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Borate complexes of X-ray iodinated contrast agents: Characterization and sorption studies for their removal from aqueous media

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ABSTRACT

Iodinated contrast media (ICM) are persistent and ubiquitous water pollutants. Because of their high water solubility and biochemical stability, their phase-separation and recovery from the aquatic environment is very difficult. Here, borate was chosen as a complexing agent of the two diagnostic aids iomeprol and iopamidol in order to provide them with a negative charge and to fix the resulting adducts on Dowex 1X4 ion exchangers. A systematic characterization study of the complex by means of capillary zone electrophoresis and ^{11}B NMR revealed that iomeprol and iopamidol interact with borate anions in aqueous solutions giving a 1:1 single-charged adduct and that the association constant at 25 °C for both contrast agents is highest at pH 10.5. These findings allowed the proper calibration of experimental parameters for further batch adsorption–desorption trials, where the two ICM were shown to be almost completely removed from the water phase and released from the solid sorbents in mild conditions, enabling the recovery of functional resin.

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1. Introduction

Diagnostic imaging of soft tissues based on X-ray radiography is performed using contrast media with high iodine content. By infusing the various body compartments with different concentrations, iodinated radiographic contrast agents attenuate the incident X-ray beam and enhance the contrast between the examined organs or vessels and the surrounding tissues. The latest generation of such diagnostic pharmaceuticals is made of highly tolerable and clinically safe species, such as iopamidol (Iopamiron®) [1] and iomeprol (Iomeron®) [2]. These belong to the class of the non-ionic and monomeric iodinated contrast media (ICM) and show unusually high water solubility that allows the formulation of very concentrated solutions for intravenous injections. These diagnostic aids are administered in high doses to patients (up to 200 g per medical application) and are rapidly excreted via urine from the human body without being metabolized [3]. Considering that thousands of tons of these compounds are synthesized worldwide every year and discharged in wastewater from medical facilities or from private households after their use, there is considerable concern now about their presence in the environment [4,5]. These very stable pharmaceuticals pass un-retained and insufficiently degraded through conventional sewage treatment plants and are then released almost unchanged in the aquatic environment [6,7]. Given their high hydrophilicity, most of the radiocontrast agents persist in surface or even groundwater, while their presence in soils or sediments due to adsorption onto solid matter is scarce [8–12]. Since not much is known about their fate and long term effects, there is a risk connected to their spread in the environment [13–17].

In this paper we present a novel approach aimed at the recovery of iodinated contrast media from wastewaters. Adsorption is perhaps the most frequently employed procedure for the treatment of polluted effluents. Today different types of dyes, drugs and pharmaceuticals are efficiently adsorbed onto charcoal [18], but ICM need to be first partially degraded (generally through ozonation processes) in order to show some affinity to activated carbons [19–21]. These are prohibitively expensive, must be regenerated after their use and show different performances depending on the type of wastewater they are in contact with [22]. Therefore low-cost and easy-to-handle polymeric sorbents have been recently studied as suitable materials for solid-phase separation of organic contaminants [23–25]. The chemical structure of these ICM is designed with the purpose of conferring high stability in the

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physiological environment and to avoid any type of interaction with other molecules [26]; hence, a simple chemical modification of the diagnostic aids would be beneficial for increasing their (generally very low) affinity towards solid polymeric sorbents.

Boric acid and borate are known to form esters with diols or polyols in aqueous solution granting a net negative charge to the complex [27,28]. These are common low-cost chemicals, compatible with water as a solvent and have low toxicity. Neutral poly-hydroxy compounds (like carbohydrates) are routinely converted into charged species with borate-based electrolytes for analytical purposes [29,30]. Since the chemical structure of the ICM comprises a core aromatic ring substituted by three iodine atoms and three OH-rich side chains, where four of them (*i.e.* two diol groups) are suitably oriented for reaction with borate, these biochemically stable molecules can be easily transformed into their respective more reactive esters.

In this work we focused on the formation of iomeprol– and iopamidol–borate complexes in aqueous solution, performing, for the first time to our knowledge, an extensive characterization study of these adducts. Capillary zone electrophoresis (CZE) and NMR were used to study the stoichiometry, stereochemistry and thermodynamics of the ICM–borate complexes and to assign the association constants of the ICM–borate complexes at different pH and temperature values. Once the experimental parameters affecting the complexation between those pharmaceuticals and borate were identified and properly adjusted to achieve maximum reaction yield, batch sorption tests on a Dowex 1X4 solid matrix could be performed. The adsorption mechanism of the negatively charged ICM–borate species on this styrene–divinylbenzene copolymer based resin (with tri-methylbenzylammonium chloride functionalities) was essentially ruled by electrostatic interactions. UV–vis spectrophotometric measurements were performed to monitor the amount of contrast medium from adsorption trials. The adsorptive properties of borate-bound iodinated contrast agents on the Dowex 1X4 resin were found to be approximately from 5- to 90-fold higher than those of the uncomplexed ICM. Furthermore, an efficient strategy for releasing the ICM–borate complex from the synthetic resin was also achieved, so that the polymeric sorbent could be re-used (three times) without any loss of sorption capacity.

2. Materials and methods

2.1. Materials

The iodinated contrast media iomeprol (Iomeron®), iopamidol (Iopamiron®) and lodomiso (precursor of iomeprol) were kindly provided by Bracco S.p.A. (Milan, Italy). Their chemical structures are reported in Supplementary data Figs. S1A–C. Industrial wastewater samples containing lodomiso were collected at the Spin Bracco Chemical Plant (Torviscosa, Italy). Borax, boric acid, boron trifluoride etherate $BF_3{\cdot}Et_2O$, acetonitrile, sodium dihydrogen phosphate, phosphoric acid, 2-amino-1-naphthalene sulfonic acid (ANS), 2-amino-1,5-naphthalene disulfonic acid (ANDS), sodium chloride, calcium chloride, magnesium chloride, calcium nitrate, ammonium nitrate, calcium sulfate and sodium acetate (see Table 2) were purchased from Sigma–Aldrich (Milan, Italy). Sodium hydroxide and hydrochloric acid were from Carlo Erba (Milan, Italy). The adsorbent material was a Dowex 1X4 resin (chloride form) and was supplied from Dow Chemicals (CO, USA). The bare fused silica capillary (50 μm ID, 375 μm OD) used for electrophoretic studies was from Alphatech (Genoa, Italy).

2.2. Capillary zone electrophoresis (CZE)

The apparatus used was an Applied Biosystem HPCE Model 270A-HT with UV detection coupled with a Turbochrom Navigator (4.0) software. A fused silica capillary tube (92 cm total length, 70 cm effective length) was used for the CZE analyses. Separations were performed at 30 °C. The detection wavelength was set at the maximum UV–visible absorbance of iomeprol and iopamidol, *i.e.* at 245 nm. A 15 or 20 kV potential was applied between the ends of the capillary in order to maintain the recorded currents below 50 μA. All runs were carried out in normal polarity. Samples were loaded under vacuum at a pressure of 16.9 kPa for 1 s. Before sample injection, the capillary was rinsed with 0.1 N NaOH for 2 min, then conditioned by flushing the running buffer for 4 min. The washes were performed at a vacuum pressure of 67.6 kPa. When the contrast media were detected as negatively-charged adducts, borax (25–100 mM, pH 9.2) or boric acid (100 mM, 5 < pH < 11) were chosen as the running electrolyte. Phosphate buffer (50 mM, pH 9.2) was instead used as running buffer to detect iomeprol and iopamidol as uncomplexed species.

Table 1
Association constants for B5–$^{-1}$ICM (iomeprol) and B6–$^{-1}$ICM (iopamidol) calculated by means of Eq. (1).

Sample	pH	K[a]
Iomeprol	9.2 9.2[b]	10.9 ± 0.6 9, 78 ± 0.2[b]
	10.5	23.8 ± 0.3
	12	22.7 ± 1.3
Iopamidol	9.2	11 ± 0.4
	10.5	28 ± 0.2
	12	18.4 ± 0.7

[a] Referred to the formation of B(5 + *n*)–$^{-1}$ICM complexes at 25 °C.
[b] Calculated for the iomeprol–borate complex formation in presence of 0.1 M NaCl.

2.3. NMR measurements

A 270 Jeol instrument operating at 67.89 MHz for ^{13}C and at 86.63 MHz for ^{11}B was used for all the experiments. In the case of ^{11}B NMR, the chemical shifts of the boron complexes were referred to an external $BF_3{\cdot}Et_2O$ standard set at 0.0 ppm. Samples were prepared by dissolving the appropriate amount of boric acid (0.08 M) and contrast medium (in the concentration range 0.012–0.09 M) in deionized water or in 0.1 M NaCl solutions. Experiments were performed at pH values of 9.2, 10.5 and 12 with temperature ranging from 25 to 55 °C. Association constants were calculated from the relative peak area of each signal at equilibrium and knowing the initial concentrations of ICM and boric acid in the analyzed sample. ^{13}C NMR spectra were recorded at 25 °C using D_2O as solvent. Methanol was used as external standard. The concentration of iomeprol and iopamidol was 0.02 M and that of borate was 0.72 M (pH 9.2).

2.4. UV–vis spectrophotometry

UV–vis spectroscopy of the samples (on a 10^{-5} M concentration scale) was performed on a CARY Model 4E (Varian) spectrophotometer. Iomeprol and iopamidol displayed the same maximum absorption wavelength at 245 nm. The path length of the quartz cell was 1 cm.

2.5. HPLC analysis

Effluent samples (containing lodomiso) from adsorption tests were analyzed by LC-UV (HP 1090 Liquid Chromatograph) using a Zorbax SB-Phenyl StableBond Analytical (Agilent Technologies) column (4.6 mm × 250 mm; 5 μm). The elution program was as follows (A = 0.015 M NaH_2PO_4 and 0.028 M H_3PO_4 solution; B = acetonitrile): 93% of A was held for 6 min, then its amount lowered to 40% over 24 min. This percentage was kept constant

for 7 min, then increased to the initial value over 3 min and left unchanged for a further 10 min. The column oven was heated at 45 °C and the injection volume was 10 μL. The flow rate of the mobile phase was set at 1 mL/min and the UV detection window at 240 nm.

2.6. Batch adsorption studies

10 mL of a 5 mM aqueous iomeprol or iopamidol solution (39 mg of contrast agent) containing borate (in the 0–100 mM concentration range, pH 10.5) were treated with 300 mg of Dowex 1X4 resin. The suspension was shaken continuously at 20 °C for 1 h in a sealed vial, avoiding incident light. The supernatant was collected, centrifuged, filtered and the concentration of residual ICM determined spectrophotometrically. Each experiment was performed in triplicate.

Industrial effluents containing about 2 mM of Iodomiso displayed an almost neutral pH (7.5–8). Borax (20 mM) was added to the samples and the pH adjusted through addition of concentrated NaOH to reach 10.5. 10 mL of the mixture were put in contact with 300 mg of Dowex 1X4 resin as described above. The supernatant was collected, centrifuged and filtered and finally analyzed through HPLC after a 1:100 dilution.

2.7. Batch desorption studies

The Dowex 1X4 resin, separated from the liquid phase after an adsorption cycle, was placed in contact with 3 mL of desorbing agent for 1 h under continuous stirring (see Table 2 for a complete list). The supernatant was then collected, centrifuged, filtered and the concentration of desorbed ICM determined spectrophotometrically.

2.8. Batch recycling tests

After a first adsorption–desorption cycle, the Dowex 1X4 resin was regenerated with a 3 mL solution containing NaCl 1 M. The mixture was put under continuous stirring for 1 h, then the liquid phase was collected, centrifuged and filtered and the remaining ICM concentration was determined spectrophotometrically.

The regenerated resin, converted into its original chloride form, was then ready for a second (or third) adsorption–desorption-regeneration cycle, which was performed as previously described in Sections 2.6–2.8.

3. Results and discussion

3.1. ICM–borate complex characterization

Very little is known about the association of iodinated contrast media with boric acid. The studies reported so far concern only its use as an elution buffer in chromatographic methods or as a reactant. On the analytical side, borate buffer has been reported as a separation medium in CZE analyses of iohexol, iothalamate and iopamidol in human serum [31,32]. Bjorsvik and co-workers have successfully employed borate as a protecting group of diol functions in an intermediate step of the synthesis of several iodine-based X-ray contrast agents [33] and claimed that the protected intermediate bears a borate ester at each available diol function of the radiocontrast medium. Since any experimental evidence of this double-negatively charged di-protected compound is lacking, we decided to tackle an in-depth characterization of the complexes formed between borate and iomeprol or iopamidol to assess their stoichiometry and main features.

3.1.1. Stoichiometry of the ICM–borate complexes

Iomeprol and iopamidol are both characterized by the presence of two diol groups in the branches linked to the iodine-containing aromatic moiety. It follows that the interaction with borate ions could in principle lead to a complex mixture of products (Scheme 1) depending on the relative amount of reactants. In order to shed light on the stoichiometry of the reaction, ^{11}B NMR, ^{13}C NMR and CZE were used. Fig. 1 reports the method of continuous variations, Job's method, in the case of the reaction between iomeprol and borate. The concentration of the ICM–borate complex, calculated from the peak at ~5.9 ppm of ^{11}B NMR spectra, was monitored as a function of the molar fraction of borate and ICM. Since the maximum of the ICM–borate complex is achieved for $X_{ICM} = X_{borate} = 0.5$, it could be concluded that the stoichiometry of the complex is 1:1. It follows that, at variance with the results previously reported [33,34], the reaction between these ICM and borate leads to the formation of the single-charged species B(5 + *n*)–^{1}ICM (for definition: see Scheme 1).

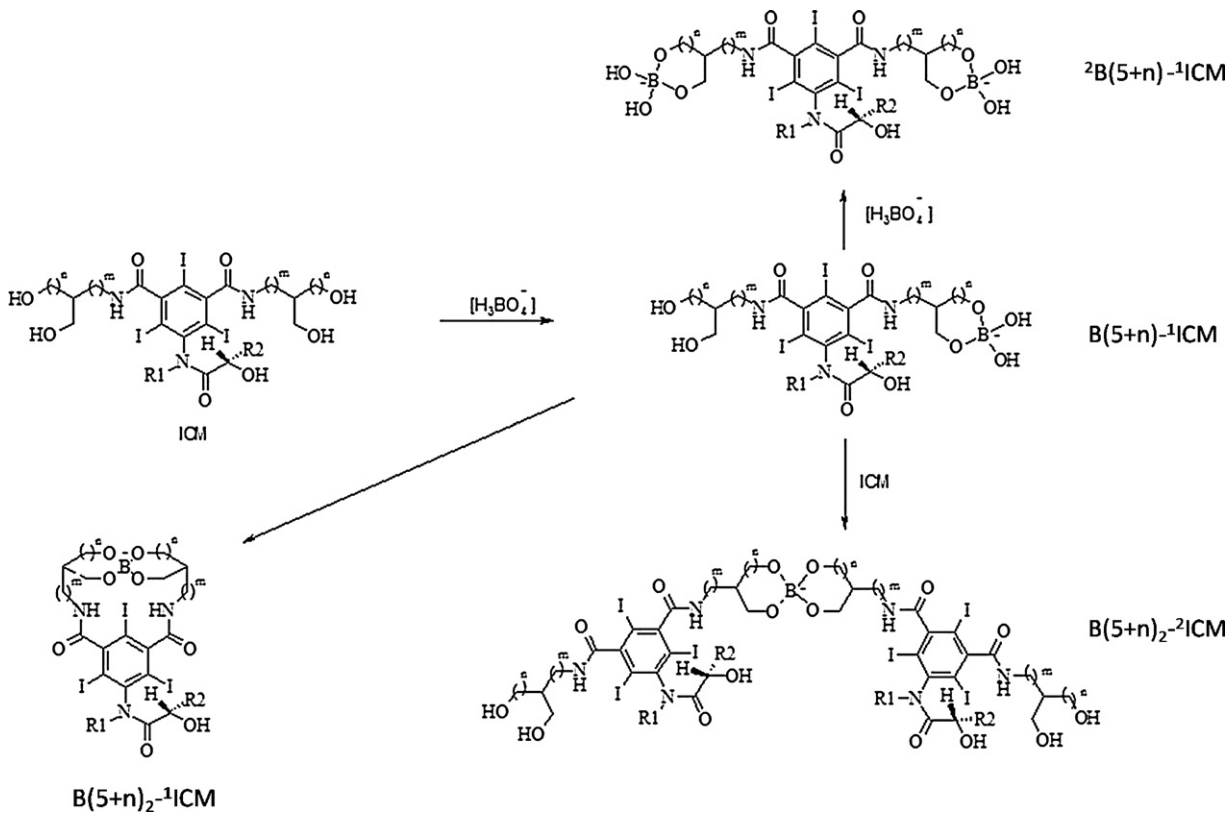
In order to evaluate possible variations in stoichiometry upon addition of an excess of borate, Capillary Zone Electrophoresis (CZE) was run with [borate]/[ICM] ratios ranging from 8 to 2000 (Fig. 2). When iopamidol (Fig. 2A) or iomeprol (Fig. 2B) samples were run at pH 9.2 in phosphate buffer, they co-migrated with the electroosmotic flow (EOF), behaving like uncharged compounds (see pale gray lines in Fig. 2). The choice of borate as the running buffer, shifted the retention times of iomeprol and iopamidol in the capillary column towards the anionic region (see dark gray and black lines in Fig. 2). Iopamidol elutes always as a single peak, while iomeprol gives rise to two signals – the conformational isomers called *endo* (76.1%) and *exo* (23.9%) – that can be efficiently separated by increasing the concentration of the complexing agent in the separation medium (Supplementary data, Fig. S1A). This well agrees with already reported HPLC and TLC data relative to iomeprol and other ICM (such as iopentol, iohexol and ioxilan but not iopamidol) in aqueous solutions [35].

Through comparison of the electropherograms of the two ICM in borate-rich medium with those of two negatively charged standards (taken in the same running conditions), it could be concluded that the ICM–borate complexes can bear only one negative charge (Supplementary data, Fig. S2). It is very likely that the coordination of a second borate group, which would lead to the formation of a double-negatively charged species, is hampered by electrostatic repulsions.

The coordination of borate ions by one of the diol groups of the ICM could also be detected by means of ^{13}C NMR analysis (Supplementary data, Fig. S3A and B).

After discarding the hypothesis of the formation of doubly-charged ICM complexes (*i.e.* ^{2}B(5 + *n*)–^{1}ICM in Scheme 1) with borate, it was decided to investigate the effect of increasing concentration of the contrast medium. To this end, ^{11}B NMR spectra of iomeprol and iopamidol were recorded with a [borate]/[ICM] ratio ranging from 6.7 to 0.9 (Fig. 3A and 3B). In the case of iomeprol (Fig. 3A), two signals (at ~13 ppm and ~5.9 ppm) were present when the highest [borate]/[ICM] ratio was used, arising from uncomplexed borate and from the B5–^{1}ICM complex, respectively. However, when the latter ratio was lowered to 0.9, an additional peak at ~10.5 ppm appeared, arising from the presence of a tetra-coordinated borate species [36]. Since the area of this peak increased upon increasing the concentration of the ICM, this signal could be safely attributed to an intermolecular tetra-coordinated boron complex, indicated in Scheme 1 as B5$_2$–^{2}ICM. Identical chemical shift values have been observed when borate anion complexes polysaccharides in aqueous solutions forming five-membered rings [35].

In contrast, when iopamidol is considered (Fig. 3B), a different overall picture is found. Besides the peak at ~2 ppm (stemming from a di-coordinated boron species: B6–^{1}ICM) and the one at



Scheme 1. Schematic representation of all possible species formed by reaction of ICM and borate ($H_3BO_4^-$). Iomeprol: R1 = CH_3, R2 = H, m = 1, n = 0; iopamidol: R1 = H, R2 = CH_3, m = 0, n = 1.

~13 ppm (from un-complexed borate), an additional peak was clearly detectable at ~5.8 ppm for [borate]/[ICM] ratio as low as 6.86. The intensity of the latter increased upon increasing iopamidol concentration. However, the ratio between the peak at ~5.8 ppm and the one at ~2 ppm was found to be 0.1, irrespective of the concentration of the ICM. For this reason, the former peak detected with ^{11}B NMR was assigned to an intramolecular tetra-coordination of the borate ion, *i.e.* to the $B6_2$–^{1}ICM species (see Scheme 1).

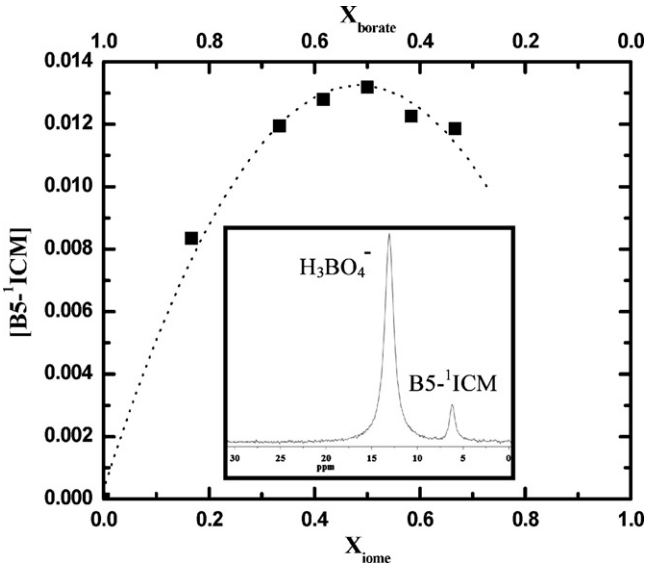


Fig. 1. Dependence of the concentration of the B5–^{1}ICM complex from the molar fraction of iomeprol (X_{iome}) and borate (X_{borate}) in solution as determined by ^{11}B NMR. The different molar fractions have been prepared by mixing different volumes of equimolar (0.1 M) iomeprol and boric acid solutions. The pH of the final solution was adjusted to 9.2. Inset: example of ^{11}B NMR for iomeprol–borate complexes. See Fig. 3A for assignations.

3.1.2. Thermodynamics of the ICM–borate complexes

Having assessed the stoichiometry of the interaction between iomeprol/iopamidol and borate, we then focused on the thermodynamics of the B(5 + n)–^{1}ICM complexes. To this end, ^{11}B NMR spectra of iomeprol and iopamidol in the presence of different amounts of borate were recorded in the interval 25/55 °C. For each temperature, the binding constant was calculated and the enthalpy and entropy of the complex formation were determined by means

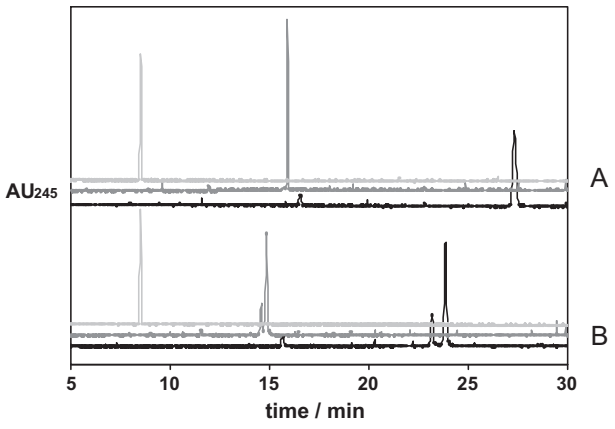


Fig. 2. Comparison of electropherograms of iopamidol (series A) and iomeprol (series B; *exo* isomer, minor peak; *endo* isomer, major peak) samples (both 0.2 mM) run in potassium phosphate buffer (pH 9.2, pale gray lines), in borax (50 mM, pH 9.2, dark gray lines) or borax (100 mM, pH 9.2, black lines).

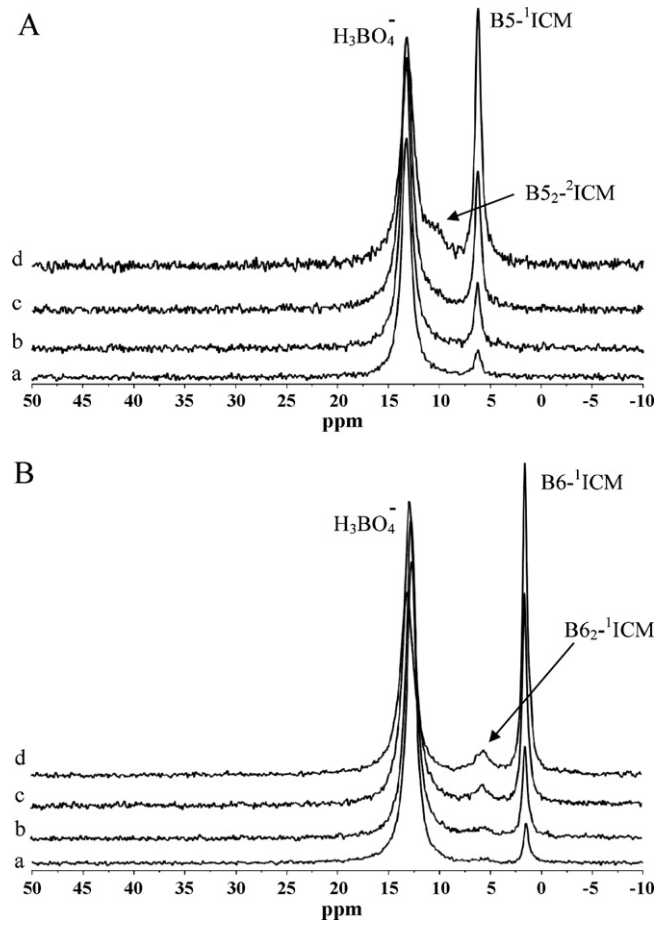


Fig. 3. ^{11}B NMR of borate treated (A) iomeprol and (B) iopamidol. The ratio [borate]/[ICM] was (a) 6.86, (b) 3.43, (c) 1.71 and (d) 0.89, respectively. Spectra have been recorded at 25 °C (pH 9.2).

of the Van't Hoff equation (1) (Supplementary data, Fig. S4). All data were collected at pH > 9.2, since at that value boric acid converts to borate and may actually bind diol functions.

$$-\frac{\Delta G^0}{R \cdot T} = \ln K = -\frac{\Delta H^0}{RT} + \frac{\Delta S^0}{R} \quad (1)$$

The values referred to the binding constants (K) are summarized in Table 1. These range from 20 to 30 M^{-1} for both iomeprol and iopamidol, thus somewhat lower than those displayed by carbohydrates (typically, glucose shows a binding constant of approximately 63) [36]. B6–^{1}ICM and B5–^{1}ICM complexes are more or less equally thermodynamically favourable. Likely, this behaviour can be traced back to the highly flexible structure of the diols present in iomeprol and iopamidol as compared with the more rigid saccharidic diol structures (*i.e.* pyranosidic form of mannose), which display larger stability differences between 5- and 6-membered boron-containing rings [36].

The dependence of the binding constant between ICM and borate on the pH of the solution deserves an additional comment: for both iomeprol and iopamidol the highest value of K has been reached at pH 10.5 while a decrease is detected for higher pH values. This behaviour has previously been discussed in the literature for borate complexes as stemming from the competition between hydroxide ions and diol groups for the complexation to boron [36]. Interestingly enough, the binding constant of iopamidol is higher than that of iomeprol at pH 10.5, while the opposite trend is found for both lower and higher pH values.

Since various ionic species are generally dissolved in ICM-contaminated effluents, the stability of the iomeprol–borate complex in presence of NaCl 0.1 M (at pH 9.2) was also studied (see Table 1, first row, point b). In such simulated wastewater, the affinity of the ICM towards borate anions was found to be only marginally affected by the high Cl^- content, as indicated by a unit decrease of the binding constant.

Thermodynamic data on the enthalpy and entropy variation of the ICM–borate complex formation highlight the different tendency of the two ICM–borate complexes to associate to water molecules, *i.e.*, disclose the hydrophobic character of the two adducts (Supplementary data, Table S5).

Table 2
List of desorbing agents (0.1 M solutions for all the salts) used in desorption trials of iomeprol from the Dowex 1X4 resin. The pH of the first three salt solutions listed was lowered through addition of concentrated HCl.

Desorbing agent	% iomeprol removal[a]
$CaCl_2$	65
$MgCl_2$	64
$Ca(NO_3)_2$	81
NH_4NO_3	45
NaCl	68
$CaSO_4$	74
CH_3COONa	70
H_3BO_3	68
HCl	71
NaOH	45

[a] With respect to the adsorbed iomeprol.

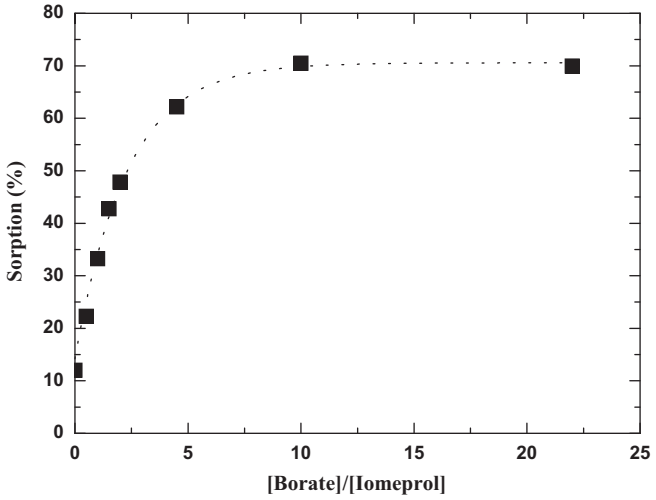


Fig. 4. Sorption (%) of iomeprol–borate complex on Dowex 1X4 resin as a function of the [borate]/[iomeprol] ratio. Adsorption tests were performed at pH 10.5 and 25 °C.

3.2. Adsorption of ICM–borate complexes

5 mM ICM solutions were used for all adsorption studies, since this concentration approaches the value detected in real effluent samples. The 10.5 pH value, optimal for the ICM–borate complexation, was selected to perform sorption tests on a Dowex 1X4 (chloride form) resin, varying the borate concentration from 2.5 mM to 112.5 mM.

As reported in Fig. 4, adsorption yields significantly increased by raising the amount of boric acid up to a [borate]/[iomeprol] ratio of 10. Further additions of borate did not show enhancement in the ICM adsorption. Therefore, all adsorption trials were carried out using a [borate]/[iomeprol] ratio equal to 10 to maximize the adsorption with the lower amount of borate. Fig. 5 reports the results on Dowex 1X4 resin adsorption obtained for iomeprol and iopamidol. First of all, it should be pointed out that, in the case of

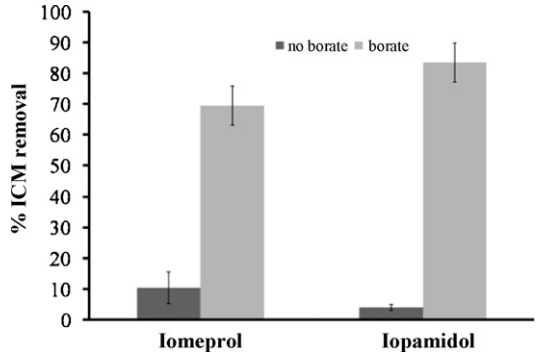


Fig. 5. Removal (%) of iomeprol and iopamidol (5 mM aqueous solutions) by Dowex 1X4 resin in presence (gray columns) or absence (black columns) of boric acid as complexing agent.

iomeprol, 15% of the ICM was absorbed by the Dowex resin even in the absence of borate. This could be attributed to an aspecific interaction between the resin and iomeprol, likely mediated by the styrene groups on the former and the triiodobenzene moiety in the latter. Conversely, in the case of iopamidol the aspecific binding did not exceed 1%. Since the aromatic moiety is very similar in the two ICM, this varying behaviour could be traced back to a different hydrophobicity of the two analytes, as previously emphasized (Supplementary data, Table S5). In addition, in the case of iopamidol, the total approach of the borate complex to the resin is likely prevented due to steric hindrance (Supplementary data, Fig. S1B).

When borate was added to the ICM, their adsorption was greatly enhanced because of the electrostatic interactions between the positively charged resin and the negatively charged $B(5+n)^{-1}$ ICM complexes. In terms of removal of iomeprol and iopamidol, approximately 5-fold or even 90-fold improvements were observed, respectively, in borate containing solution with respect to the untreated ICM.

The feasibility of the method was also evaluated on real environmental samples. HPLC analyses of lodomiso-contaminated effluents (treated with borate and Dowex 1X4 resin as described in Section 2.6), showed that up to 80% ICM removals could be reached (Supplementary data, Fig. S6A and B).

3.3. Desorption of ICM–borate complexes

As the borate–ICM adsorption mechanism on the Dowex 1X4 resin is essentially ruled by electrostatic interactions, a way to revert the process (*i.e.* to desorb ICM) could be presented by the use of saline solutions. A list of desorbing agents (mainly salts) that led to an appreciable iomeprol removal is reported in Table 2. Some salt solutions were brought to acidic pH values (through addition of concentrated HCl) in order to avoid hydroxide precipitation of alkaline earth metals. The desorption by salts was found to be very effective and percentages as high as 80% could be easily reached. Interestingly, there was a positive influence on the desorption yields of some lyotropic salts. Especially the so-called "salting-in salts", such as calcium nitrate, may destabilize hydrophobic structures, which plausibly exist to some extent when iopamidol interacts with the Dowex 1X4 polymer in solution.

Taking into account the maximum yields obtained from both adsorption and desorption procedures for iomeprol, one can conclude that, following the above reported conditions, it is possible to recover about 76 mg of iomeprol (per g resin) with respect to the 125 mg contained in the starting solution, corresponding to ca. 61% of the initial amount of ICM. In addition, considering that desorption analyses were performed using only 3 mL of saline solution, the final ICM concentration practically doubles if compared with the initial one, with a clear operational advantage. These yields could be further improved after a first activation step of the resin (see next section).

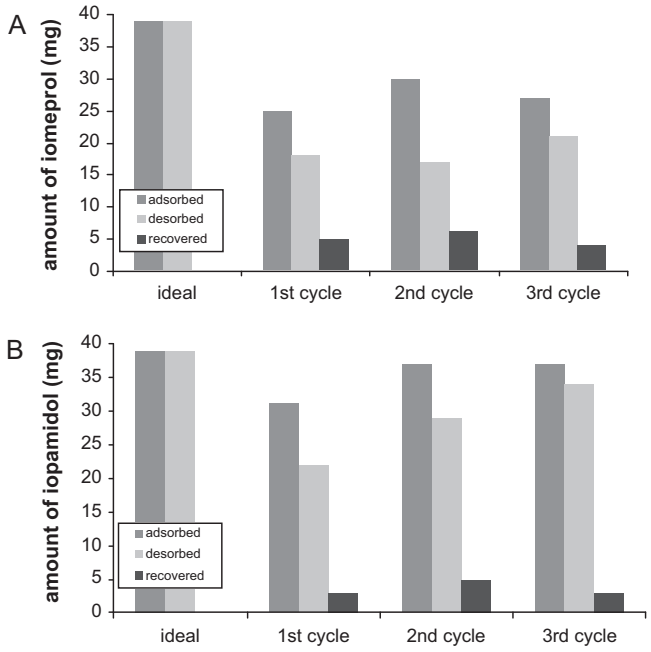


Fig. 6. Recycling performances of the Dowex 1X4 resin (300 mg) through three consecutive adsorption (dark gray columns) – desorption (light gray columns) – regeneration (black columns) steps using iomeprol (A) or ioamidol (B) solutions (39 mg of ICM) in 50 mM borate buffer as adsorbate. Desorption and regeneration of the resin were achieved employing 3 mL of a NaCl 1 M solution.

3.4. Recycling studies

The possibility to re-use the Dowex 1X4 resin after a first adsorption–desorption cycle was also assessed. In these recycling tests, desorption and regeneration steps were both performed using always a 3 mL NaCl 1 M solution. Although some salt solutions (see Table 2) were superior to NaCl in desorbing the ICM from the polymeric sorbent, NaCl was here chosen in order to ensure a complete regeneration of the resin, *i.e.*, to restore its initial chloride form.

Surprisingly, for both iomeprol and iopamidol, the resin did not show any loss of sorption capacity during recycling tests, but, on the contrary, its performance increases even more after a first activation step, *i.e.* after a first adsorption–desorption-regeneration cycle (see Fig. 6). The results obtained were compared to the ideal case (see first two columns of both histograms in Fig. 6) where the whole amount of contrast agent contained in the initial solution (39 mg) is supposed to be completely adsorbed and then desorbed already in the first stage. In the case of iomeprol, 25 mg were adsorbed in the first cycle, whereas 30 mg in the second and 27 in the third (see Fig. 6A). The results were particularly promising in the case of iopamidol: after the first adsorption step, where 31 mg of contrast agent were fixed on the Dowex resin, almost the total amount of iopamidol could be adsorbed in the second and third cycle (37 mg, 95% in both cases) (see Fig. 6B).

Regeneration procedures were found to be very effective: indeed the histograms reported in Fig. 6, show that, in the majority of cases, the sum of the recovered amount of ICM, during desorption and regeneration steps, equals the total amount of adsorbed ICM (see all the three adjacent columns in Fig. 6A and B), so that the resin adopts its original "adsorbate-free" form at the end of each cycle.

4. Conclusions

Here we proposed a new method based on the removal of iomeprol and iopamidol from aqueous mixtures by means of borate as a mediator of the, otherwise weak, interaction between the contrast agents and solid polymeric sorbents. NMR and CZE studies showed that borate complexes the two ICM forming negatively mono-charged species having 1:1 stoichiometric ratio and good stability at rather basic pH values. Through UV-vis spectrophotometry, we could demonstrate that the two investigated ICM are efficiently adsorbed onto solid Dowex 1X4 resins once borate is added to the system, reaching a significant 90% adsorption yield in the case of iopamidol. Furthermore, desorption trials on iomeprol samples gave back up to 80% of adsorbed contrast medium, leaving the polymeric matrix almost unchanged. Therefore, with respect to current ICM removal procedures, mainly performed using activated carbon as a sorbent material, this method represents an improvement both as to the yield of recovered iodine mass and as the reduction of environmental impact, being Dowex 1X4 resins easily recyclable.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jhazmat.2011.10.084.

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