Determination of iopromide in environmental waters by ion chromatography-ICP-MS

Application note

Environmental

Authors

Armando Durazo, Tarun Anumol, and Shane A. Snyder

Department of Chemical & Environmental Engineering and the BIO5 Institute, University of Arizona Tucson, AZ, USA

Abstract

The determination of iopromide in environmental waters has been accomplished using an Agilent 7700x ICP-MS coupled to an Agilent 1260 LC. The use of High Matrix Introduction (HMI) technology allows for prolonged operation with a sodium hydroxide (NaOH) eluent, and the Octopole Reaction System (ORS^3) in helium gas mode reduces polyatomic interferences on iodine (m/z 127).

Agilent Technologies

Introduction

Iopromide is an iodinated contrast medium (ICM), which is used to image internal body organs and blood vessels by x-ray or computerized tomography (CT) scan. Iopromide is generally given to patients in g/L concentrations and is excreted within 24 hours in the patient's urine [1]. It is very hydrophilic (log K_{ow} = –2.33) and non-ionic, properties that make it quite persistent in the environment. The molecular formula of iopromide is $C_{18}H_{24}I_3N_3O_8$ and its chemical structure is shown in Figure 1.
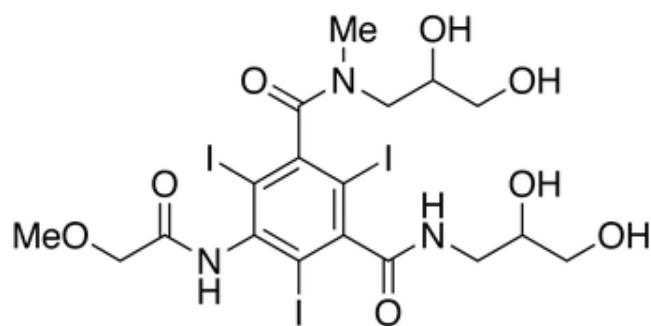

Figure 1. Chemical structure of iopromide

Iopromide's presence in surface waters and wastewaters has been widely reported as ranging from a few ng/L to as much as 10 µg/L in sewage treatment plants [2–4]. Furthermore, ICMs are known to be resistant to sewage treatment and studies have shown they are relatively poorly removed by conventional treatment processes [2, 5–7]. Due to its presence and environmental persistence, it has also been suggested that iopromide be used as a potential indicator compound of wastewater contamination [8].

Recent studies indicate that iopromide and other ICMs can form toxic iodinated disinfection byproducts (I-DBPs) during oxidation and disinfection water treatment processes [4, 9, 10]. Certain I-DBPs are known to be several times more toxic than chlorinated and brominated disinfection by-products [11–13] but are, as yet, not regulated by the US Environmental Protection Agency (USEPA) or other regulatory agencies.

Most analytical methods developed for iopromide and other ICMs involve the use of LC coupled to a mass spectrometer, generally a triple quadrupole mass spectrometer [9, 14–17]. Hybrid methods involving ion trap and nuclear magnetic resonance have also been employed. This application note describes the optimized conditions for sensitive and reproducible analysis of sub-ppb levels of iopromide in water extracts, using an Agilent 1260 LC coupled to an Agilent 7700x ICP-MS. With the use of a 500 µL injection volume, we have established a lower method reporting limit (MRL) of 0.1 ppb for iopromide in the diluted methanol extracts in our assay; in theory this corresponds to a lower MRL of 2 ppt in our environmental water samples.

Experimental

Environmental water samples were collected at established monitoring points along the rivers and creeks in the state of California, including locations near water treatment plants. The water samples were filtered through 0.7 µm filters and then extracted using an automated solid-phase extraction (SPE) system. 200 mg hydrophilic-lipophilic balance (HLB) cartridges were first preconditioned with 5 mL of methyl tertiary butyl ether (MTBE), followed by 5 mL of methanol and 5 mL of HPLC grade water. 1 L of each sample was then loaded onto a cartridge at a flow rate of 15 mL/min, after which the cartridges were rinsed with HPLC grade water followed by drying with nitrogen gas for 30 minutes. Adsorbed analytes were then eluted into 15 mL graduated conical tubes with 5 mL of methanol followed by 5 mL of 10/90 (v/v) methanol/MTBE solution. The eluent was then evaporated to a total volume less than 100 µL under flowing nitrogen followed by reconstitution to 1.0 mL total volume using methanol. 50 µL of this extract was then diluted with 950 µL of HPLC grade water to give the final extract used for IC-ICP-MS analysis.

These diluted extracts were injected into an Agilent 1260 HPLC coupled to an Agilent 7700x ICP-MS, with an injection volume of 500 µL. The chromatographic separation was performed using a Dionex AG16 4 x 50 mm guard column followed by a Dionex AS16 4 x 250 mm analytical column. A gradient elution from 2–90 mM sodium hydroxide (NaOH) was established,

using a binary gradient consisting of reagent water (A) and 100 mM NaOH (B) with a constant flow rate of 1.0 mL/min. Gradient parameters were as follows: 2% B for 18.5 minutes then increased linearly for 3.5 minutes to 40% B and held for two minutes, finally stepping up to 90% B and holding for six minutes. The gradient returned to 2% B for five minutes at the end of the run, to re-equilibrate the column, giving a total run time of 35 minutes. A 25 second needle wash using 10% aqueous methanol was used following all injections of standards and samples.

The Agilent 7700x ICP-MS was operated with HMI sample introduction (0.6 L/min dilution gas, 0.5 L/min carrier gas, sample depth = 9 mm) and in helium collision mode (He flow 3.5 mL/min). Iodine (m/z 127) intensity was monitored in time-resolved analysis (TRA) mode using a 2 second integration time over a 37 minute time window. The use of HMI allows for extended analysis of high matrix samples with minimal matrix deposition in the interface cones, and the use of the He collision cell removes potential polyatomic interferences on masses 127 such as $^{126}XeH^+$. A calibration curve for iopromide was prepared using aqueous standards with concentrations of 0.0, 0.1, 1, 10, 100 and 1000 ppb of intact compound (Figure 3).

Results and discussion

Using the method described, we have been able to detect iopromide in all non-zero standards used in our study. The chromatogram obtained for the 0.1 ppb injection is clearly distinguishable from the blank injection (as shown in Figure 2), and the calibration curve is linear over four orders of magnitude (as shown in Figure 3). This concentration range encompasses the levels at which iopromide has been observed in environmental waters including undiluted wastewater effluent.

The standards and samples in this report were analyzed during a 24 hour continuous sequence. The results obtained from this sequence are shown in Table 1. The other CCVs analyzed at the end of this sequence all agreed with their predicted values within approximately 10%.

In addition to iopromide, several other iodine containing compounds were detected in our chromatograms, as shown in Figure 4. These unknown species can be quantified based on their iodine content, using compound-independent calibrations (CIC), where the iodine content of an unknown compound is calibrated using the iodine response for a known compound, in this case iopromide. ICP-MS is ideally suited for analysis using CIC, as the high temperature ICP ion source ensures that the elemental response of the target element (iodine in this case) is essentially independent of the compound in which the target element is present. The quantitation of the iodine content in these unidentified peaks is listed in Table 2.
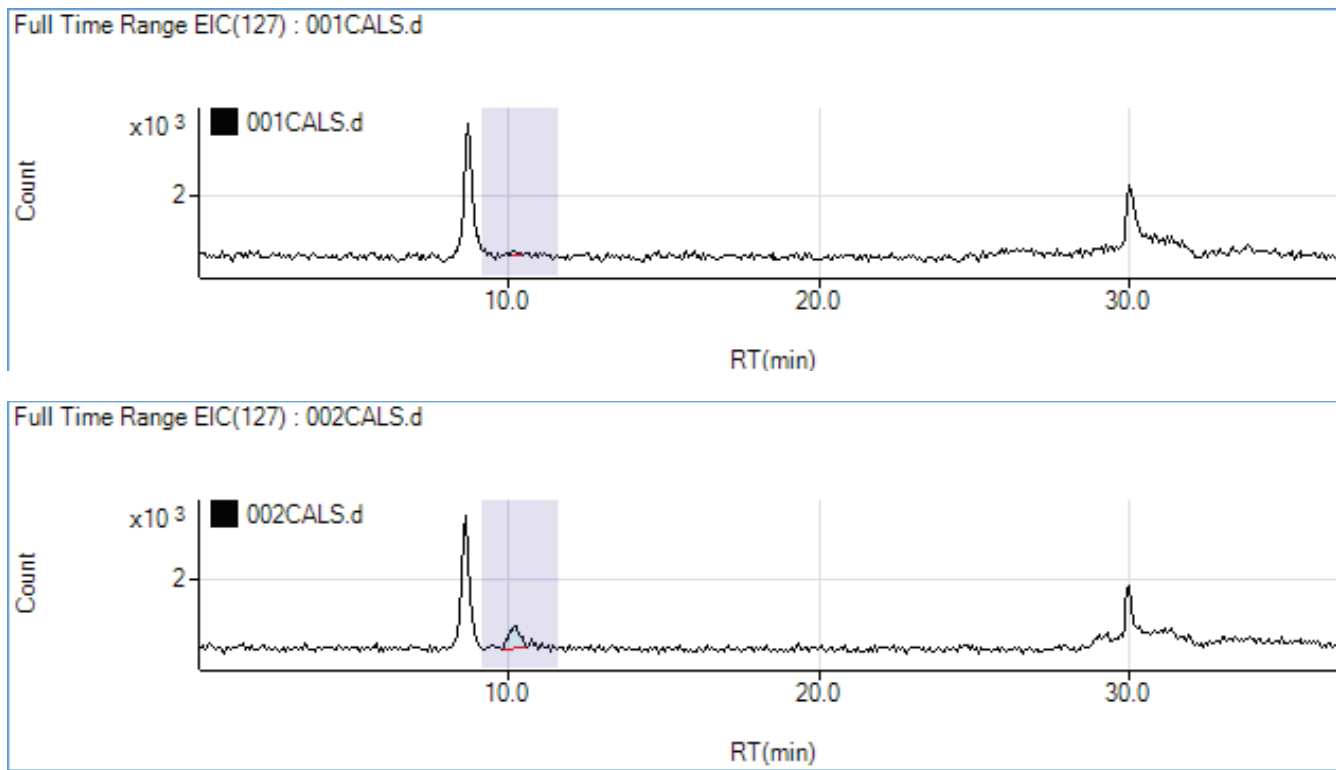
Figure 2. Comparison of the iodine chromatograms (*m/z* 127) obtained from injections of an aqueous blank extract (top) and an aqueous 0.1 ppb iopromide standard (bottom). The retention time of iopromide is 10.1 minutes.
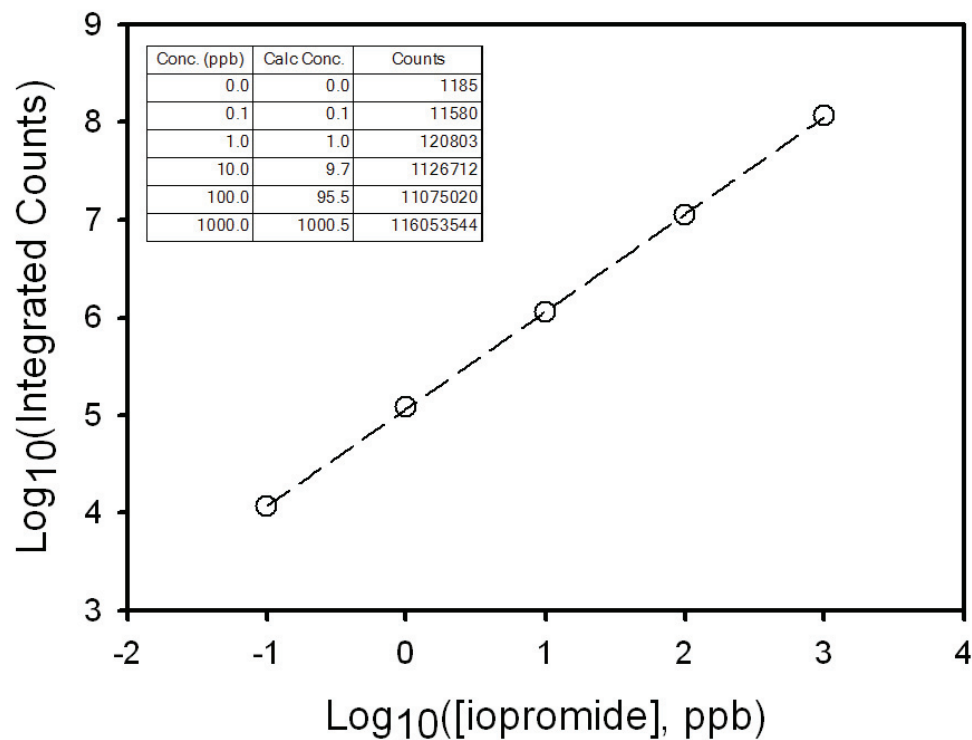

Conc. (ppb)	Calc Conc.	Counts
0.0	0.0	1185
0.1	0.1	11580
1.0	1.0	120803
10.0	9.7	1126712
100.0	95.5	11075020
1000.0	1000.5	116053544

Figure 3. Calibration curve (log log) obtained for iopromide. The concentration axis is in ppb iopromide and the calibration points are at 0.0, 0.1, 1, 10, 100, and 1000 ppb of iopromide. Inset table lists calibration standard responses.

Table 1. Summary of iopromide concentration determined in all samples measured

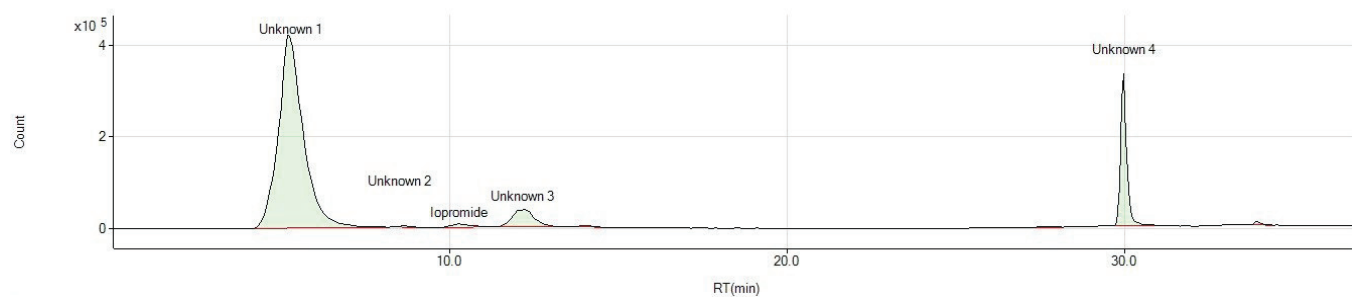| Sample				Conc. (ppb)
007SMPL.d	4/20/2012 2:03 PM	Sample	SJC1	246.19
008SMPL.d	4/20/2012 2:48 PM	Sample	LAR Ref	0.14
009SMPL.d	4/20/2012 3:33 PM	Sample	LAR Eq blank	0.19
010SMPL.d	4/20/2012 4:18 PM	Sample	LAR 6	2.53
011SMPL.d	4/20/2012 5:04 PM	Sample	LAR 5	1.97
012SMPL.d	4/20/2012 5:49 PM	Sample	LAR 4	2.44
013SMPL.d	4/20/2012 6:34 PM	Sample	LAR 3	1.86
014SMPL.d	4/20/2012 7:19 PM	Sample	LAR 2	0.57
015SMPL.d	4/20/2012 8:04 PM	Sample	LAR 1	2.19
016SMPL.d	4/20/2012 8:50 PM	Sample	Eq blank	0.00
017SMPL.d	4/20/2012 9:35 PM	Sample	100 ppb STD	107.23
018SMPL.d	4/20/2012 10:20 PM	Sample	SGR ref	0.14
019SMPL.d	4/20/2012 11:05 PM	Sample	SGR 6	32.69
020SMPL.d	4/20/2012 11:51 PM	Sample	SGR 5b	33.34
021SMPL.d	4/21/2012 12:36 AM	Sample	SGR 5a	1.68
022SMPL.d	4/21/2012 1:21 AM	Sample	SGR 5	85.22
023SMPL.d	4/21/2012 2:06 AM	Sample	SGR 3b	1.13
024SMPL.d	4/21/2012 2:52 AM	Sample	SGR 3a	108.35
025SMPL.d	4/21/2012 3:37 AM	Sample	Blank	0.05

Figure 4. Extracted ion chromatogram (*m/z* 127) of a representative sample indicating the presence of various iodinated compounds in water extracts

Table 2. Summary of the concentrations of iodinated compounds (expressed as iodine concentration) measured in all extracts. Note that the results for all compounds including iopromide are expressed as iodine concentration, so the reported values shown for iopromide expressed as iodine are approximately half the actual iopromide concentrations shown in Table 1.

Sample				Unknown 1 RT 5.2 min	Unknown 2 RT 8.5 min	Iopromide (as I)	Unknown 3 RT 12 min	Unkown 4 RT 30 min
Data file	Acq. date and time	Type	Sample name	Conc. (ppb)	Conc. (ppb)	Conc. (ppb)	Conc. (ppb)	Conc. (ppb)
007SMPL.d	4/20/2012 2:03 PM	Sample	SJC1	268.55	0.24	118.17	5.77	9.64
008SMPL.d	4/20/2012 2:48 PM	Sample	LAR Ref	1.43	0.23	0.07	0.00	55.55
009SMPL.d	4/20/2012 3:33 PM	Sample	LAR Eq blank	1.86	0.20	0.09	0.00	0.38
010SMPL.d	4/20/2012 4:18 PM	Sample	LAR 6	84.23	0.29	1.21	6.16	17.13
011SMPL.d	4/20/2012 5:04 PM	Sample	LAR 5	98.87	0.39	0.95	7.11	11.95
012SMPL.d	4/20/2012 5:49 PM	Sample	LAR 4	128.68	0.38	1.17	12.97	13.03
013SMPL.d	4/20/2012 6:34 PM	Sample	LAR 3	116.40	0.27	0.89	10.21	12.62
014SMPL.d	4/20/2012 7:19 PM	Sample	LAR 2	156.01	0.22	0.28	12.86	14.87
015SMPL.d	4/20/2012 8:04 PM	Sample	LAR 1	189.00	0.29	1.05	12.15	22.51
016SMPL.d	4/20/2012 8:50 PM	Sample	Eq blank	0.28	0.19	0.00	0.00	0.21
017SMPL.d	4/20/2012 9:35 PM	Sample	100 ppb STD	0.00	0.15	51.47	N/D	0.11
018SMPL.d	4/20/2012 10:20 PM	Sample	SGR ref	0.34	0.21	0.07	0.00	0.29
019SMPL.d	4/20/2012 11:05 PM	Sample	SGR 6	142.49	0.16	15.69	8.46	20.54
020SMPL.d	4/20/2012 11:51 PM	Sample	SGR 5b	194.45	0.12	16.00	11.20	14.92
021SMPL.d	4/21/2012 12:36 AM	Sample	SGR 5a	7.27	0.19	0.81	0.37	54.73
022SMPL.d	4/21/2012 1:21 AM	Sample	SGR 5	326.73	0.10	40.91	11.29	5.66
023SMPL.d	4/21/2012 2:06 AM	Sample	SGR 3b	24.46	0.28	0.54	3.95	6.56
024SMPL.d	4/21/2012 2:52 AM	Sample	SGR 3a	322.50	N/D	52.01	11.36	3.14
025SMPL.d	4/21/2012 3:37 AM	Sample	Blank	0.03	0.23	0.03	0.00	0.18

Conclusions

We have successfully quantified iopromide in a series of environmental water extracts using an Agilent 1260 LC coupled to an Agilent 7700x ICP-MS. This experimental arrangement allowed for us to establish an analytical method with a lower method reporting limit (MRL) of 0.1 ppb iopromide in extracts prepared via automated SPE. The use of the HMI interface allowed for an extended (>24 h) analysis to be completed (using non-volatile eluents) with minimal matrix deposition on the interface cones, and the use of He collision gas mode provides effective removal of polyatomic interferences. Not only does our work confirm and quantitate the presence of iopromide in these environmental samples, it indicates the presence of other iodinated organic compounds in these samples that are likely from anthropogenic sources and may prove to be biologically active.

References

1. Steger-Hartmann, T. et al. (2002). Investigations into the environmental fate and effects of iopromide (ultravist), a widely used iodinated x-ray contrast medium. *Water Research, 36*(1), 266–274.

2. Ternes, T. A. & Hirsch, R. (2000). Occurrence and behavior of x-ray contrast media in sewage facilities and the aquatic environment. *Environmental Science & Technology, 34*(13), 2741–2748.

3. Carballa, M., et al. (2004). Behavior of pharmaceuticals, cosmetics and hormones in a sewage treatment plant. *Water Research, 38*(12), 2918–2926.

4. Kormos, J. L., Schulz, M. & Ternes, T. A. (2011). Occurrence of iodinated x-ray contrast media and their biotransformation products in the urban water cycle. *Environmental Science & Technology, 45*(20), 8723–8732.

5. Drewes, J. E., Fox, P. & Jekel, M. (2001). Occurrence of iodinated x-ray contrast media in domestic effluents and their fate during indirect potable reuse. *Journal of Environmental Science and Health Part A — Toxic/Hazardous Substances & Environmental Engineering, 36*(9), 1633–1645.

6. Drewes, J. E., et al. (2003). Fate of pharmaceuticals during ground water recharge. *Ground Water Monitoring and Remediation, 23*(3), 64–72.

7. Snyder, S. A., et al. (2007). Role of membranes and activated carbon in the removal of endocrine disruptors and pharmaceuticals. *Desalination, 202*(1–3), 156–181.

8. Dickenson, E. R. V. et al. (2011). Indicator compounds for assessment of wastewater effluent contributions to flow and water quality. *Water Research, 45*(3), 1199–1212.

9. Duirk, S. E., et al. (2011). Formation of toxic iodinated disinfection byproducts from compounds used in medical imaging. *Environmental Science & Technology, 45*(16), 6845–6854.

10. Schulz, M. et al. (2008). Transformation of the x-ray contrast medium iopromide in soil and biological wastewater treatment. *Environmental Science & Technology, 42*(19), 7207–7217.

11. Richardson, S. D. et al. (2008). Occurrence and mammalian cell toxicity of iodinated disinfection byproducts in drinking water. *Environmental Science & Technology, 42*(22), 8330–8338.

12. Richardson, S. D. et al. (2007). Occurrence, genotoxicity, and carcinogenicity of regulated and emerging disinfection byproducts in drinking water: A review and roadmap for research. *Mutation Research-Reviews in Mutation Research, 636*(1–3), 178–242.

13. Smith, E. M. et al. (2010). Comparison of byproduct formation in waters treated with chlorine and iodine: relevance to point-of-use treatment. *Environmental Science & Technology, 44*(22), 8446–8452.

14. Putschew, A., Schittko, S. & Jekel, M. (2001). Quantification of triiodinated benzene derivatives and x-ray contrast media in water samples by liquid chromatography-electrospray tandem mass spectrometry. *Journal of Chromatography A, 930*(1–2), 127–134.

15. Hirsch, R. et al. (2000). A sensitive method for the determination of iodine containing diagnostic agents in aqueous matrices using LC-electrospray-tandem-MS detection. *Fresenius Journal of Analytical Chemistry, 366*(8), 835–841.

16. Ternes, T. A. (2001). Analytical methods for the determination of pharmaceuticals in aqueous environmental samples. *Trac-Trends in Analytical Chemistry, 20*(8), 419–434.

17. Vanderford, B. J. et al. (2011). Assessment of sample preservation techniques for pharmaceuticals, personal care products, and steroids in surface and drinking water. *Analytical and Bioanalytical Chemistry, 399*(6), 2227–2234.

www.agilent.com/chem

Agilent Technologies