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Iodinated X-ray contrast agents: Photoinduced transformation and monitoring in surface water

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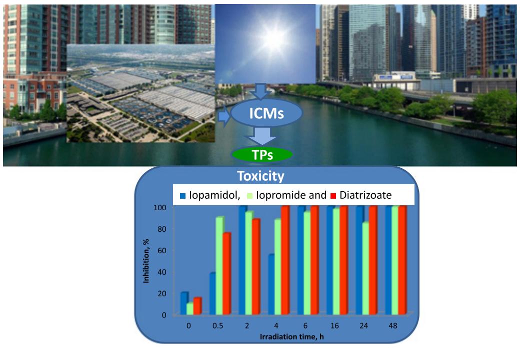
HIGHLIGHTS

- The transformation of three ICM (Iopamidol, diatrizoate and iopromide) was assessed.
- A total of forty-five TPs were detected via LC-HRMS.
- A lack of mineralization and the formation of harmful byproducts occurred for all ICMs.
- ICMs and their TPs were searched in river and WWTP effluent waters.

GRAPHICAL ABSTRACT



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ABSTRACT

Conventional wastewater treatment methods have shown to be unsuitable for a complete elimination of iodinated X-ray contrast agents (ICMs), which have thus been found in wastewater treatment plant (WWTP) effluent and in surface water. Once in the surface water, they could be transformed through different processes and form several transformation products that may need to be monitored as well. To this end, we studied the abatement and transformation of ICMs by combining laboratory experiments with in field analyses. We irradiated different aqueous solutions of the selected pollutants in the presence of TiO_2 as photocatalyst, aimed to promote ICMs degradation and to generate photoinduced transformation products (TPs) similar to those occurring in the environment and effluent wastewater. This experimental strategy has been applied to the study of three ICMs, namely iopromide, iopamidol and diatrizoate. A total of twenty-four, ten, and ten TPs were detected from iopamidol, diatrizoate and iopromide, respectively. The analyses were performed using a liquid chromatography-LTQ-FT-Orbitrap mass spectrometer. The mineralization process and acute toxicity evolution were assessed as well over time and revealed a lack of mineralization for all ICMs and the formation of harmful byproducts.

After characterizing these transformation products, WWTP effluent and surface water taken from several branches of the Chicago River were analyzed for ICMs and their TPs. HRMS with MS/MS fragmentation was used as a confirmatory step for proper identification of compounds in water and wastewater samples. All three of ICM were detected in the effluent and surface water samples, while no significant amount of TPs were detected.

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1. Introduction

Every year between 40 and 80 million doses of iodinated X-ray contrast agents (ICMs) are used for diagnostic purposes, the estimated annual production is >5000 tons (Wendel et al., 2014; Gharekhanloo and Torabian, 2012). ICMs are excreted mainly un-metabolized (>90%) (Wendel et al., 2014), so most of the drug dose enters urban wastewater after urinary elimination. Their abatement is partly achieved in secondary anoxic or anaerobic treatment, while only a small percentage is removed under aerobic conditions (Busetti et al., 2008). The yields of removal for nonionic contrast agents via ozonation in water treatment plants are 35–55% and even <20% for ionic ones (Seitz et al., 2008; Putschew et al., 2007). Reverse osmosis systems are used to remove absorbable organic halide (Drewes et al., 2001). Iopamidol and diatrizoate are stable with respect to chlorination, while iopamidol is not. (Wendel et al., 2014). Filtration-based treatments, biotransformation (Kormos et al., 2010) or direct photolysis (Doll and Frimmel, 2003; Sichel et al., 2011) have been proposed as well; however, these methods require long treatment times and exhibit low efficiency.

Due to their wide use, high biochemical stability, and low yields of abatement in treatment plants, elevated concentrations of ICMs have been detected in hospital and domestic wastewater, treated wastewater effluent (Redeker et al., 2014), surface water, groundwater and drinking water (Węgrzyn and Żabczyński, 2014; Ternes and Hirsch, 2000; Stuart et al., 2012; Kase et al., 2011, Watanabe et al. 2016).

In the present study, we focus on the photocatalyzed transformation of three ICMs: iopamidol, iopromide and diatrizoate. Iopamidol (IO) is one of the most popular and widely used non-ionic ICMs worldwide. This molecule has a good solubility in water, with a partition coefficient ($\mathrm{LogP_{OW}}$) of −2.09 and a distribution coefficient ($\mathrm{logD_{OW}}$, pH 7.4) of −2.31 (Pitrè and Felder, 1980). Standard activated sludge treatment may remove up to 35% of IO (Ternes and Hirsch, 2000, Ternes et al., 2007, Kormos et al., 2011). The concentration of IO in effluent from hospitals and municipal WWTPs are high and ranged from 0.2 to 16 μg/L (Ternes et al., 2003, Busetti et al., 2010, Kormos et al., 2011). As a result the concentration of IO in river water that is fed with this effluent may be as high as 0.386 μg/L (Bruchet et al., 2005) and >0.5 μg/L (Seitz et al., 2006). Actually, iopamidol has also been frequently detected at high concentrations (2.7–3.3 μg/L) in the source water processed into drinking water (Duirk et al., 2011, Simazaki et al., 2015). Iopamidol is also thought to be the major precursor of iodinated disinfection byproducts (Duirk et al., 2011).

Iopromide (IP) is a low osmolality, non-ionic contrast agent and one of the most common molecules used in diagnostic radiology; the production of iopromide alone is about 130 tons per year (Ning and Graham, 2008). The $\mathrm{LogP_{OW}}$ value for iopromide is −2.95, while the $\mathrm{logD_{OW}}$ (pH 7.4) is equal to −2.12 (Pitrè and Felder, 1980). It is refractory to common wastewater treatment (Kalsch, 1999) and is frequently detected in surface water, groundwater and soils (Schulz et al., 2008; Perez et al., 2006), as well as in effluent from urban areas near hospital complex in concentrations from ng/L to μg/L (Pitrè and Felder, 1980, Santos et al., 2013).

Diatrizoate (DTZ), a ionic ICM, has a $\mathrm{LogP_{OW}}$, 1.53 and $\mathrm{logD_{OW}}$ (pH 7.4) equal to −2.53, indicating a high solubility in water (Pitrè and Felder, 1980). It is essentially non-biodegradable (Seitz et al., 2008) and was detected in surface water and groundwater at concentrations up to 1 μg/L (Howard and Muir, 2011). Coated biofilm reactors (Hapeshi et al., 2013) and advanced oxidation processes (AOP, Polo et al., 2016) have been tested for treatment of wastewater containing DTZ as well.

To date, only a few studies of ICM transformation products have been carried out. Eleven TPs were prioritized and their structures elucidated by HRMS and NMR, using a screening approach not dependent upon the availability of standards (Zonja et al., 2015). LC-QTOF-MS (Singh et al., 2015) coupled with the statistical tools was used to identify TPs at environmentally relevant conditions. In this approach, unspiked wastewater samples were collected and analyzed for the presence of iopromide and its putative TPs.

Photocatalytic treatment processes using titanium dioxide ($\mathrm{TiO_2}$) hold promise for treating contaminated water with highly recalcitrant organic contaminants. Ionic ICMs like diatrizoate that had shown to be remarkably resistant to biotransformation (Kalsch, 1999, Haiss and Kümmerer, 2006) but may be degraded by photocatalytic treatment. At present, only a few studies concerning the photocatalytic treatment of ICM have been undertaken. Doll and Frimmel (2004 and 2005) studied the photocatalytic degradation of nonionic ICM (iomeprol and iopromide), suggesting significant ICM degradation and release of iodine substituents from the central ring structure, but with only a limited mineralization of organic carbon. Some transformation products of iopromide have been generated by $\mathrm{UV/H_2O_2}$ (Singh et al., 2015).

Heterogeneous photocatalysis is widely used not only to achieve the decontamination of aquatic systems, but also to simulate the abiotic transformation of pollutants occurring in the euphotic zone leading to potentially harmful transformation products. In the present study, we aim to investigate the whole ICM degradation process by studying the transformation products, the mineralization process and the toxicity of the system. Initially, laboratory experiments were performed to artificially produce transformation compounds similar to those formed in oxido/reductive pathways by adopting a photocatalytic process as a model system. This approach was previously successfully used and permitted to identify several TPs, alongside the parent compounds, in water samples (Calza et al. 2010, 2011, and 2013).

In a second phase, we analyze WWTP effluent and searched for all ICMs and their transformation products.

2. Experimental section

2.1. Materials and reagents

N,*N*′-*bis*(1,3-dihydroxy-2-propanyl)-2,4,6-triiodo-5-(lactoylamino)isophthalamide (Iopamidol, IO), 3,5-bis(acetylamino)-2,4,6-triiodobenzoic acid (Diatrizoate, DTZ, ≥98.0%), 1-*N*,3-*N*-*bis*(2,3-dihydroxypropyl)-2,4,6-triiodo-5-(2-methoxyacetamido)-1-*N*-methylbenzene-1,3-dicarboxamide (Iopromide, IP, ≥98.0%), acetonitrile (≥99.9%), acetonitrile (≥99.9%), formic acid (99%) and phosphoric acid were purchased from Sigma Aldrich, Italy. All aqueous solutions were prepared with ultrapure water Millipore Milli-Q™.

$\mathrm{TiO_2}$ P25 (Evonik Industries, Italy) was used as photocatalyst, after being subjected to irradiation and washings with ultrapure water in order to eliminate the potential interference caused by adsorbed ions such as chloride, sulfate and sodium. In all photocatalytic experiments, $\mathrm{TiO_2}$ was used at a loading of 200 mg $\mathrm{L^{-1}}$.

2.2. Irradiation procedures

Irradiation experiments were performed in stirred cylindrical closed cells (40 mm i.d. × 25 mm, made of Pyrex glass) on 5 mL of aqueous dispersions containing 20 $\mathrm{mgL^{-1}}$ of each analyte and 1000 mg/L of $\mathrm{TiO_2}$. A Blacklight Philips TLK 05 (40 W) lamp source with emission maximum at 360 nm was employed for irradiation.

The dispersions were collected from the cells at the end of the programmed irradiation period and then were filtered through 0.45 μM Millex LCR hydrophilic PTFE membranes (Millipore) before the analysis.

2.3. Analytical procedures

2.3.1. Liquid chromatography-MS

All samples were analyzed by HPLC/HRMS. The chromatographic separations, monitored using an MS analyzer, were carried out with a Phenomenex Luna C18 (2) 150 × 2.1 mm × 3 μm particle size (Phenomenex, Bologna, Italy), using an Ultimate 3000 HPLC instrument (Dionex, Thermo Scientific, Milan, Italy). The Injection volume was