

# Determination of Iopromide in Environmental Waters by Ion Chromatography-ICP-MS

Iopromide is an iodinated contrast medium (ICM), which is used to image internal body organs and blood vessels by x-ray or computerised 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.

“ We have successfully quantified iopromide in a series of environmental water extracts using an Agilent 1260 LC coupled to an Agilent 7700x ICP-MS. ”

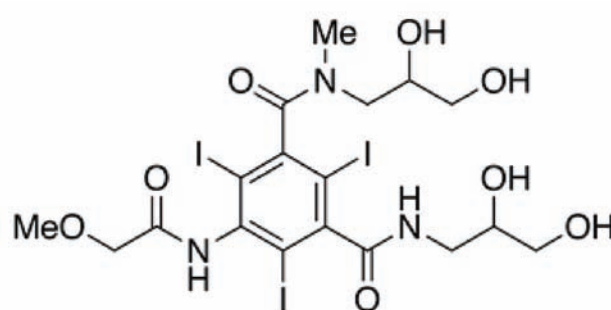


Figure 1: Chemical structure of iopromide

Iopromide's presence in surface waters and wastewaters has been widely reported as ranging from several ng/L to as much as 10  $\mu$ g/L in sewage treatment plant effluents [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 bi-products (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 bi-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 optimised 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  $\mu$ L 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

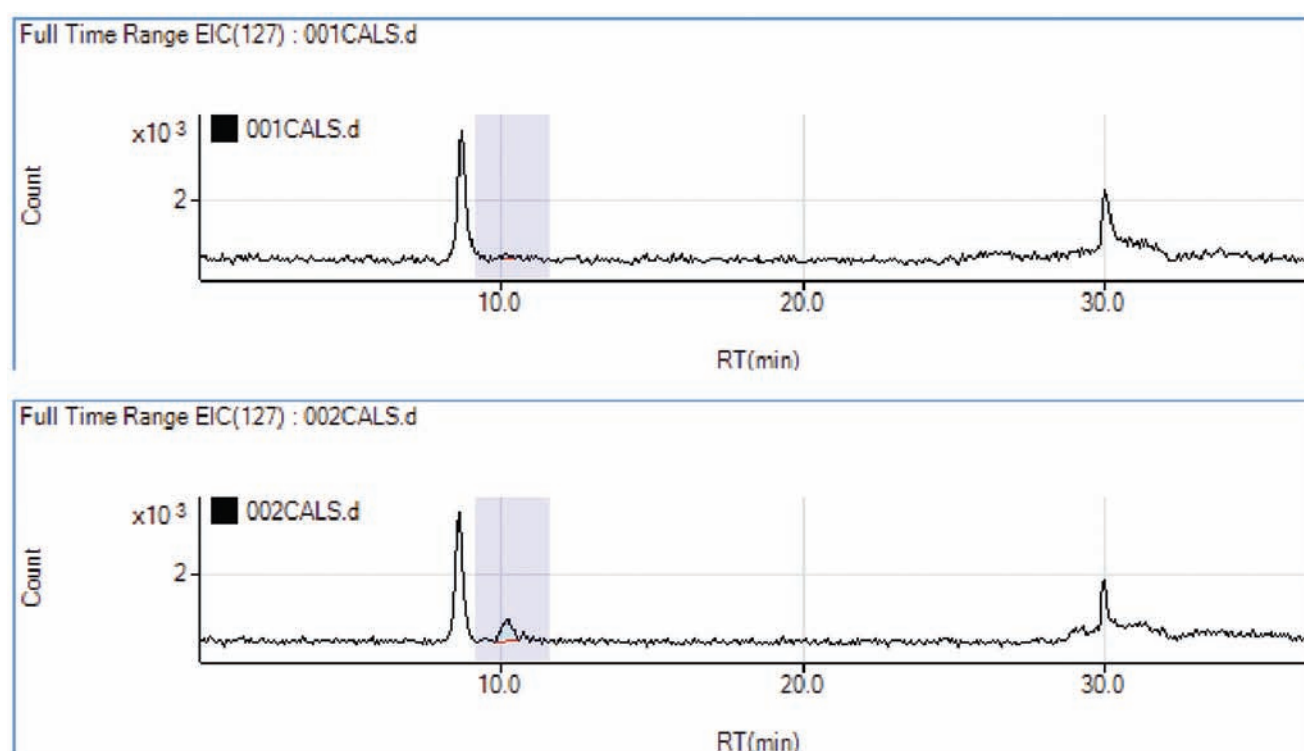


Figure 2: Comparison of the iodine chromatograms ( $m/z$  127) obtained from injections of an aqueous blank extract (top) and an aqueous 0.1 ppb iopromide standard (bottom). The retention time of iopromide is 10.1 minutes.

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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

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 <sup>126</sup>XeH<sup>+</sup>. 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 (Figure 2), and the calibration curve is linear over four orders of magnitude (Figure 3). This concentration range encompasses the levels at which iopromide has been observed in environmental waters including undiluted wastewater effluent.

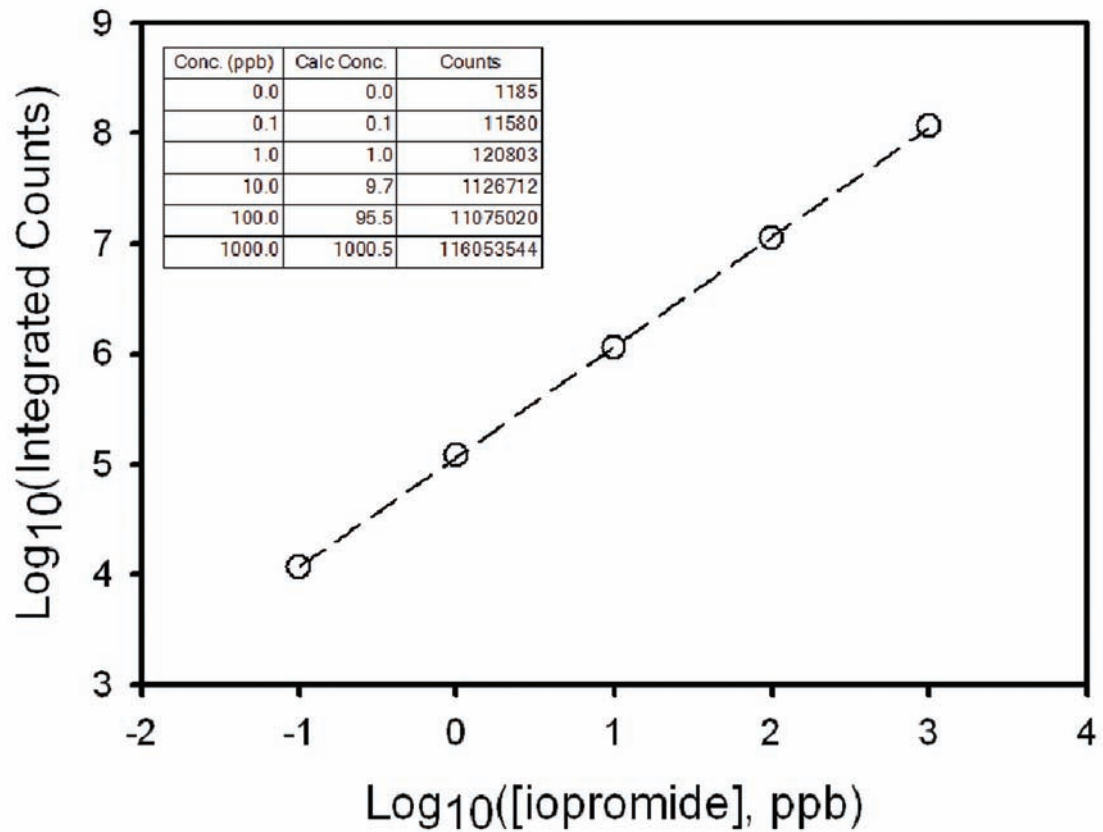


Figure 3: Calibration curve (log log) obtained for iopromide. The concentration axis is in ppb iopromide and the calibration points are at 0.0, 0.1, 1, 10, 100, and 1000 ppb of iopromide. Inset table lists calibration standard responses.

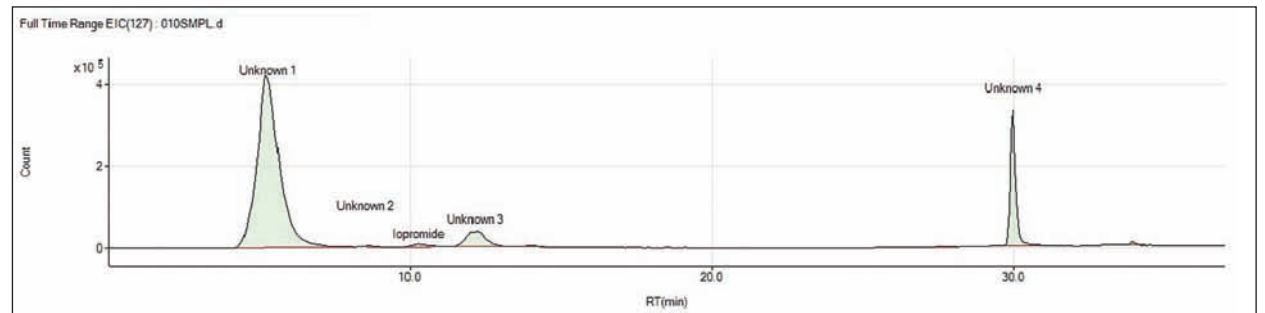


Figure 4: Extracted ion chromatogram (m/z 127) of a representative sample indicating the presence of various iodinated compounds in water extracts

The standards and samples in this report were analysed during a 24 hour continuous sequence. The results obtained from this sequence are shown in Table 1. The other CCVs analysed 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 (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

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	Acq. date and time	Type	Sample name	Unknown 1 RT 5.2 min Conc. (ppb)	Unknown 2 RT 8.5 min Conc. (ppb)	Iopromide (as I) Conc. (ppb)	Unknown 3 RT 12 min Conc. (ppb)	Unknown 4 RT 30 min 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

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.

## 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.

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