Separation of samarium and europium by solvent extraction with an undiluted quaternary ammonium ionic liquid: towards high-purity medical samarium-153†

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Long-lived europium-154 impurities are formed during the production of medical samarium-153 in a high-flux nuclear reactor. A method to separate these europium impurities from samarium was investigated using the hydrophobic quaternary ammonium ionic liquid Aliquat 336 nitrate. The separation method consists of the selective reduction of Eu³⁺ by zinc metal in an aqueous feed solution containing a high nitrate salt concentration. Subsequent extraction using undiluted Aliquat 336 nitrate leads to an efficient separation of both lanthanides in a relatively short time frame. Sm³⁺ was extracted to the neat ionic liquid phase much more efficiently than Eu²⁺. An initial approach using the addition of dicyclohexano-18-crown-6 to capture Eu⁺ failed.

Introduction

The radiolanthanide samarium-153 (¹⁵³Sm) is applied in nuclear medicine, where it is known under its commercial names Quadramet and Lexidronam.¹,² In these radiopharmaceuticals, the ¹⁵³Sm radioisotope is coordinated to an ethylenediamine tetra(methylene phosphonate) chelating ligand (¹⁵³Sm EDTMP, Fig. 1).³ ¹⁵³Sm serves well in nuclear medicine because of its favorable half-life of 46,284 h and because it decays to the stable ¹⁵³Eu nuclide. This causes no severe additional side effects in the human body after treatment. ¹⁵³Sm EDTMP is very selective towards the skeleton.⁴–⁷ The ¹⁵³Sm radionuclide is commonly produced via neutron-irradiation of an enriched ¹⁵⁴SmO₃ target, in a nuclear reactor with a high thermal neutron flux.⁸ A product with high yield, high purity and high specific activity is formed. However, since the target is usually irradiated for several days, part of the ¹⁵³Sm is already decaying during irradiation and the daughter isotope ¹⁵⁴Eu will be neutron-irradiated as well, leading to the simultaneous production of trace amounts of ¹⁵⁴Eu.⁹–¹⁰ This radiochemical impurity has a much longer half-life (8,593 year) compared to that of ¹⁵³Sm. Relatively large quantities of ¹⁵⁴Eu lead to an unacceptable radiation dose delivered to the patient. The maximum level of impurities is strictly regulated by international and national organizations (e.g. WHO, IAEA, FDA). Consequently, Quadramet has a limited shelf life of only a few days after being produced, since expiration is reached at the threshold ratio of 0.093 μCi (=3400 Bq) of ¹⁵⁴Eu per mCi (37 MBq) of ¹⁵³Sm. ¹¹–¹⁴ Additionally, long-lived ¹⁵⁴Eu impurities end up in the waste generated in the hospitals. Removal of these ¹⁵⁴Eu impurities would imply a longer product shelf-life for medical use, leading to an increased availability of ¹⁵³Sm and a lower background radioactivity of the treated patient. Waste treatment procedures in hospitals can become easier because waste containing short-lived isotopes only can be treated via decay storage. Moreover, distribution and transportation deadlines can become more flexible, opening perspectives of feeding a world-wide market. This way, an unexpected outage of a research reactor can be backed-up more easily by another research reactor, ensuring the supply of ¹⁵³Sm. Valuable and expensive enriched target material can also be used more efficiently by increasing the irradiation time because the long-lived

Fig. 1 Chemical structure of ¹⁵³Sm EDTMP (commercial names: Quadramet and Lexidronam).

† Electronic supplementary information (ESI) available. See DOI: 10.1039/c8ra03279c
Radiolanthanides are more suitable, but require more advanced short half-lives of the medical radionuclides, gravimetrical popular puri...tative. The pH of the aqueous feed solution was kept between 4 and 6.5. This way, the pH of the final feed solution remained sufficiently high to avoid re-oxidation of Eu$^{3+}$ by H$^+$ ($E^0 = +1.23$ V). The pH of the aqueous feed solution was kept between 4 and 6.5. This way, the pH of the final feed solution remained sufficiently high to avoid re-oxidation of Eu$^{3+}$ by H$^+$ ($E^0 = 0.00$ V) and sufficiently low to prevent hydrolysis of Sm$^{3+}$ or Eu$^{3+}$. Too low pH levels lead to preferential H$_2$ generation in contact with Zn$^0$, i.e. Eu$^{2+}$ will only be reduced as soon as the H$^+$ concentration is sufficiently low. Therefore, pH of the aqueous feed solution after reduction will only be slightly acidic. The pH was reduced to Eu$^{2+}$ by Zn$^0$. The water-immiscible phase of the aqueous solutions was purged with nitrogen gas during reduction of Eu$^{3+}$ to remove atmospheric and dissolved oxygen. This is necessary to prevent re-oxidation of Eu$^{3+}$ by O$_2$ ($E^0 = +1.23$ V). The pH of the aqueous feed solution was kept between 4 and 6.5. This way, the pH of the final feed solution remained sufficiently high to avoid re-oxidation of Eu$^{3+}$ by H$^+$ ($E^0 = 0.00$ V) and sufficiently low to prevent hydrolysis of Sm$^{3+}$ or Eu$^{3+}$. Too low pH levels lead to preferential H$_2$ generation in contact with Zn$^0$, i.e. Eu$^{2+}$ will only be reduced as soon as the H$^+$ concentration is sufficiently low. Therefore, pH of the aqueous feed solution after reduction will only be slightly acidic. The pH was...
measured after Eu\(^{3+}\) reduction and after extraction by means of a Hamilton Slimtrode pH electrode coupled to a Mettler-Toledo SevenCompact pH meter.

**Preparation of the water-immiscible phase**

The water-immiscible phase consisted of neat [A336][NO\(_3\)] or [A336][NO\(_3\)] containing 0.05 M DCH18C6. Neat [A336][NO\(_3\)] was prepared from commercially available [A336][Cl] by a metathesis reaction. [A336][Cl] was dissolved in acetonitrile to decrease the viscosity of the IL and to enhance phase separation. An aqueous solution containing 8 M NH\(_4\)NO\(_3\) was mixed intensively with the [A336][Cl]-acetonitrile solution. This way, chloride anions were replaced by nitrate anions, a process that is favorable according to the Hofmeister series since nitrate ions are less strongly solvated than chloride ions.\(^22\) After mixing and phase separation, the aqueous phase was removed and tested for remaining chloride by addition of a AgNO\(_3\) solution. This process was repeated until no chloride traces could be found in the aqueous phase. After achieving full conversion of [A336][Cl] to [A336][NO\(_3\)], acetonitrile was removed by means of a rotary evaporator, followed by treatment at high vacuum using a Schlenk line. Analysis of the final, dry [A336][NO\(_3\)] by total reflection X-ray fluorescence (TXRF) showed a remaining chloride concentration of ca. 4 ppm (analysis procedure in ESI).\(^20\) The ionic liquid was equilibrated with water (Milli-Q) prior to its use in solvent extraction experiments to avoid any significant volume changes during the extraction experiment.

**Extraction experiments**

The aqueous feed solutions contained both Sm and Eu. The concentration of each lanthanide was 1 g L\(^{-1}\) or 10 g L\(^{-1}\). Only stable isotopes of samarium and europium were used. The chloride or nitrate concentrations in the aqueous feed solutions were adjusted by the addition of the respective ammonium or chloride or nitrate concentrations in the aqueous feed solutions. Only stable isotopes of samarium and europium were used. The aqueous feed solutions contained both Sm and Eu. The aqueous feed solutions were performed to study the extraction rates of Sm\(^{3+}\) and Eu\(^{2+}\). For comparison and completeness, the extraction of Eu\(^{3+}\) in the same conditions was studied as well. The feed solutions were mixed with both [A336][NO\(_3\)] (IL) and [A336][Cl] solutions.

**Results**

**Selection of anion source and concentration**

In a first series of screening experiments, the extraction behavior of Sr\(^{2+}\) by the crown-ether-containing ionic liquid solution was studied as a simulant for Eu\(^{2+}\). Different anion concentrations were used in the aqueous feed solution, i.e. 0, 1, 3, 6 and 8 M. Three different sources were used to vary the anion concentration, i.e. HX, NH\(_4\)X and LiX (with X = Cl\(^-\) or NO\(_3\)\(^-\)). Experiments were performed using both [A336][NO\(_3\)] (IL) and [A336][NO\(_3\)] + 0.05 M DCH18C6 (IL + CE). Results of these screening experiments are reported in the ESI.\(^\dagger\) Based on these results, following experiments were conducted with a 6 M lithium salt aqueous feed solution.

**Time dependence of Sm\(^{3+}\)/Eu\(^{2+}\) separation**

Extraction experiments with 6 M LiX (with X = Cl\(^-\) or NO\(_3\)\(^-\)) aqueous feed solutions were performed to study the extraction rates of Sm\(^{3+}\) and Eu\(^{2+}\). For comparison and completeness, the extraction of Eu\(^{3+}\) in the same conditions was studied as well. The feed solutions were mixed with both [A336][NO\(_3\)] (IL) and [A336][Cl] solutions.
The distribution ratios of both lanthanides after extraction from a 6 M LiCl and a 6 M LiNO₃ aqueous feed solution are plotted as a function of time in Fig. 3a and 4a. It is immediately clear that high distribution ratios were obtained for the trivalent lanthanides in both systems, especially when using a nitrate aqueous feed solution. As expected, the presence of the crown ether did not influence the extraction behavior of Sm³⁺. Eu²⁺ was only reasonably well extracted in presence of the crown ether. Therefore, highest separation factors were reached without the use of a crown ether (Fig. 3b and 4b). It is also clear that separation of the Sm³⁺–Eu²⁺ couple from a nitrate aqueous feed solution is much more efficient compared to a chlorate aqueous feed solution.

Temperature dependence of Sm³⁺/Eu²⁺ separation
Extractions of Sm³⁺ and Eu²⁺ were executed at 25, 40 and 60 °C to evaluate the influence of the viscosity of the ionic liquid phase. Results of these extractions from chloride and nitrate aqueous feed solution (6 M of the respective lithium salt) are presented in Fig. 5a and b, respectively. Both graphs show that a change in temperature, and thus a change in viscosity, does not lead to any significant changes in extraction behavior of both Sm³⁺ and Eu²⁺.

Extraction behavior of Zn²⁺ impurities
Eu³⁺ can be efficiently and selectively reduced by Zn⁰, generating Zn²⁺ in the feed solution. Therefore, the extraction behavior of Zn²⁺ from both chloride and nitrate aqueous feed solutions was studied and compared to the extraction behavior of Sm³⁺ and Eu²⁺. From Fig. 6, it is clear that the extraction of Zn²⁺ strongly depends on the anions present in the extraction system. The extraction of Zn²⁺ proceeded very efficient in case of a high chloride concentration. Therefore, the extraction of Zn²⁺ from chloride media led to very high distribution ratios.

Fig. 3  (a) Distribution ratios (log scale) of Sm³⁺ (blue, squares), Eu³⁺ (green, triangles) and Eu²⁺ (red, circles) and (b) the corresponding separation factor as a function of time (5, 15, 30 and 60 min) using a 6 M LiCl aqueous feed solution. The organic phase consisted of neat [A336][NO₃] (IL, solid line, solid symbol) or [A336][NO₃] + 0.05 M DCH18C6 (IL + CE, dashed line, open symbol). Extraction parameters: O/A = 1, 60 °C and 1700 rpm.

Fig. 4  (a) Distribution ratios (log scale) of Sm³⁺ (blue, squares), Eu³⁺ (green, triangles) and Eu²⁺ (red, circles) and (b) the corresponding separation factors as a function of time (5, 15, 30 and 60 min) using a 6 M LiNO₃ aqueous feed solution. The organic phase consisted of neat [A336][NO₃] (IL, solid line, solid symbol) or [A336][NO₃] + 0.05 M DCH18C6 (IL + CE, dashed line, open symbol). Extraction parameters: O/A = 1, 60 °C and 1700 rpm.
contrary, Zn\(^{2+}\) was hardly extracted in case only nitrate anions were present in the extraction system. The extraction behavior of Zn\(^{2+}\) in nitrate media proved to be comparable to the one of Eu\(^{2+}\).

**Discussion**

**Defining two separation approaches**

In this study, the separation of samarium and europium was investigated with and without the use of a size selective extractant. Many studies report on the efficient extraction of Sr\(^{2+}\) by a 18-crown-6 (18C6) derivative as extractant.\(^{31-34}\) These 18C6-based crown ethers are able to capture a metal ion with a specific ion size in their cavity (2.6–3.2 \(\text{Å}\)). The six oxygen atoms of the crown ether serve as donor atoms to coordinate the metal ion.\(^{35}\) Therefore, they are considered to be highly size-selective.\(^{36}\) Ions that are either too large or too small do not interact properly with the crown ether. This also accounts for the trivalent lanthanides (Ln\(^{3+}\)), which have an ionic radius varying from 0.977 \(\text{Å}\) for Lu\(^{3+}\) to 1.16 \(\text{Å}\) for La\(^{3+}\) (values given for coordination number 8). Moreover, the considerable hydration energy of trivalent lanthanide ions prevents efficient coordination by the crown ether. Lowering of the oxidation state, i.e. the addition of an electron, leads to an increased ionic radius, a decreased charge density and a decreased hydration enthalpy. Thus, Ln\(^{2+}\) ions are more favorable to properly interact with 18C6-based extractants.\(^{37}\) In the lanthanide series, only europium has a relatively stable divalent state in aqueous solutions because of its half-filled 4f subshell. Therefore, the use of a size-selective extractant to selectively trap the Eu\(^{2+}\) impurities in the 18C6-cavity in the organic phase was studied as a first approach to separate the Sm/Eu couple, leaving Sm\(^{3+}\) behind in the aqueous phase. Vander Hoogerstraete *et al.* showed the efficiency of this strategy to recycle rare-earth elements from permanent magnets and nickel metal hydride batteries.\(^{23}\) Both approaches were studied in parallel throughout the experiments.

In both approaches, the water-immiscible phase consisted of neat [A336][NO\(_3\)]. Extraction parameters: O/A = 1 and 1700 rpm.

![Fig. 5](image-url) Distribution ratios (log scale) of Sm\(^{3+}\) (blue, squares) and Eu\(^{2+}\) (red, circles) as a function of time (5, 15, 30 and 60 min) using 6 M LiCl (a) and 6 M LiNO\(_3\) (b) in the aqueous feed solution at different temperatures (25, 40 and 60 °C). The organic phase consisted of neat [A336][NO\(_3\)]. Extraction parameters: O/A = 1 and 1700 rpm.

![Fig. 6](image-url) Distribution ratios (log scale) of Sm\(^{3+}\) (blue, squares), Eu\(^{2+}\) (red, circles) and Zn\(^{2+}\) (green, triangles) as a function of time (5, 15, 30 and 60 min) using 6 M LiNO\(_3\) (solid line, solid symbol) and LiCl (dashed line, open symbol) in the aqueous feed solution. The organic phase consisted of neat [A336][NO\(_3\)]. Extraction parameters: O/A = 1, 60 °C 1700 rpm.
carbon (C), hydrogen (H), oxygen (O) and nitrogen (N).\textsuperscript{44,45} This is highly important for the final disposal and waste treatment of the ionic liquid, which becomes radioactively contaminated when applied for separation of radionanethanes, an aspect that is frequently overlooked in nuclear applications on ionic liquids. (2) Ionic liquids have promising properties compared to conventional molecular solvents, leading to processes with increased safety, chemical stability and radiation-resistivity.\textsuperscript{46-48} (3) [A336][NO\textsubscript{3}] possesses a highly hydrophobic cation whereas the inorganic anion is well soluble in both the aqueous and ionic liquid phase. This ensures a minimal amount of organic compounds ending up in the aqueous phase after extraction. This is opposite to the [C\textsubscript{m}mim][TF\textsubscript{2}N] ionic liquids that are frequently used in combination with 18C6-based crown ethers.\textsuperscript{31,44-49} These ionic liquids operate via a cation extraction mechanism in case a short alkyl chain (C\textsubscript{m}) is used, losing ionic liquid cations to the aqueous phase. This, however, is unfavorable because these contaminations are not compatible with any pharmaceutical application. Additionally, radioysis of the fluorinated anion can generate harmful and hazardous compounds. (4) [A336][NO\textsubscript{3}] is a source of nitrate ions for improved extraction efficiency in a split-anion extraction mechanism in case the feed solution contains chloride ions.\textsuperscript{50} Nitrate ions are more efficient in coordinating the metal ions in crown ether complexes compared to chloride ions. The small bite angle of nitrate ions allows them to coordinate the metal ion bidentately, i.e. taking up little space in the coordination sphere, whereas chloride can only coordinate monodentately. The formation of two M–O bonds is energetically more favorable than the formation of one M–Cl bond, outweighing the considerable M–OH\textsubscript{2} bond energy. This way, the neutral [Sr(NO\textsubscript{3})\textsubscript{2}–DCH18C6] and [Eu(NO\textsubscript{3})\textsubscript{2}–DCH18C6] complexes are formed preferentially. Extraction to the ionic liquid phase occurs via neutral complex partitioning, indicated by the increase in extraction efficiency (reflected in the rising distribution ratio) with increasing anion concentration (Fig. S2, ES\textsuperscript{†}). This is similar to the extraction of alkaline earth metals by crown ethers in molecular diluents, like 1-octanol.\textsuperscript{44} Ion exchange mechanisms, like observed by Garvey et al. for [C\textsubscript{m}mim][TF\textsubscript{2}N], are unlikely to happen. In the proposed extraction mechanism, anions have to be co-extracted to maintain charge-neutrality. When extracting from chloride aqueous media, chloride anions replace the nitrate anions of the ionic liquid (eqn (4)), similar to the so-called split-anion extraction by Larsson and Binnemans.\textsuperscript{50}

\[
\text{M}^{2+}_{\text{Aq}} + 2\text{Cl}^-_{\text{Aq}} + 2[\text{A336}\text{][NO}_3\text{]}_{\text{org}} + \text{DCH18C6}_{\text{org}} \rightleftharpoons [\text{M(NO}_3)_2\text{–DCH18C6}]_{\text{org}} + 2[\text{A336}\text{][Cl]}_{\text{org}} \quad (4)
\]

This reaction, however, might be hampered because of the considerable hydration energy of the chloride ions;\textsuperscript{33,44-50} Dehydration, extraction and solvation by the ionic liquid might thus be unfavorable. The use of high salt concentrations in the aqueous feed increases the ionic strength significantly, resulting in less hydrated ions. This way, the ions are more prone to form extractable species. Extraction from nitrate aqueous solutions can proceed more efficiently because of their lower hydration energy (eqn (5)). Moreover, the ionic liquid phase is composed of nitrate ions, resulting in a more favorable transfer according to the Hofmeister series.\textsuperscript{29}

\[
\text{M}^{2+}_{\text{Aq}} + 2\text{NO}_3^-_{\text{Aq}} + \text{DCH18C6}_{\text{org}} \rightleftharpoons [\text{M(NO}_3)_2\text{–DCH18C6}]_{\text{org}} \quad (5)
\]

Selection of anion source and concentration

In a first series of screening experiments, the extraction behavior of Sr\textsuperscript{2+} as Eu\textsuperscript{2+} simulant was studied to find the optimal extraction parameters. Different anion concentrations and anion sources were used in the aqueous feed solution. Most efficient extraction of Sr\textsuperscript{2+} by [A336][NO\textsubscript{3}]–DCH18C6 was obtained using an aqueous phase with high lithium salt concentration (Fig. S1, ES\textsuperscript{†}). The use of other anion sources, i.e. HX and NH\textsubscript{4}X (with X = Cl\textsuperscript{−} or NO\textsubscript{3}\textsuperscript{−}), proved to be much less efficient, resulting in much lower distribution ratios. The lower efficiency by using HX and NH\textsubscript{4}X was most probably due to the occupation of the crown ether cavity by H\textsubscript{3}O\textsuperscript{+} and NH\textsubscript{4}+. Previous studies already proved that these ions could properly fit in this cavity because of their ion size.\textsuperscript{51,52} Li\textsuperscript{+} has a smaller ionic radius and therefore interacts less efficiently with the crown ether, resulting in better extraction results. Thus, the selection of a non-interfering source of additional anions is of high importance in these crown-ether-based extraction systems. After irradiation, the target material, i.e. Sm\textsubscript{2}O\textsubscript{3}, has to be dissolved. Most frequently, this is done by means of concentrated mineral acids, like HCl or HNO\textsubscript{3}. However, high acid concentrations are disadvantageous for two reasons. First of all, Eu\textsuperscript{2+} is extracted less efficiently by the crown ether from highly acidic media because the H\textsubscript{3}O\textsuperscript{+} ions occupy the cavity of the crown ether. Secondly, Eu\textsuperscript{2+} is unable to be stabilized in a high H\textsuperscript{+} concentration. Additionally, significant volumes of hydrogen gas would be generated during the reduction step, leading to unsafe situations. Therefore, the mixture should be adjusted to the most ideal extraction conditions after dissolution, meaning an increase in pH and anion concentration by the addition of non-interfering compounds. Evaporation to almost dryness followed by dissolution in other aqueous media is another possibility.

Because of their similar charge density and ionic radius, comparable extraction trends for Eu\textsuperscript{2+} and Sr\textsuperscript{2+} were to be expected. It was observed that Eu\textsuperscript{2+} follows indeed a similar trend as Sr\textsuperscript{2+} when extracted by DCH18C6 from chloride and nitrate aqueous media (Fig. S2, ES\textsuperscript{†}). Reasonably high distribution ratios were obtained using high salt concentrations, i.e. \( \geq 6 \) M LiX. Again, the use of nitrate aqueous media yielded in much higher extraction efficiency compared to the use of chloride aqueous media, leading to distribution ratios well above (1).

It was noted that a significant amount of Eu\textsuperscript{2+}, was also extracted towards the DCH18C6-free ionic liquid phase when using high salt concentrations. Significant extraction of Eu\textsuperscript{2+} in a DCH18C6-free system was not expected since it deviates from the behavior of Sr\textsuperscript{2+}, where no extraction was observed at all. Therefore, it is believed that a partial re-oxidation of Eu\textsuperscript{2+} to
Eu\(^{3+}\) have occurred during these experiments, whereby Eu\(^{3+}\) is extracted towards the organic phase without the interaction of a crown ether. Therefore, it is important to keep the extraction time as low as possible.

**Time dependence of Sm\(^{3+}\)/Eu\(^{2+}\) separation**

The significant extractability of Eu\(^{2+}\) by [A\(_{336}\)][NO\(_3\)] + 0.05 M DCH18C6 and the low extractability of Eu\(^{2+}\) by [A\(_{336}\)][NO\(_3\)] seem to support both separation approaches so far. To arrive at a separation system, it is important to study the extraction behavior of Sm\(^{3+}\) as well. A fast separation is advantageous taking into account the decay of \(^{153}\)Sm and possible re-oxidation of Eu\(^{2+}\). Therefore, the distribution ratios of samarium and europium were studied as a function of time. For comparison and completeness, the distribution ratio of Eu\(^{3+}\) in the same conditions was studied in parallel.

From the extraction results in Fig. 3a and 4a, from chloride and nitrate media, respectively, it was immediately clear that much higher distribution ratios were obtained for Sm\(^{3+}\) compared to Eu\(^{2+}\), with and without the use of DCH18C6. As expected, the presence of DCH18C6 in the ionic liquid did not influence the extraction behavior of Sm\(^{3+}\) because of its smaller ionic radius and higher hydration energy. The high difference in distribution ratio allows an efficient Sm/Eu separation. The DCH18C6-free system is favored because of the much lower Eu\(^{2+}\) extraction. Separation factors of 24 were reached using chloride media (Fig. 3b), whereas separation factors well above 600 were reached using nitrate media (Fig. 4b). Sm\(^{3+}\) was extracted into the ionic liquid phase via the split-anion extraction mechanism, as was described by Larsson and Binnemans (eqn (6)).

This extraction mechanism makes use of the strong affinity of nitrate ions for the IL phase, while the chloride ions have a higher affinity for the aqueous phase.

\[
\text{Sm}^{3+}_{\text{aq}} + 3\text{Cl}^-_{\text{aq}} + 5[A_{336}][\text{NO}_3]_{\text{org}} \rightleftharpoons [A_{336}][\text{Sm(NO}_3)_5]_{\text{org}} + 3[A_{336}][\text{Cl}]_{\text{org}} \quad (6)
\]

According to this extraction mechanism, the ionic liquid phase serves as a source of complexing anions. This way, no additional extractants are needed. However, chloride ions have to be transferred to the ionic liquid phase as well to ensure charge neutrality. The extraction of chloride ions is hampered because of their considerable hydration energy, as was also the case for the extraction of M\(^{2+}\) by DCH18C6 from chloride media. The much higher extraction efficiency for Sm\(^{3+}\) from nitrate aqueous media can be attributed to the lower hydration energy and higher hydrophobicity of nitrate ions. The high nitrate concentrations are needed to form extractable species. Trivalent lanthanide ions show the advantage of being able to form anionic complexes with bidentate nitrate ligands, whereas other elements cannot.

Vander Hoogerstraete et al. already showed that the trivalent lanthanides (Ln\(^{3+}\)) are extracted as pentanitrato complexes [Ln(NO\(_3\))\(_5\)]\(^{3-}\) (eqn (7)). Speciation studies using extended X-ray absorption fine structure (EXAFS) support this extraction behavior (ESI).

\[
\text{Sm}^{3+}_{\text{aq}} + 3\text{NO}_3^-_{\text{aq}} + 2[A_{336}][\text{NO}_3]_{\text{org}} \rightleftharpoons [A_{336}][\text{Sm(NO}_3)_5]_{\text{org}} \quad (7)
\]

Larsson and Binnemans already pointed out that all trivalent lanthanides (Ln\(^{3+}\)) show a similar extraction behavior with quaternary ammonium ionic liquids, with a decreasing trend in extraction efficiency across the lanthanide series.\(^{20}\) Thus, the slightly lower extraction efficiency of Eu\(^{3+}\) compared to Sm\(^{3+}\) is in full agreement with these findings (Fig. 3b and 4b). The slightly lower extractability of Eu\(^{3+}\) can probably be attributed to its slightly higher hydration energy because of its smaller ionic radius.\(^{23,24}\) Nevertheless, it is obvious that no efficient separation can be achieved without reduction of europium.

The high distribution ratios of Sm\(^{3+}\) are favorable for the second separation approach, i.e. the extraction of Sm\(^{3+}\) to the ionic liquid phase, while Eu\(^{2+}\) remains in the aqueous phase. Therefore, it can be concluded that the first separation approach, making use of a size-selective extractant to extract Eu\(^{2+}\), becomes superfluous. This also implies that different chloride or nitrate salts can be used to increase the salt concentration in the aqueous feed solution, i.e. the origin of the salt is less of importance regarding the separation method. Therefore, a salt causing less problems regarding the intended medical application can be chosen. Of course, the salt has to be highly soluble in the aqueous feed to reach the required concentration for optimal separation.

Efficient stripping of Sm\(^{3+}\) from the loaded IL phase can be achieved by decreasing the salt concentration in the aqueous phase, i.e. Sm\(^{3+}\) can be stripped by water.\(^{43}\) Reduction of the salt concentration in the system leads to a lower ionic strength. Sm\(^{3+}\) can thus be hydrated more easily, i.e. Sm\(^{3+}\) gains higher affinity for the aqueous phase. Therefore, no harsh conditions, like highly acidic media, are needed. Sm\(^{3+}\) was quantitatively (~98%) back-extracted to the aqueous phase by water in a single step. The strip solution can be slightly acidified to prevent any hydrolysis of Sm\(^{3+}\).

**Temperature dependence of Sm\(^{3+}\)/Eu\(^{2+}\) separation**

Undiluted ionic liquids are highly viscous at room temperature. This is also the case for quaternary ammonium ionic liquids containing long carbon chains, like [A\(_{336}\)][NO\(_3\)]. This high viscosity implies a more difficult mass transfer, leading to reduced extraction speed. However, the viscosity drastically decreases with increasing temperature. Therefore, the above mentioned results were all obtained at 60 °C, a temperature at which [A\(_{336}\)][NO\(_3\)] has a significant lower viscosity but at which experiments are still easy to handle. The viscosity of water-saturated [A\(_{336}\)][NO\(_3\)] decreases from 204 mPa s at 25 °C to 95 mPa s at 40 °C and 42 mPa s at 60 °C. Extractions of Sm\(^{3+}\) and Eu\(^{2+}\) were executed at these temperatures to evaluate the influence of a changing viscosity of the ionic liquid phase. The results in Fig. 5 show that a change in temperature, and thus a change in viscosity, does not lead to significant changes in the extraction behavior of both Sm\(^{3+}\) and Eu\(^{2+}\). Therefore, mass transfer might not be the rate-determining step.
**Extraction behavior of Zn\(^{2+}\) impurities**

Eu\(^{3+}\) can be efficiently and selectively reduced using chemical or electrochemical reduction methods. The chemical method makes use of Zn\(^0\) grains, which are oxidized to Zn\(^{2+}\). Hence, the introduction of extra impurities in the feed solution must be taken into account when using this chemical reduction method. Therefore, the extraction behavior of Zn\(^{2+}\) from both chloride and nitrate aqueous feed solution was studied and compared to the extraction behavior of Sm\(^{3+}\). The results in Fig. 6 clearly show that the extraction of Zn\(^{2+}\) is highly dependent on the anions present in the extraction system, i.e. Zn\(^{2+}\) is hardly extracted in case only nitrate anions are present in the extraction system, whereas the extraction of Zn\(^{2+}\) is very high in case of high chloride concentrations. This observation was expected because it is well known that the extraction of transition metals to quaternary ammonium and phosphonium chloride ionic liquids proceeds efficiently.\(^{19,35}\) Therefore, the extraction of Zn\(^{2+}\) from chloride media gives very high distribution ratios. Hence, Sm\(^{3+}\) can be efficiently separated from Zn\(^{2+}\) via selective stripping of the loaded \([A336][NO_3]\) phase. Sm\(^{3+}\) is transferred back to the aqueous phase upon reduction of the salt concentration in the system, while Zn\(^{2+}\) remains in the organic phase because of its high affinity for the ionic liquid. However, another approach is needed in case of an extraction from nitrate media, considering the low extractability of Zn\(^{2+}\) from nitrate media. In fact, the extraction behavior of Zn\(^{2+}\) is comparable to that of Eu\(^{2+}\). Therefore, reasonably good separation from samarium can already be achieved in the forward extraction step. Considering these results, Zn\(^{2+}\) impurities originating from the chemical reduction method can be efficiently removed.

**Outlook: separation scheme for the purification of samarium-153**

Based on this feasibility study, following full separation process concept to produce high purity samarium-153 can be proposed (Fig. 7): (1) dissolution of the target material by HNO\(_3\) and adjustment of the pH (4–6.5) and anion concentration (6 M NO\(_3\)) by the addition of a non-interfering nitrate salt (e.g. NH\(_4\)NO\(_3\) or LiNO\(_3\)). The total europium concentration must be adjusted by the addition of stable isotopes to facilitate the separation procedure. (2) The selective reduction of europium to its divalent state by zinc metal. (3) The forward extraction of Sm\(^{3+}\) to the ionic liquid phase, consisting of undiluted \([A336]\[NO_3]\). Eu\(^{2+}\) and Zn\(^{2+}\) remain in the aqueous phase. (4) Separation of both phases. (5) Stripping (back-extraction) of Sm\(^{3+}\) from the loaded ionic liquid phase can be easily performed by the addition of water, lowering the total salt concentration.

**Conclusion**

A feasibility study to develop an efficient method to separate samarium and europium was conducted in scope of the purification process to produce high-purity \(^{153}\)Sm for medical applications. The separation method consists of the selective reduction of Eu\(^{3+}\) by zinc metal in an aqueous feed solution containing a high chloride or nitrate salt concentration (6 M). Subsequent extraction using the quaternary ammonium ionic liquid \([A336][NO_3]\) leads to a good separation of both lanthanides in a relatively short time frame. Sm\(^{3+}\) proved to be extracted to the neat \([A336][NO_3]\) phase much more efficiently compared to Eu\(^{2+}\). A first approach using the addition of DCH18C6 to capture Eu\(^{2+}\) in the ionic liquid phase proved to be less efficient. Therefore, the separation process using neat \([A336][NO_3]\) is the preferred approach, extracting Sm\(^{3+}\) to the ionic liquid phase while Eu\(^{2+}\) remains in the aqueous phase. Moreover, it was shown that the use of a nitrate aqueous feed solution leads to a more efficient separation method compared to the use of a chloride aqueous feed solution. Zn\(^{2+}\) ions originating from the chemical reduction method showed a very low extractability in nitrate media. This way, simultaneous removal of Eu\(^{2+}\) and Zn\(^{2+}\) from Sm\(^{3+}\) can be achieved in the forward extraction step. Therefore, this separation method can be used to arrive at a purified product with extended shelf-life. This leads to an increased availability of \(^{153}\)Sm radioisotopes and a decreased background radiation of \(^{154}\)Eu in the patient after treatment. The separation method can also be applied for efficient removal of Eu\(^{2+}\) from any other Ln\(^3+\) because all trivalent lanthanide ions tend to have a similar extraction behavior as Sm\(^{3+}\).

**Conflicts of interest**

There are no conflicts to declare.
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