BATCH STUDIES FOR THE ADVANCEMENT OF THE CHROMOTOGRAPHIC SEPARATION OF ASTATINE-211

An Undergraduate Research Scholars Thesis

by

BROOKLYN D. GREEN

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This project did not require approval from the Texas A&M University Research Compliance & Biosafety office.

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ABSTRACT

Batch Studies for the Advancement of the Chromatographic Separation of Astatine-211

Brooklyn D. Green
Department of Chemistry
Texas A&M University

Faculty Research Advisor: Sherry J. Yennello
Department of Chemistry and Cyclotron Institute
Texas A&M University

Astatine, the least abundant naturally occurring element on earth, has attracted interest due to its unique fundamental chemistry and its potential use as an agent in targeted alpha therapy for cancer treatment. Further investigations in these fields rely on the cyclotron production of astatine-211 (At-211), the A=211 isotope of astatine. Traditional production utilizes the $^{209}Bi(\alpha,2n)^{211}At$ nuclear reaction pathway. This pathway requires a medium or high-energy cyclotron which is necessary to achieve an alpha-particle beam with an energy of 28.8 MeV. There are very few facilities with the capability of producing At-211 which, alongside the small quantity produced in each irradiation, makes the process of recovering At-211 from the natural bismuth target important. Research to advance this process works to maximize the quantity of material available for research. Often, the quantity of At-211 is the limiting factor in experiments involving the element.

After production of astatine-211, the irradiated bismuth target must be dissolved (typically in a nitric acid matrix), and the At-211 is then separated from the bulk target material in solution. Current methods, while effective at separating the At-211 from target material, fail to

result in free At-211. While achieving the goal of separating the At-211 from the target material and impurities, the At-211 elutes alongside organic molecules which have a high probability of rebinding to the At-211. This complicates subsequent studies as it interferes with the species being studied and therefore misrepresents the behavior of the astatine. When there is such a small quantity of material and a short window to work within, like with At-211, these issues can greatly affect the trajectory of an experiment.

In this thesis, there is a focus on designing and researching an alternative method of chromatographic separation using an ion-exchange resin. Two ion-exchange resins, Dowex 50x4 and MP Thiol, within varying nitric acid concentration matrices were tested. At-211 and the metal species previously found in the target dissolution solution were measured and quantified. This data provided information of the affinities the resins exhibited for each species at a given nitric acid condition.

Based on these affinities, both ion-exchange resins tested show promise. Additionally, nitric acid concentrations of about 2-3 M look to be the best conditions for loading. Further experimental design for column study experiments can be developed and tested based on these results. Column studies designed with this data in mind will allow testing of various reagents to ultimately find a striping agent to elute the At-211. Once an appropriate stripping agent has been identified, this method will result in free, unbound At-211.

DEDICATION

To my older sister, Marlei Green, who has always encouraged my love of learning. To my mother and father, Angela and Jerry Green, for supporting and encouraging me in every avenue I pursue. And finally, to my wonderful mentors, Gabriela Picayo and Sherry Yennello who inspire me to work for a bright future each day.

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All other work conducted for the thesis was completed by the student independently.

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NOMENCLATURE

Astatine-211   At-211

DNA   Deoxyribonucleic acid

HPGe Spectroscopy   High-purity germanium spectroscopy.

ICP-OES   Inductively coupled plasma- optical emission spectroscopy.

LET   Linear energy transfer.

TAT   Targeted alpha therapy.

1. INTRODUCTION

1.1 Motivations for Astatine-211 Production

1.1.1 Targeted Alpha Therapy

Targeted alpha therapy (TAT) has increased in attention and interest due to the successful clinical trial performance of radium-223 dichloride. Xofigo® is a radiopharmaceutical treatment for metastatic castration-resistant prostate cancer in which an alpha-emitting agent, ^{223}RaCl$_2$, is utilized to destroy targeted, malignant cells in bone metastases.[1] The success of Xofigo® serves as motivation to expand research into TAT and increase the availability of alpha-emitting radionuclides for use.[2]

While there are other radiopharmaceuticals that can target bone metastases, like samarium-153-EDTMP (Quadramet®), the radionuclides used are β particle-emitting and work to relieve bone pain therapeutically without the benefit of increasing survivability.[3] The difference in effect between the radiopharmaceuticals is due to their respective decay modes which have different characteristics. Beta particles have a low linear energy transfer (LET) which results in repairable, single-strand deoxyribonucleic acid (DNA) breaks in cells. Alpha particles like Xofigo®, however, have a high LET which results in double-strand DNA breaks in the targeted cells.[4] Additionally, alpha particles have a significantly shorter range (50-100 µm) in tissue compared to beta particles (1000-10,000 µm) and other types of ionizing radiation leading to a highly localized cytotoxic effect and minimizing harm of healthy, neighboring cells.[5] The high LET and short path length of alpha-particles make them especially effective for use in cancer treatment.

In light of the success of Xofigo®, researchers have focused their interest on the A=211 isotope of astatine, At-211, due to its promise as an alpha-emitter for application in TAT. It's moderately short half-life and simple, alpha-emitting decay scheme make At-211 well suited for use in a clinical setting.[6,7] Recent pre-clinical studies of mouse models have shown potential success of At-211 in treating cancer.[8–10] However, further research is needed to develop and approve the use of radiotherapeutics with At-211 as the agent. This requires special attention to efficient production, separation, and delivery of At-211 to laboratories involved in the research.

1.1.2 Fundamental Chemistry

Due to the element's unique position on the periodic table at the intersection of the halogens and metalloids, astatine is an interesting element with diverse chemistry.[11–13] Various oxidation states of astatine have been reported including At^-, At^0, At^+, At^{3+}, At^{5+}, and At^{7+}, but little is known about their respective chemistry and speciation behavior.[14] There remains debate on what chemical form astatine takes on in solution with the possibility of its behavior resembling iodine (At^-), a halogen, or polonium (At^+), a metallic element.[15,16] Further studies and theoretical calculations on astatine's chemistry are necessary to understand the element.

Astatine's fundamental chemistry remains relatively unexplored because of its low abundance: the lowest of any naturally occurring element on earth, with an estimated 0.07 g existing at any given time[17]. The low abundance of astatine can be attributed to its lack of stable isotopes and the short half-lives of its two longest-lived isotopes, At-210 ($t_{1/2}$=8.1 h) and At-211 ($t_{1/2}$=7.2 h). Therefore, investigations furthering the research into astatine's fundamental chemistry and the alpha-emitting radionuclide At-211 as a TAT agent rely on the cyclotron production and efficient onsite separation of At-211.

1.2   Current Methods of Astatine-211 Separation

Standard At-211 production relies on alpha particle bombardment of a natural bismuth target in a medium-energy cyclotron. This production is reliant on the ^{209}Bi(α,2n)^{211}At nuclear reaction pathway.[18] A medium-energy cyclotron is necessary to achieve an incident alpha-particle beam energy of 28.8 MeV, the energy required for At-211 production (without the co-production of At-210) according to the nuclear reaction cross section.[19] Unfortunately, there are very few sites with medium-energy cyclotrons and facilities suitable for producing medical At-211. Worldwide, there are only 29 facilities with the capability of At-211 production of which seven are within the Unites States.

After production, the At-211 must be separated from the bulk bismuth target material for further experimentation. Most recently, the separation of At-211 from bismuth has been achieved by extraction chromatography using 1-octanol or 3-octanone impregnated resin. Ethanol is subsequently employed as a stripping agent to strip the resin of and elute the adsorbed At-211.[20] While effective, this method's use of ethanol causes the coelution of 1-octanol or 3-octanone bound and unbound to At-211. These organic molecules cause a misrepresentation of astatine's behavior in subsequent experiments due to the interference of the At-211 and 1-octanol or 3-octanone complexes. Devising an alternative method using ion-exchange chromatography is a potential solution to avoiding this misrepresentation as there is a lack of organically impregnated resin introducing the 1-octanol or 3-octanone into the solution. This alternative method will circumvent this, allowing for more consistent data on astatine's behavior. Additionally, less post-separation chemistry will be necessary for At-211 studies maximizing the time and quantity of material available for experiments.

1.3   Advancements in Chromatographic Separation

To make advancements in the ion-exchange chromatography separation of At-211, a resin with the ideal behavior must be used in column studies. For the separation of astatine-211 from the bulk target material, bismuth and various metal impurities from the target material and aluminum target frame must show a low affinity for the resin under conditions where astatine-211 shows a high affinity. After the column is loaded with astatine, and the At-211 has adsorbed to the resin, a stripping agent can be employed to elute the At-211 from the resin.

Experiments to find the affinity of several (extraction and ion-exchange) resins for At-211 were done at a variety of molar nitric acid concentrations. High purity germanium (HPGe) spectroscopy was used to quantify the activity of the species in each phase to determine the associated affinity. Based on this data, two ion-exchange resins with relatively high affinities for At-211 were chosen for use in further experiments into the behavior of the bulk target material present alongside the At-211 in dissolution.

Subsequent experiments involved determining the affinities of the two chosen ion-exchange resins for the metal impurities and target material species present in dissolution solutions. This was tested at various molar nitric acid concentrations. To measure the uptake of these elements in these ion-exchange resins, a trace metal analysis instrument, ICP-OES (inductively coupled plasma- optical emission spectroscopy), was employed. This allowed quantification of the concentration of the metal in the resin and aqueous phase.

In the future, this data will be used to determine a resin or resins for use in column studies. Data will also help to determine what loading conditions to use in the studies and possible striping agents or conditions. Column studies will lend to experiments on how to elute At-211 from the column, eventually resulting in an alternative separation procedure using ion-

exchange chromatography. This will serve to decrease complications in pre-experiment

preparation and increase consistency in At-211 behavior experiments, opening the door to more

research on targeted alpha therapy and fundamental chemistry as it relates to At-211.

2.   MATERIALS & METHODS

2.1   Astatine-211

2.1.1   *Production*

Astatine-211 was produced via medium-energy cyclotron through the $^{209}Bi(\alpha,2n)^{211}At$ nuclear pathway. The metallic targets used in the irradiation were made using natural bismuth on a thin aluminum frame. The incident α-particle beam used for the bombardment of the bismuth target had an energy of 28.8 MeV. This production was continued and monitored overnight. Additional information on astatine-211 production can be found in the literature.[21] The irradiated target material— including bismuth, metal impurities, and At-211—was dissolved in a ~9 -10 M nitric acid solution. The dissolution procedure for At-211 and the bulk target material was completed onsite, rapidly, via an automated dissolution apparatus utilizing LabVIEW to remotely control the column valves.[22] **WARNING:** At-211 is radioactive and was handled under ALARA principles within an appropriate laboratory with the capability to handle radioactive materials.

2.1.2   *Materials*

Nitric acid solutions of varying concentrations in the 0.2 – 4 M range were made using concentrated nitric acid (67-70% w/w Aristar Plus HNO_3) and purified water (ELGA LabWater PureLab Flex Ultrapure Laboratory Water Purification System, operating at 18.2 MΩ). The resulting nitric acid solutions were titrated and found to be 0.16 M, 0.66 M, 1.16 M, 2.11 M, 3.02 M, and 4.10 M nitric acid.

The resins used in this experiment included Dowex 50x4 200–400 mesh (H) and Dowex resin purchased from Alfa Aesar and MP thiol 100–200 mesh resin purchased from Supra Sciences.

2.1.3 Batch Study Method

The batch studies were each done in 1.5 mL tubes. In each tube, 20-30 mg of resin and 500 µL of the desired nitric acid concentration were combined. These solutions were spiked with a target dissolution solution containing At-211. Samples were mixed using a tube rotator for a minimum of 10 min. Once mixed, these samples were centrifuged (SCILOGEX D1008 Mini Centrifuge) for a minimum of 1 min. The aqueous phase was decanted from the sample into 2 mL spin tubes containing filters (Corning™ Costar™ Spin-X™, nylon filter with 0.22 µm pore size). These tubes were centrifuged, again, for a minimum of 1 min. This separated any remaining solid resin from the solution. All experiments were done at least in duplicate.

2.1.4 HPGe Detection

Quantification of At-211 in the samples was done using γ-ray spectroscopy via high-purity germanium detectors (HPGe, Canberra Model GC2020). The software used for obtaining and analyzing the spectra was Genie-2000. At-211 quantification was done by measurement of the 76.9 keV, 79.3 keV, 89.8 keV, and 92.3 keV X-rays and the 687 keV γ-ray.

The initial activity of At-211 in each sample was found before separating the resin from the aqueous phase. After each sample had gone through the batch study method procedure, the activity of the resulting, filtered aqueous phase was measured. These initial and final activity measurements were used in the distribution coefficient, K_d, calculations.

2.1.5   Distribution Coefficient Calculation

Distribution coefficients were calculated using the activities measured by HPGe detector. Values were calculated according to the following equation.

$$K_d = \frac{I_o - I_{aq}}{I_{aq}} \, x \, \frac{V_{aq}\,(mL)}{M_{resin}\,(g)} = \frac{I_{resin}}{I_{aq}} \, x \, \frac{V_{aq}\,(mL)}{M_{resin}\,(g)} \tag{1}$$

In this equation, I_o and I_{aq} are net count rates of the measured radionuclide in the aqueous phase before and after separating the phases. These counts have been volume- and decay-corrected. V_{aq} is the volume of the aqueous phase in milliliters. M_{resin} is the mass of resin in grams. All experiments and, therefore, K_d calculations were done at least in duplicate.

2.2   Bismuth and Rare Earths

2.2.1   Materials

Nitric acid solutions of varying concentrations in the 0.1 – 4 M range were made using concentrated nitric acid (67-70% w/w Aristar Plus HNO_3) and purified water (ELGA LabWater PureLab Flex Ultrapure Laboratory Water Purification System, 14.4 MΩ). After preparing these nitric acid solutions, they were titrated using a standardized NaOH solution (1.04 ± 0.02 M, Fisher Chemical NaOH) to obtain their respective molarities. These titrations were done in triplicate. The resulting nitric acid solutions were found to be 0.509 ± 0.001 M, 1.004 ± 0.006 M, 2.176 ± 0.002 M, 3.188 ± 0.002 M, and 3.992 ± 0.005 M nitric acid. Additionally, a 2% nitric acid solution was prepared by weighing out 14 g of concentrated nitric acid into a 500 mL volumetric flask and diluting to the mark with purified water. This 2% solution was subsequently used to prepare calibration sets for ICP-OES analysis and a stock solution for the batch studies.

A 10 ppm stock solution containing the metal species of interest was prepared by aliquoting 100 µL of a bismuth instrumental standard solution (BDH, 999 ± 6 µg/mL Bi in 5% HNO_3) and 1000 µL of a 100 ppm rare-earth instrumental standard (Inorganic Ventures, 100

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μg/mL Ce, Er, Gd, La, Nd, Sm, Tb, Tm, Yb, Dy, Eu, Ho, Lu, Pr, Sc, Th, U, and Y in 7% HNO_3)

into a 100 mL volumetric flask. This was diluted to the mark with 2% nitric acid.

A dissolution solution was prepared by aliquoting 57 μL of a 1000 ppm Rh internal

standard solution (Inorganic Ventures, 1002 ± 5 μg/mL Rh in 2.5% HNO_3) into a 50 mL

volumetric flask and diluting to the mark with 2% HNO_3. Aliquots of this solution were

transferred into 50 mL tubes using a 2.5 mL volumetric pipet. Once spiked with the sample, this

dilution solution served as a 1 ppm Rh internal standard and to provide enough volume for ICP-

OES analysis.

The resins used in this experiment included: Dowex 50x4 200–400 mesh (H) purchased

from Alfa Aesar and MP thiol 100–200 mesh resin purchased from Supra Sciences.

2.2.2 Batch Study

Dowex 50x4 resin (20 ± 2 mg) and MP Thiol (20 ± 2 mg) were weighed out in five

triplicate sets into centrifuge tubes. In each tube, 50 μL of the stock was aliquoted. Then, 450 μL

of the appropriate nitric acid solution was aliquoted to achieve triplicate trials for each acid

concentrations for both resins.

The tubes were shaken manually for 10 minutes. Once mixed, these samples were

centrifuged (SCILOGEX D1008 Mini Centrifuge) for a minimum of 1 min. The aqueous phase

was decanted from the sample into 2 mL spin tubes containing filters (Corning™ Costar™ Spin-

X™, nylon filter with 0.22 μm pore size). These tubes were centrifuged, again, for a minimum of

1 min. This separated any remaining solid resin from the solution.

2.2.3 ICP-OES Analysis

In 15 mL centrifuge tubes, 2.5 mL of the prepared 2% nitric acid dilution solution

containing the Rh internal standard was volumetrically pipetted. Aliquots of 350 μL of each

sample were micro-pipetted into the dilution solution tubes. Alongside these samples, 50 µL of the stock solution and 450 µL 2% nitric acid was micro-pipetted into these dilution solution tubes to measure the concentration of the initial solution. This initial concentration solution was prepared for analysis in triplicate. Measuring the concentration of the initial solution allows the concentration in the resin to be quantified by ICP-OES (ThermoScientific iCAP Pro ICP-OES) and the K_d values to be calculated (Equation 1). Each sample reading was repeated four times.

2.2.4   Distribution Coefficient Calculation

$$K_d = \frac{[M^+]_o - [M^+]_{aq}}{[M^+]_{aq}} \; x \; \frac{V_{aq} \, (mL)}{M_{resin} \, (g)} = \frac{[M^+]_{resin}}{[M^+]_{aq}} x \; \frac{V_{aq} \, (mL)}{M_{resin} \, (g)} \tag{2}$$

In the equation above, $[M^+]_o$ is the concentration of the metal in the initial solution without having gone through the batch study method procedure. The $[M^+]_{aq}$ is the concentration of the metal in the aqueous solution of the batch study samples. V_{aq} is the volume of the aqueous phase in milliliters. M_{resin} is the mass of the exchange material (the resin) in grams.

$[M^+]_{aq}$ is subtracted from the $[M^+]_o$ to determine the $[M^+]_{resin}$, or the concentration of the metal species of interest in the resin. This is necessary as ICP-OES is unable to analyze solid samples like resin. The concentration of metal species of interest is required to calculate the K_d value.
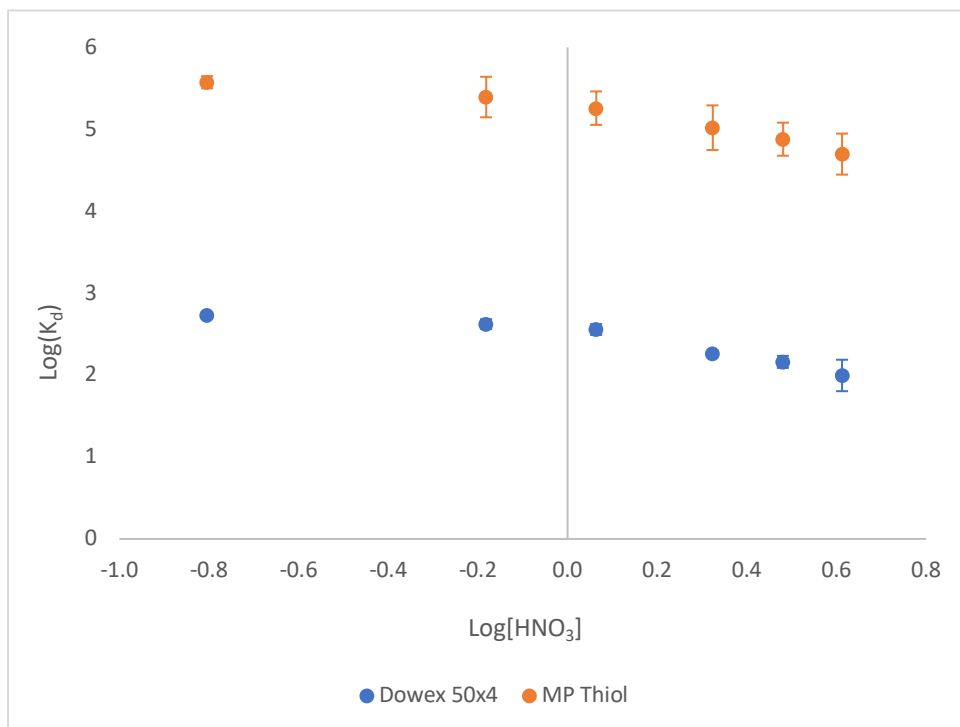
3.   RESULTS

3.1   Astatine-211

Figure 1: Log values of experimentally determined distribution coefficients for At-211 plotted alongside the log values of the molar nitric acid concentrations used in the experiments. Values for Dowex 50x4 resin are plotted in blue and MP Thiol resin in orange.

3.1.1   Dowex 50x4

In the data resulting from the Dowex 50x4 resin batch studies with At-211, the K_d values range from about 100 to 500 mL/g. At a nitric acid molarity of 0.16 M, the K_d value was measured at 535 ± 27 mL/g. For 0.66 M nitric acid, the measured K_d was 420 ± 57 mL/g. For 1.16 M nitric acid, the measured K_d was 360 ± 54 mL/g. For 2.11 M nitric acid, the measured K_d was 183 ± 9 mL/g. For 3.02 M nitric acid, the measured K_d was 145 ± 25 mL/g. For 4.10 M nitric acid, the measured K_d was 99 ± 44 mL/g. The K_d values show a monotonically decreasing

trend with the highest K_d value associated with the lowest nitric acid concentration and the lowest K_d value associated with the highest nitric acid concentration.

The logarithmic K_d values were plotted alongside the logarithmic nitric acid concentration values in figure 1. The logarithmic value for 0.16 M HNO_3 was -0.804 and the associated logarithmic K_d value was 2.73 ± 0.02. The logarithmic value for 0.66 M HNO_3 was -0.182 and the associated logarithmic K_d value was 2.62 ± 0.06. The logarithmic value for 1.16 M HNO_3 was 0.064 and the associated logarithmic K_d value was 2.56 ± 0.07. The logarithmic value for 2.11 M HNO_3 was 0.323 and the associated logarithmic K_d value was 2.26 ± 0.02. The logarithmic value for 3.02 M HNO_3 was 0.480 and the associated logarithmic K_d value was 2.16 ± 0.07. The logarithmic value for 4.10 M HNO_3 was 0.612 and the associated logarithmic K_d value was 2.00 ± 0.19.

The slope of the trendline for the logarithmic K_d values of Dowex 50x4 plotted in figure 1 was -0.5 with a slope uncertainty of 0.1. The y-intercept was 2.43 with an uncertainty of 0.05. This trendline had a correlation coefficient of 0.85.

3.1.2 MP Thiol

In the data resulting from the MP Thiol batch studies with At-211, the K_d values range from about 50,000 to 400,000 mL/g. At a nitric acid molarity of 0.16 M, the K_d value was measured at $375,000 \pm 64,000$ mL/g. For 0.66 M nitric acid, the measured K_d was $250,000 \pm 140,000$ mL/g. For 1.16 M nitric acid, the measured K_d was $180,000 \pm 85,000$ mL/g. For 2.11 M nitric acid, the measured K_d was $100,000 \pm 66,000$ mL/g. For 3.02 M nitric acid, the measured K_d was $76,000 \pm 35,0000$ mL/g. For 4.10 M nitric acid, the measured K_d was $50,0000 \pm 29,000$ mL/g. Like seen with At-211 and Dowex 50x4, the K_d values for MP Thiol show a

monotonically decreasing trend with the highest K_d value associated with the lowest nitric acid concentration and the lowest K_d value associated with the highest nitric acid concentration.

The logarithmic K_d values were plotted alongside the logarithmic nitric acid concentration values in figure 1. The logarithmic value for 0.16 M HNO_3 was -0.804 and the associated logarithmic K_d value was 5.57 ± 0.1. The logarithmic value for 0.66 M HNO_3 was -0.182 and the associated logarithmic K_d value was 5.39 ± 0.2. The logarithmic value for 1.16 M HNO_3 was 0.064 and the associated logarithmic K_d value was 5.26 ± 0.2. The logarithmic value for 2.11 M HNO_3 was 0.323 and the associated logarithmic K_d value was 5.02 ± 0.3. The logarithmic value for 3.02 M HNO_3 was 0.480 and the associated logarithmic K_d value was 4.88 ± 0.2. The logarithmic value for 4.10 M HNO_3 was 0.612 and the associated logarithmic K_d value was 4.70 ± 0.3.

The slope of the trendline for the logarithmic K_d values for MP Thiol plotted in figure 1 was -0.6 with a slope uncertainty of 0.1. The y-intercept was 5.19 with an uncertainty of 0.04. This trendline had a correlation coefficient of 0.91.

3.2 Bismuth and Rare Earths
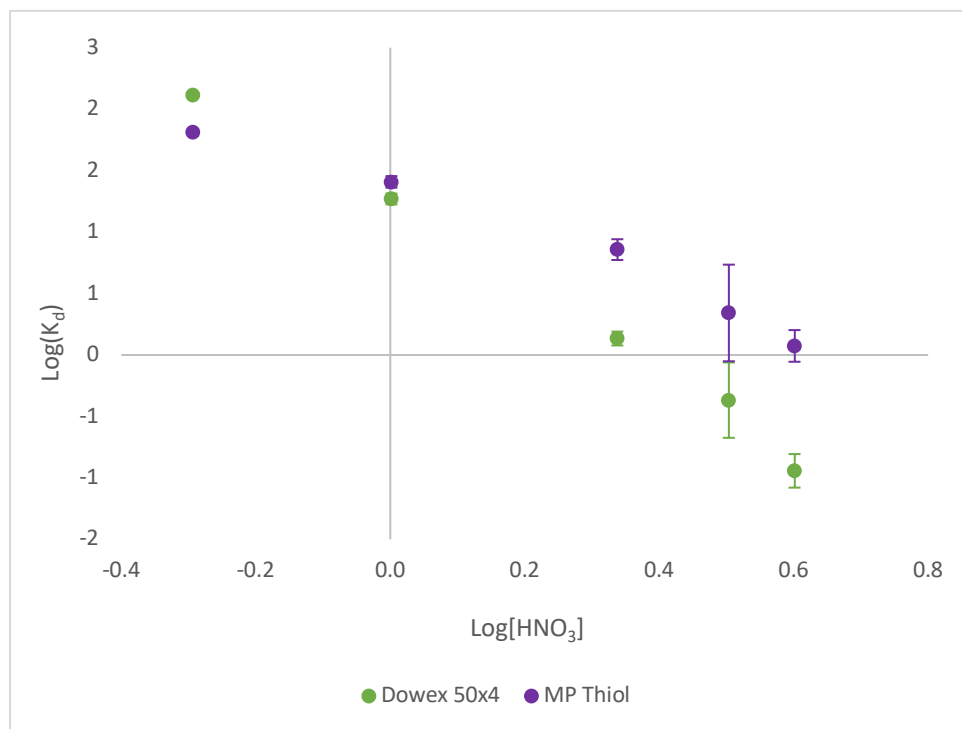
3.2.1 Bismuth

Figure 2: Log values of experimentally determined distribution coefficients for bismuth plotted alongside the log values of the molar nitric acid concentrations used in the experiments. Values for Dowex 50x4 and MP Thiol resin studies are plotted.

3.2.1.1 Dowex 50x4

Based on the data collected from the Dowex 50x4 resin batch studies, the K_d values of bismuth range from about 0.1 to 100 mL/g. At a nitric acid molarity of 0.509 M, the K_d value was measured at 130.4 ± 3.6 mL/g. For 1.004 M nitric acid, the measured K_d was 18.6 ± 1.9 mL/g. For 2.176 M nitric acid, the measured K_d was 1.4 ± 0.2 mL/g. For 3.188 M nitric acid, the measured K_d was 0.4 ± 0.3 mL/g. For 3.992 M nitric acid, the measured K_d was 0.1 ± 0.4 mL/g.

The logarithmic K_d values of bismuth were plotted alongside the logarithmic nitric acid concentration values in figure 2. The logarithmic value for 0.509 M HNO_3 was -0.293 and the associated logarithmic K_d value was 2.12 ± 0.01. The logarithmic value for 1.004 M HNO_3 was -

0.0017 and the associated logarithmic K_d value was 1.27 ± 0.04. The logarithmic value for 2.176 M HNO_3 was 0.338 and the associated logarithmic K_d value was 0.13 ± 0.056. The logarithmic value for 3.188 M HNO_3 was 0.5035 and the associated logarithmic K_d value was -0.37 ± 0.3. The logarithmic value for 3.992 M HNO_3 was 0.601 and the associated logarithmic K_d value was -0.94 ± 0.1.

The slope of the trendline for the logarithmic K_d values for Dowex 50x4 shown in figure 2 was -3.3 with a slope uncertainty of 0.16. The y-intercept was 1.21 with an associated error of 0.07. This trendline had a correlation coefficient of 0.99.

3.2.1.2 MP Thiol

In the data resulting from the MP Thiol resin batch studies with bismuth, the K_d values range from about 0.1 to 2 mL/g. At a nitric acid molarity of 0.509 M, the K_d value was measured at 65 ± 4 mL/g. For 1.004 M nitric acid, the measured K_d was 25.6 ± 2.8 mL/g. For 2.176 M nitric acid, the measured K_d was 1.4 ± 0.9 mL/g. For 3.188 M nitric acid, the measured K_d was 2.2 ± 2.0 mL/g. For 3.992 M nitric acid, the measured K_d was 1.2 ± 0.3 mL/g.

The logarithmic K_d values of bismuth were plotted alongside the logarithmic nitric acid concentration values in figure 2. The logarithmic value for 0.509 M HNO_3 was -0.293 and the associated logarithmic K_d value was 1.81 ± 0.03. The logarithmic value for 1.004 M HNO_3 was -0.0017 and the associated logarithmic K_d value was 1.41 ± 0.05. The logarithmic value for 2.176 M HNO_3 was 0.338 and the associated logarithmic K_d value was 0.86 ± 0.08. The logarithmic value for 3.188 M HNO_3 was 0.5035 and the associated logarithmic K_d value was 0.34 ± 0.39. The logarithmic value for 3.992 M HNO_3 was 0.601 and the associated logarithmic K_d value was 0.07 ± 0.13.

The slope of the trendline for the logarithmic K_d values for MP Thiol and bismuth was -1.92 with a slope uncertainty of 0.18. The y-intercept was 1.24 with an associated error of 0.07. This trendline had a correlation coefficient of 0.98.
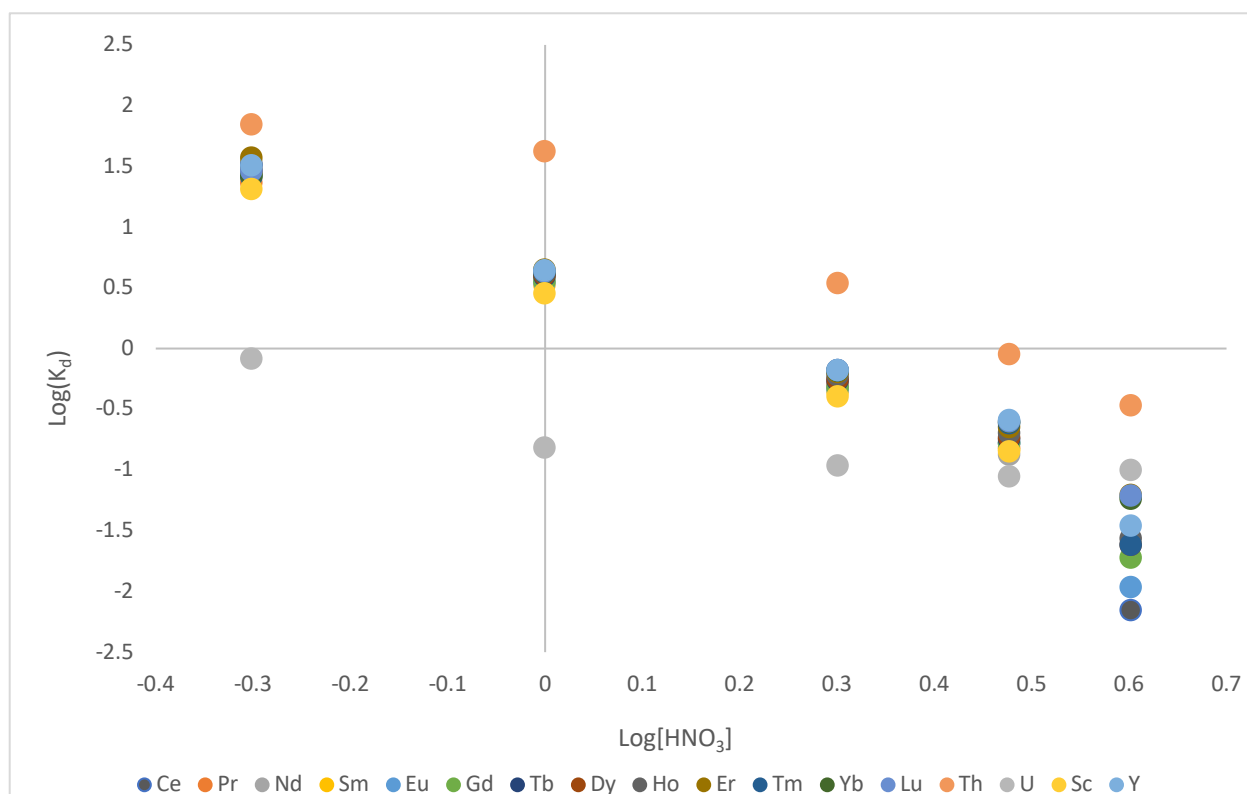
3.2.2 Rare Earths

3.2.2.1 Dowex 50x4

Figure 3: Log values of experimentally determined distribution coefficients for each of the rare earth elements plotted alongside the log values of the molar nitric acid concentrations used in the experiments. Values for Dowex 50x4 are plotted.

As shown in figure 3, the K_d values for Dowex 50x4 were relatively similar for all the tested rare earth species at each tested nitric acid condition, with deviation from thorium and uranium. Thorium was, on average, a magnitude higher in the associated K_d values than the other rare earths. Similarly, uranium was on average a magnitude lower in the associated K_d values

than the other rare earths. Additionally, there are some differences between rare earths at the 4 M nitric acid condition. However, for purpose of analysis, this data will be reported as an average across the rare earths in a general sense.

The logarithmic K_d values ranged from about -2.5 to 2. At a nitric acid molarity of 0.509 M, the K_d values for each rare earth was about 30 mL/g. For 1.004 M nitric acid, the K_d values for each rare earth was about 4 mL/g. For 2.176 M nitric acid, the K_d values were about 0.5 mL/g. For 3.188 M nitric acid, the K_d values were about 0.15 mL/g. For 3.992 M nitric acid, the K_d values were about 0.005 mL/g.

3.2.2.2 MP Thiol

The K_d values for MP Thiol were insignificant for the rare earths in each of the nitric acid concentrations. Values calculated were essentially 0 for each concentration and species. Therefore, this data has not been included as a figure. Data from the literature demonstrates precedence for this observance and confirms its validity which will be discussed in the analysis of the data within the following section.
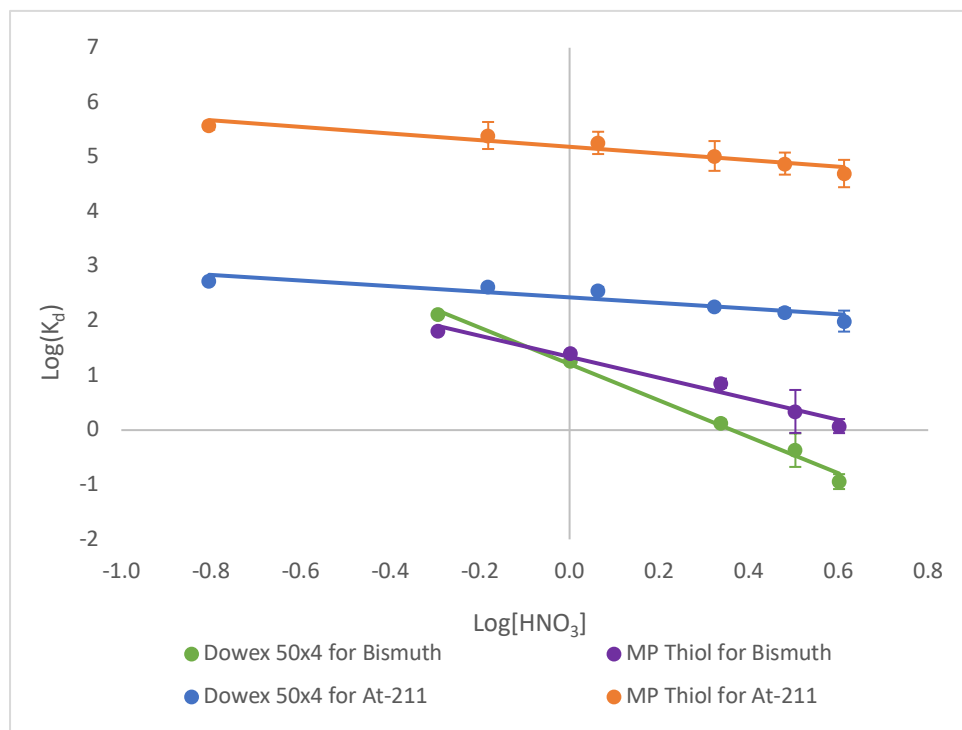
.

4.   ANALYSIS

Figure 4: Log values of experimentally determined distribution coefficients for bismuth and At-211 for both resins plotted alongside the log values of the molar nitric acid concentrations used in the experiments.

4.1   Dowex 50x4

4.1.1   At-211

Dowex 50x4 resin showed a high adsorption of At-211 for the 0.2-4 M nitric acid concentrations. At all concentrations, about 100 to 1000 times the amount of At-211 partitioned into the resin rather than staying in the aqueous phase. This is advantageous for the chromatographic separation and purification of At-211. If the contaminants being separated away from the At-211 show a poor level of adsorption for Dowex 50x4 at the nitric acid conditions, these impurities can be eluted leaving only At-211 within the resin for later stripping.

4.1.2   Bismuth

Bismuth had a relatively low adsorption to Dowex 50x4 resin, compared to At-211, according to the data collected. This is especially true for the 3 M and 4 M acid conditions for which about 10 times the amount of bismuth stays in the aqueous phase than in the resin. For 2 M nitric acid, the data shows about as much bismuth stays in the aqueous phase than partitions to the resin. For 0.5 M and 1 M nitric acid, the bismuth favors the resin with about 10 to 100 times the bismuth adsorbing to the resin rather than remaining in the aqueous phase.

While bismuth has a lower affinity for the Dowex 50x4 than At-211 at all concentrations, the lower nitric acid concentrations (0.5, 1, 2 M) still demonstrate a significant affinity for the resin. This is problematic as bismuth is likely to remain adsorbed to the resin alongside the At-211, complicating the separation process and leading to a high level of impurities. To properly elute the bulk target material contaminants when loading the target dissolution solution, a loading nitric acid concentration of 3 M or 4 M would be the most advantageous. This allows most of the bismuth to elute immediately.

4.1.3   Rare Earths

Further complicating choosing the ideal parameters for a Dowex 50x4 procedure, the rare earths exhibit similar affinity for the resin as does bismuth. With the same goal in mind of eluting these contaminants immediately after loading, a nitric acid concentration that exhibits a low affinity for the resin is the most advantageous. Therefore, using a loading solution of 3 or 4 M nitric acid would provide the best results, as similarly concluded from the bismuth data. At 3 and 4 M nitric acid, all of the rare earths remain primarily in the aqueous phase and not adsorbed to the Dowex 50x4 resin.

4.2   MP Thiol

4.2.1   At-211

     In the batch studies using MP Thiol resin, At-211 showed a very high affinity for the resin at all nitric acid concentrations. These results were significantly higher than the results for At-211 and Dowex 50x4. At all nitric acid concentrations, the data concludes that about 10^5 to 10^6 times the At-211 adsorbed to the resin than remained in the corresponding concentration nitric acid aqueous phase. If MP Thiol resin is used in an ion-exchange chromatography procedure, this behavior is beneficial as it means the resin will retain a high degree of the activity without eluting it. This helps in the chromatographic procedure and in the yield.

4.2.2   Bismuth

     Based on the results of the MP Thiol batch study, bismuth showed a relatively low affinity for the resin. However, the affinity of MP Thiol and bismuth at these concentrations was higher than for Dowex 50x4. For all nitric acid concentrations, the logarithmic value of the distribution coefficient was above 0 meaning the bismuth favors the resin. Even at the highest nitric acid concentration of 4 M, the data concluded that about an equal amount of bismuth remained in the aqueous phase than adsorbed to the resin.

     Although these distribution coefficient values for bismuth are higher than Dowex 50x4 resin, they must be compared to the At-211 distribution coefficient values for that resin. For MP Thiol, the affinity for At-211 is at such a high degree of magnitude that the bismuth does not pose much of an issue. Due to the large amount of At-211 being retained in the resin, the small amount of bismuth sticking along is not significant. Additionally, putting it through the column twice (or more) could further decrease the amount of bismuth present and lead to a purer result.

4.2.3 Rare Earths

MP Thiol resin did not have significant distribution coefficient results for the rare earths at the tested nitric acid concentrations. This is because of the poor affinity it has for the rare earths leading to low, virtually zero amounts of them adsorbed to the resin.

This is not a surprising occurrence due to precedence in the literature. CYANEX 301, a resin commonly used to separate actinides from lanthanides, also contains a thiol group like MP Thiol does. This resin is effective in separating actinides from lanthanides due to soft donor atoms like nitrogen or sulfur (present in thiol) having a lower affinity for the lanthanides than the actinides. Therefore, a thiol-containing resin can be predicted to have a low affinity for the rare earths.[23]

5.   DISCUSSION

5.1   Dowex 50x4

As discussed within the analysis, there is a significant difference between the affinity of Dowex 50x4 for At-211 and bismuth. This magnitude of difference is especially significant at lower nitric acid concentrations. This difference in affinities between the two species make it possible to use Dowex 50x4 to separate them. However, the presence of other species in the target dissolution solution and similar distribution coefficients of these species to bismuth could lead to complications.

Based upon the data collected, the most advantageous conditions to test for a Dowex 50x4 column study would be at 2 M which has a significant between each species and At-211. This high value for At-211 will allow this species of interest to remain adsorbed in the resin while the low values for bismuth and the rare earths would allow the majority of the contaminants to elute from the column once loaded.

5.2   MP Thiol

From the analysis of the data in the previous section, it can be concluded that there is a significant difference between the affinity of At-211 and bismuth. It is also discussed that the rare earth elements have an insignificant affinity for MP Thiol, as expected for a thiol-based resin. This avoids complication of other elements and provides a large separation factor for column studies.

The data collected shows a large gap between affinities at about 2 or 3 M nitric acid. At these molar nitric acid concentrations, the At-211 has a large affinity while bismuth has a

relatively low affinity. When loading the column, based on these affinities, bismuth will elute in its majority once loaded. The At-211 will be adsorbed by the resin while the bismuth and other contaminants elute first. This makes 2 or 3 M the ideal loading conditions for MP Thiol resin-based column studies.

5.3   Further Work

The significant difference in affinity for MP Thiol between At-211 and the bulk target material elements makes this ion-exchange resin a promising choice in column separation, especially with a diluted load solution of 2 M nitric acid. Dowex 50x4 also shows promise as an ion-exchange resin used in a new method of separation but more caution may be needed to ensure a pure final product.

However, further investigations into how to strip the adsorbed At-211 need to be undertaken. Due to the high affinity of either of these resins for At-211 at this nitric acid concentration range, changing the acid conditions to strip At-211 would not be adequate. The At-211 would remain mostly adsorbed to the resin at any reasonable nitric acid concentration. It would instead require a stripping agent to pull off the At-211 and elute it. Based on the results from these batch studies, column studies to find an appropriate stripping agent will be done.

Once a method has been developed to load and purify At-211 from its dissolution solution, it will be easier and more efficient to use in chemical studies. With less time spent on preparation of the At-211 and more time spent on conducting investigations into fundamental chemistry and TAT cancer research of this interesting radionuclide, more progress can be made within these two promising fields.

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