THESIS

INVESTIGATION OF THE EXTRACTION OF STABLE ^{45}Sc AND CARRIER FREE ^{44}Sc FOR THERANOSTIC APPLICATIONS

Submitted by

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ABSTRACT

INVESTIGATION OF THE EXTRACTION OF STABLE ^{45}Sc AND CARRIER FREE ^{44}Sc FOR THERANOSTIC APPLICATIONS

Scandium is an element of interest when it comes to theranostic applications. There are mainly two isotopes of scandium utilized in medical applications, Sc-44 and Sc-47. Sc-44 is a positron emitter and is used for imaging. Sc-47 is utilized as a beta emitter for targeting tumors. Together, the pair make a theranostic agent. This research focuses on Sc-44. To utilize the isotope after production, it must be separated and purified from target material, in this case titanium. One of the quickest and most efficient way to separate radioisotopes is extraction chromatography. The goal of this research is to understand and improve the separation of scandium from titanium by employing a variety of different chromatographic resins in a fast manner. Previous studies in the literature yielded data from several groups that examined the uptake of scandium and titanium onan extraction chromatographic resin based on a tetraoctyl diglycolamide, DGA. These groups employed either stable or radioactive scandium for their experiments. While the uptake of titanium was consistent between the studies, all groups have reported different values for the uptake of scandium. The aim of this part of the work is to compare both the uptake of stable and radioactive scandium to further elucidate the discrepancies between the studies reported in the literature. Radioactive Sc-44 for tracer studies will be obtained by “milking” a Ti-44 generator in regular intervals. Both stable and radioactive results obtained in this research will be compared.

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CHAPTER 1: BACKGROUND

1.1 Background

The use of radioactive isotopes to target cancer cells has been successful in many cases since they were first utilized after the discovery of ^{131}I in 1938. Before radioisotopes were usedas radiopharmaceuticals, they were utilized as tracers and labeled onto pharmaceuticals. I-131 was used in a variety of different ways for observing the thyroid. It was the first radiopharmaceutical approved by the FDA and paved the way for the investigation and expansion of other widely used radiopharmaceuticals.[1]

Over time, radiopharmaceuticals have been crafted to specifically target certain types of cancer and limit radiation exposure to surrounding healthy tissue.[2] A more recent process for targeting cancer via radiopharmaceuticals is the idea of theranostic agents. Theranostic radiopharmaceuticals can consist of a single radioisotope that can be used to both image and treatcancer cells or a pair of radioisotopes of the same element, where one is used for imaging and theother for treatment. The advantage to theranostic agents is they are designed to specifically target tumors in the body while having no additional chemical effects such as diverting treatment to different parts of the body. By using the same element, the negative effects to the body of different chemical interactions is negated .[3,4]

Production of radioactive isotopes for radiopharmaceuticals can happen using a variety of

different methods. The radioisotopes can be made in a nuclear reactor or at an accelerator, via proton irradiation or similar nuclear reactions. Once the isotopes have been produced, the most important step is to purify the radioisotope of interest from the starting material (often referred to as a target) either in a nuclear reactor or at an accelerator. In order to be labeled onto the pharmaceutical, the radionuclidic purity must be >99.9%.[5] A variety of different methods have been developed to ensure such purity is reached. These methods include, but are not limited to, high-performance liquid chromatography (HPLC), size exclusion chromatography (SEC), ion exchange chromatography (IX), and extraction chromatography (EXC).[6] These methods can be used individually or in sequence to achieve high purity radioisotopes for labeling.

The goal for this research is to understand the separation of scandium from its titanium target material via EXC. Various groups have investigated this separation in the past, but all havereported conflicting values for the uptake of scandium on a resin coated with N,N,N',N'-tetra-n- octyldiglycolamide or DGA resin. This research aims to elucidate the differences in reported uptake values for scandium on DGA and other resins by examining the effects of contact time, acid concentration, and radioactive versus stable scandium. The principles of EXC as well as its methodology will be discussed in Chapter 2. The understanding of scandium and its applications as a theranostic radiopharmaceutical will be discussed later in this chapter in Section 1.3.

1.2 The Chemistry of Scandium & Titanium

The chemical properties of scandium and titanium are similar due to their positions in thetransition metal block of the periodic table. This section will discuss the similarities and

differences between the two elements and the general chemical properties of both.

1.2.1 The Chemistry of Scandium

Scandium is the twenty-first element in the periodic table, and the first transition metal. The element appears as a soft, silvery-white metal, has a molecular weight of 44.9559 g mol^{-1} and an ionic radius of 2.63 Å.[7,8] The idea of scandium's existence was first theorized by Dmitry Mendeleev in 1871. In 1879, the first oxide of scandium was discovered by Lars Fredrick Nilson found in a rare earth matrix with gadolinite and euxenite.[7] The first discovery of the element itself did not come until 1923 when Francis William Aston discovered ^{45}Sc, the only stable isotope of scandium, using accelerated anode rays (now called protons).[9] Scandium is the 50^{th} most abundant element on earth and is mainly found in tin, tungsten, and uranium ores. It can also be extracted from the ore thortveitite, which can contain up to 34% scandium. While it is fairly rare on earth, it has a high cosmic abundance.[7]

Scandium is a fairly reactive element. As a metal, it oxidizes in air over time and turns a yellow or pink color. The color change is due to oxidation. Scandium is easily dissolved in a variety of acids and reacts rapidly in acidic solutions. While scandium metal does not tend to react violently with water, it does react with water when heated, forming the hydrated Sc^{3+} ion insolution.[7]

Scandium is also considered a rare earth metal (REM), which is a class of metals that includes the lanthanide series and usually extends to include scandium and yttrium. Despite the name, these metals are not necessarily rare. They do, however, have extremely similar properties

and are rather difficult to separate from one another.[10] One distinguishing feature of the REMs, including scandium, is that they are typically found in the +3 oxidation state. Scandium also has chemical properties and characteristics that closer align with yttrium and the other REMs than its transition metal neighbors such as aluminum or titanium.

While scandium is considered a REM, it exhibits many chemical properties that differ from the rare earths. First, scandium has a much smaller radius that that of the lanthanide series,even when the lanthanide contraction is considered. Second, scandium is not usually found in matrices with other REMs present. Last, it has magnetic properties that resembles the transition elements and not REMs.[11] For these reasons, it is often excluded as a true REM, though it is stillused as a lanthanide homolog in certain chemical instances.

Scandium has a wide variety of uses in daily life. It is used to produce “high-intensity lights” via the production of the compound Sc_2O_3. Radioactive ^{46}Sc is used as a tracer agent forcrude-oil refining. Another valuable use of scandium is combining it with iodine to create the compound scandium iodide (ScI), which is added to mercury lamps to create light sources that realistically resemble the light spectrum emitted by the sun. Scandium is also a valuable component in aerospace applications, particularly in building space craft, because it is a relatively light metal but has a higher melting point than aluminum.[7] Finally, radioactive ^{44}Sc and ^{47}Sc have been investigated for use as imaging and therapy agents, respectively, in the radiopharmaceutical industry. This thesis is related to that final use case and will involve elucidating the true separation factor of scandium from titanium for theranostic applications in nuclear medicine. This will be discussed more below in section 1.3.

1.2.2 The Chemistry of Titanium

Titanium is the twenty-second element on the periodic table and comes directly after scandium. It is the second metal in the transition block and was first discovered by William Gregor in 1791.[12] The element was later named by Martin Klaproth in 1795 but was not observed in its pure form until 1910 by Matthew Hunter.[7] Titanium has a molecular weight of 47.87 g mol^{-1} and an ionic radius of 2.57 Å.[7,8] There are five stable isotopes of titanium (^{46}Ti, ^{47}Ti, ^{48}Ti, ^{49}Ti, & ^{50}Ti) with ^{48}Ti being the most abundant.

In its elemental form, titanium appears as a white, lustrous metal with high corrosion resistance, making it useful in various applications. Unlike scandium, titanium is very abundant on earth and easily found in Earth's crust. While titanium metal has a low density, it still retains high strength. The metal can also be ductile but only in oxygen free environments. Titanium willburn when exposed to both air and nitrogen and is the only element to burn in a nitrogenous environment. All of these characteristics make titanium a very valuable metal because it can be utilized in various scenarios and situations.

Titanium is also a rather reactive element. As mentioned above, it will ignite upon exposure to air or nitrogen. For this reason, titanium is usually not found in its metal form but rather in an oxidized form of titanium, in an alloy, or as a chloride, to name a few. By having the metal present in one of these forms, it allows for titanium to be used in both nitrogen and oxygenrich environments while still harnessing the chemical traits of titanium metal. Titanium is the main component for alloying when added to aluminum, molybdenum, and manganese, among others. In the chloride form, titanium is commonly found as a tetrachloride ($TiCl_4$). In

the oxide form, titanium is most commonly found as titanium dioxide (TiO_2). Uses for these different forms are discussed below.

Titanium dioxide is used as paint. The uses of titanium dioxide paints range from artist's paint to more industrialized applications such as use in solar observations due to the compound's ability to reflect infrared light. Alloys of titanium are primarily used in aerospace applications, more specifically in aircraft and missiles. The combination of titanium's light weight, strength, and high melting point make it a great candidate for structural design and integrity of aircraft andmissiles. Chloride forms of titanium are used for producing colored or iridized glass or for producing smoke screens due to the fumes produced when exposed to air.[7] Overall, titanium is a very common transition metal that can be utilized in many different settings.

1.2.3 Comparison of Scandium & Titanium Chemical Properties

Scandium and titanium lie directly beside one another on the periodic table as the first and second elements, respectively, in the d-block or transition metal section. While the d-block experiences no formal trend, scandium has a slightly larger atomic radius (2.63 Å) than titanium(2.57 Å), which adheres to the overall atomic radius trend in the periodic table.[8,13] Although there is a slight difference in atomic size, this has not been found to be an effective means for separation. Instead, chemical properties must be exploited. The two elements are similar in color and both have relatively low densities and high melting points, though titanium does melt 121°C higher than scandium.[14] Both scandium and titanium metals react with air, though titanium metal typically passivates rapidly while scandium metal oxidizes

slowly and is therefore susceptible to corrosion. Both scandium and titanium can be found in the +3 oxidation state in solution, though titanium can also occupy the +2 or +4 oxidation states. While titanium can form the +3 oxidation state in solution, it is more stable in the +4 state.[7] While the elements exhibit some similar physical characteristics, the additional oxidation states available to titanium offer a way to successfully separate the two.

1.3 Nuclear Medicine

Shortly after the discovery of radiation, scientists discovered that they could harness the emissions for various uses. One of these was imaging. Wilhelm Roentgen first discovered this property in 1895 directly after his discovery of x-rays. This discovery provided the foundation for radiation to be a useful tool in medical diagnosis and treatment. Later in the 1930's, the

Joliot-Curies' discovered artificial radioactivity via irradiation of stable elements with a neutron source. This led to the discovery of the positron or β^+ particle. During this same period, Ernest Lawrence engineered the first cyclotron. Lawrence was also interested in artificial radioactivity. The work from both groups lead to the discovery of both iodine-131 (^{131}I) and technetium-99m (^{99m}Tc).[15] These artificial radionuclides would later become the face of nuclear imaging and medicine.

There are many useful radionuclide imaging techniques and machines used today for nuclear medicine applications. The two most common imaging techniques were discovered in 1950 and 1963, respectively, as Positron Emission Tomography (PET) and Single Photon Emission Computed Tomography (SPECT). PET scans rely on positron emission from the

nucleus to diagnose masses or tumors inside the body that may not be seen by other methods. PET was first conceptualized by William Sweet and Gordon Brownell in 1950. Two years later, the pair had the first clinical PET device active at Massachusetts General Hospital. In a similar manner, SPECT scans detect gamma rays emitted from the nucleus of a radioisotope. SPECT canbe utilized with more radioisotopes than PET due to the greater number of radioisotopes that emit photons in the SPECT gamma range.[16,17] Roughly ten years after the first clinical PET device was active, David Kuhl and Roy Edwards were exploring SPECT scans as another imaging device that does not rely solely on positron emission.[18] These two nuclear imaging techniques lead the way for nuclear medicine to expand and become the relevant diagnostic and treatment tool it is today.

Technetium was one of the first man-made radiotracers to be utilized as a radiopharmaceutical. Tc-99m was first investigated by Powell Richards and Paul Harper at Brookhaven National Laboratory. The radioisotope was produced in a generator via the decay of the parent molybdenum-99 (^{99}Mo). The radioisotope was measured via SPECT scan due to its transition from the metastable state to the ground state prior to decay by beta (β^-) emission. It was found to have qualities that made it an ideal candidate for nuclear medicine. These qualities included: light particle emission (beta), easily labeled, short enough half-life to enter the body and target a tumor but not commit too much unnecessary radiation to surrounding tissue, and ease of availability via generator.[19] All of these characteristics make technetium a viable candidate for nuclear imaging still today.

While technetium has long been a standard for radiopharmaceuticals and imaging, it is

not a comprehensive cure all. Technetium is mainly used in brain and thyroid scans in the body. While research has been able to label the ^{99m}Tc radioisotope onto other compounds and direct it to other parts of the body, such as the liver and bone marrow, it is not an all-inclusive.[19] Also, ^{99m}Tc is only used to image and test organ functionality.[20] For these reasons, other potential radioisotopes needed to be investigated to expand the field of nuclear medicine. Since the discovery of ^{99m}Tc, scientists have been investigating other viable candidates for both imaging and treating malignancies in the body. They have focused on elemental chemistry to target various parts of the body and come up with labeling techniques to tailor radioisotopes to attack specific areas and kill abnormal cells. Theranostic agents have become one of the newest methods for both diagnosing and treating abnormalities and cancer. Theranostics have the advantage of having the same elemental chemistry in the body for both diagnosing and treating. This allows scientists to track and know the whereabouts of the radioisotope throughout the process, thus providing improved control of exposure to the patient.[17] While technetium paved the way for nuclear medicine, theranostic agents have the ability to move the field forward evenfarther by allowing radioisotopes to be personalized to the specific needs of the patient.

One of the new elements of interest as a theranostic agent is scandium. Some of the first studies of scandium as a potential theranostic agent took place at Brookhaven National Laboratory in the 1990s. It was not until the early 2000s that scandium became widely investigated.[21] Since then, scandium has been utilized in many preliminary tests as well as earlyclinical trials to target cervical, ovarian, and prostate cancers.[22] While trials and testing

are still taking place, scandium has shown to be a promising theranostic agent that can be tailored to the specific need of the patient.

Scandium has twenty-five known radioisotopes. Of the twenty-five, three have propertiessuitable for nuclear medicine and more specifically as theranostic agents. The three isotopes of interest are ^{43}Sc, ^{44}Sc, and ^{47}Sc. Sc-43 has a half-life of 3.89 hours and decays via positron emission (β^+) to ^{43}Ca. Sc-44 has a half-life of 3.97 hours and decays primarily by positron emission and occasionally by electron capture (EC) to ^{44}Ca, as shown below in Figure 1. Finally, ^{47}Sc decays by beta emission (β^-) to ^{47}Ti with a half-life of 3.34 days shown below in Figure 2. These radioisotopes can be produced using calcium, titanium, or vanadium targets.[21] The scope of this research is limited to scandium/titanium separations, so the production routes will be limited to titanium target material.

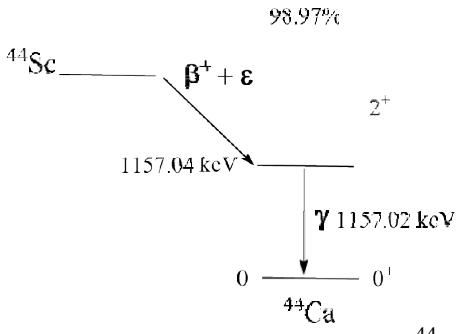

Figure 1: Decay scheme of ^{44}Sc

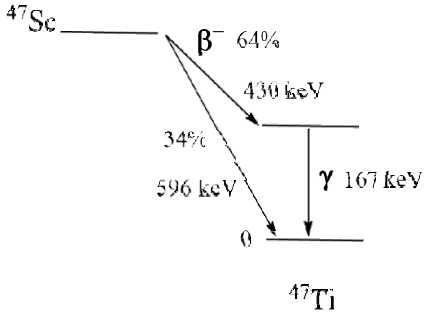

Figure 2: Decay scheme of ^{47}Sc

1.3.1 Sc-43 Production Routes

The only production route for ^{43}Sc via titanium targets is the proton irradiation of enriched (typically 97%) ^{46}Ti. The reaction shown below was investigated by Domnanich et al.at a medical cyclotron.[23]

$$^{46}\text{Ti}\,(p,\alpha)\,^{43}\text{Sc}$$

The results yielded roughly 200 MBq of high radionuclidic purity (>98%) after a seven-hour irradiation time. This reaction was found to be more favorable than the calcium target reaction asit did not co-produce other radioisotopes of scandium and had a high radionuclidic purity.[23]

1.3.2 Sc-44 Production Routes

There are two main routes for the production of ^{44}Sc via titanium as starting material. Thefirst is the proton irradiation of enriched ^{47}Ti in a cyclotron. The reaction, shown below, is a novel reaction investigated by Loveless et al.

$$^{47}\text{Ti}\,(p,\alpha)\,^{44}\text{Sc}$$

The process results in the co-production of ^{46,47}Sc alongside the target isotope of ^{44}Sc.[24] This can affect single radionuclidic purity but, for the purposes of theranostic agents, it is not a problem. The addition of ^{43}Sc is not a chemical concern because it has the same elemental chemistry as ^{44}Sc, but could potentially cause greater dose to the patient due to varying decay energies. Therefore, it will not cause any unwanted side reactions in the body. However, it should be takeninto consideration that additional dose exposure to the patient happens with the introduction of another radioisotope.

The other route for production of ^{44}Sc is via a titanium generator. It should be noted that the radiochemical batch studies discussed later involved the use of ^{44}Sc produced via generator.[25] The generator starts with the parent ^{44}Ti, which has a half-life of roughly 60 years. It decays to ^{44g}Sc via EC in the decay scheme shown below in Figure 3.

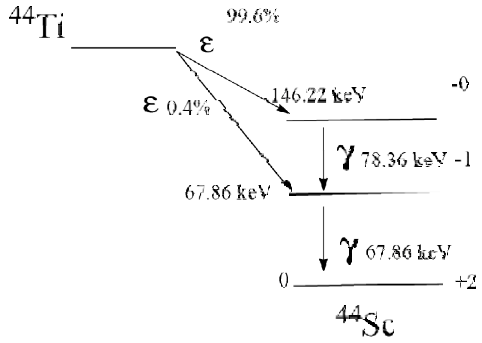

Figure 3: Decay scheme of ^{44}Ti for a ^{44}Ti/^{44g}Sc generator

Titanium generators are not a popular way of obtaining scandium radioisotopes. Although the generator method has been around for many years, most researchers and medical professionals refrain from utilizing the titanium generator due to the long half-life of the parent (^{44}Ti) as well as the difficulty of producing the parent isotope. The longevity of ^{44}Ti can cause many problems,such as long-lived radioactive waste and need for containment. The primary difficulty related to ^{44}Ti production is the small cross section for the production reaction (below).[26]

$$^{45}\text{Sc (p,2n) } ^{44}\text{Ti}$$

1.3.3 Sc-47 Production Routes

For ^{47}Sc, there are three different routes for production that use titanium as starting material. The first method takes place in a nuclear reactor via fast neutron irradiation according to the reaction shown below.

$$^{47}\text{Ti (n,p) } ^{47}\text{Sc}$$

Enriched titanium targets are required for this reaction to be effective.[26] While this may be feasible for reactors with high neutron flux such as the HFIR reactor at Oak Ridge National Laboratory, it is not ideal for long term production.[21] Long term production would lead to a largeamount of energy being consumed to produce one isotope as well as production of many long- lived radioisotopes that are harmful to people and the environment. The other downside to reactor produced ^{47}Sc is the co-production of ^{46}Sc, which is a long-lived radionuclide impurity. Sc-46 is not useful in nuclear medicine, much less as a theranostic agent, since it does not possess the qualities needed for radiopharmaceutical use by having a longer half-life and a high gamma energy. Thus, the production of ^{46}Sc decreases the radionuclidic purity of ^{47}Sc making this reaction an undesirable route for ^{47}Sc production.[26]

The second method of ^{47}Sc production is via proton irradiation at a cyclotron. In the reaction shown below, ^{48}Ti is irradiated with protons to produce ^{47}Sc.

$$^{48}\text{Ti (p,2p) } ^{47}\text{Sc}$$

This reaction is favorable due to the high abundance and low cost of ^{48}Ti. The downsides are the low cross-section of ^{48}Ti and the co-production of ^{46}Sc which, again, dilutes radionuclidic

purity. The co-production also adds higher risk and unnecessary dose to the patient as the two isotopes ^{46,47}Sc cannot be separated from one another.[21]

The last production route of ^{47}Sc utilizes photonuclear production via the reaction shown below. The photonuclear or gamma reaction was first reported by Yagi et al in 1977.[27] This reaction resurfaced recently in a paper by Rotsch et al at Argonne National Laboratory.[28]

$$^{48}\text{Ti}\ (\gamma,p)\ ^{47}\text{Sc}$$

The downside to this reaction is the co-production of ^{46,48}Sc which are nonviable radionuclides for radiopharmaceutical use.[27,28] Rotsch et al. reported the elimination of ^{48}Sc co-production by using enriched titanium target material. While using enriched targets increases radionuclidic purity, it does not eliminate the production of the long-lived ^{46}Sc. This is another reaction that is not ideal for producing scandium for radiopharmaceutical use.

Overall, scandium has been proven to be a viable theranostic agent. While the need for production routes continues, the demand for radiochemical separations, particularly the partitioning of scandium/titanium, is obvious. The next chapter will outline separation methods as well as experimental methodology utilized for this research.

1.4 Carrier Free Solutions

Carrier free (CF) solutions are void of stable isotopes of the same element. The goal of carrier addition is to “carry” the radioactive atoms to the desired destination. Both CF and carrier added solutions are utilized every day. Which type of solution to use is highly dependent on the nature of the research as well as the experimental procedures utilized.

CF solutions have many advantages. Radiation can be detected in picogram quantities. This allows for small amounts of radiation to be utilized while still obtaining high-quality data. CF solutions all exhibit extremely high radiochemical and nuclidic purity. This is important in applications such as nuclear medicine.[29]

While CF solutions have many advantages, there are also many disadvantages to these solutions. CF solutions have orders of magnitude fewer atoms than carrier or even stable solutions. This can cause negative effects in a few different ways. The results using CF solutionsmay yield unfavorable results meaning the expected outcome may be less than what was previously thought because there are not as many atoms available to experiment with. Second, atoms will be lost due to adsorption. Adsorption occurs everywhere all the time. It is unavoidable. The downside to CF solutions is that there are so few atoms to being with that losing more to adsorption can also cause a decrease in expected results.[30]

Addition of a carrier can help in two ways. The first is to make sure as much of the radioactive solution gets into solution as possible. The second, and also subsequent way, is by preventing loss of radioactive atoms to adsorption. While not all radioactive atoms will be prevented from adsorbing to various containers and transfer devices, there will be much fewer radioactive atoms lost in the presence of a carrier. The trade off to adding a carrier is the decrease in radiochemical and nuclidic purity as well as specific activity. Depending on the nature of the sample, the advantages of adding a carrier may be outweighed by losing purity.[29]

For this research, ^{44}Sc is the only radioisotope used for experimental procedures in this research. It is produced by the decay of ^{44}Ti in a generator set up which will be discussed in depth in Chapter 3. Since scandium comes directly from the decay of titanium, there are no carriers present in solution. The kinetic batch studies conducted for this research all employed CF solutions. An understanding of how the radioisotope behaves in solution on its own is obtained in the following research.

1.5 Gamma Dose of ^{44}Sc

When considering radiation exposure by ^{44}Sc, the biggest concern is the 1157 keV gamma ray associated with the decay of ^{44}Sc to the 2+ excited state of ^{44}Ca. The gamma constant

Γ for ^{44}Sc was found to be 0.00036 (mSv/h)/MBq.[31] This will be utilized to understand the radiation effects to the resin. It can also be used as an understanding of human dose if no ALARA measures were taken and how much gamma dose is received from ^{44}Sc. This calculation is shown below in Appendix C for calculations in section C.1. It should also be noted that the calculation was done for the maximum contact time of two hours, and this would be the theoretical maximum gamma dose received. The calculation showed a dose of 0.0119 mSv in two hours which computes to a dose rate of 0.00596 mSv/h.

CHAPTER 2: CHEMICAL SEPARATIONS

2.1 Necessity of Scandium/Titanium Separations

Scandium/titanium separation and purification methods are needed to isolate and purify scandium for theranostic radiopharmaceutical use. To be an effective theranostic agent, scandium must be of high purity and not contain other radioisotopes that are not useful for radiopharmaceutical applications. Another thing to consider is the half-lives of the three isotopes of interest. Because the half-lives range from hours to days, it is imperative to have a quick, effective separation method to get the radioisotopes labeled and to the patient for treatment. This section will review various separation methodologies that have been previously considered for this purpose, such as solvent extraction and ion exchange chromatography.

2.1.1 Solvent Extraction Separations

Solvent extraction (SX) is a separation method that can be utilized in both chemical and radiochemical separations involving metals. The premise of the separation is to have the analyte of interest extracted from one immiscible phase to another. For radiochemical separations, the two immiscible phases are typically an organic phase and an aqueous phase, usually both in the liquid state. The metal analyte is normally contained in the aqueous phase to begin with and extracted into the organic phase after sufficient contact. Organic ligands are designed to target various metal ions depending on the matrix of other ions in solution. The ligands are dissolved in process-relevant solvents that vary depending on what application.[32]

One advantage of SX is that organic ligands used for extraction can be synthesized to be selective for individual elements of interest. On the other hand, a disadvantage of SX is that

liquid-liquid extraction techniques produce a large amount of liquid waste at the end of the process. For radiochemical separations, the waste will contain small amounts of radioactivity and must go through proper disposal protocol for radioactive waste. Another disadvantage is that the organic solvents utilized to dissolve the organic extraction ligands can be harmful to the environment or people if not handled properly. Most SX applications are performed on a large, industrial scale or are being investigated to eventually scale up the process. This would mean large quantities of highly volatile and harmful organic solvents are being utilized.[33]

Another concern with SX is the retention of organic ligands or solvents with the radiometal which are not suitable for radiopharmaceutical production. Even a small amount can cause harm if injected with the radiometal. Organic ligands and solvents could cause side reactions that could be very harmful to the patient. Kirkbright et al. reported organic contaminants retained in the final solution of scandium when utilizing SX as a large matrix separation method.[34] In a similar manner Qui et al. reported having to utilize other purification techniques after extracting scandium from solution via SX.[35] SX may be able to isolate scandium from large matrices but it does not have the ability to purify it from organic residues in the process. Overall, SX was a former front runner for separations, but new methods have been developed to get away from this separation method. It is for these reasons that SX will not be explored in this research.

2.1.2 Ion Exchange Chromatography Separations

Ion exchange (IX) resins employ cation- or anion-functionalized organic polymers that trap oppositely charged ions to enable separations. IX involves a stationary phase (resin) with a mobile phase (solution) passed over it and is typically performed in a column orientation. This technique is commonly utilized for radiochemical separation methods that exploit radiometals

with a difference in electric charge. The resins are utilized to separate a mixture of radiometals based on their charge and charge dispersal at the time of separation. Cation exchange resins are typically utilized for lower valence state metals that are typically +1, +2, or +3. Anion exchangeresins are much more common. They have the ability to form anionic complexes with strong acids which are commonly utilized in radiochemical separations.[32] These resins have the ability to separate radiometals effectively.

One of the main attractions to ion exchange resins is various particle sizes (mesh) and cross-linking. Smaller particles lead to better IX kinetics. Cross-linking refers to the amount of interconnectivity in the beads. Less cross-linking means the solution can flow through the beadsfaster and is typically utilized to separate particles with large size differences. Large metals would be retained longer while smaller metals would flow easily through the resin. More cross- linking would have the opposite effect and take a much longer time for the solution to filter through.[32] IX is commonly utilized for purification purposes and can exploit various chemical and physical properties to separated different elements.[36] While IX has many attractive properties, it also has several disadvantages that keep it from being an ideal candidate for scandium/titanium separations.

The disadvantages of IX are slow speeds and inefficient separation of similar sized ions. As mentioned before, high degree of cross-linkage provides high separation efficacy. While this is a great quality, especially for purification, the downside is the amount of time it takes for the separation to occur. The high cross-link only allows so much solution through at a time, meaningseparation can take extended periods of time to occur.[36] When scaled up, this results in inefficient separations and can mean loss of radioactive material to decay. The other downsidethat is applicable to scandium/titanium separations is that scandium and titanium

have very similar ionic radii and valance states. While titanium has more accessible valance states than scandium, it still maintains a very similar ionic radii to that of scandium.

Several groups have utilized IX to separate scandium from titanium and various other metals in a matrix. Hamaguchi et al. reported titanium to have the lowest distribution coefficient for cation exchange from a multi-metal matrix of thorium, zirconium, iron, aluminum, calcium, and scandium. The highest distribution coefficient for titanium reported was 10 and decreased with increasing molarity of the ammonium thiocyanate eluent. This was much lower than the highest reported distribution coefficient for scandium which was roughly 2,500.[37] The distribution coefficients of the two metals show significant separation of scandium from titanium but not the high-level separation needed for radiopharmaceutical use.

Deilami-Nezhad et al. also investigated scandium separations via IX. This group, however, focused their separation methods on radiopharmaceutical use. They reported high radiochemical purities of 98%, 99%, and 88% for the produced $^{47}ScCl_3$ for the different methodologies used. The downside to their methodology is that it called for the use of a mixture containing hydrofluoric acid (HF) to elute the cation column. While the solution was only 0.4 M HF, it is still very dangerous to work with any concentration of HF, and large quantities would be needed if the process were to be scaled up.[38] In this case, the use of HF makes IX not ideal forscandium separation and purification.

The two separation methods presented have shown value in separating scandium but have many drawbacks especially when considering scale-up. The next section will explore extraction chromatography (EXC) as a separation method for scandium and titanium.

2.2 Extraction Chromatography

There are several radiochemical separation methods that could be viable for separating

scandium from titanium. However, this research focuses on extraction chromatography (EXC) toseparate the two. EXC is a newer separation method that combines the selectivity of SX with the solid phase and the chromatographic approach of IX. EXC uses a porous, inert polymer backbone that is thinly coated with an organic ligand to form a selective resin that the analyte solution is then passed over, typically in a column. Figure 4 shown below gives an up-close visual representation of an EXC resin bead as the mobile phase is passed over it.[32,39]

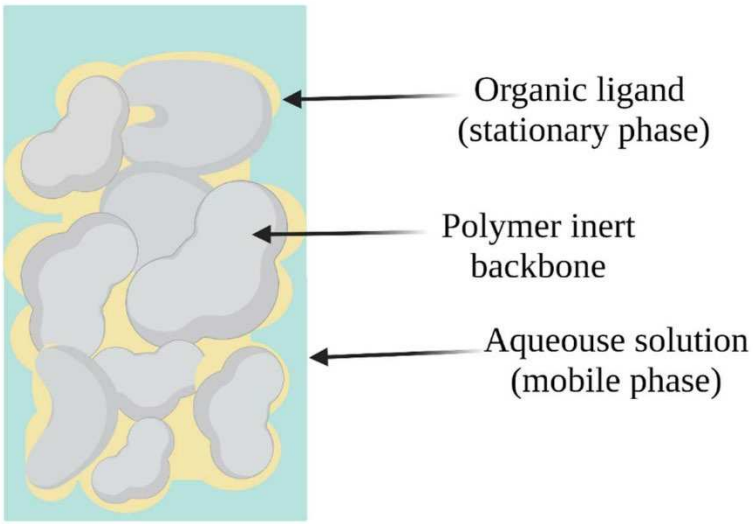

Figure 4: EXC resin bead

Just like SX, EXC has an organic and an aqueous phase. The organic phase is the organicligand that is thinly coated onto the resin beads. This is the stationary phase. The aqueous phase contains the analyte in an acidic mixture and is passed over the resin as the mobile phase. After the solution has passed over the column, the analyte which is bound to the resin can be removed by addition of a different solution to the column. The new solution can consist of different acid

concentrations, oxidizing agents, or complexing agents. After this is added, the analyte will elute off the column ideally leaving it pure and separated from the mixture.[39]

EXC was developed to be a better alternative to SX by reducing the amount of liquid waste produced. It has been found that EXC is particularly useful in separating actinides and lanthanides.[39] This is helpful in scandium-titanium separations for two reasons. The first reason is that actinides and lanthanides are very similar in size despite the large change in atomic number from the lanthanide group to the actinide group.[40] EXC allows for the separation of thesegroups despite similar physical qualities. This is useful for the scandium and titanium separation, because they too have similar ionic radii and physical characteristics.[39] The second reason is unlike titanium, scandium behaves like a REM since it has chemical properties akin to the lanthanide series.[11] By exploiting these two factors, EXC can separate scandium from titanium successfully and yield a high radiochemical purity of scandium without any additional separations required.

While there are many advantages to EXC, there are a few disadvantages that need to be discussed. The first is the use of organic solvents and ligands. Since the method still utilizes organic ligands to extract metals like SX does, it still requires harsh chemicals to facilitate the separation process. Second is the need for repeated separations. This mainly applies to rare earths since their chemistry is so similar but can be a downside to the process. The third disadvantage is column packing. Typically, EXC resins are very fine particulates that are much smaller than those of IX. This makes packing a column extremely difficult as air bubbles can cause channeling, which will reduce the effectiveness of the separation. The column must be packed tediously and precisely to ensure accurate results.[32] While there are disadvantages to EXC, it is still a highly efficient separation technique.

The results in EXC are based on the ratio of organic phase concentration to aqueous phase concentration at equilibrium (the distribution ratio, *D*) from SX. The distribution ratio

can be converted to the parameter *k',* which is defined as the number of free column volumes to the elution profile peak maximum or the resin capacity factor. To convert from *D* to *k'*, the volumes of the station phase (v_s) and the mobile phase (v_m) must be utilized. This conversion is shown in equation 1.[41]

$$k' = D \cdot \frac{v_s}{v_m} \tag{1}$$

While converting from *D* is possible, it is much simpler to measure the weight distribution factor (D_w) and convert to the distribution ratio *D* or resin capacity factor *k'*. To obtain D_w, the amount of analyte retained on the resin is measured against the initial weight of the resin. This equation is shown as equation 2.[41]

$$D_w = \frac{A_0 - A_s}{A_s} \cdot \frac{V}{w} \tag{2}$$

Above, A_0 refers to the initial analyte activity or concentration in the known volume of solution. Similarly, A_s denotes the final analyte activity or concentration after contact with the resin. Here $A_0 - A_s$ indicates the analyte activity or concentration which sorbed to a known resin weight, *w*, utilizing the known total volume of solution, *V*, where *w* is in grams and *V* is in mL. The equation for converting the weight distribution factor D_w to the distribution ratio *D* is shown in equation 3.[41]

$$D = D_w \cdot \frac{d_{extr}}{WF} \cdot \frac{v_s}{v_m} \tag{3}$$

In equation 3, d_{extr} is the extractant density and *WF* is the weight fraction of extractant loading. Extractant loading is measured in grams per grams of resin. A direct relation of *k'* to D_w

can be obtained by substituting equation 3 into equation 1 which results in equation 4 shown below.[41,42]

$$k' = D_w \cdot \frac{d_{extr}}{WF} \cdot \frac{v_s}{v_m} \quad (4)$$

These equations, specifically equation 4, can be utilized to compute the weight distribution factor of the resin to a form that is easily understood and graphed, which is *k'*. Thisresearch will have results plotted in *k'* on a log-log scale and will be shown in Chapter 5.

The next section will discuss previous literature involving the use of EXC for separating scandium from titanium. It will highlight the use of the popular resin DGA and the various methodologies that have possibly led to such large discrepancies in the true uptake value of scandium on DGA resin. The EXC resins utilized in this research will be discussed in detail in Chapter 3.

2.3 Previous Literature Results & Discrepancies

This section will discuss the discrepancies found in previous studies of the separation ofscandium from titanium utilizing DGA resin. Four different literature findings on this specific topic will be discussed. The premise for this research is to discern the true uptake value for scandium - both radioactive and stable - on DGA resin as well as elucidate why these groups reported such large discrepancies in their *k'* values. The groups include: Roman et al., Alliot et al., Dirks, and Boron-Brenner. The methodologies as well as results from each group will be discussed below in separate subsections.

2.3.1 Roman et al. Methodologies & Results

Before conducting the experiment, Roman preconditioned the resin for an hour on a shaker table. After precondition, the group reported a one-hour contact time with a known amount of the resin added to the solution in a 2 mL Bio-Spin column. An aliquot of solution was taken and filtered before being analyzed. The samples were analyzed on either an inductively coupled plasma-atomic emission spectroscopy (ICP-AES) instrument or via a 5x5 inch sodium iodide (NaI) detector depending on the nature of the samples.[43]

The acid ranges examined were 0.01 M – 16 M for nitric acid and 0.01 M – 11 M for hydrochloric acid. The group reported data in both nitric and hydrochloric acids, with nitric acid providing the best results, which are shown in Figure 5. They also pointed out that the absorption of scandium is dependent on acid concentration. In both hydrochloric and nitric acids, the limit of detection (LOD) was reached at higher acid concentrations ≥ 2.0 M. The *k'* values increased with increasing nitric acid concentration, while the *k'* values for hydrochloric acid decreased from 0.1 M – 1 M before increasing to the LOD at 2 M. While the results yielded good uptake values of scandium on the DGA column, it did show that it would be difficult to elute scandium from the column with either of the acids at practically any acid concentration.[43] While the group's motivation was not for production of theranostic radioscandium, they did prove that DGA is very effective at separating scandium from a matrix in both hydrochloric and nitric acids.

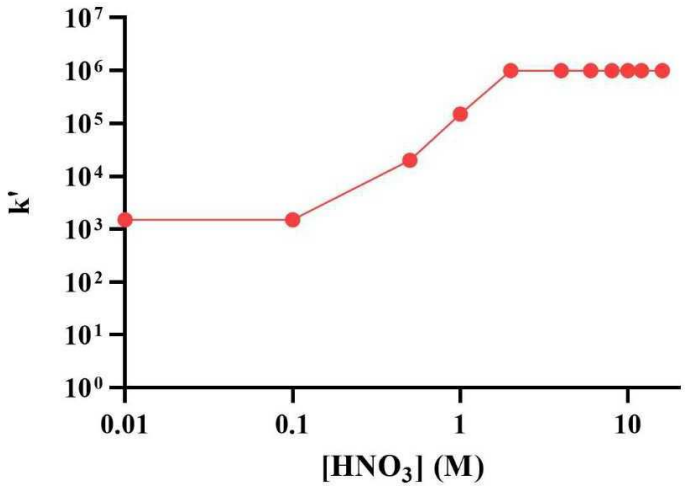

Figure 5: Roman et al. retention data of scandium on DGA[43]

2.3.2 Alliot et al. Methodologies & Results

Alliot et al. began the procedures by preconditioning the DGA resin with nitric acid and reconstituting the cyclotron produced ^{47}Sc three times in either hydrochloric or nitric acid. The group employed a two-hour contact time with the scandium solution and DGA resin and ICP-AES analysis for detecting the analyte. Radiochemical purity was also measured via a high purity germanium (HPGe) detector. The group utilized calcium targets to produce ^{47}Sc. This section will only focus on the batch study of scandium uptake on DGA resin. Although the radioisotope produced in the cyclotron was ^{47}Sc and is not the isotope of interest in this research, the data are still useful when comparing batch studies and uptake values of scandium on titanium because all isotopes of scandium have the same chemical behavior.[44]

The acid ranges for this group were 0.1 M - 6 M nitric acid and 0.05 M – 4 M hydrochloric acid. The group reported better retention rates of scandium with low nitric acid concentrations from 0.10 M – 2 M than the other groups., From 2 M and 4 M, Alliot et al.

reported hydrochloric acid produced better *k'* values. The group also reported eluting scandiumwith 0.1 M. The results are shown in Figure 6.[44] While the group reported conflicting values when compared to Roman et al, they still proved that DGA is a suitable resin for retaining scandium.

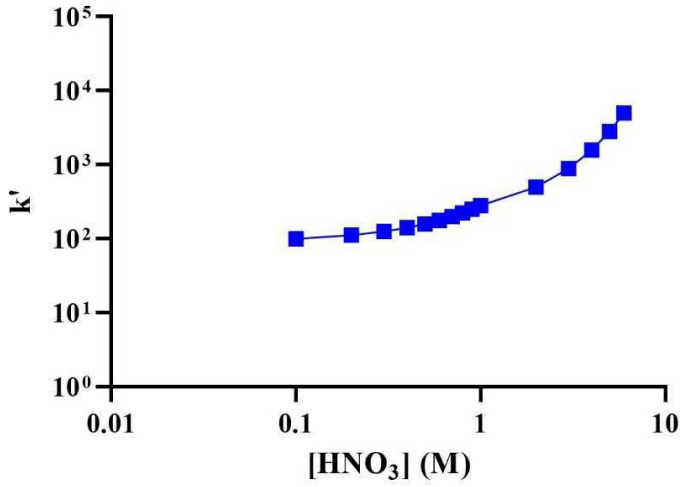

Figure 6: Alliot et al. retention data of scandium on DGA[44]

2.3.3 Dirks Methodology & Results

Dirks began the research by preconditioning the resin before addition of the analyte. Forscandium separations, she focused on the separation of scandium from titanium for nuclear medicine use. She utilized stable ^{45}Sc in her studies. For her experimental methodology, she employed a 30-minute contact time for scandium solution and DGA resin. This was determined to yield the best time from previous batch studies by Dirks. The solution was separated via centrifugation and measured on an ICP-MS to determine analyte quantity retained in solution. Batch studies with both hydrochloric and nitric acid were reported.[45]

The acid ranges reported were 0.001 M – 12 M nitric acid and 0.001 M – 10 M hydrochloric acid. Similar to Roman et al., Dirks reported higher *k'* values for scandium uptake in nitric acid than in hydrochloric acid. The best uptake concentration for both acids was reported to be 3 M. In hydrochloric acid, the *k'* values steadily decreased until a slight increase at 10 M. In nitric acid, the *k'* values increased up to 1 M, then decreased briefly and subsequently showed large fluctuations with increasing acid concentration. These values are shown below in Figure 7.[45] While the reported values are consistent with Roman et al., it is hard to say if the ideal concentration for scandium separations on DGA resin in nitric acid is 3 M when compared to the Roman data. The Roman data were at LOD, so the two data sets cannot quantitatively be compared.

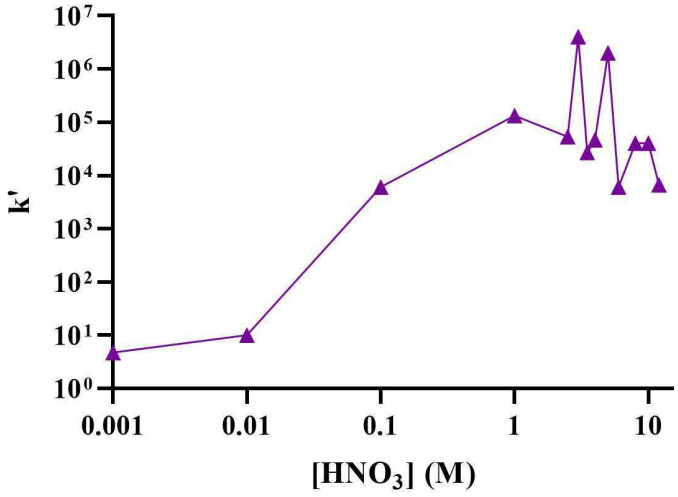

Figure 7: Dirks retention data of scandium on DGA[45]

2.3.4 Boron-Brenner Methodology & Results

The last data set was provided by Boron-Brenner. To begin the experiments, the resin was preconditioned on a shaker table and then allowed to sit for a certain amount of time. His methods included kinetic batch studies with shake times including one hour and 2.5 hours. The solutions were filtered with a syringe and 0.45 μm PTFE filter and analyzed on one of the following instruments: ICP-AES, inductively coupled plasma-mass spectrometry (ICP-MS).[46]

Acid concentrations ranged from 0.01 M – 10.5 M for nitric and 0.01 M – 8 M for hydrochloric acid. The best concentration for scandium uptake in nitric acid occurred at 2.5 M but the results plateau from there. The LOD was reached, so the true *k'* values are unknown beyond this point. The best acid concentration for hydrochloric occurred at 2.5 M since it yieldedthe highest k' values of scandium on DGA resin. The upper acid concentrations also hit a plateau here, and once again LOD was likely reached. The interesting find in the data was that *k'* values for nitric acid were higher than those of hydrochloric acid but only at low concentrations. This is similar to what Alliot et al. reported previously. The other thing to note about the data was that nitic acid samples reached the theoretical LOD at lower concentrations than those in hydrochloric acid. These results are shown in Figure 8.[46] While the results were on par with Alliot et al., they did not elucidate the true value of uptake for scandium on DGA resin.

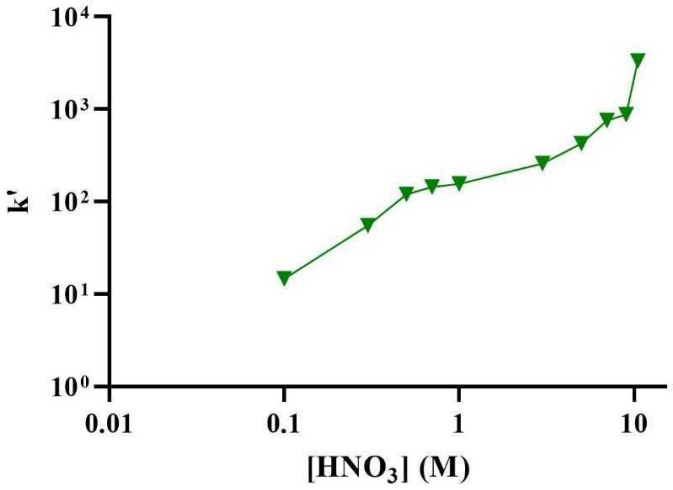

Figure 8: Boron-Brenner retention data of scandium on DGA[46]

2.3.5 Motivation for Research

The motivation for this research is to elucidate the true value of uptake for scandium on DGA resin. Figure 9 outlines the wide range of *k'* values shown in nitric acid. This is a visual representation of the discrepancies discussed in this chapter. While there are other resins that could be utilized that do not present the conflicting data that DGA does, DGA is a promising resin that is widely available and shows good scandium retention. The question this research seeks to answer is: what has contributed to the variation seen in scandium retention on DGA? This research will investigate using kinetics studies to see if the differing contact time has anything to do with the large discrepancies. It will also investigate the use of radioactive (^{44,47}Sc)scandium versus stable scandium (^{45}Sc). The methods utilized will be outlined in Chapter 4.

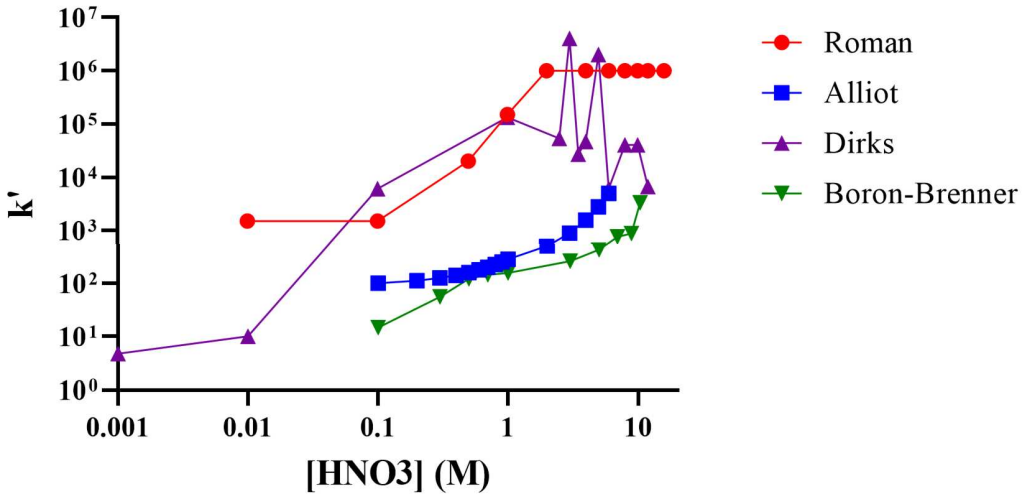

Figure 9: Previous DGA uptake data in nitric acid comparison

CHAPTER 3: METHODOLOGY

This chapter will discuss materials utilized for this research as well as the titanium generator and measurement techniques. The analytical tools include ICP-MS for stable scandiumand gamma counting for radioactive samples.

3.1 Materials

The scandium standard utilized for this research was an ICP-MS certified reference from British Drug House (BDH) at 1000 μg/mL. The nitric solutions prepared for ICP-MS use were made from ARISTAR Plus grade material, which contains <1 ppb metal impurities, from BDH. The nitric acid solutions utilized for the experiments with radioactive scandium were made using 68-70% ACS grad acid from BDH. All acid solutions were made utilizing 18.2 MΩ deionized water from a Millipore purification filter and system. Acid titrations were performed to validate the molarity of each acid concentration with either 0.1 N or 1.0 N sodium hydroxide solution and phenolphthalein indicator purchased from Sigma Aldrich. Pipette tips utilized for batch studies were all Eppendorf pipettes and tips purchased from VWR. Sample shaking and contacting was carried out utilizing Labquake™ shaker tables purchased from Thermo Scientific or an Incubating Rocker purchased from VWR. Samples contacted on the Incubating Rocker were shaken without utilizing the incubation. Vials utilized in research for both batch studies and calibration curve samples for ICP-MS (2 mL, 5 mL, 15 mL, and 50 mL) were all made of polypropylene and purchased from VWR. Laboratory glassware and glass bottles utilized to store acid solutions were all made of borosilicate glass and also purchased from VWR.

Batch contact studies in this research utilized four EXC resins: DGA, Ln, Ln2, and Ln3. All had the same bulk 50-100 μm particle size and all were purchased from Eichrom Technologies. These resins will be discussed in detail in section 3.3. Resins were weighed into vials utilizing disposable antistatic microspatulas purchased from VWR. Filtration of analyte samples was performed using a 5 mL BD Luer-lock syringes purchased from VWR and syringefilters using 0.45 μm or 0.25 μm polytetrafluoroethylene (PTFE) membranes purchased from VWR.

3.2 Titanium-44 Generator

The titanium-44 for the generator was supplied by the U.S. Department of Energy IsotopeProgram, managed by the Office of Science, and produced at Los Alamos National Laboratory. The Ti-44 solution was certified as 1 mCi on February 17, 2021. This is the date that will be utilized to correct for radioactive decay when data analysis occurs. The solution had a volume of 1.32 mL with a quantity of 1 mCi ^{44}Ti and 1 mCi ^{44}Sc. The two isotopes have the same activity due to their secular equilibrium. The chemical form of the solution is Ti (IV) dissolved in 6 M HCl. It was determined to have 0.76 mCi/mL by the quantification of ^{44}Ti via the 78.3 keV gamma emission. It was also determined to have a specific activity of 4.4 Ci/g by measurementon an inductively coupled mass spectrometry – optical emission spectrometry (ICP-OES) titanium analysis.

While the main isotope of focus is ^{44}Ti, there are other elements that were produced that remain in solution. These elements and concentrations were all stable and identified as: 0.95 mg/L aluminum, 2.95 mg/L calcium, 3.07 mg/L sodium, 8.35 mg/L niobium, 12.1 mg/L scandium, 172.8 mg/L titanium, 3.59 mg/L zinc, and 1.07 mg/L zirconium. All of the elements

are stable and should not interfere with nuclear measurements that will be conducted on experimental samples. It is important to note these contaminants, however, to understand there are other elements in solution should non-nuclear instruments be utilized to measure samples.

3.3 Extraction Chromatographic Resins

As previously mentioned, four EXC resins were evaluated in this research. These resins are DGA, Ln, Ln2, and Ln3. All resins will be discussed in detail below, and a visual representation of each structure will be shown. A comparison of resin performance as well as analysis methods will be reported in Chapters 4 and 5.

3.3.1 DGA Resin

DGA or N,N,N',N'-tetra-n-octyldiglycolamide is an EXC resin developed by Triskem. The resin is available in either a branched or normal form. For the purposes of this research onlythe normal form will be utilized. Figure 10 shows the structure for DGA-normal.[47]

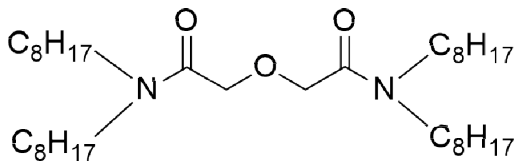

Figure 10: Structure of EXC resin DGA-normal

While DGA is mainly utilized for actinide and lanthanide separations, it has shown promising results for scandium separations as reported in Chapter 2.[47,48] DGA is known to have high affinity for REMs particularly in the trivalent or +3 state.[48] This makes DGA a good fit for scandium separations, since it is considered a REM and only resides in the trivalent state outsideof the ground state. According to the Triskem technical documentation, DGA exhibits,

"stability against interfering agents like…Ti (IV)." While the document is referring to Ti(IV) in environmental samples that contain americium, this is still an advantage for scandium radiopharmaceutical separations. The technical document did not provide any information about the retention of scandium on DGA.[44]

3.3.2 Ln Resin

The Ln resin is a part of the Ln series of resins containing three very similar extractants. Ln is the first in the series and contains a dialkyl phosphoric acid as ligand. It also has the strongest acidity of the resin series. The structure for Ln resin is shown in Figure 11.[47]

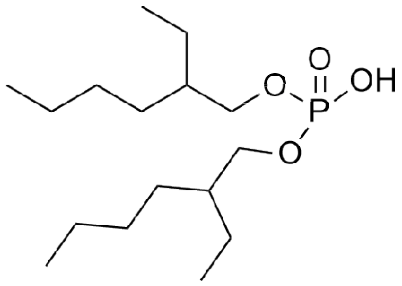

Figure 11: Structure of EXC resin Ln

The resin series is utilized for adjacent, trivalent REM and actinide separations. Ln has been utilized in combination with DGA to produce some of the most pure, high specific activity REM nuclides for nuclear medicine applications. Ln also produces similar separation factors to that of Ln2. The separation factor and contributing constituents of Ln2 and Ln3 will be discussed in their respective subsections. Scandium produced *k'* values of $> 10^4$ for all concentrations of nitric acid on Ln resin. The selective separation of scandium proved to be the best separation of the REMs on Ln resin in nitric acid.[49] These results show a promising

separation factor as well asthe ability to achieve high specific activity for radiopharmaceutical applications.

3.3.3 Ln2 Resin

Ln2 is the second of the trio of Ln EXC resins. It contains a dialkyl phosphonic acid as ligand and is has the median acidity of the three. The structure for Ln2 is shown in Figure 12.[47]

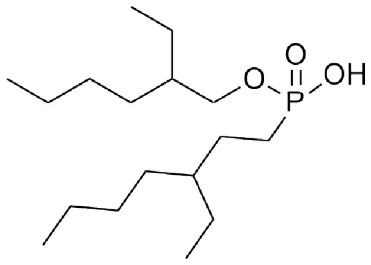

Figure 12: Structure of EXC resin Ln2

Ln2, like Ln, can be utilized in combination with DGA to produce highly effective radiochemical separations. The two resins differ only by one oxygen atom where Ln has two andLn2 only has one. In a similar manner, Ln2 has shown *k'* values for scandium retention to be $> 10^4$ in nitric acid. This again has to do with the structure of the resin and its affinity for trivalent metal ions. The upside to Ln2 as opposed to Ln is that the recovery of REMs has been found to happen in more dilute acids than that of Ln. Ln2 also provides better results for scandium retention in nitric acid over hydrochloric acid.[49] Overall, Ln2 is a comparable EXC resin to Ln but can be utilized with more dilute acid concentrations.

3.3.4 Ln3 Resin

Ln3 is the third and final resin in the Ln series of resins. It differs the most structure wisefrom the series. Ln3 has a dialkyl phosphinic acid as ligand with the weakest acidity of the series. Figure 13 shows the resin structure for Ln3.[47]

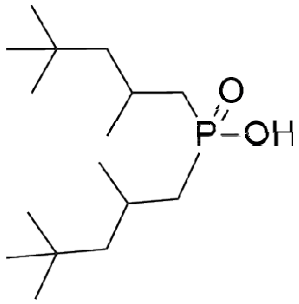

Figure 13: Structure of EXC resin Ln3

Ln3, unlike Ln and Ln2, has not been reported to be utilized in combination with DGA for high radiochemical purity. Ln3 shows a greater difference in retention for trivalent REMS when compared to Ln2 than Ln2 does when compared to Ln. This is due to the steric hindrance which is greater for Ln3 because it has no oxygen atoms to disperse the forces. Ln3 requires evenlower acid concentrations to be effective than that of Ln2. While this may appear as an advantage for the resin, in reality, it is not. Extremely low acid concentrations along the range of 10^{-3} M are hard to obtain and not practical for scaled up industrial uses. This makes Ln3 the least practical of the resins for REM separations. It has also been utilized for higher valance state metal ions which is not ideal for separating trivalent scandium.[49] While Ln3 shows the least promise for scandium separation of the series, it will still be investigated. It is expected that Ln3 retention of scandium will be much lower than that of Ln or Ln2.

3.4 Instrumentation

3.4.1 Inductively Coupled Plasma Mass Spectrometry (ICP-MS)

The instrument utilized to measure samples was a Perkin Elmer NexION 350. Sample evaluation begins with an aliquot, typically in a liquid form. A portion of the aliquot is taken up through tubing where it then enters the sample introduction system. This system is comprised of both a nebulizer and spray chamber. After passing through the introduction system, the sample is aerosolized. It is then injected into the plasma via sample injector. The plasma has various temperature gradients to dry, vaporize, atomize, and eventually ionize the sample for evaluation. The ICP-MS detected charged ions produced by the extremely high temperature plasma.[50] After the ions are formed, they are separated based on a mass to charge ratio before being analyzed by the detector. The ability to produce single ions provides the ICP with the ability to detect ultra- trace results.[51]

The ICP is often coupled with a mass spectrometry (MS) analyzer. The MS is made up offive different parts: sample inlet, ion source, mass analyzer, detector, and data system. The sample inlet is where the sample enters the detector. In this case, it comes in after passing through the ICP. When it enters, it is exposed to low pressures. From here, the sample passes into the ion source where the sample is vaporized and converted to ions. The ions travel through an electromagnetic field and are accelerated towards the mass analyzer. Once the ions reach the mass analyzer, they are separated by their mass-to-charge ratio. Finally, they reach the detector and are counted then processed by the data system.[52] Data can be retrieved from the data system for analysis.

The LOD for this instrument was calculated utilizing the IUPAC method. The IUPAC method for LOD determination was utilized due to the analytical nature of the samples being evaluated. A calibration curve was employed to determine k' values for the samples making the IUPAC the method of choice. Equation 5 shows the equation utilized for LOD determination of the ^{45}Sc experiments.

$$\mathrm{LOD_{IUPAC}} = \frac{3 \cdot \sigma_b}{m} \tag{5}$$

For the IUPAC definition, σ_b is the standard deviation of the blank and *m* is the slope of the calibration curve.[53] For these experiments, *m* is the average slope determined from multiple calibrations curves in each experiment. It should also be noted that the LOD for each resin was determined by the highest LOD for the instrument since multiple experiments were done for eachkinetics graph.

3.4.2 Gamma Spectroscopy

The instrument used to measure radioactive samples was a Wallac 1470 automated gamma counter. The gamma counting method implored relies on gamma spectroscopy via a thallium doped sodium iodide detector (NaI(Tl)). The detector utilized an inorganic scintillator to detect gamma radiation emitted from radionuclides. This is one of the oldest and most reliable methods in gamma detection and it is still relevant today.

The mechanism for NaI(Tl) detection is via a crystal lattice. When the radiation enters thelattice, it excites electrons in the crystal causing them to seek out a higher valance state. In this mechanism, the electron jumps from the lower band or the valance band up to the upper band or the conduction band. The space in between the two bands is called the band gap, and

the space in the band gap is known as the forbidden gap. Electrons cannot reside in this space in pure crystals. If an electron is excited in a pure crystal, it will jump to the conduction band and de- excite over time. The de-excitation will emit light, but since the gap is so large it will not be emitted in a visible frequency and therefore not register in the detector.

In this case, thallium is added to the lattice as an activator. Since the crystal is no longer pure, more states are added to the band gap in the forbidden region. This allows for electrons to de-excite through these newly formed states and greatly increases the probability of visible light being emitted.

Radiation excites a great number of electrons upon entrance into the lattice. When electrons are excited from the ground state of the lattice, holes are formed in the lower band. These are referred to as electron-hole pairs. While the electron is excited, the positive hole can also drift. In this case, the hole will be drawn to a thallium atom and ionize it. The hole seeks outthe thallium activator due to a much lower ionization energy compared to the rest of the crystal. After the excitation, electrons are allowed to move freely through the crystal lattice until they find an ionized recombination site to recombine with. When recombination occurs, the electron becomes part of an excited atom with distinct excited energy states. The excited state may have an allowed transition to the ground state. If the de-excitation is allowed, visible light may be emitted. If de-excitation is forbidden, the atom remains in an excited state until thermal energy excites it into a state that can complete the transition. This delay of de-excitation is known as phosphorescence and can contribute significantly to background light depending on the circumstances.

Choice of activator is imperative for timely and accurate results. Thallium has been the standard for inorganic scintillators and is used as the comparison method for new materials. There are many advantages to NaI(Tl) detection. They are usually cost efficient and can be used as field instruments. They also employ various geometries and have large counting areas. They also provide high detection efficiency due to the high average atomic number of the detector material. Finally, they have the ability to change activators depending on the element of interest. Activators can make a difference depending on sample nature and desired properties of the scintillator.

While these are great qualities, they also have disadvantages such as lower energy resolution along the lines of 5-10% and slow timing. Inorganic scintillators have excited state half-lives ranging from 5-500 ns. Another disadvantage is the fragility of the crystal. They are extremely hygroscopic and fragile. They must be kept in an airtight container at all times. Failureto do so will result in degradation of the detector crystal. Though the NaI(Tl) may have some disadvantages, it is a robust detector that has been the standard for many years. It was chosen as the detection method for radioactive scandium for this project.[54]

For the radioactive experiments, the Currie method was utilized to determine the LOD forthe experiments. The Currie method was employed because of fluctuations associated with the data due to the randomness of radiation. This method is outlined in equations 6 and 7.

$$\mathrm{LOD_{Currie}} = \frac{N_d}{60} + \bar{x}_b \tag{6}$$

Here, $\bar{x}_b$ is defined as the average blank and N_d is defined in equation 7.

$$N_d = 4.653 \cdot sN_b + 2.706 \tag{7}$$

Where sN_b is the $\sqrt{\sigma_b}$ and σ_b is the standard deviation of the blank. The resulting numberis total counts which is needed to calculate the LOD for radioactive samples.[55]

CHAPTER 4: BATCH CONTACT STUDIES UTILIZING EXTRACTION CHROMATOGRAPHIC METHODS

This section will focus on the methodologies of batch contact studies conducted in this research. All parameters were established from previous literature data from Roman et al., Alliot et al., Dirks and Boron-Brenner.[43-46] As mentioned above in section 2.3, the goal was to obtain true retention values for scandium and explain the large discrepancies reported among the four groups. Below will entail the experimental methodologies used of both stable and radioactive scandium batch contact studies.

4.1 Batch Contact Methodologies

Two of the main considerations in these batch studies were contact time and acid concentration. All groups reported varying contact times as well as acid concentrations. The goal of these studies was to investigate a wide range of contact times as well as acids to see how they would affect the scandium retention on DGA or the other EXC resins investigated. Contact timesincluded: 10 minutes, 30 minutes, 1 hour, and 2 hours. Only nitric acid was utilized in these experiments at 11 different concentrations, ranging from 0.01 M – 10.0 M. In depth procedures are described below.

4.1.1 Batch Contact Methodology of ^{45}Sc

All experiments were conducted with the materials described above in section 3.1. Since these experiments were conducted with stable scandium, the ICP-MS was utilized to analyze samples. ACS grade acid of high purity was utilized to prevent interferences and minimize data error.

To begin, a known amount of resin was weighed into pre-labeled microcentrifuge tubes and the weight was recorded. The resin was preconditioned with 1.0 mL of nitic acid and allowed to sit overnight. The next day, the resin was spiked with 0.5 mL of the same nitric acid concentration containing 2.5 ppm ^{45}Sc. Next, the resin was contacted with the acid and analyte solution for a predetermined amount of time on a shaker table. When the time was up, the tubes were removed and placed upright to allow the resin beads to settle at the bottom. A 1.0 mL aliquot was taken from the solution and filtered through a syringe with at least a 0.45 μm filter on the end into a 15 mL centrifuge tube. The solution was then diluted up to 10 mL with distilled water and transported to be measured on the ICP-MS.

4.1.2 Batch Contact Methodology of ^{44}Sc

All experiments were conducted with materials described above in section 3.1 except forthe ARISTAR Plus nitric acid purchased from BDH. The nitric acid solutions were made with 68-70% ACS grade nitric acid from BDH. The radioscandium utilized is described in section 3.2.

To begin, a known amount of resin was weighed into pre-labeled microcentrifuge tubes and the weight was recorded. The resin was preconditioned with 1.49 mL of nitic acid and allowed to sit overnight. The next day, the resin was spiked with 100 μL of a prepared stock solution of ^{44}Sc containing between 15,180-18,040 Bq. The range is indicative of difference in stock preparation which ranged from one to two hours. The stock solution preparation is described below in section 4.2.4. Next, the resin was contacted with the acid and analyte solution for a predetermined time on a shaker table. When the time was up, the tubes were

removed and placed upright to allow the resin beads to settle at the bottom. A 1.0 mL aliquot was taken from the solution and filtered through a syringe with at least a 0.45 μm filter on the end into a gamma tube and capped. Solutions were placed in racks and measured on the automated gamma counter.

4.2 Solution Preparation

4.2.1 Nitric Acid Preparation

All nitric acid solutions utilized in the experiments with stable scandium were ultra-high purity ACS grade, meaning few impurities were found in the acid. Solutions were made from a stock solution of concentrated nitric acid with a molarity of ~16 M. To obtain the ideal molarity of the nitric acid solutions, dilution with DI water must occur. Amount of stock needed was calculated from equation 8.

$$C_1V_1 = C_2V_2 \tag{8}$$

Here C_1 is the concentration of the stock which is the concentrated nitric acid at 16 M. V_1 is the amount of solution in mL that is going to be made, and $C2$ is the ideal concentration of acid. V_2 is left and it is the amount of stock solution needed to make the ideal solution concentration by dilution. This equation leads to the finale equation 9. This is obtained by dividing C_1V_1 by C_2.[7]

$$\frac{C_1V_1}{C_2} = V_2 \tag{9}$$

All nitric acid solutions were prepared with this methodology regardless of purity. The acid solutions for the radioactive scandium were prepared with non-ACS grade nitric acid stock since they did not need to be free of impurities. The radioactive samples were measured by

gamma counting i.e., emission of radiation, so there are no interferences from stable elements present in the acid. The stock solution of the non-ACS nitric acid was also ~16 M.

After all solutions were prepared and thoroughly mixed, titrations were performed for each solution to obtain the exact acid concentration. As mentioned above in section 3.1, solutions were titrated with either 1.0 or 0.1 N sodium hydroxide solution coupled with a phenolphthalein indicator. Three replicates were done of each acid concentration for statistical analysis. Data for two high purity and ACS grade nitric acid solutions can be found in Appendix A.

4.2.2 Calibration Curve Standards Preparation

Calibration curve standards were made to use with samples on the ICP-MS. The best data points for the standard curve were determined with the help of the ICP-MS instrument coordinator, Dr. Jacqueline Chaparro. Seven points were determined based on previous literature data of how much scandium would be left in solution and measured by the ICP-MS. A blank was also utilized as a baseline to know how much scandium was in the nitric acid solution. All standards were made in the same manner. All standards were made in 50 mL centrifuge tubes and remade periodically to ensure fresh DI 18.2 Ω milli-Q water and scandium solution was usedfor the best results.

First, nitric acid was added to the vials. Every standard contained 5 mL 0.1 M HNO_3. Next, the appropriate amount of scandium stock solution was added to the vial. Last, the solutions were diluted up to 50 mL with DI water. The following details how much scandium stock each standard contained. Standard 1 had a concentration of 8 ppb of stable scandium and

contained 4 μL of 0.1 M ^{45}Sc stock. Standard 2 had a concentration of 40 ppb of stable scandiumand contained 20 μL of 0.1 M ^{45}Sc stock. Standard 3 had a concentration of 200 ppb of stable scandium and contained 0.1 mL of 0.1 M ^{45}Sc stock. Standard 4 had a concentration of 400 ppb of stable scandium and contained 0.2 mL of 0.1 M ^{45}Sc stock. Standard 5 had a concentration of 800 ppb of stable scandium and contained 0.4 mL of 0.1 M ^{45}Sc stock. Standard 6 had a concentration of 4 ppm of stable scandium and contained 2 mL of 0.1 M ^{45}Sc stock. Standard 7 had a concentration of 7.2 ppm of stable scandium and contained 3.7 mL of 0.1 M ^{45}Sc stock. The 8th solution was the blank which only contained 0.1 M HNO_3. The signal from these solutions was used to determine the amount of stable scandium remaining in solution after contact with the resin while correcting for background interferences.

4.2.3 Sc-45 Stock Solution Preparation

Stock solutions of the stable scandium were prepared in order to have scandium in a nitric acid solution as well as in a concentration of nitric acid that was suitable for instrumentation purposes. Stock solutions were prepared from a 1.5 M nitric acid solution containing ~1000 μg/mL scandium. The concentration of scandium was too high for instrumentation purposes. Therefore, a 2 mL aliquot of the BDH solution was dried down on a hot plate and reconstituted in the appropriate nitric acid concentration. Scandium stock solutions were made for all 11 concentrations of nitric acid investigated in this research. The 0.1 M scandium stock was also utilized in calibration standards for the ICP-MS.

4.2.4 Sc-44 Stock Solution Preparation

Stock solutions of ^{44}Sc were all made in 0.1 M nitric acid. Stock solutions were

preparedevery day that experiments took place due to the relatively short half-life of the radioisotope. First, the generator was milked with 1.0 mL of the load solution of 0.1 M oxalic/0.2 M hydrochloric acid mixture. The solution was dried down in a 100 mL wide bottom flask to maximize the surface area in contact with the heating block. Next, 0.5 mL of 3% hydrogen peroxide was added to the solution and dried down to destroy the oxalate ions. Last, the desired nitric acid concentration ranging from 0.01 – 10.0 M was added in 200 μL increments threetimes and dried down to replace the chloride ions with nitride ions. The solution was then brought up in ~7.0 mL of 0.1 M nitric acid and mixed thoroughly.

4.3 Investigation of DGA Extraction Chromatographic Resin

4.3.1 Sc-45 Experimental Procedures & Results

Two kinetic batch studies with three replicates per data point were conducted on the uptake of stable scandium on DGA resin. Both batch studies were conducted in accordance with the methods outlined in section 4.1.1. All nitric acid solutions utilized were BDH. Samples were measured on an ICP-MS.

The results of the first study conducted is shown in Figure 14. The figure shows the highest k' values at 7.5 – 10 M nitic acid at slightly higher than 1 x 10^5. The values for these concentrations are slightly higher than 0.01 M and the trio from 0.50 – 1.0 M. It is theorized that these values are close to the limit of detection (LOD) of the ICP-MS. The interesting part of the data is the large drop in uptake values from 0.01 – 0.5 M and 1.0 – 7.5 M nitric acid. It also shows large discrepancies in uptake based on contact time. These large dips were not observed inprevious data. A second batch study was conducted to see if these results were reproducible.

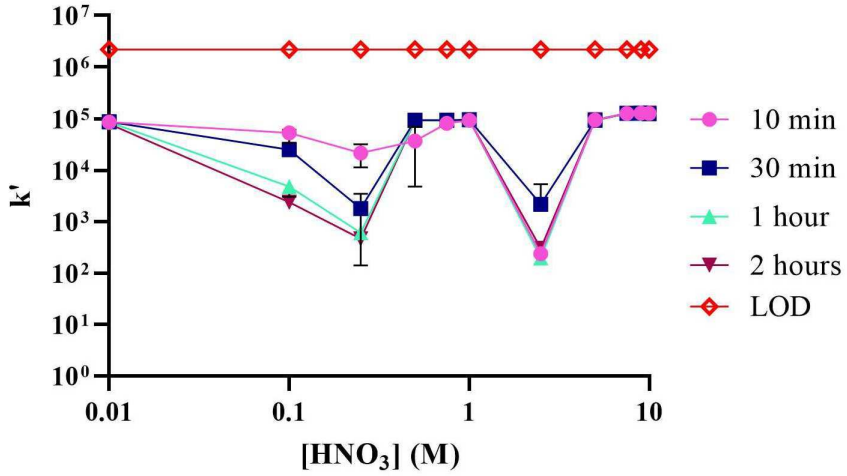

Figure 14: First batch study of ^{45}Sc on DGA

The results of the second batch study conducted is shown in Figure 15. These results are more consistent with previously published results than the first batch study. The data shows that lower nitric acid concentrations had lower k' values from 0.01 – 0.1 M. They also shows that the retention at lower concentrations was slightly better at higher contact times. This is likely due to less nitrate ions available in solution to complex with the scandium. Higher contact times show slightly better retention due to more interactions of the resin with scandium. It is also possible that equilibrium was not reached at shorter contact times for lower acid concentrations. The data leveled out at 0.1 M and were mostly consistent through the range of concentrations. One thing to note is that the higher concentrations of 7.5 – 10.0 M produced slightly higher k' values than the other concentrations.

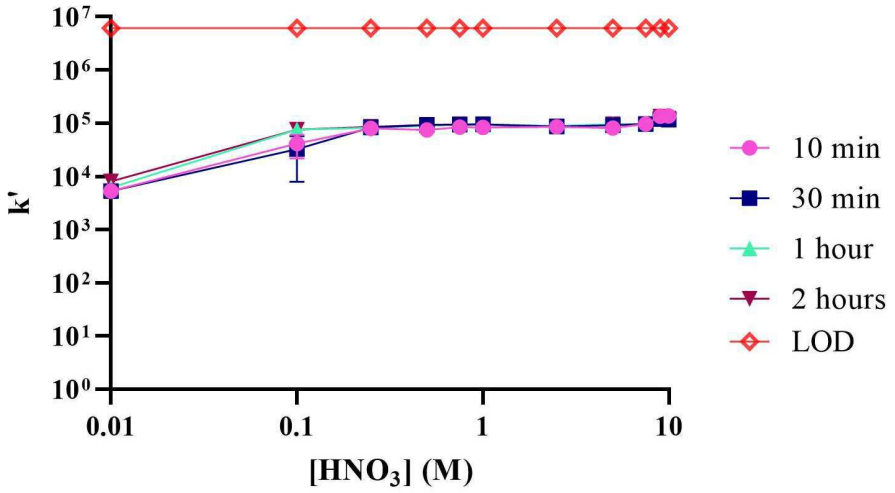

Figure 15: Second batch study of ^{45}Sc on DGA

4.3.2 Sc-44 Experimental Procedures & Results

One batch study of ^{44}Sc uptake on DGA was conducted with three replicates per data point. The results from these experiments are shown in Figure 16. The 30-minute contact time showed better retention of ^{44}Sc than the other contact times. It is believed that equilibrium is reached around the 30-minute mark. The data showed mostly increasing retention with increasing acid concentration with the highest k' value at 5.0 M nitric acid. A decrease in scandium retention after 5.0 M was observed. While the decrease is not large, it is noticeable andobserved at 10 minutes, 30 minutes, and one hour contact time. The lowest retention was observed at a two-hour contact time. Both 10 minute and one hour contact times showed similar retention with one hour contact times retaining slightly more radioscanidum at the intermittent acid concentrations than the 10-minute contact time. This could likely be due to the one-hour contact time reaching full equilibrium where the 10-minute contact time did not. The results also showed that lower acid concentrations produced little to no ^{44}Sc uptake. This was

caused by fewer nitrate ions in solution. The scandium complexed with the nitrate ions before being retained on the resin. With less ions in solutions, fewer complexes were formed and thus less radioscandium was retained on the resin. Discrepancies in the batch studies between ^{45}Sc and ^{44}Sc will be discussed in Chapter 5.

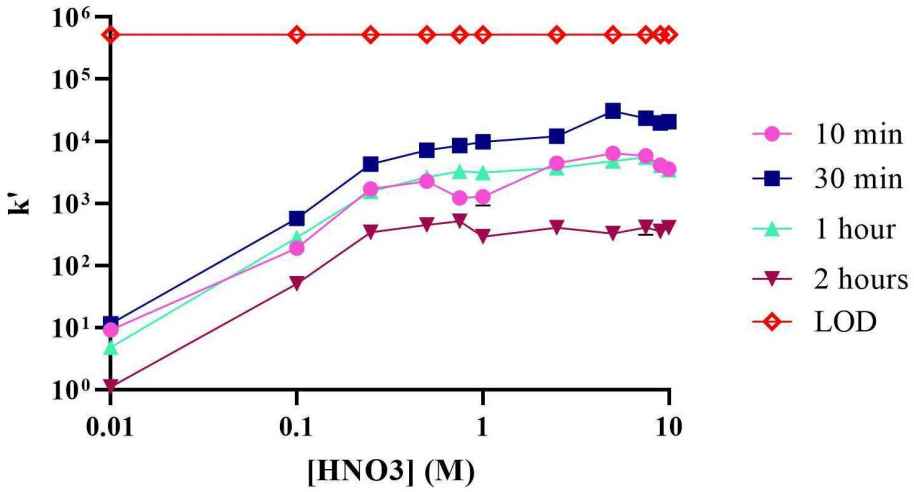

Figure 16: Batch study of ^{44}Sc on DGA

4.4 Investigation of Ln Extraction Chromatographic Resin

4.4.1 Sc-45 Experimental Procedures & Results

A single batch study with three replicates per data point was conducted for the Ln resin. The data for stable scandium on Ln resin was previously obtained by Dr. Boron-Brenner.[46] Thesedata were obtained with a 30-minute contact time and measured via ICP-MS. Slightly different acid concentrations were used in these experiments, but the data do not differ from what is expected from this series. A full kinetic study with the other three contact times was not performed due to time constraints and expenses of running the ICP-MS.

The data show a consistent uptake of ^{45}Sc across all acid concentrations. The k' values determined in these experiments are roughly 10^4 showing good retention of scandium on the resin.[46] These data will be compared to the radioscandium data and the other resins in Chapter 5.

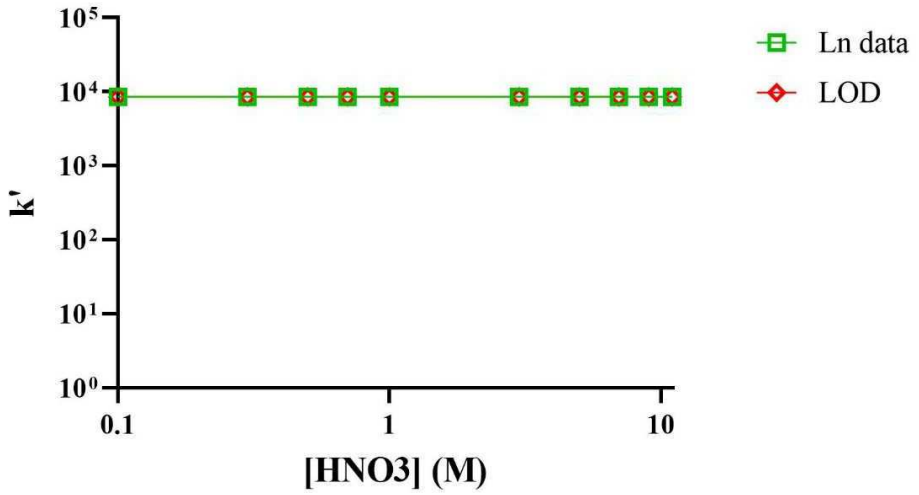

Figure 17: Batch study of ^{45}Sc on Ln by Dr. Boron-Brenner[46]

4.4.2 Sc-44 Experimental Procedures & Results

One kinetics batch study with three replicates per data point was obtained for the uptake of ^{44}Sc on Ln resin. The highest retention of scandium was found at the 30-minute mark. It is theorized that equilibrium is met around this contact time. The lowest retention of radioscandium was seen at the 10-minute contact time. Retention was significantly lower for this contact time than the other contact times, especially at lower acid concentrations. These data are another indication that equilibrium of the solution and resin was not observed until the 30-minute contact time. Both the one hour and the two hour contact times produced lower

retention values, but they followed the same trends as those for a 30-minute contact time. The highest retention of ^{44}Sc occurred at 5.0 M. Retention slightly decreased at higher acid concentrations for the 30 minute, one hour, and two hour contact times. These results will be compared to the stable scandiumexperiments in Chapter 5.

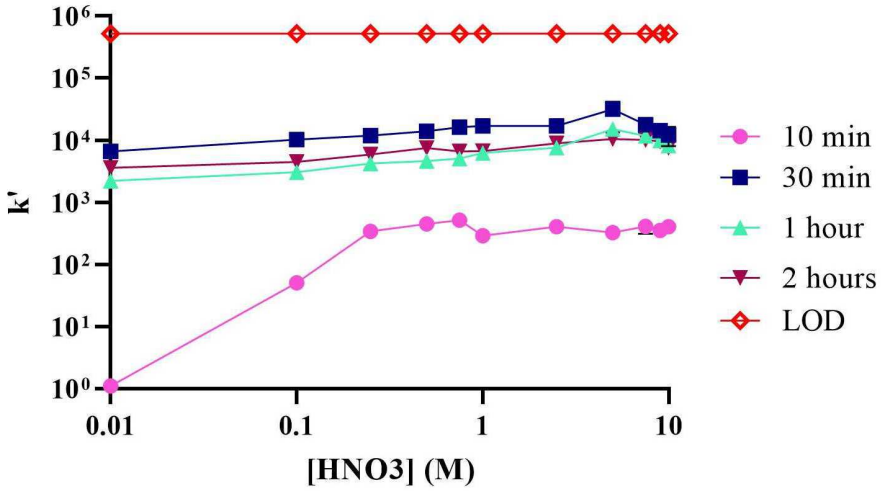

Figure 18: Batch study of ^{44}Sc on Ln

4.5 Investigation of Ln2 Extraction Chromatographic Resin

4.5.1 Sc-45 Experimental Procedures & Results

One kinetics batch study with three replicates per data point was conducted for Ln2 resin. The data showed a mostly consistent trend in uptake of ^{45}Sc across all contact times and acid concentrations. There are two observable retention decreases at 1.0 M and 5.0 M concentrationsbut they are negligible. This was observed at all four contact times. All contact times produced the same k' values meaning equilibrium was reached at or before the 10-minute contact time. These results will be compared with the other resins in Chapter 5.

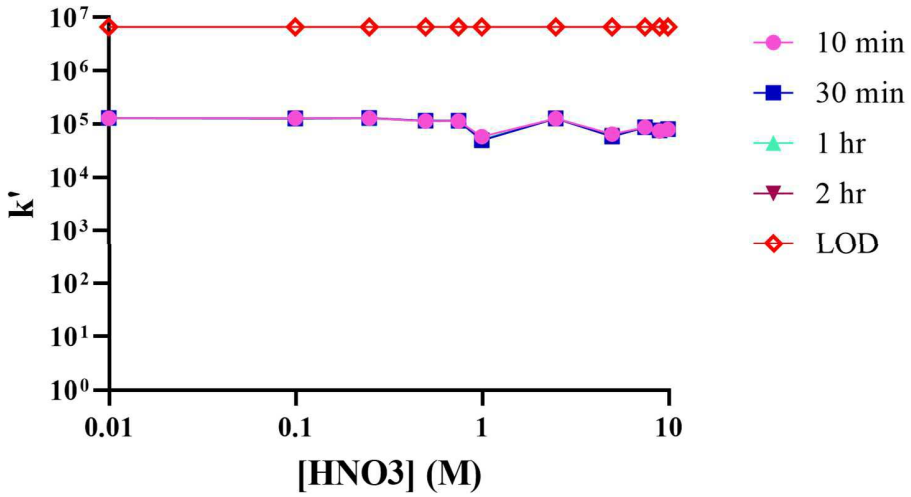

Figure 19: Batch study of ^{45}Sc on Ln2

4.5.2 Sc-44 Experimental Procedures & Results

One kinetics batch study of radioactive with three replicates per data point scandium on Ln2 resin conducted and is shown in Figure 20. The results showed that the best retention occurred at one hour and two hours. The one-hour contact time had slightly better retention at thehigher acid concentrations. The lowest retention occurred at the 10-minute contact time with the 30-minute contact time showing slightly better retention. Equilibrium is not reached until at or before the one-hour contact time for Ln2. It was also observed that all four contact times showed a decrease in retention at higher acid concentrations.

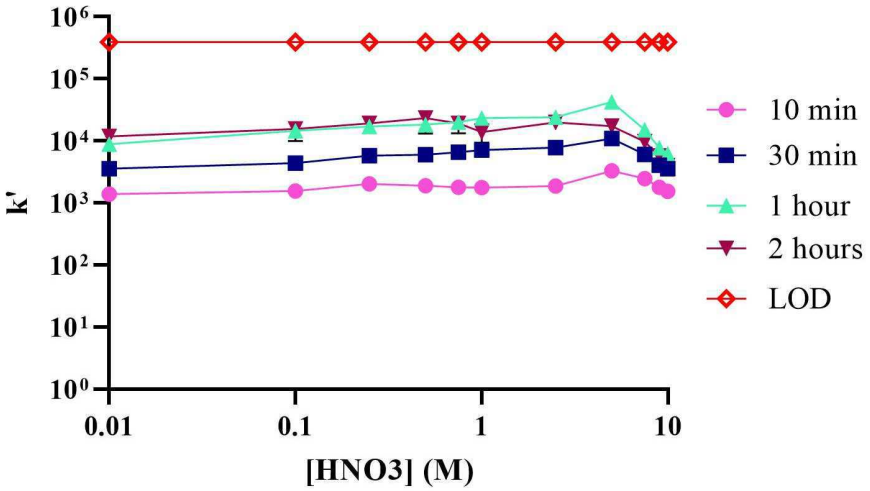

Figure 20: Batch study of ^{44}Sc on Ln2

4.6 Investigation of Ln3 Extraction Chromatographic Resin

4.6.1 Sc-45 Experimental Procedures & Results

One kinetics batch study with three replicates per data point of ^{45}Sc retention on Ln3 wasconducted and the results are shown in Figure 21. Good retention of scandium was observed at lower concentrations at all contact times. Two dips were observed at 0.75 M and 2.5 M before a large decrease at higher acid concentrations. These retention decreases were observed at all contact times. Two slight discrepancies to note are at 0.1 M and 1.0 M for the 10-minute contact time. This was likely due to experimental error since the other concentration data points line up with the other contact times.

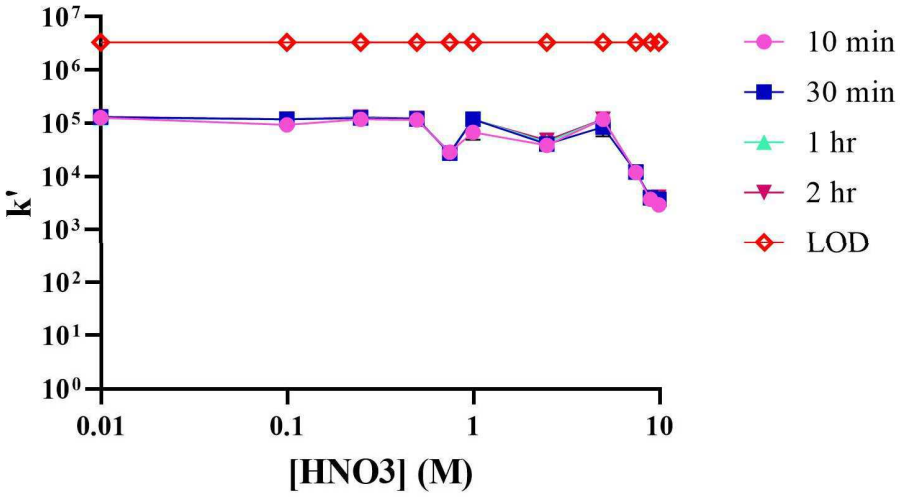

Figure 21: Batch study of ^{45}Sc on Ln3

4.6.2 Sc-44 Experimental Procedures & Results

One kinetics batch study with three replicates per data point of radioactive scandium on Ln 3 was conducted and is shown in Figure 22. The best retention for Ln3 occurred at a one-hourcontact time with the greatest retention occurring at 0.75 M nitric acid. The two-hour contact time showed comparable retention except at intermediate acid concentrations, where retention was slightly less. Retention at 10 minutes and 30 minutes was less than the other two contact times. This means equilibrium of this resin was likely reached at of before the one-hour contact time but after 30 minutes. Another interesting observation for these data was the drastic decrease in retention at higher acid concentrations for all contact times. This decrease began after 5.0 M and decreased steadily to 10.0 M. Discrepancies in the stable and radioactive data will be discussed in Chapter 5.

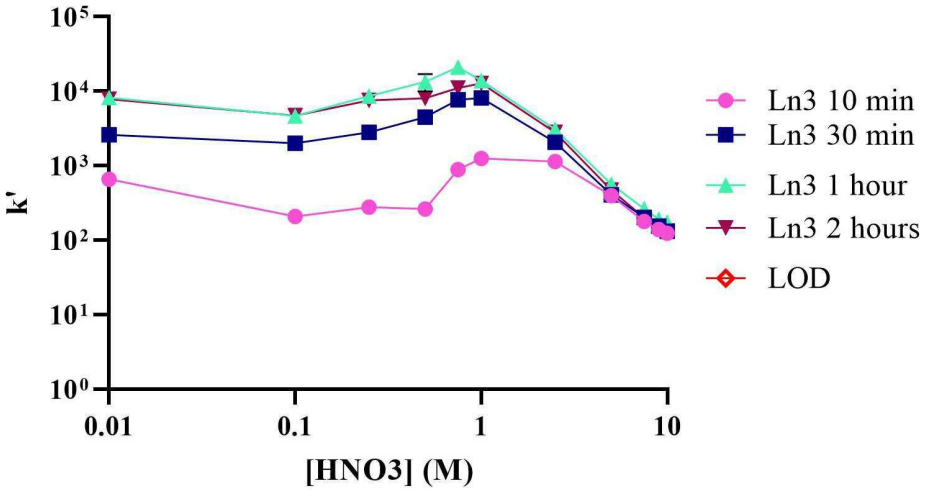

Figure 22: Batch study of ^{44}Sc on Ln3

CHAPTER 5: DISCUSSION

This chapter includes the discussion of the differences between data obtained with stable and radioactive isotopes for the four EXC resins evaluated.

5.1 DGA Comparison

Two kinetic batch studies of ^{45}Sc on DGA were conducted. DGA was the only resin to have two stable kinetic experiments. This was due to large discrepancies with the first data set. The results of the first kinetic batch study did not align with previous results whatsoever. Discrepancies in the first data set were likely due to experimental error. Uncertainties in resin mass were caused by loss of resin during the addition of acid to the micro centrifuge tubes. Massuncertainty as well as non-uniformity likely led to the large discrepancies and drops in retention noticed in the data at 0.5 M and 5.0 M nitic acid concentrations.

The two batch studies of ^{45}Sc produced drastically different results shown in Figure 23. The first batch study showed two major dips in k' values in the middle of the data at 0.5 M and 5.0 M nitric acid, respectively. The results also showed lower contact time was better for scandium retention than higher contact times. This data set was not at all consistent with previous literature results. It is believed that these large discrepancies are due to experimental error. The second DGA data set showed a much more consistent retention for all contact times. Itshowed an increase in retention from 0.01 M to 0.1 M acid concentration. This was expected due to the lack of nitrate ions in solution at 0.01 M. While the 0.1 M also had fewer ions in solution, it had more ions available to complex with the stable scandium than the lower acid

concentration. The results of the second study indicated the first data set was experimental error. The results were more consistent with the expected outcome of ^{45}Sc uptake on DGA. The first DGA kinetic data are shown as a comparative to the second DGA kinetic data set but will not becompared to the ^{44}Sc results.

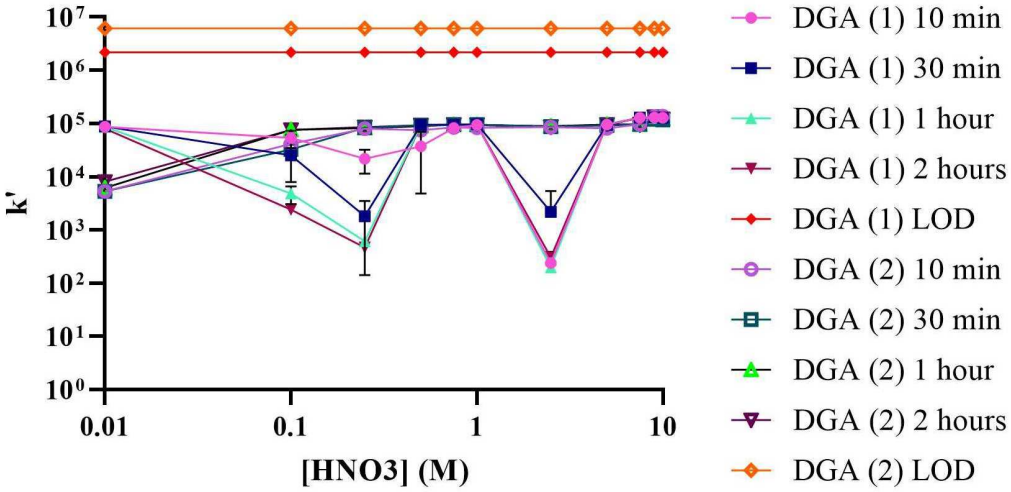

Figure 23: Comparison of batches 1 and 2 of ^{45}Sc on DGA

The second DGA batch study was more consistent with the previous literature results. Ofprevious results, the second DGA kinetic data results agreed most consistently with the data obtained by Roman et al. A comparative graph of the two data sets is shown in Figure 24. It should be noted that the Roman group utilized radioactive ^{44}Sc in these studies where the experimental results shown from these studies utilized ^{45}Sc. The only difference was the Roman data show k' values an order of magnitude higher than those reported in the second batch study. This may be due to a higher LOD than what was seen on the ICP-MS at the Proteomics Facility. The other main difference is the Roman study reported lower k' values at

lower nitric acid concentrations than reported here. The lower concentrations were almost an order of magnitude lower than those reported here. These discrepancies are likely due to a lower amount of ^{44}Sc ionsin solution to interact due to the use of radioactive scandium. The main takeaway is the data curves are very similar as well as higher uptake with increasing acid concentrations. This is promising when trying to discern the true uptake of scandium in nitic acid on DGA resin.

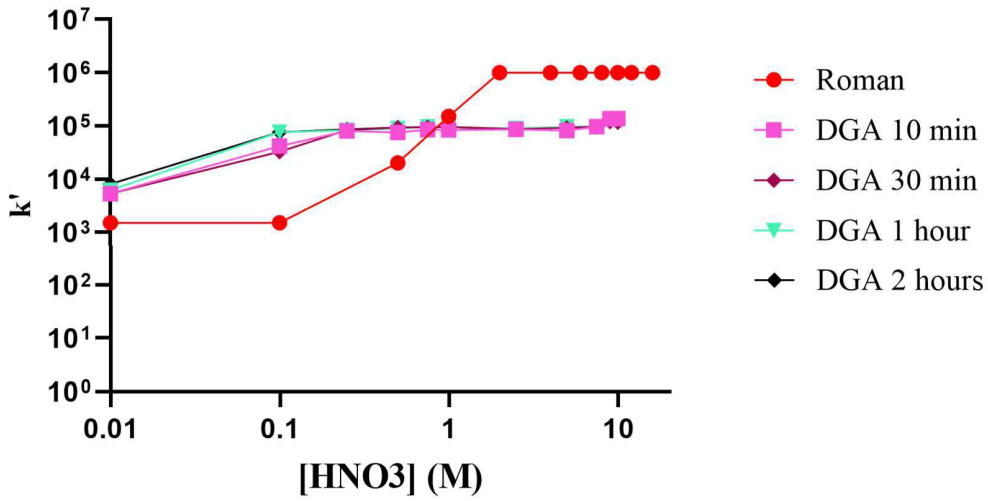

Figure 24: Comparison of Batch 2 DGA and Roman data[43]

After comparing the previous literature experiments to the ^{45}Sc data obtained from this research, the data for this paper were compared for both ^{45}Sc and generator obtained ^{44}Sc. Results for these experiments are shown in Figure 25. The results showed a higher uptake of ^{45}Sc than ^{44}Sc at all contact times. While ^{45}Sc had consistent uptake across all four contact times, ^{44}Sc varied widely. Time to reach equilibrium for ^{44}Sc in solution was also much longer than ^{45}Sc. This was likely due to the lack of available radioscandium in solution. There was also a large

decrease in ^{44}Sc retention at the two-hour contact time. This is likely due to radiolysis of the resin after being in contact with high amounts of ^{44}Sc for extended periods. The one trend that held true for both radioactive and stable scandium was the increase in uptake of scandium with increasing acid concentration. This was expected as there are fewer nitrate ions in solution available to complex with scandium- regardless of their nature.

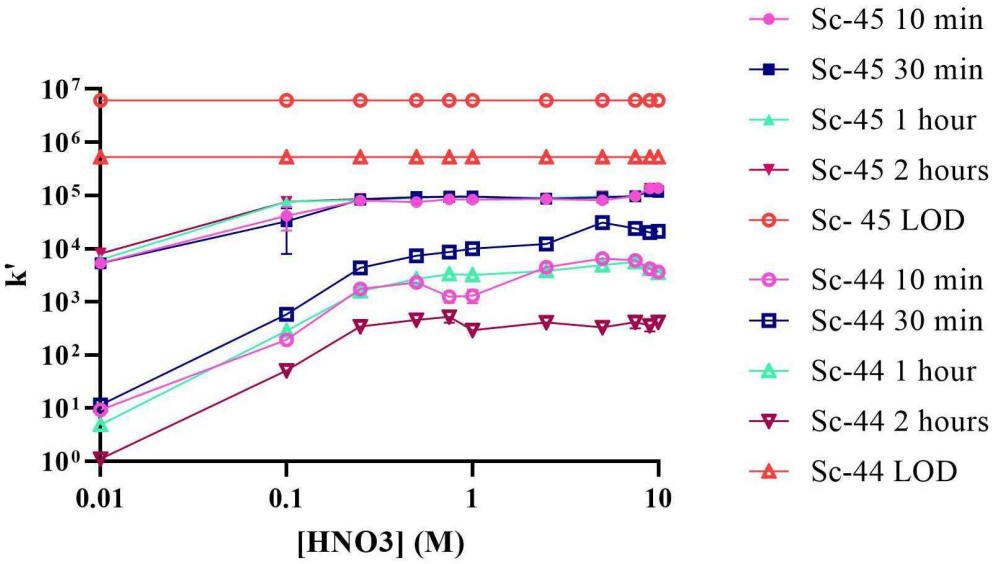

Figure 25: Comparison of ^{44,45}Sc on DGA

Figure 26 shows the vast difference in uptake of radioscandium compared to stable scandium. As mentioned previously, this had to do with the limited availability of radioscandium atoms in solution. A calculation of the amount of average available ^{44}Sc atoms in solutions compared to the average available ^{45}Sc atoms in solution can be found in Appendix C. Equations 10 – 13 demonstrate how the values were obtained.

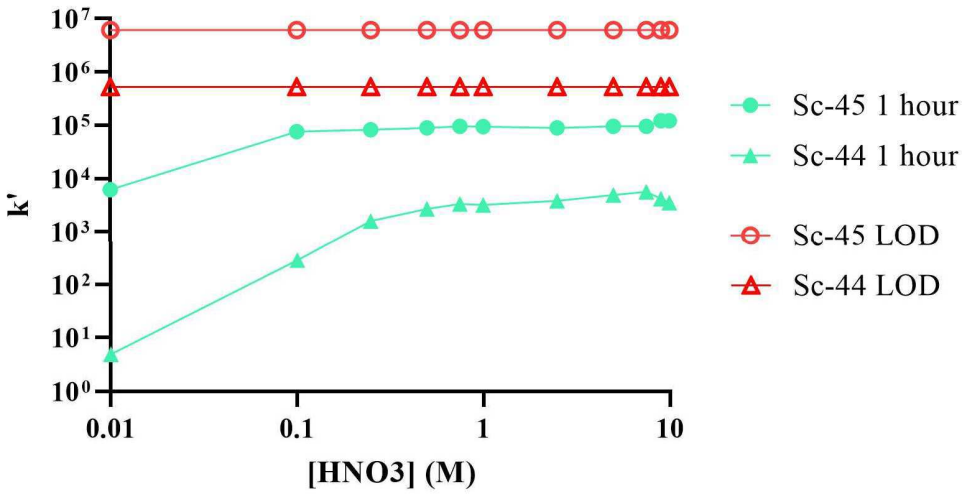

Figure 26: Comparison of ^{44,45}Sc at one hour contact time

First, the equation for converting activity to dose is shown in equation 10.

$$D = A_0 \times \Gamma \times t \tag{10}$$

Where D is dose in mSv, A0 is initial activity in MBq, Γ is the gamma constant in (mSv/h)/MBq for a specific isotope at one meter, and t is time in h. This should take into consideration handling of the isotope and that dose will increase if distance decreases below one meter. While this was not necessary for converting activity to the number of atoms in solution, it will be useful in understanding the dose from ^{44}Sc and comparing it to the number of atoms found in solution.

Next, the decay equation for radioactive decay was utilized as shown in equation 11.

$$A = A_0 \times e^{-\lambda t} \tag{11}$$

Where A is the activity after a certain time has passed, A_0 is initial activity, λ is the isotope specific decay constant, and t is the time that has passed.

The final equation utilized is for the conversion of activity to number of atoms of ^{44}Sc in solution. It is shown in equations 12 and 13.

$$A = \lambda N \tag{12}$$

Where,

$$N = \frac{A}{\lambda} \tag{13}$$

The calculation showed approximately 96,000 atoms for ^{44}Sc and 2.2 x 10^{20} atoms for ^{45}Sc. This is a very large difference in the number of available atoms in solution. The other factor to be considered was adsorption to various surfaces that come in to contact with the solutions. Adsorption occurs when atoms or molecules in solution stick to the walls of containers, vessels, transfer devices, etc. This translates to loss of atoms in solution. For ^{45}Sc adsorption did not affectthe number in solution because there were many atoms available with which to work.

5.2 Ln Comparison

The comparison of Ln resin with ^{44,45}Sc yielded interesting results. It should be noted thatthere is only one contact time of 30 minutes for stable scandium. The experiments were previously conducted by Boron-Brenner.[46] The results showed the uptake for both ^{45}Sc and ^{44}Sc were comparable. Figure 27 displayed the k' values for ^{45}Sc sit in the middle of the data for ^{44}Sc. It should, however, be recognized that the k' values for ^{45}Sc were at the LOD for this experiment. It was likely that the values for Ln are much higher than what is indicated on this graph which is consistent with the previous conclusions from the DGA studies that fewer ^{44}Sc

atoms were available to react in solution. It should also be noted that all contact times for ^{44}Sc, except 10 minutes, were mostly consistent in uptake values. These results were expected for this resin.

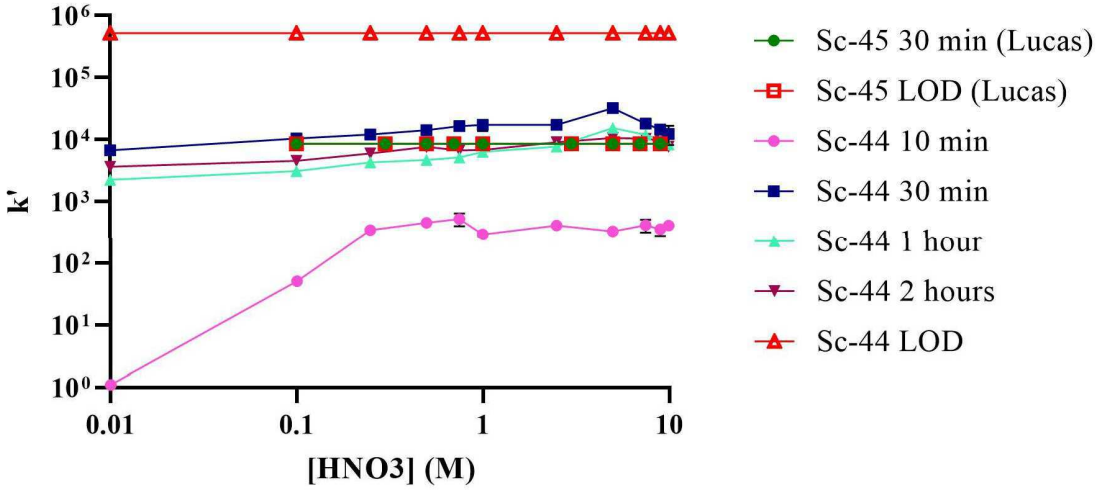

Figure 27: Comparison of ^{44,45}Sc on Ln resin[46]

5.3 Ln2 Comparison

The comparison of Ln2 resin with ^{44,45}Sc yielded results that were expected. Both resultsare shown in Figure 28. The k' values for ^{44}Sc were consistent with previous results as well. Increased contact time resulted in increasing uptake, with one hour contact time yielding the best results. It should also be noted that there was only about one order of magnitude difference between stable and radioscandium uptake. One difference was the slight drop in k' values at 1.0 M nitric acid that was observed for ^{45}Sc but not for ^{44}Sc. The decrease in uptake was likely due to experimental error. Overall, the uptake of ^{44}Sc was more consistent with previous results.

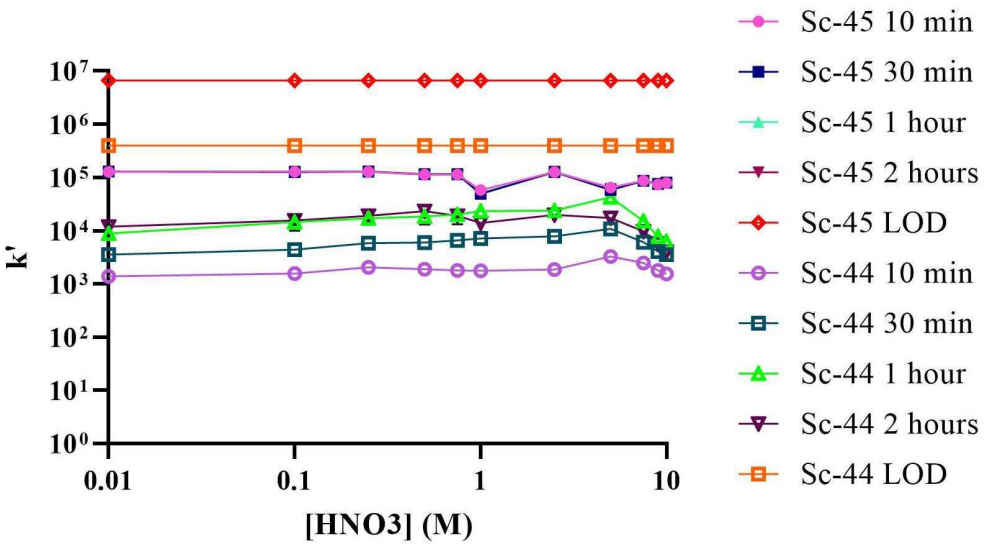

Figure 28: Comparison ^{44,45}Sc on Ln2 resin

5.4 Ln3 Comparison

The results for uptake of ^{44,45}Sc on Ln3 resin were also interesting. Shown in Figure 29, the k' values for ^{45}Sc showed a consistency in uptake until 1.0 M nitric acid where there was a noticeable decrease in scandium retention and a large continual decrease in retention at the three highest acid concentrations. This was almost the opposite of the k' values reported for ^{44}Sc. The uptake of ^{44}Sc showed a slight decrease at lower acid concentrations before increasing to the highest uptake values around 1.0 M nitric acid and then steadily decreased again after that. The highest k' value for ^{44}Sc overlapped the drop in k' at 1.0 M nitric acid. This overlap likely implied experimental error occurred in the ^{45}Sc experiments. The steady decrease observed in ^{44}Sc as well as the sharp decrease in ^{45}Sc can be attributed to competition in solution with an abundance of nitride ions which was discussed previously. Generally, the values were somewhatconsistent with what was expected from these experiments.

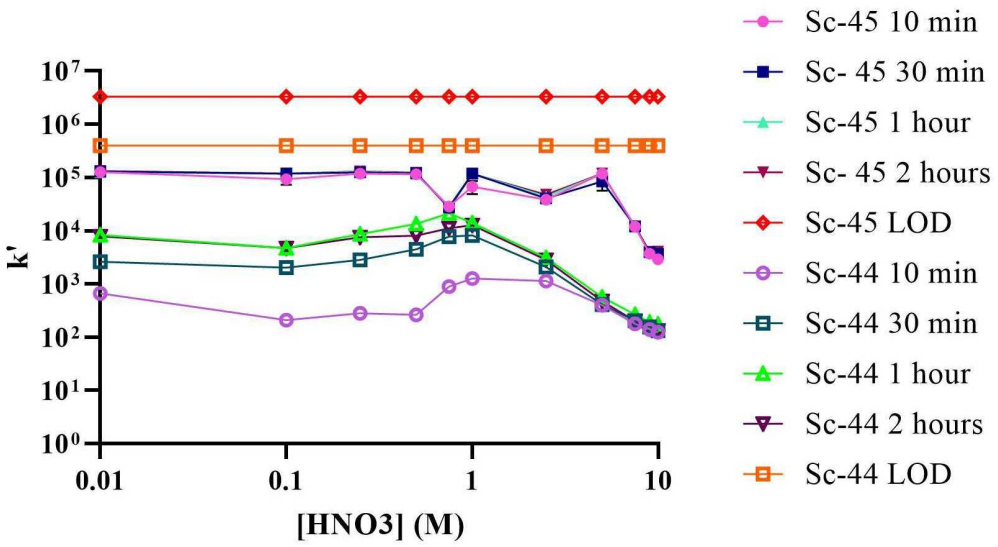

Figure 29: Comparison of ^{44,45}Sc on Ln3 resin

5.5 Overall Resin Comparison

Overall, the resins were mostly comparable to one another. DGA, Ln2, and Ln3 all produced similar uptake values for ^{45}Sc around 10^{5}. DGA resin varied with slightly lower k' values at lower acid concentrations. It should also be noted that contact time had no effect on uptake for the ^{45}Sc studies with all of the resins. This means that equilibrium was reached quickly with the abundance of stable scandium ions in solution. For ^{45}Sc, Ln2 was the best resin as it had consistent uptake values at all acid concentrations and contact times.

The same conclusions cannot be said for ^{44}Sc. The resins produced interesting uptake values when in solution with radioscandium. Experimental results showed that both DGA and Lnreached equilibrium first at or before 30 minutes of contact but after 10 minutes. Ln2 and Ln3 reached equilibrium at or before one hour of contact but after 30 minutes. These resins took longer to reach equilibrium likely because of the decreasing number of oxygen atoms

available to interact on the resins as they increase up the series, i.e., Ln has four, Ln2 has three, and Ln3 has two. This should be considered when working with the short half-life of ^{44}Sc. The best uptake values were observed for Ln and Ln2 resins. Ln3 k' values fluctuated greatly, but the highest value was found at a lower acid concentration of 0.75 M nitric acid. This is important when scaling up experiments due to hazard level. Lower acid concentrations are preferred especially when used in large quantities. While DGA is widely preferred, it produced steadily increasing k' values with the best uptake occurring at upper acid concentrations. The resin also showed slightly less uptake than the other resins with radioscandium across all acid concentrations. In addition to these factors, it is believed the resin may have undergone radiolysis at the two-hour contact time, while the other resins did not show decreased uptake at prolonged exposure periods. Overall conclusions will be provided in the next chapter as well as future steps for this project.

CHAPTER 6: CONCLUSIONS & FUTURE DIRECTIONS

This chapter will consist of overall conclusions drawn from these experiments, as well as suggestions for future work to extend the understanding of this topic.

6.1 Conclusions

The stable results were obtained to establish a baseline for experimental procedures andas a comparison to the radioactive results. Since ^{45}Sc is not applicable or useful to nuclear medicine, the results will not be discussed in this chapter at length.

The findings for DGA yielded promising results. The radioscandium data showed lower uptake values when compared to the stable scandium data especially at lower acid concentrationsbut was consistent with what was expected. Since the solution was carrier-free, these findings displayed good results for the small amount of radioactive scandium atoms in solution. If scaled up, larger amounts of radioactive scandium would be present for radiopharmaceutical applications. This means it is likely there would be larger uptake values similar to the ones observed for ^{45}Sc, because more scandium would be available in solution. It would likely reach equilibrium quicker as well. Overall, the results of the DGA experiments are promising but also need to be investigated further. While some results of all the DGA studies are similar, none align exactly. This may be due to experimental conditions. Overall, ^{44}Sc uptake on DGA is best at a contact time of 30 minutes and nitric acid concentration of 7.5 M.

The Ln studies are not complete. The stable data studies were only conducted at a contact time of 30 minutes. With that being said, it is likely variation in contact time with ^{45}Sc would not

yield any major fluctuations. However, the true value of uptake for ^{45}Sc on Ln resin is not knownsince all results were at LOD. Apart from this, the Ln series showed the most promise for radioscandium uptake. The k' values were consistent at all acid concentrations and small discrepancies between contact times-with the exception of the 10-minute contact time-and equilibrium reached at 30 minutes of contact. It should also be noted that if scaled up for radiopharmaceutical work, there would likely be greater uptake due to more available atoms as mentioned for DGA. Overall, this resin displayed good uptake values of radioscandium especially at low acid concentrations.

The Ln2 studies were not as comparable as Ln. There were larger differences in k' valuesfor stable and radioactive scandium. While it was expected to have lower uptake values for radioscandium, the k' values observed for Ln2 were lower than Ln in comparison to the stable values previously found. It should still be noted that the Ln values were at LOD, but the data show the uptake of radioscandium for Ln2 was below the stable values. It also took around one hour of contact time for solutions to reach equilibrium with Ln2. While this is likely due to the lack of an oxygen atom on the resin, it is still a differentiating factor when it comes to scaling up the process. It is also likely that the time to reach equilibrium will decrease as more material is introduced and diffusion stops being the limiting factor.

Ln3 studies had the largest discrepancies. The results showed that the uptake of ^{44}Sc was lower than ^{45}Sc, which, again, was expected. The differences lie within the curve created at various acid concentrations. The highest uptake for ^{44}Sc overlapped with the dip in uptake for ^{45}Sc at 1.0 M nitric acid. The values for uptake of ^{44}Sc were overall much lower than ^{45}Sc

except for the overlap at intermediate acid concentrations. It also took the radioscandium one hour to reach equilibrium in solution. While this, again, will likely decrease at radiopharmaceuticalconcentration levels, it should still be considered for future work.

After reviewing all of the resins, the best resin for ^{44}Sc uptake was Ln. These conclusions are purely based on scandium uptake and do not take into account separation factors. Ln was the best resin because it reached equilibrium with ^{44}Sc around 30 minutes and exhibited good uptake at lower acid concentrations. After that, DGA is the next best resin. It also reached equilibrium at around 30 minutes but did not have great uptake at lower acid concentrations. It also likely exhibited radiolysis at prolonged contact with the radioisotopes. The next best resin was Ln2. It reached equilibrium around one hour of contact and showed good uptake values across all acid concentrations. The last and worst resin from these experiments was Ln3. It also reached equilibrium around one hour of contract time but differed greatly from the ^{45}Sc data. While it did show some overlaps of uptake, the data were very different from previous results and needs moreinvestigation.

6.2 Future Work

There are four main experiments that should be considered for future work on this project. They will be discussed in greater detail in the subsections below. These studies are: carrier added to ^{44}Sc solutions, radiolysis studies of the resins, separation factor (SF) studies, andcompletion of the Ln data series with ^{45}Sc.

6.2.1 Carrier Added Studies

All solutions with ^{44}Sc were prepared as CF solutions and had very few atoms available

to react in solution. The next step would be to do an experiment and add increasing amounts of ^{45}Sc to a solution containing Sc-44 to see how much is needed to get agreement with the measurements performed with only Sc-45. The goal would be to start with very little carrier and increase it in small increments. It should be noted that stable scandium does impact the radiopurity of the solution and can be harmful in radiopharmaceutical work. However, in small amounts, it can be used to get a more effective uptake of ^{44}Sc. Therefore, these studies would bebeneficial to this work.

6.2.2 Radiolysis Studies

Radiolysis studies should be conducted on all resins at various radiation levels and contact times. This would be useful to have since, again, radiopharmaceuticals would require higher radiation levels. The goal is to understand when radiation begins to degrade the resin andfor how long it can be in contact before degradation begins. In conjunction with these studies, it would be ideal to have a supplementary studies of the using advanced surface and material analytical techniques, e.g. FT-IR or SEM, before and after radiation introduction. This would give a better understanding of the scope and location of the degradation when it occurs. These studies would be of great benefit to future scale up work.

6.2.3 Separation Factor Studies

Separation factor studies would help understand which resin is the best at selectively separating scandium from titanium targets. The experiments outlined above only address which resin is the best at scandium uptake. SF experiments would include uptake of both stable and radioactive titanium on the same resins at all four contact times with the experimental proceduresprevious described. The highest SF would indicate the best resin as long as all

other factors such as equilibrium and acid concentration were manageable for scale up. These experiments would provide a much better understanding of which of the resins is truly the best for separationof scandium from titanium.

6.2.4 Completion of Ln Data with ^{45}Sc

The last step to finalizing this research is the completion of the Ln data series with ^{45}Sc. This would likely include a redo of the 30-minute data with the experimental procedures outlined earlier. The reason this was not done for this work were time constraints due to Covid-19 related laboratory closures. A full data workup of ^{45}Sc uptake on Ln would likely yield a lower LOD andpotentially higher k' values. Overall, this would provide a complete understanding of the Ln resin series on both ^{44,45}Sc as well as acid dependency and equilibrium.

6.3 Final Thoughts

Overall, these experiments provided a large amount of useful data for the uptake of scandium on EXC resins. While the data did not elucidate a true uptake value for scandium on DGA resin, they did provide more information on the topic. It also provided new understandingsof the Ln resin series as well as offered insights into the large discrepancies seen with DGA. While there are further experiments to be done, this information can help researchers move forward with utilizing scandium as a potential theranostic agent for radiopharmaceuticals.

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APPENDICIES

Appendix A: Nitric Acid Titration Data

Table 1: High purity nitric acid titration data

Stock Conc (M)	Average	Date made
0.01	0.011	10/27/2020
0.10	0.096	9/10/2020
0.25	0.244	10/27/2020
0.50	0.472	1/21/2020
0.75	0.697	1/21/2020
1.00	0.933	1/21/2020
2.50	2.493	10/27/2020
5.00	4.543	1/21/2020
7.50	7.930	11/5/2020
9.00	8.363	1/21/2020
10.00	9.553	1/21/2020
0.10	0.095	2/12/2020
0.10	0.139	1/3/2020
0.10	0.098	3/6/2020
0.10	0.095	10/27/20
0.25	0.234	1/21/2020
0.01	0.011	1/21/2020
2.50	2.870	1/3/2020
7.50	7.227	1/21/2020

Table 2: ACS grade nitric acid titration data

Stock Conc (M)	Average	Date made
0.009	0.010	12/6/2021
0.100	0.101	12/6/2021
0.251	0.333	12/6/2021
0.503	0.510	12/6/2021

0.754	0.750	12/6/2021
1.006	1.033	12/6/2021
2.516	2.500	12/6/2021
5.033	5.195	12/6/2021
7.550	7.410	12/6/2021
9.060	9.147	12/6/2021
10.660	9.787	12/6/2021
0.009	0.011	2/1/2022
0.251	0.257	2/1/2022
0.503	0.330	2/1/2022
0.754	0.710	2/1/2022
1.006	0.970	2/1/2022
2.516	2.475	2/1/2022
5.033	5.025	2/1/2022
7.550	7.350	2/1/2022
9.060	8.967	2/1/2022
10.660	9.933	2/1/2022

Appendix B: Raw Data

Table 3: Raw data for Figures 14 & 23

HNO3 Conc (M)	Contact Time (min)	k'	Standard Deviation
0.01	10	87189.6	1998.4
0.10	10	53594.9	19493.2
0.25	10	21748.3	10414.9
0.50	10	37380.1	32536.7
0.75	10	82674.0	11674.0
1.0	10	94501.4	1300.1
2.5	10	237.4	35.1
5.0	10	95555.2	2270.0
7.5	10	128292.4	1781.4
9.0	10	129181.5	757.4
10.0	10	127473.3	1980.5
0.01	30	87581.8	2643.3
0.10	30	25326.2	35573.8

0.25	30	1809.0	1668.6
0.50	30	94151.4	830.9
0.75	30	93680.2	1327.8
1.0	30	96388.6	422.8
2.5	30	2198.8	3195.6
5.0	30	94556.8	1829.8
7.5	30	128256.2	2286.7
9.0	30	129388.6	283.9
10.0	30	126976.9	1559.3
0.01	60	86966.5	3668.5
0.10	60	4810.6	1741.1
0.25	60	609.0	47.7
0.50	60	94384.7	2615.0
0.75	60	92961.3	2460.3
1.0	60	94927.6	776.0
2.5	60	196.8	32.4
5.0	60	96452.6	1015.4
7.5	60	127295.9	2316.2
9.0	60	127082.2	2525.5
10.0	60	126351.7	2260.3
0.01	120	79972.1	4955.4
0.10	120	2415.4	229.6
0.25	120	469.2	79.8
0.50	120	94421.9	1908.4
0.75	120	94130.6	1723.7
1.0	120	94612.2	2424.7
2.5	120	304.1	80.1
5.0	120	96531.0	582.2
7.5	120	127298.8	2284.0
9.0	120	127508.1	2366.6
10.0	120	129549.2	379.4

Table 4: Raw data for Figures 15, 23, 24, 25, & 26

HNO3 Conc (M)	Contact Time (min)	k'	Standard Deviation
0.01	10	5321.9	269.3
0.10	10	41211.9	19454.8
0.25	10	80216.8	183.3
0.50	10	86375.9	7441.8
0.75	10	79344.0	3428.4
1.0	10	90171.7	6272.8
2.5	10	86078.5	3034.9
5.0	10	94469.6	179.8
7.5	10	96226.4	118.7
9.0	10	131520.6	8520.2
10.0	10	118499.1	2588.8
0.01	30	5295.7	253.0
0.10	30	32481.5	24545.8
0.25	30	82733.8	529.8
0.50	30	92970.7	800.1
0.75	30	94457.3	661.9
1.0	30	95328.2	424.7
2.5	30	86705.5	1264.5
5.0	30	91106.2	8053.3
7.5	30	96184.7	368.9
9.0	30	127103.9	7596.0
10.0	30	135509.3	319.4
0.01	60	6143.9	215.2
0.10	60	76033.0	1398.3
0.25	60	82498.2	4072.6
0.50	60	89430.6	8189.5
0.75	60	95144.8	610.8
1.0	60	93793.9	837.5
2.5	60	88769.5	1380.2
5.0	60	95165.7	606.3
7.5	60	95699.3	688.0
9.0	60	121256.9	759.8
10.0	60	127047.6	9665.0

0.01	120	6161.1	151.7
0.10	120	75814.4	2425.9
0.25	120	86096.8	1367.7
0.50	120	93125.7	1563.6
0.75	120	95425.8	247.6
1.0	120	94425.8	1357.3
2.5	120	86884.8	421.2
5.0	120	94800.5	661.7
7.5	120	95704.5	460.4
9.0	120	123686.8	7620.7
10.0	120	130672.8	7796.9

Table 5: Raw data for Figures 16, 25, & 26

HNO3 Conc (M)	Contact Time (min)	k'	Standard Deviation
0.01	10	9.2	1.0
0.10	10	191.0	28.4
0.25	10	1728.3	47.2
0.50	10	2299.9	486.8
0.75	10	1237.0	285.9
1.0	10	1301.3	365.4
2.5	10	4480.9	150.4
5.0	10	6475.6	240.2
7.5	10	5948.9	319.0
9.0	10	4169.5	175.7
10.0	10	3628.0	360.5
0.01	30	11.5	0.4
0.10	30	578.6	50.0
0.25	30	4324.9	812.2
0.50	30	7289.5	656.1
0.75	30	8647.3	696.7
1.0	30	9975.1	1188.7
2.5	30	12186.6	1810.3
5.0	30	30982.6	3557.5

7.5	30	23850.0	623.9
9.0	30	19967.4	1883.5
10.0	30	21067.9	3078.9
0.01	60	4.8	0.5
0.10	60	284.5	21.1
0.25	60	1576.6	84.1
0.50	60	2677.4	209.2
0.75	60	3334.1	193.1
1.0	60	3183.4	123.0
2.5	60	3781.8	99.7
5.0	60	4873.5	533.0
7.5	60	5563.2	606.4
9.0	60	4141.5	226.7
10.0	60	3508.3	301.3
0.01	120	1.1	0.0
0.10	120	50.9	3.1
0.25	120	343.6	35.9
0.50	120	455.9	57.0
0.75	120	521.6	121.5
1.0	120	293.4	3.1
2.5	120	409.3	61.2
5.0	120	327.5	57.9
7.5	120	412.4	98.5
9.0	120	355.5	79.1
10.0	120	411.0	0.8

Table 6: Raw data for Figures 18 & 27

HNO3 Conc (M)	Contact Time (min)	k'	Standard Deviation
0.01	10	1285.1	384.1
0.10	10	1165.4	31.7
0.25	10	2080.1	676.7
0.50	10	3205.8	192.0
0.75	10	3571.1	387.9
1.0	10	4039.9	302.8
2.5	10	4053.9	413.8
5.0	10	7451.4	335.9
7.5	10	4594.6	533.5
9.0	10	3744.4	122.1
10.0	10	2990.7	107.7
0.01	30	6714.9	69.2
0.10	30	10434.7	852.7
0.25	30	12147.2	782.2
0.50	30	14162.8	777.7
0.75	30	16468.1	1694.6
1.0	30	17220.5	3496.0
2.5	30	17302.4	2045.4
5.0	30	32206.3	4161.8
7.5	30	18136.8	2159.6
9.0	30	14604.1	925.0
10.0	30	12379.5	4219.7
0.01	60	2261.1	56.6
0.10	60	3091.0	92.9
0.25	60	4285.6	287.1
0.50	60	4717.4	146.1
0.75	60	5134.7	59.4
1.0	60	6327.0	817.5
5.0	60	15426.0	1522.3
7.5	60	12017.7	1690.9
9.0	60	10020.8	808.8

10.0	60	8370.8	18.3
0.01	120	3660.3	116.4
0.10	120	4519.8	87.8
0.25	120	5979.8	249.2
0.50	120	7660.0	701.3
0.75	120	6725.7	426.6
1.0	120	6827.6	449.9
2.5	120	9028.1	526.9
5.0	120	10682.8	1020.4
7.5	120	10294.1	1325.2
9.0	120	9675.2	390.3
10.0	120	7709.0	250.3

Table 7: Raw data for Figures 19 & 28

HNO3 Conc (M)	Contact Time (min)	k'	Standard Deviation
0.01	10	128556.5	886.7
0.10	10	128226.9	791.0
0.25	10	127514.9	1307.9
0.50	10	113668.6	611.7
0.75	10	114064.9	773.3
1.0	10	50587.9	3065.3
2.5	10	126990.2	452.4
5.0	10	64851.5	3672.8
7.5	10	86418.4	1024.7
9.0	10	73991.6	1126.7
10.0	10	78444.5	1087.4
0.01	30	129421.3	447.3
0.10	30	126743.0	313.2
0.25	30	129081.4	522.3
0.50	30	114343.4	645.2
0.75	30	114690.4	1104.9

1.0	30	46893.6	202.9
2.5	30	126783.3	1802.2
5.0	30	62310.9	428.0
7.5	30	86169.7	468.4
9.0	30	75807.5	590.4
10.0	30	79498.9	1069.9
0.01	60	127686.0	1930.1
0.10	60	126541.5	2260.8
0.25	60	126005.3	628.4
0.50	60	114784.5	1170.0
0.75	60	113921.5	1023.6
1.0	60	47303.3	2637.9
2.5	60	128876.8	1016.9
5.0	60	61190.9	4021.8
7.5	60	86476.2	188.6
9.0	60	74907.9	416.6
10.0	60	79241.3	2054.4
0.01	120	127506.1	409.8
0.10	120	127595.5	701.4
0.25	120	127700.8	2347.9
0.50	120	113929.5	438.6
0.75	120	113483.3	344.0
1.0	120	49246.1	1588.4
2.5	120	127856.2	520.6

Table 8: Raw data for Figures 20 & 28

HNO3 Conc (M)	Contact Time (min)	k'	Standard Deviation
0.01	10	1392.7	86.3
0.10	10	1562.9	38.5
0.25	10	2040.5	333.5
0.50	10	1884.3	159.0
0.75	10	1795.9	120.1
1.0	10	1774.4	295.4
2.5	10	1867.6	334.3
5.0	10	3282.7	64.4
7.5	10	2468.3	34.2
9.0	10	1783.3	148.7
10.0	10	1536.9	15.4
0.01	30	3551.6	107.1
0.10	30	4389.5	342.0
0.25	30	5800.1	610.9
0.50	30	5990.7	456.7
0.75	30	6546.6	447.1
1.0	30	7134.3	662.6
2.5	30	7801.7	87.1
5.0	30	10869.7	989.6
7.5	30	6065.8	733.7
9.0	30	4049.3	93.1
10.0	30	3559.0	204.6
0.01	60	8820.1	592.2
0.10	60	14487.8	4533.0
0.25	60	17146.2	1583.5
0.50	60	18375.4	5276.7
0.75	60	20146.0	2337.6
1.0	60	23378.3	2887.5
2.5	60	24003.8	3001.1
5.0	60	42326.5	5927.6
7.5	60	15088.7	1111.0
9.0	60	7680.5	274.8

10.0	60	6206.1	365.7
0.01	120	11798.8	1281.9
0.10	120	15554.7	3407.7
0.25	120	19102.4	2672.5
0.50	120	23241.3	3875.2
0.75	120	19068.5	5814.7
1.0	120	13942.4	4545.8
2.5	120	19838.2	3646.3
5.0	120	17294.6	1942.0
7.5	120	9770.3	192.6
9.0	120	5714.4	353.7
10.0	120	4023.1	266.4

Table 9: Raw data for Figures 21 & 29

HNO3 Conc (M)	Contact Time (min)	k'	Standard Deviation
0.01	10	126706.3	2292.9
0.10	10	116976.2	769.8
0.25	10	118227.2	4926.7
0.50	10	115278.1	1709.4
0.75	10	28398.0	1233.9
1.0	10	86753.8	22968.3
2.5	10	33299.8	24.8
5.0	10	117424.1	693.1
7.5	10	11919.9	82.0
9.0	10	3406.5	50.5
10.0	10	2893.6	73.8
0.01	30	129560.4	391.0
0.10	30	117949.3	1000.1
0.25	30	124129.6	1169.1
0.50	30	119508.1	835.4
0.75	30	27465.3	1288.8
1.0	30	117735.1	767.6
2.5	30	40051.5	2570.9
5.0	30	117595.2	838.6
7.5	30	11987.2	204.6
9.0	30	4156.8	107.2
10.0	30	3699.0	269.8
0.01	60	123914.8	9293.6
0.10	60	117833.9	364.6
0.25	60	127135.6	1362.2
0.50	60	120401.0	858.5
0.75	60	29709.5	416.7
1.0	60	118110.2	1139.1
2.5	60	43518.3	1789.4
5.0	60	117250.0	1237.0
7.5	60	12050.9	101.7

9.0	60	3962.9	181.6
10.0	60	3815.0	264.4
0.01	120	131166.3	883.2
0.10	120	117367.0	793.3
0.25	120	129089.0	109.3
0.50	120	122425.6	1871.1
0.75	120	26740.9	727.9
1.0	120	116906.9	639.9
2.5	120	47421.1	3281.6
5.0	120	117937.2	628.9
7.5	120	11854.7	204.0
9.0	120	3989.5	250.6
10.0	120	4061.1	232.3

Table 10: Raw data for Figures 22 & 29

HNO3 Conc (M)	Contact Time (min)	k'	Standard Deviation
0.01	10	657.6	119.1
0.10	10	207.5	19.2
0.25	10	278.4	18.8
0.50	10	262.4	31.2
0.75	10	886.0	4.7
1.0	10	1255.7	124.2
2.5	10	1136.5	9.2
5.0	10	396.1	13.6
7.5	10	178.1	4.3
9.0	10	138.9	2.8
10.0	10	123.5	3.8
0.01	30	2593.4	51.2
0.10	30	2007.2	399.5
0.25	30	2817.2	119.0
0.50	30	4470.0	456.7
0.75	30	7714.4	309.4
1.0	30	8124.9	500.4
2.5	30	2065.9	113.3
5.0	30	408.4	21.3
7.5	30	201.6	6.3
9.0	30	154.2	2.4
10.0	30	131.6	7.5
0.01	60	8236.2	627.4
0.10	60	4684.5	201.6
0.25	60	8586.6	353.4
0.50	60	13452.8	3524.2
0.75	60	21041.0	2565.8
1.0	60	13946.4	883.8
2.5	60	3079.7	146.4

5.0	60	564.2	3.4
7.5	60	265.9	24.0
9.0	60	190.2	3.5
10.0	60	176.0	6.9
0.01	120	7866.8	472.0
0.10	120	4697.9	715.1
0.25	120	7510.2	1351.4
0.50	120	8063.3	79.8
0.75	120	11109.0	424.2
1.0	120	12717.4	1523.2
2.5	120	2818.1	129.4
5.0	120	470.7	4.6
7.5	120	200.9	6.9
9.0	120	142.2	6.8
10.0	120	132.3	1.5

Appendix C: Calculation of ^{45}Sc atoms & CF ^{44}Sc atoms

C.1 Determination of Dose of ^{44}Sc Spike Solution

The spike solution of ^{44}Sc was determined to be 16547.2 Bq per sample. This was determined by averaging the spikes for each experiment. Difference occurred in spike amount due to the varying times it took to dry down the sample and reconstitute.

Here, equation 10 will be used to calculate gamma dose.

$$D = A_0 \times \Gamma \times t \quad (10)$$

D = dose (mSv)

A_0 = initial activity of the spike (Bq)

Γ = gamma dose constant for ^{44}Sc ((mSv/h)/MBq)

t = time in contact with radiation (h)

$\Rightarrow A_0 = 1.65 \times 10^4$ Bq per spike (100 μL spike) = 16.5 MBq

$\Gamma = 0.00036$ (mSv/h)/MBq

t = 2 h

$$\Rightarrow \quad D = 16.5472 \text{ MBq} \times 0.00036 \frac{\frac{\text{mSv}}{\text{h}}}{\text{MBq}} \times 2 \text{ h}$$

$$\Rightarrow \quad D = 0.0119 \text{ mSv}$$

$$\Rightarrow \quad \text{Dose rate} = \frac{D}{2 \text{ h}} = \frac{0.0119 \text{ mSv}}{2 \text{ h}}$$

$$\Rightarrow \quad \text{Dose rate} = 0.00596 \frac{\text{mSv}}{\text{h}}$$

C.2 Determination of Atoms in ^{45}Sc Spike Solution

Here, the number of atoms in the spike solution of stable ^{45}Sc will be determined. Samples were spiked with 0.5 mL of a stock solution containing 33333.33 ppb ^{45}Sc. The molar mass of scandium is 44.95591 g/mol.

A_0 = initial spike (ppb)

mm = molar mass of elemental scandium (g/mol)

$\Rightarrow A_0 = 3.33 \times 10^4$ ppb $= 3.33 \times 10^4$ μg/L

mm = 45.0 g/mol

$$\Rightarrow \quad 3.33 \times 10^4 \frac{\mu\text{g}}{\text{L}} \times \frac{10^{-6} \text{ g}}{1 \mu\text{g}} = 3.33 \times 10^{-2} \frac{\text{g}}{\text{L}}$$

$$\Rightarrow \quad 3.33 \times 10^{-2} \frac{\text{g}}{\text{L}} \times \frac{1 \text{ mol}}{45.0 \text{ g}} \times 5 \times 10^{-4} \text{ L} = 3.71 \times 10^{-7} \text{ mol}$$

$$\Rightarrow \quad 3.71 \times 10^{-7} \text{ mol} \times 6.02 \times 10^{23} \frac{\text{atoms}}{\text{mol}} = 2.23 \times 10^{17} \text{ atoms}$$

In conclusion, there were 2.23 x 10^{17} atoms of ^{45}Sc in every 0.5 mL spike.

C.3 Determination of Atoms in ^{44}Sc Spike Solution

The spike solution of ^{44}Sc was determined to be 16547.2 Bq per sample. This was determined by averaging the spikes for each experiment. For this calculation, equations 11 and 13 will be utilized.

Here, equation 11 will be utilized to decay correct for the loss of ^{44}Sc due to radioactive decay.

$$A = A_0 \times e^{-\lambda t} \quad (11)$$

For equation 11,

A = activity after time t has passes (Bq)

A_0 = initial acitity (Bq)

λ = dose coefficient (1/h)

T = time (h)

$\Rightarrow$ For the number of atoms in ^{44}Sc spike

A_0 = 1.50 x 10^6 Bq

λ = 0.172 1/h

t = 1.5 h of drying time

$\Rightarrow$ $$A = 1.50 \times 10^6 \text{ Bq} \times e^{-0.172 \frac{1}{h} \times 1.5 \text{ h}} = 1.16 \times 10^6 \text{ Bq}$$

Now that A is known, it can be used and plugged into equation 13 to calculate the number of atoms of ^{44}Sc.

$$N = \frac{A}{\lambda} \quad (13)$$

N = number of atoms (atoms)

A = decay corrected activity (Bq)

λ = dose coefficient (1/h)

Where,

A = 1.16 x 10^6 Bq

λ = 0.172

$$\Rightarrow \quad \frac{1.16\ x\ 10^6\ Bq}{0.172} = 6.72 \text{ x } 10^6 \text{ Bq}$$

Solutions were constitued in 7.0 mL of nitric acid.

$$\Rightarrow \quad 6.72 \text{ x } 10^6 \text{ Bq} / 7.0 \text{ mL} = 1.65 \text{ x } 10^5 \frac{Bq}{mL}$$

Replugging into eqaution 13 yeilds the number of Bq in a 7 mL stock solution.

$$\Rightarrow \quad \frac{1.65 \text{ x } 10^5 \frac{Bq}{mL}}{0.172} = 9.60 \text{ x } 10^5 \frac{Bq}{mL}$$

Now, the number of Bq per spike needs to be calculated which is

$$\Rightarrow \quad 1.65 \text{ x } 10^5 \frac{Bq}{mL} \text{ x } 0.1 \text{ mL} = 1.65 \text{ x } 10^4 \text{ Bq}$$

Now one last replug in equation 13 to yeild the number of ^{44}Sc atoms per spike

$$\Rightarrow \quad \frac{1.65\ x\ 10^4\ Bq}{0.172} = 9.60 \text{ x } 10^4 \text{ atoms per spike}$$

In conclusion, roughly 9.60 x 10^4 atoms of ^{44}Sc were avaible in each spike.