***Highlights (3 to 5 bullet points (maximum 85 characters including spaces per bullet point)**

Highlights:

- Rapid and sensitive direct injection method for analysis of seven target ICMs
- The method was validated in complex aqueous matrices such as secondary effluent, groundwater and drinking water
- Removal of seven target ICMs by LPUV/H_2O_2, LPUV/Cl_2 and LPUV/NH_2Cl

*Title Page

A direct injection liquid chromatography tandem mass spectrometry method for the kinetic study on iodinated contrast media (ICMs) removal in natural water

Authors: Israel J. Lopez-Prieto[a], Shimin Wu[a,b], Weikang Ji[a], Kevin D. Daniels[a,c], and Shane A. Snyder[a,d,]

[a]University of Arizona, Department of Chemical & Environmental Engineering, 1133 E. James E Rogers Way, Harshbarger 108, Tucson, AZ 85721-0011, United States

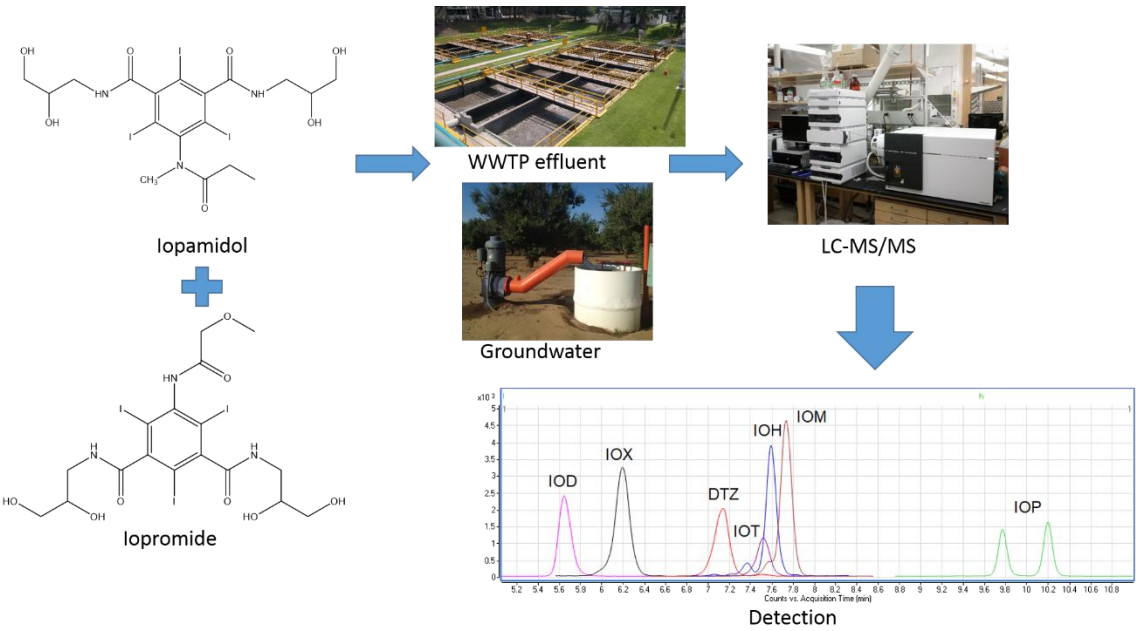
[b]EREnvironmentalProtectionEngineeringTechnologyCo., Ltd.,Shenzhen518071, China

[c]Hazen and Sawyer, 1400 E. Southern Avenue, Suite 340, Tempe, AZ 85282, United States

[d]Nanyang Technological University, Nanyang Environment & Water Research Institute, Clean Tech One, 1 Cleantech Loop, #06-08, Singapore 637141, Singapore

Corresponding author, email: ssnyder@ntu.edu.sg

Graphical abstract



*Revised manuscript with no changes marked

A direct injection liquid chromatography tandem mass spectrometry method for the kinetic study on iodinated contrast media (ICMs) removal in natural water

Authors: Israel J. Lopez-Prieto[a], Shimin Wu[a,b], Weikang Ji[a], Kevin D. Daniels[a,c], and Shane A. Snyder[a,d,]

[a]University of Arizona, Department of Chemical & Environmental Engineering, 1133 E. James E Rogers Way, Harshbarger 108, Tucson, AZ 85721-0011, United States

[b]EREnvironmentalProtectionEngineeringTechnologyCo., Ltd.,Shenzhen518071, China

[c]Hazen and Sawyer, 1400 E. Southern Avenue, Suite 340, Tempe, AZ 85282, United States

[d]Nanyang Technological University, Nanyang Environment & Water Research Institute, Clean Tech One, 1 Cleantech Loop, #06-08, Singapore 637141, Singapore

Corresponding author, email: ssnyder@ntu.edu.sg

Abstract

Iodinated contrast media (ICMs) are a class of X-ray contrast media worldwide utilized for radiographic procedures. Since they cannot be removed efficiently during water treatment, they can be found in surface and groundwater. In this work, a rapid and sensitive direct injection liquid chromatography-tandem (LC-MS/MS) method for the simultaneous analysis of seven ICMs media (iopamidol, ioxitalamic acid, diatrizoic acid, iothalamic acid, iohexol, iomeprol and iopromide) in complex aqueous matrices has been developed and validated. The MDLs for the analytes ranged from 0.7 to 21 ng L^{-1} in ultrapure water, and recoveries ranged from 86 to 100% in drinking water, 85 to

103% in groundwater and 84 to 105% in WWTP effluent. A stereo-isomer for iopromide was separated. This analytic method was applied to investigate the removal of target ICMs by low pressure ultra violet light (LPUV) advanced oxidation processes with three oxidants, hydrogen peroxide, free chlorine and monochloramine in groundwater. Results showed that the addition of oxidants did not enhance attenuation of ICMs, since fluence-based decay apparent rate constants were similar (K_{UV}= 3.2X10^{-3}, $K_{UV\text{-}Cl2}$= 3.6X10^{-3} and $K_{UV\text{-}NH2}$= 3.4X10^{-3} 10^{-3} cm^2 mJ^{-1}). This yielded direct photolysis is the main mechanism to attenuate target ICMs.

Keywords: Iodinated contrast media, Direct injection, Liquid chromatography-tandem mass spectrometry, Complex aqueous matrices, UV-based oxidation processes

1. Introduction

A current major challenge for water analysis is to develop a simple, sensitive and robust method for the detection and quantification of emerging contaminants at trace levels in complicated matrices such as surface water and wastewater effluents. In recent years, iodinated contrast media (ICMs) as the most widely administered intravascular pharmaceuticals in medical X-ray have become one of the most prevalent emerging contaminants. Owing to their high polarity and biological stability, ICMs are usually difficult to remove by conventional wastewater treatment (Busetti et al., 2008; Pauwels & Verstraete, 2006). Hence ICMs have been detected at μg L^{-1} levels in aqueous environments, including surface water, groundwater, and even drinking water (Ternes and Hirsch 2000;Weissbrodt et al. 2009). Although ICMs are non-toxic to the human body, they have received increasing attention as potential precursors of iodinated disinfection by-products (I-DBPs) which have been proven to be highly cytotoxic and

genotoxic to mammalian cells (Duirk et al., 2011). It has been reported in recent years that I-DBPs are generally of much higher developmental toxicity and growth inhibition than their bromo- and chloro-analogues (Richardson et al., 2008). There are two types of ICMs based on their charges at a neutral pH. Non-ionic ICMs have been more heavily studied than ionic ones since they are more abundant in surface waters (Pérez & Barceló, 2007; Westerhoff et al., 2005). The most common methods involve liquid chromatography coupled to an ultra violet detector (LC-UV) or tandem mass spectrometry (LC-MS/MS). Tian et al., (2014) developed a method utilizing LC-UV detector for quantification of iopamidol, with a detection limit of 5µg L^{-1}. Ternes & Hirsch (2000) developed a sensitive LC-MS/MS method with solid-phase extraction (SPE) step using a non-polar cartridge and achieved a level of quantification of 10 ng L^{-1}. In addition, Sacher et al., (2005) developed a method to analyze six ICMs using ion chromatography (IC) for separation and inductively coupled plasma mass spectrometry (ICP-MS) for quantification which obtains limits of detection of about 0.2 µg L^{-1} without pre-concentration. Table 1 shows a summary of different methods developed for ICM quantification.

Most current analytical methods for the determination of ICMs in aqueous matrices include a SPE as a pre-concentration step in order to enrich the analytes, clean them up from the interfering matrices, and achieve lower detection limits (Ternes et al., 2005). However, SPE procedure is costly and time-consuming, and may result in a loss of analytes (Sacher & Brauch, 2005). Large volume injection LC-MS/MS methods have become popular since they do not require a pre-concentration step with SPE. They also increase the overall recoveries of the analysis, whereas achieve lower limits of detection (LOD) (Tarun A. et al., 2013).

The objective of this study was to develop a rapid, sensitive and robust direct injection LC-MS/MS method for the simultaneous analysis of seven ICMs (iopamidol, ioxitalamic acid, diatrizoic acid, iothalamic acid, iohexol, iomeprol and iopromide) in environmental waters such as secondary effluent, ground water and drinking water. This current method was applied to investigate the removal of target ICMs by low pressure ultra violet (LPUV) advanced oxidation processes with three oxidants (hydrogen peroxide, free chlorine and monochloramine) in groundwater.

[Table 1]

2. Materials and methods

2.1. Chemicals

Diatrizoic acid (DTZ) was purchased from Sigma-Aldrich (St. Louis, MO, USA). iothalamic acid (IOT) and ioxitalamic acid (IOX) were purchased from Toronto Research Chemicals (Ontario, Canada). Iohexol (IOH), iopamidol (IOD), and iopromide (IOP) were obtained from the United States Pharmacopeial Convention Inc. (Rockville, MD, USA). Iomeprol (IOM) was purchased from LGC Standards (Manchester, NH, USA). The isotopically labeled surrogate standards (ILSS), iohexol-d_5 (IOH-d_5) and iopamidol-d_3 (IOD-d_3), were also obtained from Toronto Research Chemicals (Ontario, Canada) LC/MS grade methanol, acetonitrile, formic acid and acetic acid were purchased from Fisher Scientific Co. (Fair Lawn, NJ, USA). Ammonium acetate (NH_4Ac) and ammonium formate (NH_4Fo) were obtained from Sigma-Aldrich (St.

Louis, MO, USA). Ultrapure water with a resistivity of 18.1 MΩ·cm was obtained from a Milli-Q system (Millipore, Billerica, MA).

Stock solutions of each target ICM and isotope surrogate standard were prepared at 1.0 mg mL^{-1} in methanol. A standard mix (sub-stock solution) of all the analytes at 10 μg mL^{-1} and of the two isotopically labeled surrogates at 1.0 μg mL^{-1} were prepared in methanol. Working standard solutions at concentrations of 10, 20, 50, 100, 200, 500, 1000, 2000, 5000, 10000 and 20000 ng L^{-1} were prepared weekly by serially diluting the mixed sub-stock solution of analytes in methanol, and then spiking ILSS at 1000 ng L^{-1} afterward. Stock solutions were stored in the freezer at −20 °C.

2.2. Sample collection and preparation

Groundwater samples were collected from two monitoring wells downstream the WWTP outfall. WWTP effluent was collected after secondary treatment to prior chlorination basin. Drinking water from the university tap water was collected as well. All samples were collected in 1 L amber glass bottles, which were rinsed with methanol and ultrapure water and pre-baked at 400 ^{o}C prior to collection and stored at 4 °C for a maximum of two weeks before analysis.

A 1000 ng L^{-1} of ILSS mixture was spiked into one mL of each water sample. The samples were then filtered with a 0.2 μm pore size polyethylene sulfonate (PES) syringe filter from Agilent Technologies (Palo Alto, CA) and placed in an autosampler vial for analysis.

2.3. Instrumentation

The LC separation was carried out using an Agilent 1290 UHPLC system (Agilent Technologies, Palo Alto, CA). Separation was conducted with an Agilent Poroshell 120 EC-C8 column (4.6×100 mm, 2.7 μm particle size) maintained at 30 °C with a constant flow rate of 0.5 mL/min. Ultrapure water containing 0.1% (v/v) formic acid (A) and methanol containing 0.1% (v/v) formic acid (B) were used as the mobile phases. The gradient was as follows: B was initiated at 2%, and linearly increased to 20% in 8.0 min, then increased to 100% in 0.5 min and held for 2.5 min. A 4.0 min equilibration at 2% B was used at the end of each run. The injection volume was 80 μL.

Mass spectrometric detection was performed utilizing an Agilent 6490 triple quadrupole mass spectrometer (Agilent Technologies, Palo Alto, CA) equipped to a Jet Stream dual electrospray source and iFunnel technology. The instrument was tuned and optimized to obtain adequate sensitivity and resolution using the Agilent tune solution (p/n: G1969-85000) in all peak windows. The instrument was conducted utilizing an electrospray ionization source (ESI) in positive mode, with optimized parameters as follows: gas temperature, 275^{o}C; gas flow, 18 L/min; sheath gas temperature, 350^{o}C; sheath gas flow, 12 L min^{-1}; nebulizer, 45 psi; fragmentor, 380 V. The optimized MRM transition parameters for target ICMs and surrogate standards are listed in Table 2.

[Table 2]

2.4. Identification and quantification

Identification of the target ICMs was succeeded by comparing the retention time and the relative intensities (RI) of the two detected product ions (Table 2). The tolerance of relative retention time (RRT) was ±2%. The tolerances for various RIs were as follows:

150 ±20% for RI >50%, ±25% for RI >20–50%, ±30% for RI >10–20%, and ±50% for RI
151 ≤10% (André et al., 2001). All target ICMs were quantified internally utilizing
152 isotopically labeled surrogate standards. The surrogate standard applied for each analyte
153 is shown in Table 2. At least one lab blank and one lab fortified blank sample utilizing
154 ultrapure water were carried out for every 10 samples. Data acquisition and analysis
155 were conducted with Agilent MassHunter Workstation Software (Ver. B.06.01).
156 For quantification, a calibration curve of at least seven points was constructed over the
157 concentration range of 10–20000 ng L^{-1} for each ICM with 1000 ng L^{-1} of ILSSs. All
158 target analytes were calibrated internally using linear regression with *1/x* weighting
159 based on the relative response factors (RRFs) for the analytes and their corresponding
160 isotopically labeled surrogate compound (Table 2). The instrument detection limit (IDL)
161 was determined as the minimum injected mass (ng) that yielded into a signal to noise
162 ratio (S/N) of >3. The method detection limit (MDL) was driven by processing seven
163 fortified replicates at concentration 2-5 times the estimated IDL. The MDL was
164 computed as the product of the standard deviation of the measured concentrations and
165 the student's t critical value for the 99% of confidence level with 6 degrees of freedom
166 (for seven replicate determinations the t-value is 3.143) (Kirchmer, 1982).
167 Recovery experiments were carried out utilizing tap water, groundwater and secondary
168 effluent. Five fortified replicate samples were prepared by spiking 100 ng L^{-1} of seven
169 ICMs into each water matrix. The recovery was computed as the difference between the
170 measured concentration in the fortified and unfortified sample divided by the fortified
171 concentration times one hundred in order to express as a percentage.
172
173 **1.5. UV dose determination on collimated beam device**
174

A collimated beam UV device (CBD 11-1, ITT Wedeco) equipped with 4 LP-UV Hg lamps (NLR2036, radiation flux of 9 watts) that produces a monochromatic light at a wavelength of 253.7 nm was used for this experiment. The UV irradiance was determined by a calibrated UV detector (SED 240, international light) coupled to a radiometer (IL 1700, International Light). These values were adjusted by correction factors based on Bolton & Linden (2003) on the equation (1):

$$E' = E_0 \times PF \times RF \times WF \times DF \qquad (1)$$

Where E' is the weighted average UV irradiance (mW cm^{-2}); E_0 is the radiometer measurement at the surface area of the liquid within the Petri dish and at the center of the UV beam collimated device (mW cm^{-2}); PF is the Petri factor (non-uniformity of incident fluence rate across the dish area); RF is the reflection factor (small portion of the beam light which is reflected off the media); WF is the water factor (decrease of the irradiance due to the distance between light source and solution); and DF is the divergence factor (decrease of the UV beam due to the distance between the light source and surface media).

$$\text{UV dose} = E' \times t \qquad (2)$$

The irradiance value calculated in the water is used as the average fluence rate (mW cm^{-2}). The inverse of this number is the t value, exposure time (s), which was used to obtain the UV dose (mJ cm^{-2}) by multiplying the exposure time by the UV irradiance E'. The LP UV dosage or fluence, used in this study were 0, 100, 200, 400, 600 and 800 mJ cm^{-2}.

Briefly, 200 mL of the prepared sample (groundwater spiked with ICMs) was transferred to a crystallization petri dish (inner diameter 12.5 cm) and sodium hypochlorite was added. For each sample, 10 mL was taken out to measure the concentration of free chlorine by a Hatch colorimeter immediately before and after UV irradiation. The remaining volume was then aliquoted for the ICMs analysis. This was repeated for the UV/H_2O_2 experiments, where H_2O_2 concentrations were measured using a hydrogen peroxide colorimeter kit I-2016 (CHEMetrics) both before and after UV irradiation. The remaining volume was also aliquoted for ICMs analysis. To ensure that the oxidant reaction time was equal to the UV irradiation exposure time, an excess amount of sodium sulfite was prepared to quench the free chlorine and monochloramine after UV irradiation.

3. Results

3.1 Optimization for liquid chromatography conditions

To maximize separation efficiently of the seven target ICMs, Agilent Poroshell 120 EC-C8 column (4.6×100 mm, 2.7 μm particle size) was chosen, while water containing 0.1% (v/v) formic acid and methanol containing 0.1% (v/v) formic acid were applied as mobile phases. As shown in Fig. 1, under the optimized LC conditions, baseline separation was achieved for the isomers—DTZ and IOT, which were difficult to separate (Ens et al., 2014). Also, the two stereoisomers of IOP were separated. However, since no single standards were available for IOP stereoisomers, the two peaks were combined to quantify the concentration of IOP.

[Fig. 1]

3.2. Method linearity and limits of detection

The DI LC-MS/MS method was validated utilizing drinking water, groundwater and secondary effluent spiked with 200 ngL^{-1} of target ICM into each water matrix by seven replicates. The recovery for target ICMs was 86 to 100% in drinking water, 85 to 103% in groundwater and 84 to 105% in WWTP effluent. A ten-point calibration curve was prepared in MQ water ranging from 20-20000 ng L^{-1} in order to test LC-MS/MS response. Calibration curves for target ICMs had good linearity (R2>0.996). As shown in Table 3, IDLs for target ICMs ranged from 0.5-1.5 ng L^{-1}, and MDLs ranged from 0.7-21 ng L^{-1} in ultra pure water. The work of chromatographic separation is shown in Fig 2.

[Table 3]

[Fig. 2]

3.3.Removal of ICM during LPUV/H_2O_2, LPUV/Cl_2 and LPUV/NH_2Cl treatment

A pseudo-first order kinetics was observed for the degradation of seven ICMs and plotted by linear relations between ln([C]/[C_0]) versus UV dose (mJ cm^{-2}) during UV exposure (0, 100, 200, 400, 600 and 800 mJ cm^{-2}) with an addition of 0, 3.5 and 7 mg L^{-1} of hydrogen peroxide and 0, 2.5 and 5 mg L^{-1} of free chlorine and monochloramine

respectively. Since the fluence (mJ cm^{-2}) delivered into the sample is the product of the exposure time (s) and the fluence rate (mW cm^{-2}) at the same wavelength range, Eq (3) is equivalent to Eq (4) (Wang et al.,2012). From the slope of each plot, the apparent rate constant for each condition were determined experimentally

$$\ln\left(\frac{C}{C_0}\right)_{UV-OXI} = -K_{UV-OXI}t = -(K_{UV} + K_{OXI})t \quad (3)$$

$$\ln\left(\frac{C}{C_0}\right)_{UV-OXI} = -K_{UV-OXI}f = -(K_{UV} + K_{OXI})f \quad (4)$$

Where C_0 and C are the concentration of ICMs before and after the treatment, the K_{oxi} represents different oxidants (i.e. H_2O_2, Cl_2, and NH_2Cl) at different concentrations explained above, and f is the fluence rate. The direct photolysis linear plots of $\ln[C]/[C_0]$ versus fluence (UV dose) for all ionic and non-ionic ICMs are shown in Fig. 3. Generally, the addition of H_2O_2 and oxidants such as Cl^- and NH_2Cl during UV treatment can significantly improve the degradation of organic contaminants due to the contribution of •OH, •Cl and •NHCl (Buxton & Ross, 1988; Fang & Shang, 2014; Patton et al., 2017). However, the addition of each oxidant did not promote an extent in the attenuation of target ICMs, which indicates UV direct photolysis is the primary mechanism to attenuate these photolabile organic compounds. Table 3 shows fluence decay apparent rate constant. Even at UV doses of 100 mJ cm^{-2} without additional of oxidants, 37% attenuation was observed. Furthermore, the formation of •OH did not appreciably promote the attenuation of photo-susceptible ICMs during AOP treatment, which could be due to rapid degradation attributed from direct photolysis (Kim & Tanaka, 2009; Pereira & Singer, 2007).

[Table 4]

[Fig. 3]

The photo-degradability performance relies mainly on two compound-specific features such as the quantum yield (ϕ) at specific wavelength (λ) and the molar absorption coefficient (ε) to which it is exposed (Sanches & Pereira, 2010; Tian et al., 2014). The quantum yield is the ratio between decomposed molecules and the total numbers of photons absorbed by the compound, while the molar absorption coefficient is a measurement of the capacity of a compound to absorb light at a specific wavelength from the UV spectrum. Even the use of low UV doses can promote the degradation of photolabile organic compounds by direct photolysis due to their potential to absorb light. Therefore, the abatement of all ICMs by direct photolysis was mainly associated to the photochemical reaction since more photons are absorbed.

[Table 5]

Since aqueous hydrogen peroxide, free chlorine, and monochloramine components have different extinction coefficient at 254 nm, when samples are exposed to LPUV, the fraction of UV absorbed by the sample is different in each case. Thus, different pseudo first order decay constant can be obtained. The average removal of ICM under each treatment is presented ahead. As shown in Fig. 3, increasing the UV dose increase the destruction of target ICM. Nevertheless, increasing the oxidants dose (hydrogen peroxide and free chlorine) does not enhance ICM removal. This could be due to their high product of molar absorption coefficient and quantum yield. This yields in the very high photo-degradability compound, neglecting the need of oxidants to the extent the

300 removals (Allard et al., 2016; Yu et al., 2015). Table 5 shows basic properties of ICMs
301 along with molar absorption and quantum yield.
302
303 **4. Conclusion**
304
305 This direct injection method yielded lower method detection limits of 0.7-21 ng L^{-1} and
306 recoveries above 95% in groundwater, drinking water and secondary effluent.
307 Validation experiments under LPUV illustrated that direct photolysis is the main
308 mechanism to attenuate seven target ICM in groundwater. Oxidants such as hydrogen
309 peroxide, free chlorine and monochloramine did not enhance the removal of ICM. The
310 use of free chlorine and monochloramine as a radical under AOP may have some
311 adverse consequence such as the formation of a variety of iodinated disinfection by
312 products of low-high molecular weight that are still unknown.
313
314 **5. Acknowledgments**
315
316 The authors would like to acknowledge The University of Arizona, Department of
317 Chemical and Environmental engineering for providing the facility for UV experiments.
318 We especially wish to acknowledge Xylem Wedeco for providing collimated beam
319 device low-pressure ultra violet light reactor. We also appreciate Agilent Technologies
320 for their assistance with the acquisition and maintenance of the instrumentation used in
321 this study.
322
323 **6. References:**
324 Allard, S., Criquet, J., Prunier, A., Falantin, C., Le Person, A., Yat-Man Tang, J., Croué,

J.P., 2016. Photodecomposition of iodinated contrast media and subsequent formation of toxic iodinated moieties during final disinfection with chlorinated oxidants. Water Res. 103, 453–461. https://doi.org/10.1016/j.watres.2016.07.050

André, F., De Wasch, K.K.G., De Brabander, H.F., Impens, S.R., Stolker, L.A.M., Van Ginkel, L., Stephany, R.W., Schilt, R., Courtheyn, D., Bonnaire, Y., Fürst, P., Gowik, P., Kennedy, G., Kuhn, T., Moretain, J.P., Sauer, M., 2001. Trends in the identification of organic residues and contaminants: EC regulations under revision. TrAC - Trends Anal. Chem. 20, 435–445. https://doi.org/10.1016/S0165-9936(01)00085-1

Bolton, J.R., Linden, K.G., 2003. Standardization of methods for fluence (UV dose) determination in bench-scale UV experiments. J. Environ. Eng. 129, 209–215. https://doi.org/10.1061/(ASCE)0733-9372(2003)129:3(209)

Busetti, F., Linge, K.L., Blythe, J.W., Heitz, A., 2008. Rapid analysis of iodinated X-ray contrast media in secondary and tertiary treated wastewater by direct injection liquid chromatography-tandem mass spectrometry. J. Chromatogr. A 1213, 200–208. https://doi.org/10.1016/j.chroma.2008.10.021

Buxton, G. V., Greenstock, C.L., Helman, W.P., Ross, A.B., 1988. Critical Review of rate constants for reactions of hydrated electrons, hydrogen atoms and hydroxyl radicals (·OH/·O−in Aqueous Solution. J. Phys. Chem. Ref. Data 17, 513–886. https://doi.org/10.1063/1.555805

Duirk, S.E., Lindell, C., Cornelison, C.C., Kormos, J., Ternes, T.A., Attene-Ramos, M., Osiol, J., Wagner, E.D., Plewa, M.J., Richardson, S.D., 2011. Formation of toxic iodinated disinfection by-products from compounds used in medical imaging. Environ. Sci. Technol. 45, 6845–6854. https://doi.org/10.1021/es200983f

Ens, W., Senner, F., Gygax, B., Schlotterbeck, G., 2014. Development, validation, and

application of a novel LC-MS/MS trace analysismethod for the simultaneous quantification of seven iodinated X-ray contrast media and three artificial sweeteners in surface, ground, and drinking water. Anal. Bioanal. Chem. 406, 2789–2798. https://doi.org/10.1007/s00216-014-7712-0

Fang, J., Fu, Y., Shang, C., 2014. The roles of reactive species in micropollutant degradation in the UV/free chlorine system. Environ. Sci. Technol. 48, 1859–1868. https://doi.org/10.1021/es4036094

Kim, I., Yamashita, N., Tanaka, H., 2009. Photodegradation of pharmaceuticals and personal care products during UV and UV/H2O2 treatments. Chemosphere 77, 518–525. https://doi.org/10.1016/j.chemosphere.2009.07.041

Kirchmer, C.J., 1982. Trace analyses for wastewaters. Environ. Sci. Technol. 16, 430A. https://doi.org/10.1021/es00102a706

Patton, S., Li, W., Couch, K.D., Mezyk, S.P., Ishida, K.P., Liu, H., 2017. Impact of the ultraviolet photolysis of monochloramine on 1,4-dioxane removal: New insights into potable water reuse. Environ. Sci. Technol. Lett. 4, 26–30. https://doi.org/10.1021/acs.estlett.6b00444

Pauwels, B., Verstraete, W., 2006. The treatment of hospital wastewater: An appraisal. J. Water Health 4, 405–416. https://doi.org/10.2166/wh.2006.025

Pereira, V.J., Weinberg, H.S., Linden, K.G., Singer, P.C., 2007. UV degradation kinetics and modeling of pharmaceutical compounds in laboratory grade and surface water via direct and indirect photolysis at 254 nm. Environ. Sci. Technol. 41, 1682–1688. https://doi.org/10.1021/es061491b

Pérez, S., Barceló, D., 2007. Fate and occurrence of X-ray contrast media in the environment. Anal. Bioanal. Chem. 387, 1235–1246. https://doi.org/10.1007/s00216-006-0953-9

375 Richardson, S.D., Fasano, F., Ellington, J.J., Crumley, F.G., Buettner, K.M., Evans, J.J.,
376 Blount, B.C., Silva, L.K., Waite, T.J., Luther, G.W., Mckague, A.B., Miltner, R.J.,
377 Wagner, E.D., Plewa, M.J., 2008. Occurrence and mammalian cell toxicity of
378 iodinated disinfection byproducts in drinking water. Environ. Sci. Technol. 42,
379 8330–8338. https://doi.org/10.1021/es801169k
380 Sacher, F., Raue, B., Brauch, H.J., 2005. Analysis of iodinated X-ray contrast agents in
381 water samples by ion chromatography and inductively-coupled plasma mass
382 spectrometry. J. Chromatogr. A 1085, 117–123.
383 https://doi.org/10.1016/j.chroma.2005.01.031
384 Sanches, S., Barreto Crespo, M.T., Pereira, V.J., 2010. Drinking water treatment of
385 priority pesticides using low pressure UV photolysis and advanced oxidation
386 processes. Water Res. 44, 1809–1818. https://doi.org/10.1016/j.watres.2009.12.001
387 Tarun Anumol, Shimin Wu, S.M. and S.S., 2013. Analysis of Trace Organic
388 Contaminants in Water by Direct Injection Using Agilent 6490 LC / MS / MS with
389 Pos / Neg. Appl. note, Environ. Agil. 1–10.
390 Ternes, T.A., Bonerz, M., Herrmann, N., Löffler, D., Keller, E., Lacida, B.B., Alder,
391 A.C., 2005. Determination of pharmaceuticals, iodinated contrast media and musk
392 fragrances in sludge by LC tandem MS and GC/MS. J. Chromatogr. A 1067, 213–
393 223. https://doi.org/10.1016/j.chroma.2004.10.096
394 Ternes, T.A., Hirsch, R., 2000. Occurrence and behavior of X-ray contrast media in
395 sewage facilities and the aquatic environment. Environ. Sci. Technol. 34, 2741–
396 2748. https://doi.org/10.1021/es991118m
397 Tian, F.X., Xu, B., Lin, Y.L., Hu, C.Y., Zhang, T.Y., Gao, N.Y., 2014.
398 Photodegradation kinetics of iopamidol by UV irradiation and enhanced formation
399 of iodinated disinfection by-products in sequential oxidation processes. Water Res.

58, 198–208. https://doi.org/10.1016/j.watres.2014.03.069

Wang, D., Bolton, J.R., Hofmann, R., 2012. Medium pressure UV combined with chlorine advanced oxidation for trichloroethylene destruction in a model water. Water Res. 46, 4677–4686. https://doi.org/10.1016/j.watres.2012.06.007

Weissbrodt, D., Kovalova, L., Ort, C., Pazhepurackel, V., Moser, R., Hollender, J., Siegrist, H., Mcardell, C.S., 2009. Mass flows of x-ray contrast media and cytostatics in hospital wastewater. Environ. Sci. Technol. 43, 4810–4817. https://doi.org/10.1021/es8036725

Westerhoff, P., Yoon, Y., Snyder, S., Wert, E., 2005. Fate of endocrine-disruptor, pharmaceutical, and personal care product chemicals during simulated drinking water treatment processes. Environ. Sci. Technol. 39, 6649–6663. https://doi.org/10.1021/es0484799

Yu, H.-W., Anumol, T., Park, M., Pepper, I., Scheideler, J., Snyder, S.A., 2015. On-line sensor monitoring for chemical contaminant attenuation during UV/H 2 O 2 advanced oxidation process. Water Res. 81, 250–260. https://doi.org/10.1016/j.watres.2015.05.064

Tables and figures
Click here to download Table: Tables and figures .docx

A direct injection liquid chromatography tandem mass spectrometry method for the kinetic study on iodinated contrast media (ICMs) removal in natural water

TABLES

Table 1 Summary of different methods for quantification of ICMs

Compound	Separation & detection	Recovery (%)	Level of detection (ng L^{-1})	Reference
IOD, IOP, DTZ, IOT, IOX, IOM	SPE-LC-(+)-ESI-MS-MS	70 % (surface water)	10-30	(Ternes and Hirsch, 2000)
DTZ, ITA, IXA, IOD, IOM, IOP	SPE-LC-(+)-ESI-MS-MS	63-74% (tap water and WWTP effluent)	10-50	(Hirsch et al., 2000)
DTZ, IOP, IOT, IOX	SPE-LC-(+)-ESI-MS-MS	DTZ: 100% OP:100% IOT:55% IOX:90%	50	(Putschew et al., 2001)
DTZ, ITA, IXA, IOD, IOM, IOP, IOX	LC-(+)-ESI-MS-MS	DTZ:97% ITA:98% IXA:98% IOD:109% IOM:96% IOP:98% IOX:99% (surface water and drinking water)	110-210	(Sacher et al., 2001)
IOD, IOM, IOX, DTZ, IOT, IOP, IXA, IDP	LC-(+)-ESI-MS-MS	100-108% 93-102% (MQ water and WWTP effluent)	IOD: 222, IOM: 730, IOX:800, DTZ:830, ITA:970, IOP:200, IXA:110, IDP:110	(Busetti et al., 2008)
IOH, IOM, IOD, IOP, IOX, DTZ	IC-ICP-MS	94-103% 94-109% (Tap water and surface water)	IOH:70, IOM:100, IOD:`120, IOP:130, IOX:110, DTZ:120	(Sacher et al., 2005)
IOH, DTZ, IDP	LC-UV	92-116% (MQ water and tap water)	50,000	(Borowska et al., 2015)
IOD	LC-UV	--	5000	(Tian et al., 2014)

IOD: iopamidol. IOH: iohexol, IOM: iomeprol, IOP: iopromide, IDP: iodipamide, DTZ: diatrizoate, IOX: ioxitalamic acid, IOT: iothalamic acid, IXA: ioxaglic acid

Table 2 Optimized MRM conditions of target ICM and surrogate standards.

Compound	Abbr.	RT (min)	Surrogate Assignment	Prec Ion	Prod Ion	CE (V)	ESI Mode
Iopamidol	IOD	5.64	IOD-d3	777.9	558.7	28	Positive
				777.9	387.0	44	Positive
Ioxitalamic acid	IOX	6.19	IOD-d3	644.8	301.9	48	Positive
				644.8	428.8	28	Positive
Diatrizoic acid	DTZ	7.15	IOH-d5	614.8	233.0	52	Positive
				614.8	361.0	20	Positive
Iothalamic acid	IOT	7.51	IOH-d5	614.8	360.9	28	Positive
				614.8	177.1	56	Positive
Iohexol	IOH	7.58	IOH-d5	821.9	803.8	20	Positive
				821.9	375.0	56	Positive
Iomeprol	IOM	7.73	IOH-d5	777.9	404.9	48	Positive
				777.9	531.8	32	Positive
Iopromide *	IOP	9.77 &	IOH-d5	791.9	572.8	28	Positive
		10.20		791.9	299.8	60	Positive
Surrogate							
Iopamidol-d3	IOD-d3	5.62	−	781.0	562.0	22	Positive
Iohexol-d5	IOH-d5	7.56	−	826.9	810.0	20	Positive

* two isomer peaks

RT: retention time; Prec: Precursor; Prod: product; CE: collision energy

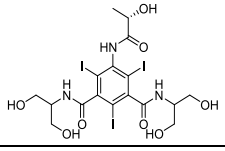
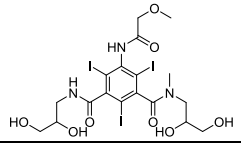
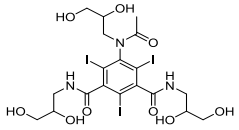
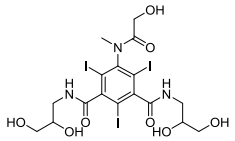
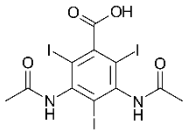
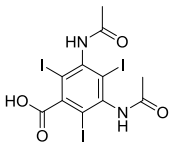
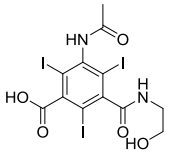
Table 3 Linearity, IDLs, MDLs and recovery for target ICMs

Compound	R^2	IDLs (ng L^{-1})	MDLs (ng L^{-1})	Recovery (%, n=7)		
				Drinking water	Ground water	WWTP Effluent
IOD	0.9960	0.5	3.1	92±5	97±3	94±4
IOX	0.9996	0.5	6.2	90±6	85±3	84±4
DTZ	0.9988	1.5	15	97±4	99±2	101±2
IOT	0.9997	1.5	21	100±3	103±2	105±3
IOH	0.9987	0.5	5.4	86±4	87±6	85±5
IOM	0.9996	0.5	4.5	92±3	91±4	96±4
IOP	0.9996	0.1	0.7	99±3	100±3	103±4

Table 4 Fluence-based decay apparent rate constant (10^{-3} cm^2 mJ^{-1}) by LPUV treatment along different oxidants at different concentrations

	IOD	IOX	DTZ	IOT	IOH	IOM	IOP
K_{UV}	3.3	3.3	3.5	3.2	3.3	3.1	3.0
$K_{UV\text{-}H2O2\text{-}3.5}$	3.7	3.6	3.8	3.4	3.9	3.6	3.6
$K_{UV\text{-}H2O2\text{-}7}$	4.0	3.7	3.9	3.6	4.3	4.0	3.9
$K_{UV\text{-}Cl\text{-}2.5}$	3.6	3.4	3.8	3.4	3.4	3.1	3.1
$K_{UV\text{-}Cl\text{-}5}$	3.6	3.5	3.8	3.4	3.8	3.2	3.3
$K_{UV\text{-}NH2\text{-}2.5}$	3.3	3.3	3.5	3.2	3.5	3.1	3.0
$K_{UV\text{-}NH2\text{-}5}$	3.4	3.4	3.5	3.3	3.5	3.1	3.2

Table 5 Basic properties of target ICMs with molar absorptivity and quantum yield at 254 nm

Name	Molecular Weight and Formula	Structure	Water Solubility (g/L)[a]	Log Kow[b]	Molar absorption[c] ε_{254}	Quantum yield[d] ϕ_{254}
Iopamidol (IOD)	777.09 $C_{17}H_{22}I_3N_3O_8$		134	-1.38	22	3.4
Iopromide (IOP)	791.12 $C_{18}H_{24}I_3N_3O_8$		287	-2.49	22.1	3.9
Iohexol (IOH)	821.14 $C_{19}H_{26}I_3N_3O_9$		1000	-2.81	27.7	4.1
Iomeprol (IOM)	777.09 $C_{17}H_{22}I_3N_3O_8$		427	-1.35	20	N.A.
Diatrizoic acid (DTZ)	613.92 $C_{11}H_8I_3N_2O_4$		1000	1.37	15.9	7.1
Iothalamic acid (IOT)	613.92 $C_{11}H_9I_3N_2O_4$		1000	1.47	19.1	3.8
Ioxitalamic acid (IOX)	643.94 $C_{12}H_{11}I_3N_2O_5$		1000	0.50	N.A.	N.A.

[a] from ACD/Labs 6.0; [b] from KowWIN v1.68; [c] (10^3) (M^{-1} cm^{-1}); [d](10^{-2}) (mol $Einsten^{-1}$)

N.A.= Not available

FIGURES

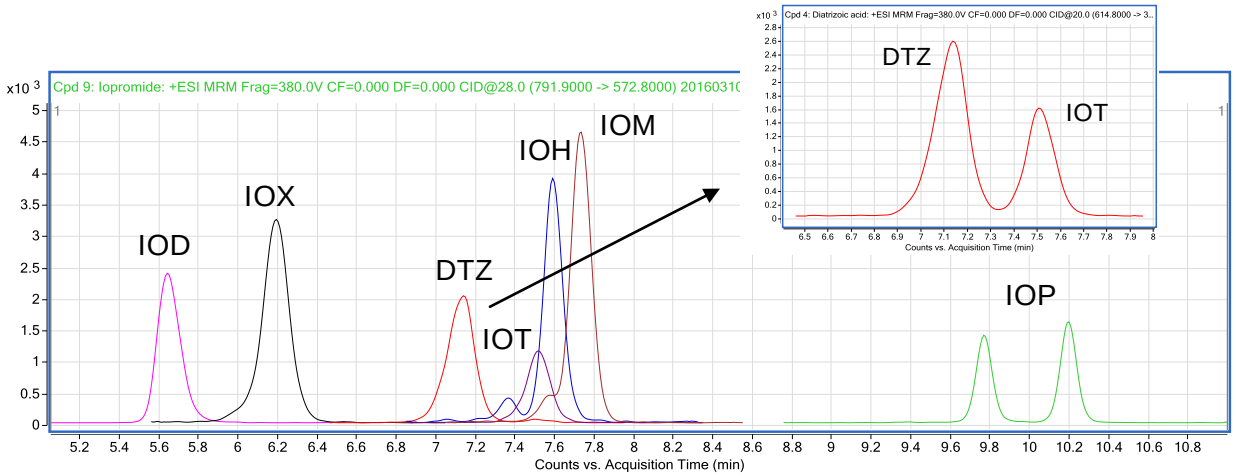


Fig. 1 LC-MS/MS Chromatogram of seven target ICM at 500 ng L^{-1}.

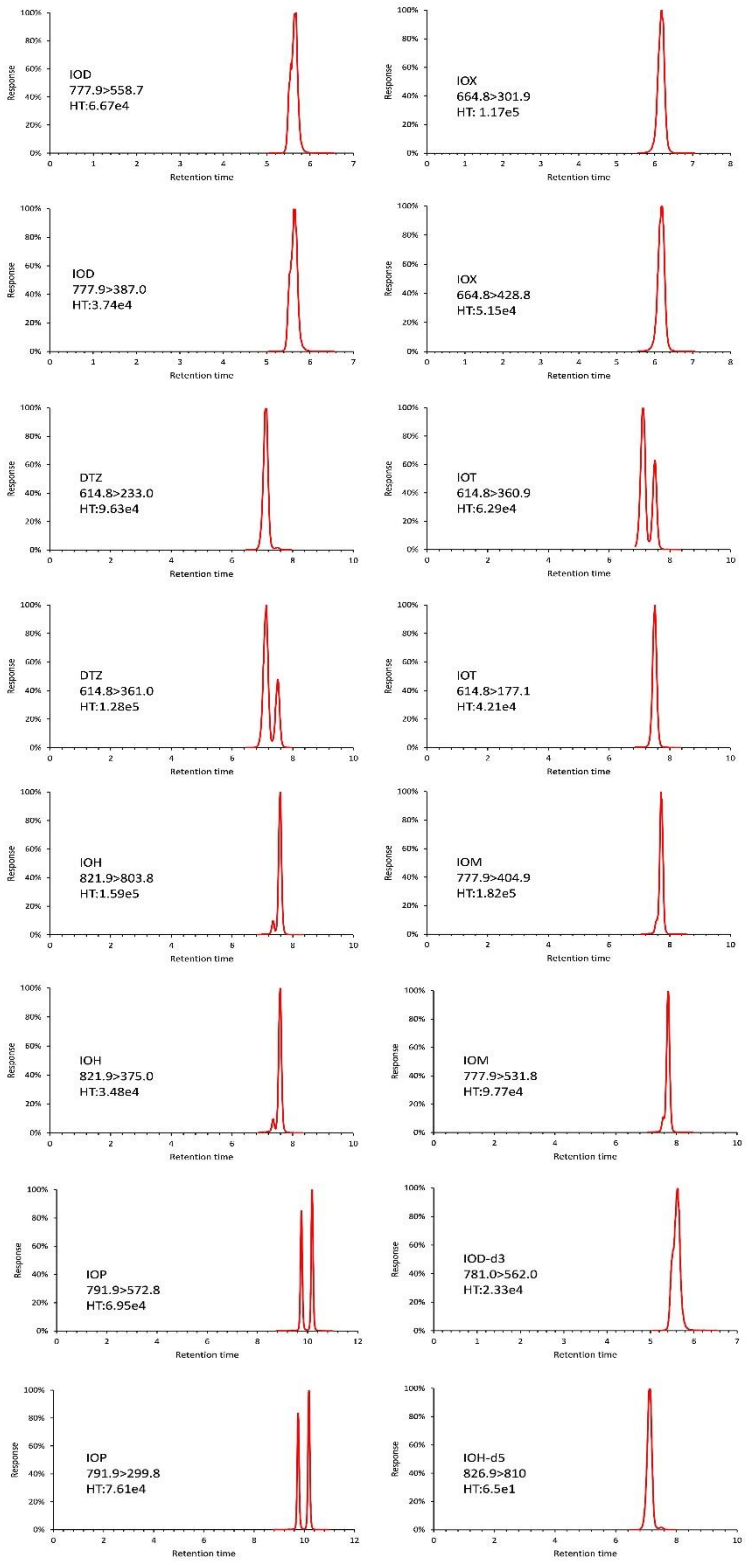


Fig 2 LC-MS/MS chromatogram of all analytes at 20µg L^{-1} and surrogate standards at 10 µg L^{-1} (HT is the counts of height peak).

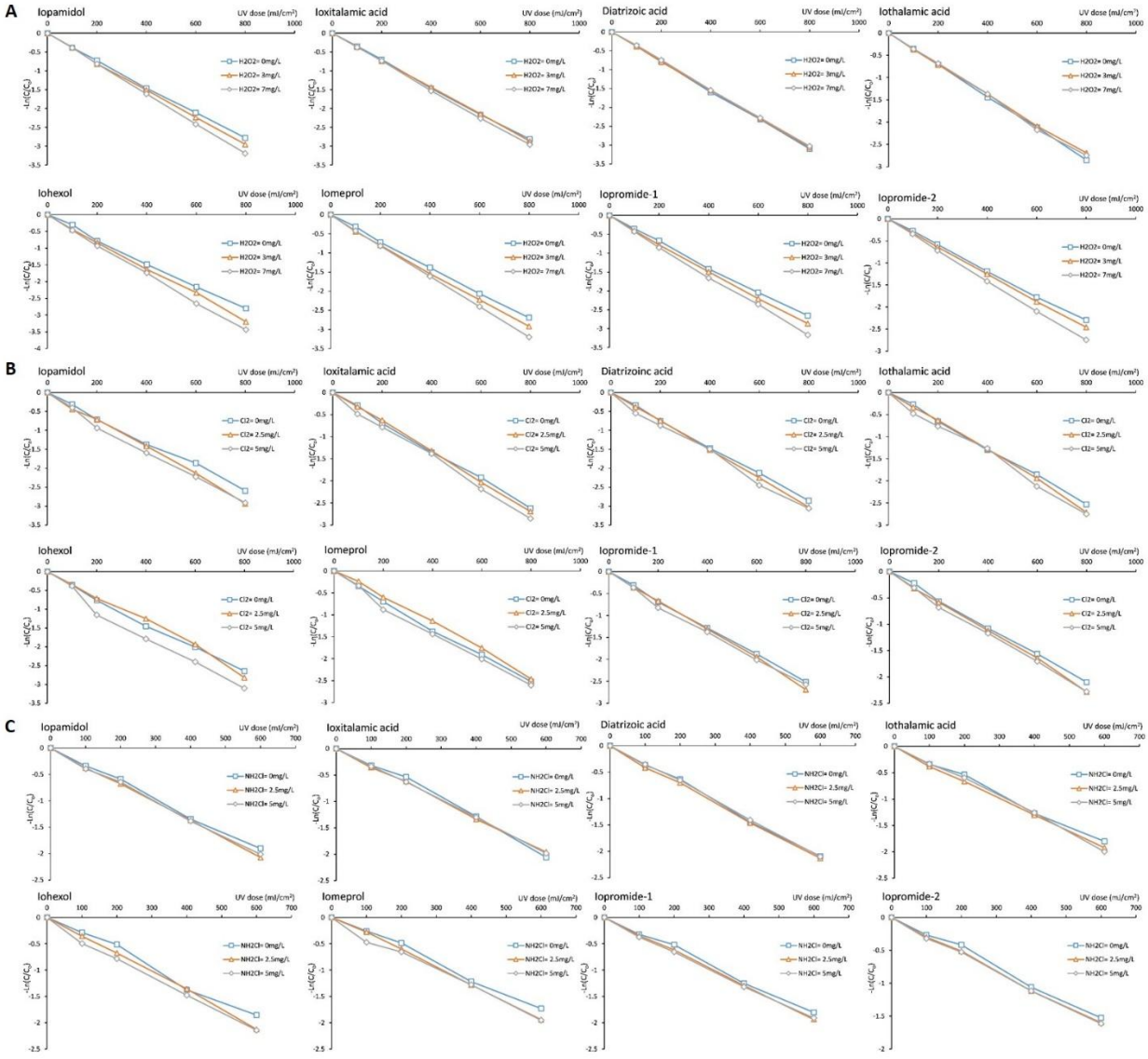


Fig. 3 ICMs attenuation through LPUV A) H_2O_2 B) Cl_2 and C) NH_2Cl