbaki et al., 2016). Tertiary treatments involving oxidation have been recommended for recalcitrant PPCPs that are only partially removed through conventional processes (Ahmed et al., 2017; Rivera-Utrilla et al., 2013). Chlorination is one of the cost-effective oxidation methods used in wastewater treatment plants. Primarily aiming for disinfection, chlorination was also found to be capable of removing some PPCPs with aromatic moieties, such as caffeine, acetaminophen, and diclofenac (Lin et al., 2011; Mousel et al., 2017; Quintana et al., 2010; Westerhoff et al., 2005).

Nevertheless, wastewater treatment processes may transform PPCPs into other substances, resulting in the occurrence of unpredictable transformation products (TPs) in the effluent (Scheurer et al., 2012). Most of the previously reported TPs of PPCPs are biological degradation products and mammal metabolites, such as hydroxyl derivatives and glucuronide conjugates (Lonappan et al., 2016; Pico and Barcelo, 2015; Tiwari et al., 2017). Aside from the biodegradation products, water disinfection through chlorination or ozonation and other advanced oxidation processes may also result in the generation of TPs (Bletsou et al., 2015). Similar to the formation of disinfection by-products from natural organic matter (NOM), strong oxidation processes form reactive hydroxyl and chlorine radicals, which may transform PPCPs into various forms of TPs.

Aromatic compounds are particularly vulnerable to halogenated TP formation during water chlorination (Grbovic et al., 2013; Pico and Barcelo, 2015; Postigo and Richardson, 2014; Santos et al., 2012; Vikesland et al., 2013; Westerhoff et al., 2005). Laboratory studies have demonstrated that the disinfection of pure water using hypochlorite transforms acetaminophen into chlorinated products, monochloro-4-acetamidophenol, and dichloro-4-acetamidophenol, which accounted for 7% of the initial acetaminophen (Bedner and Maccrehan, 2006). Chlorination using 10-mg/L Cl_2 can transform salicylic acid into mono and dichlorinated salicylic acids as well as bromo- and bromochloro-salicylic acids under the presence of bromide (Quintana et al., 2010). Formation of stable chloro-diclofenac and chloro-decarboxy-diclofenac through electrophilic substitution on the aromatic ring has been confirmed (Quintana et al., 2010; Soufan et al., 2012). Mono and dichlorinated triclosans have been identified in chlorinated water (Vanderford et al., 2008; Vikesland et al., 2013). Chlorination may cause the substitution of one to four chlorines onto bisphenol A (Vikesland et al., 2013). These halogenated TPs may possess greater molecular weights and higher hydrophobicity levels, rendering them more persistent, bioaccumulative, and toxic than the parent PPCPs (Agueera et al., 2013). However, these TPs have not been thoroughly investigated partly due to the difficulty of characterisation.

High-resolution mass spectrometry (HRMS) can be used to identify unknown compounds and therefore can be used for TP characterisation (Agueera et al., 2013; Bletsou et al., 2015; Zedda and Zwiener, 2012). In contrast to most targeted analyses for PPCPs that use triple quadrupole mass spectrometry (MS) with unit mass resolution, in which qualification depends on the retention time and ion transitions of the analyte standard, non-targeted analysis through HRMS can be used to characterise an unknown compound on the basis of its accurate mass. Time of flight MS, a commercial HRMS analyser, can provide up to 3-ppm mass accuracy (Krauss et al., 2010). This high mass accuracy allows for a small mass error when matching a spectrum feature to a candidate compound, which would shorten the list of probable compounds and increase certainty when identifying a TP. The TP candidates could be nominated on the basis of the results obtained through searching on commercial databases, online chemical libraries, and in-house libraries. Fragment ions produced through collision-induced dissociation (CID) provided by quadrupole-time of flight (QTOF) may facilitate the elucidation of the molecular structure of a TP, which should share some structural properties with its parent PPCP (Agueera et al., 2013; Bletsou et al., 2015; del Mar Gomez-Ramos et al., 2011; Zedda and Zwiener, 2012).

In this bench-scale study, we developed a non-targeted analytical method for the systematic identification of the TPs of multiple aromatic PPCPs, specific to those generated through water chlorination. HRMS and its compatible techniques were applied to screening for TP candidates, indicating molecular formulae, and elucidating chemical structures.

2. Methods

2.1. Chemicals and reagents

Standards of 10 aromatic PPCPs, including three anti-inflammatory drugs (acetaminophen, acetylsalicylic acid, and diclofenac), four parabens (methylparaben, ethylparaben, propylparaben, and butylparaben), bisphenol A, oxybenzone, and triclosan (Fig. S1), which were in high purity grade (≥99.8%) were supplied by Sigma-Aldrich (Saint Louis, MO, USA). Sodium hypochlorite solution (available chlorine concentration: 10%–15%) was supplied by Sigma-Aldrich. Reagent-grade sodium thiosulfate pentahydrate was supplied by Merck (Kenilworth, NJ, USA). Dimethyldichlorosilane, toluene, formic acid, acetic acid, acetone, methanol, and dichloromethane used for sample preparation were analytical or high-performance liquid chromatography (LC) grade. LC–MS grade acetonitrile for LC mobile phase was supplied by J.T. Baker (Center Valley, PA, USA). Milli-Q water for LC aqueous phase was produced by a water purification system (Merck KGaA, Darmstadt, Germany).

2.2. Water chlorination

A model water sample was prepared by spiking the 10 aromatic PPCPs into 100 mL of Milli-Q water (5000 ng/L). In the chlorinated group (CM, n = 6, Exp. 1), the model water was added with 1050 μL of freshly prepared sodium hypochlorite solution (66.7 mg/L) to result in an initial free chlorine concentration of 0.7 mg/L, which was measured using a chlorine test photometer (Chlorine eXact EZ, Industrial Test Systems, Rock Hill, SC, USA) immediately after the addition of sodium hypochlorite$_{(aq)}$ and vigorous hand-shaking. The model water was shaken at 110 rpm for 10 min using an orbital shaker (United Corps, New Taipei, Taiwan), and the residual chlorine (0.6 mg/L) was subsequently quenched using 200 μL of 10-mM sodium thiosulfate$_{(aq)}$. The model water in the untreated group (UM, n = 6) did not undergo chlorination and chlorine quenching. Chlorinated (n = 6) and untreated (n = 6) milli-Q blanks were used to evaluate the background interference.

In addition to Exp. 1, we performed the following chlorination experiments to evaluate if the workflow of unknown feature screening and TP identification can be transferred to another condition or to wastewater: (a) the model water was chlorinated at a lower dose (0.2 mg/L) and a longer reaction time (30 min) in accordance with the information that a local water recycling centre provided (n = 6,