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Ion exchange behavior of astatine and bismuth†

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Astatine and bismuth sorption on several ion exchange resins from nitric acid media has been studied. This work covers commercially available resins Dowex 50 × 4, MP thiol, Dowex 1 × 8, and TEVA. One of the main advantages of using ion exchangers for astatine separation and purification is the absence of any organic media in the effluent in comparison with extraction chromatography resins. The behavior of the above-mentioned metals was investigated in up to 4 M HNO₃ solutions. The determined distribution coefficients are greater than 1 for all the resins studied, reaching 10⁴ for MP thiol and TEVA resins. The interaction of nitric acid with an anion exchanger in Cl-form results in an exchange reaction, where AtO⁺ chloro complexes can form. To understand the astatine behavior under these conditions, stability constants of AtOCl and AtOCl₂[−] complexes have been reevaluated and discrepancy in the literature values has been eliminated. For each resin a thermodynamic model has been developed to suggest a possible mechanism of astatine sorption. Literature and new experimental data on bismuth sorption by studying resins in nitric acid media have been reviewed and a mathematical model to describe its behavior has been suggested. A ratio of corresponding fit functions of At and Bi assigned to the same resin and acidity has been used to estimate the separation factors of these elements.

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Introduction

Radiotherapy is one of the most effective approaches to treat cancer. Radiopharmaceuticals based on alpha emitting radionuclides have gained a lot of attention due to the high therapeutic effect and minimal damage of surrounding healthy tissue.¹ So far, there has been only one Federal Drug Administration (FDA) approved product based on an α -emitter, namely Xofigo[®] (²²³RaCl₂).² Yet the superior results of targeted alpha therapy (TAT) have prompted study on additional candidates such as astatine-211 (²¹¹At). It has a convenient half-life of 7.2 h and a short decay chain, matching requirements of therapeutic

α -emitting radionuclides.³ However, astatine is still one of the least chemically studied elements and the main obstacle is that the number of production facilities is barely above 20 worldwide.⁴ It is impossible to avoid radiochemical studies of astatine because there are no stable isotopes of this element and the most long-lived one, ²¹⁰At, has a half-life of 8.3 h. Therefore, prior to clinical studies of astatinated biomolecules there is a demand to understand astatine fundamental chemical properties that must be met by radiochemical studies.

Astatine, belonging to the group of halogens, demonstrates multiple oxidation states, namely −1, 0, +1, +3, +5, and +7.^{5–7} However, the aqueous chemistry of astatine deals with −1, +1, and +3 states only.⁸ The astatine neutral species, oxidation state 0, is believed to escape aqueous media.⁹ To confirm the two highest oxidation states, +5 and +7, the presence of aggressive oxidizing agent xenon difluoride is required.^{10,11} And this means that these species exist outside of the window of stability for water.^{8,12}

It is believed that AtO⁺ is the most stable species in the aqueous phase, representing the +3 oxidation state.^{13–17} However, At⁺ can also be found in acidic solutions.⁹ If reducing agents are applied, then anionic At[−] can be formed.^{18,19} It must be noted

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that AtO^+ can form complexes with different ligands,^{16,20} including the formation of negatively charged complexes.^{12,20–26}

The fundamental properties of astatine are also relevant in the study of superheavy elements. In order to study elements at the bottom of the periodic table,^{27–29} it is necessary to investigate the chemical properties of their homologs. For example, astatine is a homolog³⁰ of tennessine (transactinide element, Ts, $Z = 117$).^{31–33}

Currently, the most popular way to produce medically relevant amounts of ^{211}At is the $^{209}\text{Bi}(\alpha, 2n)^{211}\text{At}$ nuclear reaction,³⁴ where a metallic Bi target^{22,35–39} is irradiated with 29 MeV α -beam.^{4,40,41} The target bombardment is intentionally performed not at the maximum of a corresponding excitation function to avoid co-production of ^{210}At , which decays to radiotoxic ^{210}Po .

Isolation of At from Bi is a required next step after the end of the target bombardment. Historically, a dry distillation method was employed first,^{22,35,36} despite safety concerns and procedure reproducibility issues. Nevertheless, this approach led to an automated setup, successfully employed in Sweden.⁴² An alternative route is wet chemistry where the target is dissolved in nitric acid.^{37–39} The dissolution and purification processes can also be automated to reduce the dose to personnel, and this strategy has been realized in the USA.^{42–45} However, some research studies after the target dissolution again apply elevated temperatures to evaporate the solution to dryness as a required step to convert their matrix to hydrochloric medium.⁴⁶ Keeping in mind the At volatility and corresponding radiation safety concerns, a new approach to remotely separate At from Bi in nitric acid media was developed by our team.^{14,45,47} The principal difference is that the target dissolution solution (nitric acid) without any chemical manipulation is loaded onto a column, selectively sensitive only to At, while Bi and radioimpurities (^{18}F , ^{24}Na , ^{58}Co , $^{66,67}\text{Ga}$, $^{109,111}\text{In}$, ^{170}Lu) pass through the column. So far, we tested two extraction chromatography resins using our automated device, namely 3-octanone and 1-octanol impregnated beads,⁴⁵ both resulting in up to 95% recovery yield. Our previous paper expands the range of applicable extraction chromatography resins with respect to mechanisms of both At and Bi sorption from nitric acid media.⁴⁸

This paper is devoted to commercially available ion exchangers to study At and Bi behavior in up to 4 M HNO_3 . There is a limited number of papers studying this topic. Watanabe *et al.*⁴⁹ studied At recovery from 8 M HNO_3 on an anion exchange MonoSpin SAX resin (tetraalkylammonium chloride bonded to inert support),⁵⁰ showing 55% yield. A strongly acidic cation exchange Dowex 50 \times 8 resin was used to study At behavior in the presence of nitric, hydrochloric, and sulfuric acids along with 5 mM dichromic acid as an oxidizing agent or in the pH range 1–7.^{20,21,51,52} These results were used to estimate AtO^+ interaction with NO_3^- , Cl^- , HCr_2O_7^- , HSO_4^- , ClO_4^- , and OH^- anions. In order to expand knowledge on At and Bi behavior in nitric acid media, a set of cation (Dowex 50 \times 4, MP thiol) and anion (Dowex 1 \times 8, TEVA) exchangers was considered along with thermodynamic modeling of the element interactions with resins.

Experimental

Chemicals

Nitric acid (67–70% Aristar[®] Plus, HNO_3) was purchased from BDH chemicals; TEVA 100–150 μm resin was purchased from Eichrom; Dowex 50 \times 4 200–400 mesh (H) and Dowex 1 \times 8 100–200 mesh (Cl) resins were purchased from Alfa Aesar. MP thiol 100–200 mesh resin was purchased from Supra Sciences. In this manuscript we have used two cation exchangers (Dowex 50 \times 4 and MP thiol) and two anion exchangers (Dowex 1 \times 8 and TEVA). Dowex 50 \times 4 is a strong acid sulfonated ($-\text{SO}_3\text{H}$) resin capable of exchanging H^+ from the functional group with other cations in the solution.⁵³ MP thiol resin instead of $-\text{SO}_3\text{H}$ utilizes a thiophenol group ($-\text{PhSH}$), which is also involved in H^+ exchange with cations in solution.⁵⁴ Dowex 1 \times 8⁵³ and TEVA⁵⁵ resins are very similar. They are amine-based resins with Cl^- -anion involved in exchanges with anionic species in solutions. ICP Bi standard was purchased from Inorganic Ventures. Deionized (DI) H_2O was obtained from an ELGA LabWater Purelab Flex ultrapure laboratory water purification system operated at 18.2 M Ω cm at 25 °C. Radionuclide ^{207}Bi in 4 M HNO_3 was purchased from Eckert & Ziegler.

^{211}At production

Astatine-211 was produced by the $^{209}\text{Bi}(\alpha, 2n)^{211}\text{At}$ nuclear reaction *via* 28.8 MeV α -particle bombardment of a natural Bi metallic target overnight. Details on the At production, targeting, beam intensities, and activity produced can be found elsewhere.¹⁵ The target material was dissolved in ~ 10 M HNO_3 . An automated dissolution apparatus was employed to chemically treat the irradiated target.⁴⁵

Methods

Quantitative analysis of radionuclides was performed *via* γ -ray spectroscopy using high-purity germanium detectors (HPGe, Canberra Model GC2020 and BE2020) equipped with Genie-2000 software for ^{211}At and an automatic NaI gamma counter (2480 Wizard, PerkinElmer) for ^{207}Bi assay. The ^{211}At was tracked directly by measurement of the 76.9 keV, 79.3 keV, 89.8 keV, and 92.3 keV X-rays and 687 keV γ -ray; the ^{207}Bi was tracked by its characteristic X-rays at ~ 75 keV. Stable Bi was analyzed by ICP-OES. The equilibrium acidity of the radioactive aqueous solutions was determined using a Titroline 5000 automatic potentiometric titrator (SI Analytics) with 0.1 M NaOH. It should be noted that the radioactive solutions were first allowed to decay for at least 10 half-lives of ^{211}At (> 3 days). WARNING: ^{211}At is highly radioactive and was handled under ALARA principles in laboratories equipped to handle radioactive materials appropriately, and a radiological biosafety cabinet was employed.

Resin batch studies

Each batch experiment was performed in a 1.5 mL plastic screw cap tube by adding 20–30 mg of dry resin along with 0.5 mL of nitric acid solution of desired concentration (up to 4 M) spiked with a target dissolution solution containing ^{211}At , or 4 M HNO_3 containing ^{207}Bi . The system was mixed by vigorous

shaking for several seconds followed by end-over-end tumbling on a tube rotator at roughly 18 rpm for a minimum of 10 min for ^{211}At and overnight for $^{207,209}\text{Bi}$. Each tube was measured with the HPGe γ -detector or the NaI automatic gamma counter to determine the initial activity of the sample or by ICP-OES to determine the initial concentration of stable Bi. The samples were then centrifuged on a SCILOGEX D1008 Mini Centrifuge at 7000 rpm for at least 1 min. An aliquot (usually 400 μL) of aqueous phase was placed into a spin column and centrifuged again to completely separate a small amount of floating beads from solution. An aliquot of this centrifuged solution (usually 200–300 μL) was measured with the HPGe γ -detector or the NaI automatic gamma counter for radioactive samples and with the ICP-OES for stable Bi.

Distribution coefficients (K_d) were calculated according to

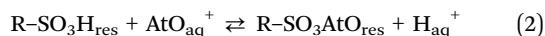
$$K_d = \frac{I_0 - I_{\text{aq}}}{I_{\text{aq}}} \cdot \frac{V_{\text{aq}}}{m_{\text{res}}} \quad (1)$$

Where I_0 and I_{aq} are volume- and decay-corrected net count rates of the measured nuclide in the aqueous phase before and after phase separation; V_{aq} and m_{res} are the aqueous phase volume (mL) and resin mass (g), respectively. All experiments were performed at least in duplicate.

Results and discussion

Dowex 50 \times 8, Dowex 50 \times 4, and MP thiol resins

As mentioned above, the majority of published work devoted to At chemistry on ion exchangers deals with Dowex 50 \times 8 resin. This section is to expand the available data on cation exchangers by including other commercially available resins, namely Dowex 50 \times 4 and MP thiol, showing the lowest and the highest K_d values, respectively. Due to the fact that the MP resin also exchanges its protons with cations in solution,⁵⁶ here we provide reactions only for the sulfonated Dowex resin, because they are similar to those of thiol-based one. The cation exchange reaction between AtO^+ and the resin can be written as

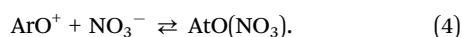


and a sorption constant is

$$K_{\text{CIX_At}} = \frac{[\text{R-SO}_3\text{AtO}]_{\text{res}} \cdot a_{\text{H}_{\text{aq}}^+}}{[\text{AtO}^+]_{\text{aq}}}, \quad (3)$$

where activity in the aqueous phase is $a = \gamma \cdot [\text{H}^+]$ and activity coefficients γ for nitric acid solutions were derived from the literature.⁵⁷

It is known from the literature that AtO^+ forms a weak complex with the NO_3^- -anion²⁰ according to



The stability constant of this kind of complex is 0.88 according to our previous work,¹⁶ and can be described as

$$K_1 = \frac{[\text{AtO}(\text{NO}_3)]}{[\text{AtO}^+] \cdot a_{\text{NO}_3^-}}. \quad (5)$$

Champion *et al.*⁹ suggested a reduction process of astatine in the aqueous acidic solutions



where the redox reaction constant is

$$K_{\text{redox}} = \frac{[\text{At}^+]}{[\text{AtO}^+] \cdot a_{\text{H}^+}^2}. \quad (7)$$

Analogously, the autoreduction process of Cu^{3+} to Cu^{2+} in acidic media was also mentioned in the literature.⁵⁸ Equations to describe At^+ -based systems are similar to eqn (2) and (3). It must be mentioned that there is no literature data on nitrate complex formation of At^+ . According to the definition of a distribution coefficient, the following equation can be used

$$K_{\text{d_CIX}} = \frac{[\text{R-SO}_3\text{AtO}]_{\text{res}} + [\text{R-SO}_3\text{At}]_{\text{res}}}{[\text{AtO}^+]_{\text{aq}} + [\text{AtO}(\text{NO}_3)]_{\text{aq}} + [\text{At}^+]_{\text{aq}}}. \quad (8)$$

Incorporating eqn (3), (5) and (7), one can get a function $K_{\text{d_CIX}} = f(a_{\text{NO}_3^-})$ to fit experimental data. Assuming $[\text{H}^+]_{\text{aq,eq}} = [\text{NO}_3^-]_{\text{aq,eq}}$, the best function to fit both Dowex 50 \times 4 and MP thiol data is

$$K_{\text{d_CIX}} = \frac{K_{\text{CIX_AtO}}/a_{\text{NO}_3^-} + K_{\text{CIX_At}} \cdot K_{\text{redox}} \cdot a_{\text{NO}_3^-}}{1 + K_1 \cdot a_{\text{NO}_3^-} + K_{\text{redox}} \cdot a_{\text{NO}_3^-}^2}. \quad (9)$$

This function has only three unknown parameters that can be determined by fitting (see Fig. 1). The estimated values of these unknown constants are summarized in Table 1.

It is clear that in both cases astatine was adsorbed mostly in the form of At^+ . Apparently, interaction of the acidic solution, containing AtO^+ , with these resins results in astatine reduction.

Cation exchangers have been extensively studied in terms of metal sorption from mineral acids. Strelow *et al.* investigated

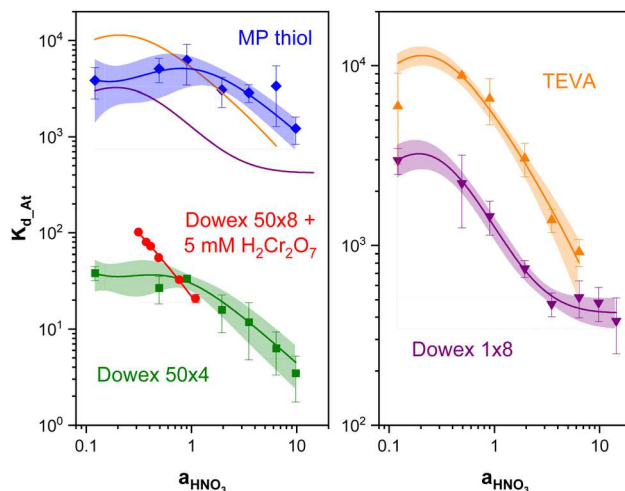
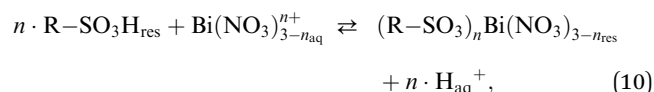


Fig. 1 Astatine sorption from nitric acid media by different ion exchange resins. Dowex 50 \times 8 data (red) are taken from literature²¹ with the fit function described in our previous work.¹⁶ Dowex 50 \times 4 and MP thiol resin data were fitted using eqn (9). Dowex 1 \times 8 and TEVA resin data were fitted using eqn (26) (only fit functions shown on the left panel). Shades represent 95% confidence intervals.

Table 1 Results of Dowex 50 × 4 and MP thiol resins fitting according to eqn (9)

Resin	$K_{\text{CIX_AtO}}$	$K_{\text{CIX_At}}$	K_{redox}
Dowex 50 × 4	3.0 ± 1.0	45 ± 8	3.4 ± 1.7
MP thiol	300 ± 140	$12\,000 \pm 1800$	1.3 ± 0.5

sorption of 49 cations by AG 50W × 8 resin (analogue of Dowex 50 × 8) up to 4 M nitric acid media.⁵⁹ Marsh *et al.* studied the behavior of 53 metals in the presence of different cation exchangers from 3 to 12 M HNO₃.⁶⁰ This acidity range is mostly outside of the scope of our work, however very low Bi uptake was observed for Dowex 50 × 4 resin. Distribution coefficient data for Bi under these conditions are shown in Fig. 2. In order to fit these data points, one should consider Bi interactions with both NO₃[−] and OH[−] anions. The corresponding stability constants are known from the literature.^{61,62} The cation exchange between positively charged Bi species and the resin can be written as



where $n = 1, 2$, and 3 (only cationic species). An analogous reaction can be written for hydroxy-species of Bi. A corresponding constant of this sorption reaction is

$$K_{\text{sorb_Bi}(\text{NO}_3)_{3-n}^{n+}} = \frac{[(\text{R-SO}_3)_n\text{Bi}(\text{NO}_3)_{3-n}]_{\text{res}} \cdot a_{\text{H}_{\text{aq}}^+}^n}{[\text{Bi}(\text{NO}_3)_{3-n}^{n+}]_{\text{aq}}}, \quad (11)$$

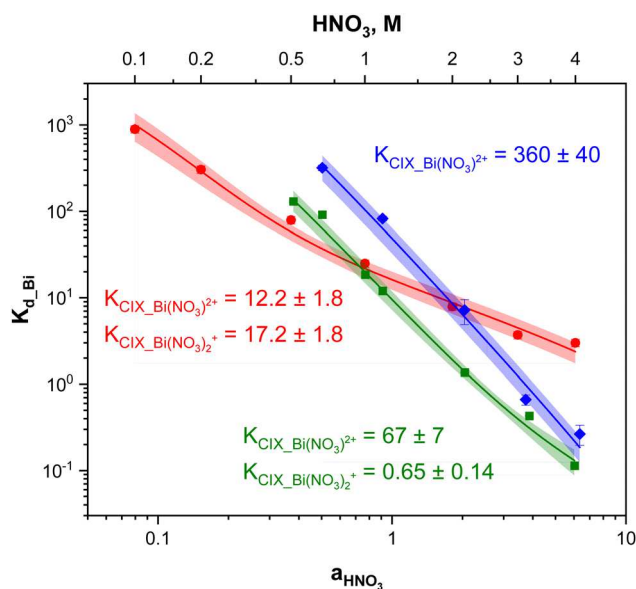


Fig. 2 Distribution coefficient values for Bi absorbed by AG 50W × 8 (red), MP thiol (blue), and Dowex 50 × 4 (green) cation exchange resins from nitric acid media. Experimental data for AG 50W × 8 were taken from the literature.⁵⁹ The solid lines are fit results according to eqn (13).

Thus, the K_d value of this process is

$$K_{d_CIX} = \frac{\sum [(\text{R-SO}_3)_n\text{Bi}(\text{NO}_3)_{3-n}]_{\text{res}} + \sum [(\text{R-SO}_3)_n\text{Bi}(\text{OH})_{3-n}]_{\text{res}}}{\sum [\text{Bi}(\text{NO}_3)_x^{3-x}]_{\text{aq}} + \sum [\text{Bi}(\text{OH})_x^{3-x}]_{\text{aq}}}, \quad (12)$$

where $x = 0, 1, 2, 3$, and 4 (all possible species).

The best fit of experimental data shown in Fig. 2 was found using the equation

$$K_{d_CIX} = \frac{K_{\text{CIX_Bi}(\text{NO}_3)_2^+} \cdot \beta_1 / a_{\text{NO}_3^-} + K_{\text{CIX_Bi}(\text{NO}_3)_2^+} \cdot \beta_2 \cdot a_{\text{NO}_3^-}}{1 + \sum \beta_x \cdot a_{\text{NO}_3^-}^x + \sum \beta'_x \cdot a_{\text{OH}^-}^x}. \quad (13)$$

Having fit functions for At and Bi, one can estimate the corresponding separation factors as a ratio of derived equations. Fig. 3 shows separation factors for MP thiol, Dowex 50 × 4, and Dowex 50 × 8 resins. The latter is not favorable due to K_{sep} values close to 1. The former in turn demonstrates good separation with $K_{\text{sep}} > 10$ at > 0.5 M HNO₃, reaching 10 000 at 4 M HNO₃. It can be seen that sorption of $\text{Bi}(\text{NO}_3)_2^{2+}$ species decreases in the order MP thiol > Dowex 50 × 4 > Dowex 50 × 8. Sorption of $\text{Bi}(\text{NO}_3)_2^+$ was found to be negligibly small for MP thiol resin, and sorption of this species decreases in reverse order. It should be noted that the MP thiol resin is not chemically stable at ≥ 8 M HNO₃. And Dowex 50 × 4 resin can be used for efficient At and Bi separation at 1–2 M HNO₃ ($K_{d_At} < 10$ at > 2 M HNO₃, see Fig. 1).

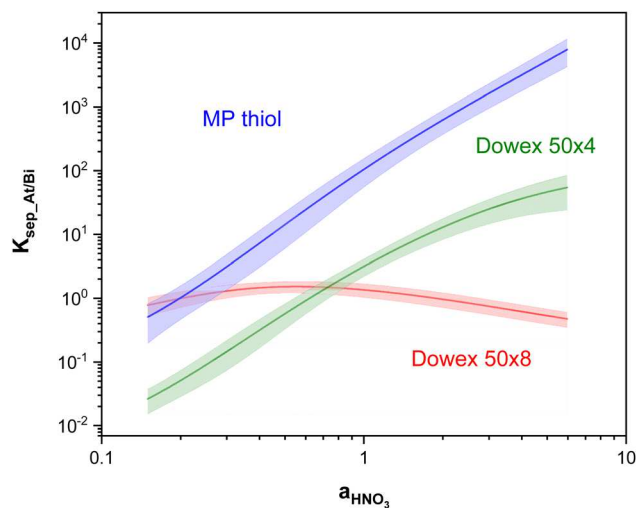
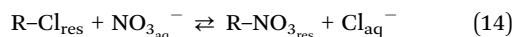


Fig. 3 Separation factor of the At and Bi mixture in nitric acid media utilizing Dowex 50 × 8 (red), Dowex 50 × 4 (green), and MP thiol (blue) resins. Astatine in the presence of Dowex 50 × 8 was oxidized by 5 mM H₂Cr₂O₇ according to literature data.²¹ Separation factors were calculated as a ratio of the corresponding fit functions. Shade represents 95% confidence interval.

Dowex 1 × 8 and TEVA resins

Both Dowex 1 × 8 and TEVA⁵⁵ resins are anion exchangers in Cl[−]-form and they show very high K_d values of astatine distribution in a wide range of nitric acid concentrations (see Fig. 1). This means that there must be negatively charged species of At in the solution. There is no data in the literature indicating that nitrates can form negatively charged complexes with AtO⁺. Also, it is very unlikely that AtO⁺ can be reduced to At[−] without any chemical pretreatment. This leaves the AtOCl₂[−] complex, which is more probable because of its very high stability constant of $\beta_2 \approx 2.5 \times 10^5$.^{20,21} We provide equations here for Dowex 1 × 8 resin only, because they are very similar to those for TEVA resin. Each resin will be slowly converted to the NO₃[−]-form upon passage of nitric acid solutions through them according to



It is important to note that Dowex 1 resin contains a small number of tertiary and secondary nitrogen atoms which can retain protons and release them upon washing with water.^{63–65} Thus, assuming that the concentration of released protons from the resin is proportional to $1/[\text{H}^+]_{\text{aq}}$ (the higher the solution acidity the more protons are trapped by the resin amino groups and the fewer protons are released to the aqueous phase), the charge balance in the solution is $[\text{H}^+]_{\text{aq,eq}} + 1/[\text{H}^+]_{\text{aq,eq}} = [\text{NO}_3^-]_{\text{aq,eq}} + [\text{Cl}^-]_{\text{aq,eq}}$. The selectivity constant of the anion exchange reaction can be written as

$$K_{\text{NO}_3, \text{Cl}} = \frac{[\text{R-NO}_3]_{\text{res}} \cdot a_{\text{Cl}_{\text{aq}}^-}}{a_{\text{NO}_3^-}} = \frac{a_{\text{Cl}_{\text{aq}}^-}^2}{a_{\text{H}_{\text{aq}}^+} + 1/a_{\text{H}_{\text{aq}}^+} - a_{\text{Cl}_{\text{aq}}^-}} \quad (15)$$

and the value of this constant is equal to 3.8 for Dowex 1 × 8 resin.⁶⁶ By solving quadratic eqn (15), it is possible to estimate the concentration of Cl[−] anions in solution. In our experiments, the phase ratio was not equal to unity, so a correction factor f must be used

$$a_{\text{Cl}_{\text{aq}}^-} = \frac{-K_{\text{NO}_3, \text{Cl}} + \sqrt{K_{\text{NO}_3, \text{Cl}}^2 + 4 \cdot K_{\text{NO}_3, \text{Cl}} \cdot (a_{\text{H}_{\text{aq}}^+} + f/a_{\text{H}_{\text{aq}}^+})}}{2} \quad (16)$$

where $f = m_{\text{res}}/(\rho_{\text{res}} \cdot V_{\text{aq}})$, including m_{res} – resin mass, g; ρ_{res} – resin density, g mL^{−1}; V_{aq} – volume of aqueous phase, mL. Density values of air dry resins were taken from the literature.⁵⁵ This equation shows how Cl[−] concentration depends on the

acidity of the solution, leading to the formation of the AtO⁺ chloro complexes

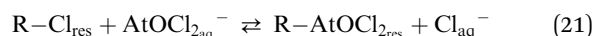


where equations for the stability constants are

$$\beta_1 = \frac{[\text{AtOCl}]}{[\text{AtO}^+] \cdot a_{\text{Cl}^-}}, \quad (19)$$

$$\beta_2 = \frac{[\text{AtOCl}_2^-]}{[\text{AtO}^+] \cdot a_{\text{Cl}^-}^2}. \quad (20)$$

So, sorption of AtOCl₂[−] by the anion exchange resin can be described as



and a thermodynamic constant of this reaction takes the form

$$K_{\text{AIX-At}} = \frac{[\text{R-AtOCl}_2]_{\text{res}} \cdot a_{\text{Cl}_{\text{aq}}^-}}{[\text{AtOCl}_2^-]_{\text{aq}}}. \quad (22)$$

At elevated acidity the following reaction requires inclusion



where a protonation constant is

$$K_a = \frac{[\text{HAtOCl}_2]_{\text{aq}}}{[\text{AtOCl}_2^-]_{\text{aq}} \cdot a_{\text{H}_{\text{aq}}^+}}. \quad (24)$$

This HAtOCl₂ acid can also be absorbed by the resin and then the distribution coefficient is as shown in eqn (25).

Using the equations above, one can simplify this expression and present it as a function $K_{\text{d-AIX}} = f(a_{\text{H}^+})$ to fit experimental data, as shown in eqn (26), where $a_{\text{Cl}^-} = f(a_{\text{H}^+})$ according to eqn (16).

It was mentioned above that the stability of astatine chloro complexes was estimated in the literature.^{20,21} We decided to re-evaluate published constants, assuming that the AtO⁺ dominates in the solution, because the β_1 values are different by a factor of ~2. It turns out that in 1968, when the authors²¹ published their results, the stability constants of AtO⁺ complexes with NO₃[−] and HCr₂O₇[−] anions were not yet known. However, these two ligands were present in their HCl system and must be considered. In our previous paper¹⁶ we analyzed the results of Norseyev *et al.*²¹ and derived equations, describing AtO⁺ sorption by Dowex 50 × 8 from nitric acid solutions in

$$K_{\text{d-AIX}} = \frac{[\text{R-AtOCl}_2]_{\text{res}} + [\text{HAtOCl}_2]_{\text{res}}}{[\text{AtO}^+]_{\text{aq}} + [\text{AtO}(\text{NO}_3)]_{\text{aq}} + [\text{At}^+]_{\text{aq}} + [\text{AtOCl}]_{\text{aq}} + [\text{AtOCl}_2^-]_{\text{aq}} + [\text{HAtOCl}_2]_{\text{aq}}}. \quad (25)$$

$$K_{\text{d-AIX}} = \frac{K_{\text{AIX-At}} \cdot \beta_2 \cdot a_{\text{Cl}^-} + K_{\text{sorb-HAtOCl}_2} \cdot \beta_2 \cdot K_a \cdot a_{\text{H}^+} \cdot a_{\text{Cl}^-}^2}{1 + K_1 \cdot a_{\text{NO}_3^-} + K_{\text{redox}} \cdot a_{\text{H}^+}^2 + \beta_1 \cdot a_{\text{Cl}^-} + \beta_2 \cdot a_{\text{Cl}^-}^2 \cdot (1 + K_a \cdot a_{\text{H}^+})}, \quad (26)$$

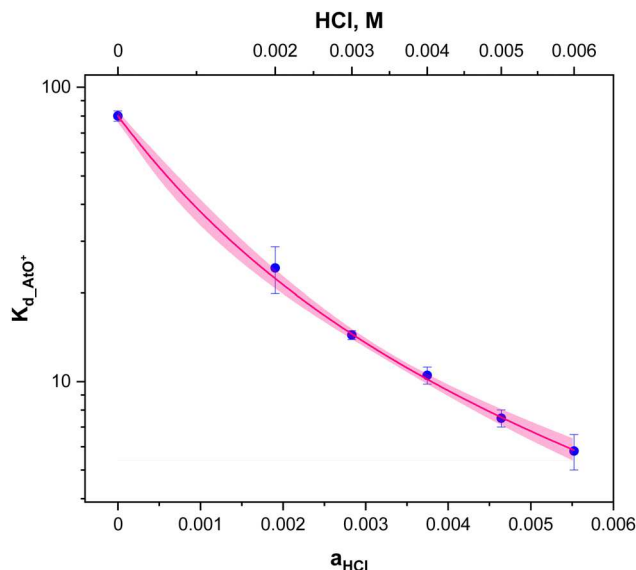
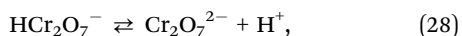


Fig. 4 Astatine sorption by Dowex 50 \times 8 from HCl solutions in the presence of 0.5 M HNO_3 and 5 mM $\text{H}_2\text{Cr}_2\text{O}_7$. Experimental data points were taken from the literature.²¹ The solid line is a fit according to eqn (30). Shade represents 95% confidence interval.

the presence of 5 mM $\text{H}_2\text{Cr}_2\text{O}_7$

$$K_{d,\text{At}} = \frac{K_{\text{CIX,At}}/a_{\text{H}^+}}{1 + K_1 \cdot a_{\text{NO}_3^-} + K_{\text{dichrom}} \cdot p \cdot a_{\text{HCr}_2\text{O}_7^-}}, \quad (27)$$

where p describes the deprotonation of the HCr_2O_7^- anion



$$p = \frac{a_{\text{H}^+}}{a_{\text{H}^+} + K_a}. \quad (29)$$

The $\text{p}K_a$ value of the reaction described by eqn (28) is equal to 1.18.⁶⁷ The same paper²¹ also considers AtO^+ sorption by Dowex 50 \times 8 from 0.5 M HNO_3 solution in the presence of 5 mM $\text{H}_2\text{Cr}_2\text{O}_7$ as a function of HCl concentrations. In this case the distribution ratio is

$$K_{d,\text{At}} = \frac{K_{\text{CIX,At}}/a_{\text{H}^+}}{1 + K_1 \cdot a_{\text{NO}_3^-} + K_{\text{dichrom}} \cdot p \cdot a_{\text{HCr}_2\text{O}_7^-} + \beta_1 \cdot a_{\text{Cl}^-} + \beta_2 \cdot a_{\text{Cl}^-}^2}, \quad (30)$$

where $[\text{H}^+] = [\text{HNO}_3] + [\text{H}_2\text{Cr}_2\text{O}_7] + [\text{HCl}]$.

Activity coefficients for HCl solutions were taken from the literature.⁶⁸ Eqn (30) was used to fit the experimental data shown in Fig. 4. Tyung *et al.* also studied stability constants of astatine with chloride anions in the presence of dichromic acid and Dowex 50 \times 8 resin;²⁰ however, in this case nitric acid was substituted with perchloric acid. They studied At interaction with perchloric acid and found that AtO^+ does not form a complex with the ClO_4^- anion, which was confirmed by electromigration studies of At behavior under these conditions.⁶⁹ In other words, parameter $K_1 \cdot a_{\text{NO}_3^-}$ in eqn (30) can be omitted to fit data (see Fig. S1 and S2 in the ESI†) published elsewhere.²⁰ Activity coefficients for corresponding molar

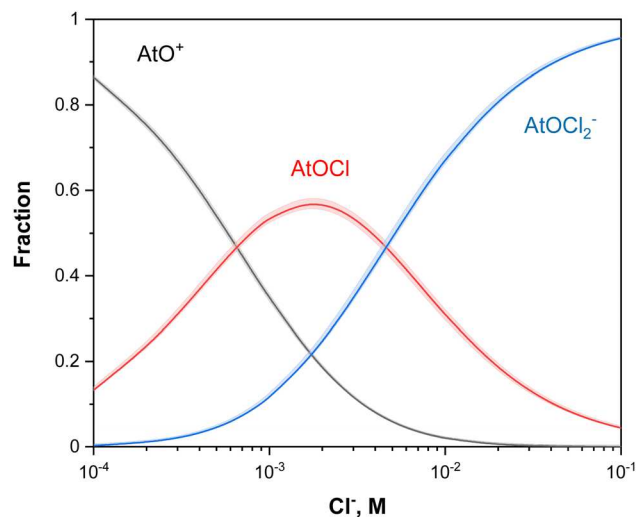


Fig. 5 Astatine speciation in the Cl^- media if $[\text{H}^+] \geq 0.3$ M (no hydrolysis). Shade represents propagated uncertainties.

Table 2 Reevaluated stability constants of astatine chloro complexes published in literature

β_1	β_2	Comment
1600 ± 80	$(33.4 \pm 1.5) \times 10^4$	0.3 M HClO_4 , data from ref. 20
1880 ± 220	$(27 \pm 5) \times 10^4$	0.5 M HClO_4 , data from ref. 20
1220 ± 140	$(36 \pm 4) \times 10^4$	0.5 M HNO_3 , data from ref. 21
1530 ± 70	$(33.3 \pm 1.3) \times 10^4$	Weighted average

concentrations of HClO_4 were interpolated based on literature values.^{70,71} The results of this analysis are presented in Table 2.

Taking uncertainty into account, the new stability constant values from different authors are in good agreement.

Once stability constants of AtO^+ in HCl media from different authors agree with each other, one can reconstitute the speciation diagram (Fig. 5). It can be seen that at 0.1 M HCl concentration and above, At is predominantly in the AtOCl_2^- form. This means that such HCl or saline solution can be used to strip At from cation exchangers.

These new stability constant values of AtO^+ chloro complexes were used to fit corresponding data in Fig. 1. Results are summarized in Table 3. In both cases, the best fit was found under the assumption that there is no AtO^+ reduction to At^+ . This is supported by previous findings where complexation may occur fast enough to preclude reduction. For example, with ketones¹⁷ and Tl^{3+} complexation with Cl^- .⁷² Apparently, the TEVA data set does not have enough experimental points to determine the constants of HAtOCl_2 sorption.

Thus, investigation of astatine sorption on the different ion exchange resins provided in this work show that astatine

Table 3 Results of Dowex 1 \times 8 and TEVA resins fit according to eqn (26)

Resin	$K_{\text{AIX,At}}$	K_a	$K_{\text{sorb,HAtOCl}_2}$
Dowex 1 \times 8	86 ± 9	0.83 ± 0.32	430 ± 30
TEVA	266 ± 13	0.17 ± 0.05	—

uptake decreases in the order MP thiol \approx TEVA $>$ Dowex 1 \times 8 $>$ Dowex 50 \times 4. Taking into account results of At sorption by extraction chromatography resins,⁴⁸ the uptake decreases in the order MP thiol \approx TEVA $>$ Dowex 1 \times 8 $>$ TRU \gtrsim UTEVA $>$ TK 400 \gtrsim SR $>$ LN \gtrsim Dowex 50 \times 4.

Conclusions

A set of four ion exchange resins have been tested to adsorb astatine from nitric acid media. The two cation exchangers Dowex 50 \times 4 and MP thiol show the lowest and the highest distribution coefficients for astatine, respectively. The K_d values for Dowex 50 \times 4 do not exceed 40, while the MP Thiol resin demonstrates values on the order of 4×10^3 . Of the two anion exchange resins examined, TEVA demonstrates sorption efficiency very close to MP thiol resin, whereas Dowex 1 \times 8 has K_d values greater than 10^3 only below a nitric acid concentration of 1 M. For each resin a thermodynamic-based mathematical model has been derived and used to fit experimental data. The results from this analysis show that the cation exchange resins Dowex 50 \times 4 and MP thiol most likely adsorb astatine in its +1 oxidation state. The anion exchangers Dowex 1 \times 8 and TEVA adsorb a negatively charged complex AtOCl_2^- , which is formed due to release of Cl^- anions upon washing of the resins with nitric acid. The concentration of chlorides in the aqueous phase has been mathematically estimated as a function of nitrates. There is some discrepancy across stability constant values for chloro complexes of AtO^+ reported in the literature. The published results on astatine stability complexation have been re-evaluated based on mathematical equations derived in this study. Uptake of astatine from nitric acid media by the studied resins decreases in the order: MP thiol \approx TEVA $>$ Dowex 1 \times 8 $>$ TRU \gtrsim UTEVA $>$ TK 400 \gtrsim SR $>$ LN $>$ Dowex 50 \times 4. Sorption of Bi by MP thiol, Dowex 50 \times 8, and Dowex 50 \times 4 resins in nitric acid media has also been mathematically modeled. The results obtained have been used to estimate At/Bi separation factors. These calculations led to a conclusion that MP thiol and Dowex 50 \times 4 resins can potentially be deployed to separate At from the bulk Bi matrix.

Author contributions

E. E. T.: conceptualization, formal analysis, methodology, validation, investigation, data curation, writing – original draft, visualization, funding acquisition. J. D. B.: validation, investigation, data curation, writing – review & editing, funding acquisition. S. J. S.: investigation, resources, writing – review & editing. G. A. P.: investigation, writing – review & editing. L. A. Mc., G. C. T.: investigation, resources. L. A. M.: investigation, resources, writing – review & editing, project administration, funding acquisition. B. D. G., A. A., M. B., E. E., K. H., T. H., B. H., L. H., K. L., S. R., R. R., M. S., A. T., D. T., J. T., Z. T.: investigation. S. J. Y.: writing – review & editing, supervision, project administration, funding acquisition.

Conflicts of interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Jonathan D. Burns, Evgeny E. Tereshatov, Lauren A. McIntosh, Gabriel C. Tabacaru, Sherry J. Yennello have patent #PCT/US21/25156 “Rapid At-211 purification method” pending to Texas A&M University; Evgeny E. Tereshatov, Jonathan D. Burns, Lauren A. McIntosh, Gabriel C. Tabacaru, Sherry J. Yennello have patent #PCT/US21/63241 “Systems and methods for automated separation and recovery of astatine” pending to Texas A&M University.

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