IC-ICP/MS analysis of Iodinated X-ray Contrast Media after Ozonisation

The use of contrast media in non-invasive diagnostics facilitates targeted imaging of organs and distinction between healthy and unhealthy tissue. One differentiates between contrast media for magnetic resonance imaging (MRI) and X-ray examinations.

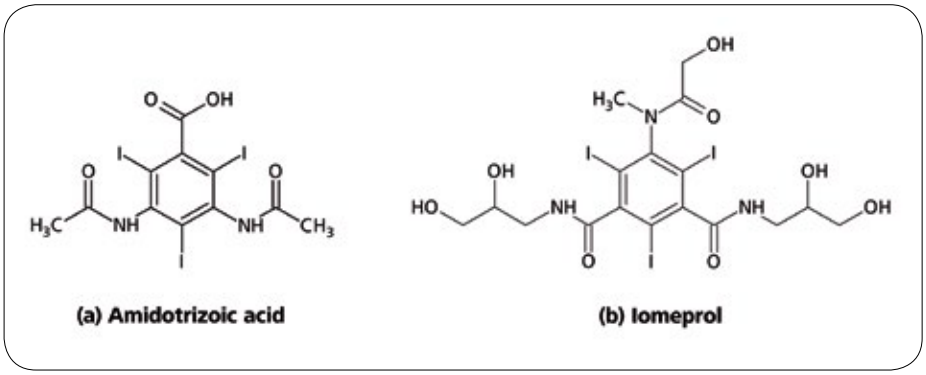

Fig. 1: Chemical structures of two X-ray contrast media, (a) Amidotrizoic acid and (b) Iomeprol

While MRI is based on the use of magnetic fields caused by charged elementary particles, X-ray contrast media change the radiodensity of an organ by absorbing the X-rays. X-ray positive contrast media such as iodine and barium compounds absorb the X-rays more effectively than body tissue, thereby providing a stronger contrast.

The preparations currently in use (Fig. 1) are organically bound iodides which are almost all derived from triiodobenzoic acid. These compounds are inert and therefore safe to be administered intravenously or orally. Unmetabolised, they are excreted after a few hours and on account of their poor biodegradability, even after passing through waste water treatment plants, find their way into the environment where they can be detected in elevated concentrations. X-ray contrast media can be found in most European receiving waters at µg/l levels.

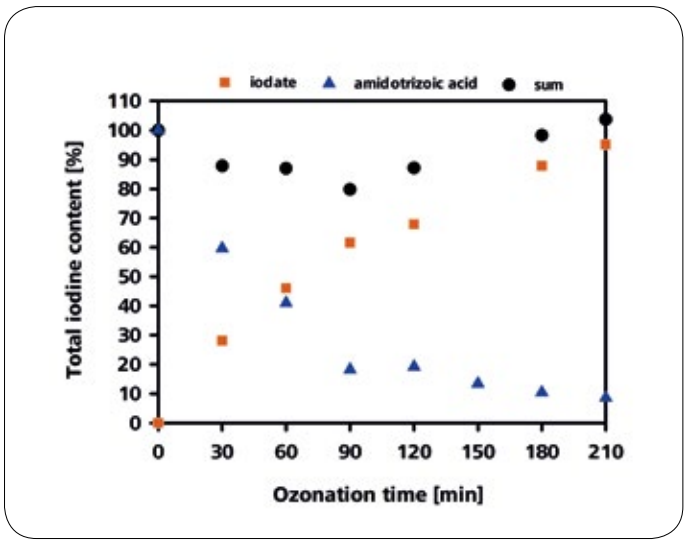

Fig. 2: Recovery rate of the iodine in the form of iodate and amidotrizoic acid depending on the duration of the ozonisation process.

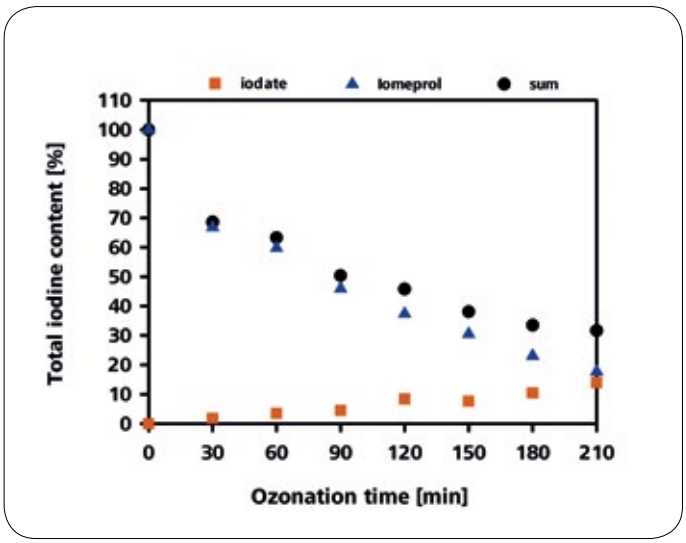

Fig 3: Recovery rate of the iodine as iodate and iomeprol depending on the duration of the ozonisation process.

Ozonisation

Apart from the advantages of killing off viruses, fungi and bacteria, ozonisation is considered an environmentally friendly method for degrading persistent organic pollutants. There is, however, a drawback. Ozonisation can transform otherwise harmless substances into toxic compounds. In the case of iodised X-ray contrast media, there is a considerable need for more research regarding what happens during degradation and the emergence of oxidation products.

Analysis

IC-ICP/MS offers, as clarification of the reaction behaviour, the possibility to determine other iodised degradation products besides inorganic oxidation products such as iodate and iodide. For this purpose, watery solutions of the model components iomeprol and amidotrizoic acid (Fig. 1) are subjected to different doses of ozone so that the residual X-ray contrast media and the degradation products can be examined. The results serve to optimize ozonisation and estimate any potential dangers.

Experiments

IC-ICP/MS makes it possible to differentiate between various oxidation levels (speciation), therefore between free and bonded iodine ions and consequently to determine the effect of ozonisation on the iodine-containing X-ray contrast media (ICCM).

The ozonisation took place in an ozonisation reactor (provided by the local authorities association for regional water supply) for watery solutions of 21.3 mg/l amidotrizoic acid (13.21 mg/l iodine) and 20.4 mg/l iomeprol (9.99 mg/l iodine), respectively. The ozone concentration in the ozone reactor was maintained at 3 mg/l and samples were taken at 30 minute intervals over a period of 3.5 to 4 hours.

The separation of the ionic, iodine-containing, degraded products took place under isocratic elution on a Metrosep A Supp 3 column. The amidotrizoic acid and iomeprol were determined on an RP-18 HPLC column (Phenomenex Envirosep-PP, 125 × 4.6 mm) under gradient elution. The quantification of both the X-ray contrast media and the degraded products was achieved using the standard addition method. The IC-ICP/MS analysis system used for the quantification of the ozonisation products (ozonisation by-products, OBPs) consisted of an 850 Professional IC (Metrohm) and a VG PQ ExCell ICP/MS (ThermoScientific); the determination parameters of the ICP/MS are shown in Table 1, the IC parameters in the captions of Figures 4 and 5.

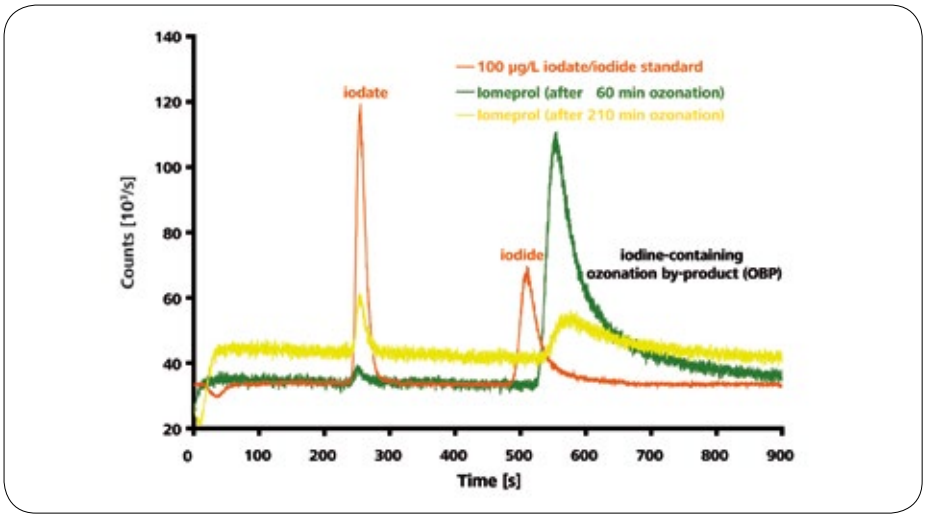

Fig 4: IC-ICP/MS-chromatogram of a 100 µg/l iodate and iodide standard in comparison with an iomeprol solution after 60 and 210 minute ozonisation process, respectively. Column: Metrosep A Supp 3 - 250/4.0; eluent: 6.8 mmol/l $NaHCO_3$ and 7.2 mmol/l Na_2CO_3, 1 ml/min; Column temperature: 30 °C; Sample volume: 20 µl.

Results

a) Amidotrizoic Acid

Contrary to its ionic character, the amidotrizoic acid itself could not be analysed as an evaluable peak using IC-ICP/MS. However, iodate could be detected as the only ozonisation product. The quantification of the iodate in Figure 2 shows that after only 210 minutes 95% of the total amount of iodine present was in the form of iodate. An LC-UV analysis carried out in parallel on the remaining amidotrizoic acid showed that after 210 minutes only 8% of the total amount of iodine was still present as amidotrizoic acid. The recovery rate of 103% of the iodine excludes any further occurrence of ozonisation products.

b) Iomeprol

Iomeprol, on the other hand, showed a considerably slower degradation with regard to the amount of iodate produced. After 210 minutes only 14% of the total amount of iodine present was in the form of iodate. The LC-UV analysis carried out on the remaining iomeprol showed that after 210 minutes of ozonisation only 16%

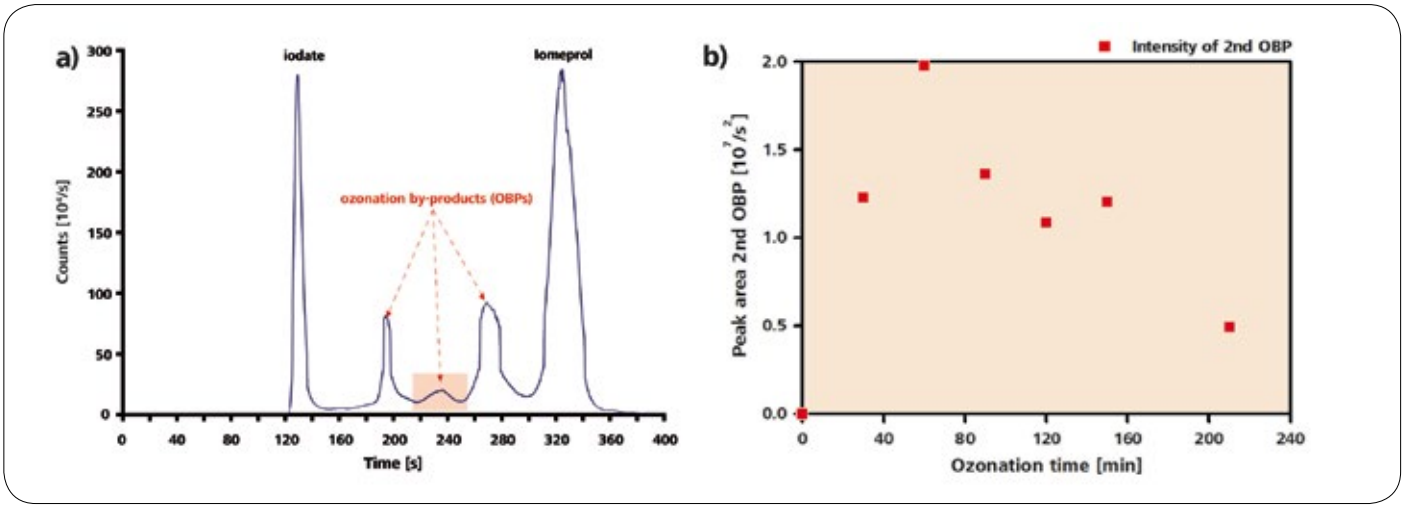

Fig 5: a) HPLC-ICP/MS chromatogram of an iomeprol solution after a 120 minute ozonisation. Column: Phenomenex Envirosep-PP 125 × 4.6 mm, Eluent A: 0.1% formic acid in water (v/v), Eluent B: acetonitrile, 0.5 ml/min, gradient: 0-0.5 min: 95% A, 5% B, 0.5-5.7 min: 60% A, 40% B; 5.7-10 min: 95% A, 5% B. b) course of the peak area of the second OBP-peak (1:100 dilution) depending on the ozonization time.

Mode:		Nogas
Power:		1200 W
Atomizer:		Concentric flow rate: 1 ml/min
Flows	Plasma gas:	Ar, 13 l/min
	Auxiliary gas:	Ar, 1 l/min
	Atomizer gas:	Ar, 1 l/min
Detection:		^{127}I

Table 1: ICP/MS determination parameters.

of the iodine was in the form of iomeprol. This means that the total recovery rate of the iodine lies at only 30% (Fig. 3).

The rest of the iodine must therefore be in the form of various iodine-containing degradation products. At least one of these degradation products can be detected using IC-ICP/MS.

A comparison of the chromatograms of a 100 µg/l iodate/iodide standard with the 60 and 210 minute long ozonised iomeprol solution shows that on the basis of the significant differences in the retention times the second peak could not be that of the earlier eluting iodide.

The HPLC-ICP/MS measurement presented in Figure 5 suggests that this peak is caused by one or several ionic degradation products of the iomeprol. An exact quantification of this peak was not carried out. On lengthening the duration of the ozonisation, an increase in the peak area can be observed which decreases again after 60 minutes. This seems to be evidence of a further iomeprol oxidation product which builds up quickly initially but with further ozonisation, is once again degraded.

Conclusion

On the basis of the tests carried out using IC-ICP/MS, it is possible to discover the effectiveness of the ozonisation of iodised X-ray contrast media from the amount of iodate produced. While a 210 minute ozonisation degrades almost all of the amidotrizoic acid to iodate, under the same ozonisation conditions, 16% of the iomeprol is still present. As in the absence of iodide only 14% is present as iodate and in the ion chromatogram other, yet to be identified peaks occur, it can be assumed that other iodine-containing degradation products are present. That being said, under the chosen ion chromatographic conditions, it is not possible to document the intact iodised X-ray contrast media.

Reference

Seitz W. *et al.:* Chemie in Labor und Biotechnik, Heft 12, 456–460 (2004)

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