Isotope separation by DC18C6 crown-ether for neutrinoless double beta decay of $^{48}\text{Ca}$

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Abstract. The isotope separation via liquid-liquid extraction (LLE) using crown-ether (DC18C6) was carried out in order to demonstrate the feasibility of calcium isotope enrichment, which aimed to find a cost-effective way to enrich calcium-$^{48}\text{Ca}$ for the study of neutrinoless double beta decay ($^{0}\nu\beta\beta$) in the CANDLES project. The LLE results revealed that the extraction was solvent dependent in the presence of HCl and the distribution coefficient (D) increased approximately threefold ($0.0546\pm0.0012$) with 12 M HCl solvent under a 3.9 M CaCl$_2$ (aq) (30% w/w) system. Furthermore, the HCl solvent maintained the calcium content attached to the crown-ether at lower feed concentrations. The reaction cell ICP-MS (Agilent 7900) with an additional H$_2$ gas was used to analyze the isotopic composition. The single-stage separation factor of organic phase was found to be $0.992\pm0.003$, $0.994\pm0.003$, $0.996\pm0.004$ for $^{48}\text{Ca}/^{42}\text{Ca}$, $^{48}\text{Ca}/^{43}\text{Ca}$, and $^{48}\text{Ca}/^{44}\text{Ca}$, respectively in the extracted organic phase of 3.3 M CaCl$_2$ (aq) (30% w/w) system. The obtained results were comparable with the HCl solvent system. As a result, without the addition of an acidity reagent, the production of the enriched $^{48}\text{Ca}$ isotope via LLE was highly feasible. To improve the mass production of enriched $^{48}\text{Ca}$, filter separation was applied in order to shorten the time required and to study various volumes of the extraction system. The results indicated that the extraction efficiency of filter LLE was comparable to conventional LLE. Filter LLE resulted in more than threefold reduction in time required (approximately 10 minutes for a complete single-stage separation) in comparison with a conventional LLE, consequently implying great potential in the enrichment and mass production via filter LLE.

1. Introduction
Calcium-40 ($^{40}\text{Ca}$) is the most abundance calcium isotopes of 96.94%, while the remaining stable isotopes are $^{42}\text{Ca}$, $^{43}\text{Ca}$, $^{44}\text{Ca}$, $^{46}\text{Ca}$, and $^{48}\text{Ca}$, which occur at 0.65%, 0.14%, 2.09%, 0.004%, and 0.19%,
respectively. At the present, calcium isotopes are widely used in various applications, including academic research and medical application [1]. In particular for $^{48}$Ca, which accounts for 0.19% of all calcium isotope, it is used as a key component for synthesizing super heavy nuclei by bombarding into heavy elements [2]. Furthermore, CANDLES (CAlcium fluoride for studies of Neutrino and Dark matters by Low Energy Spectrometer) project has been studied on the neutrinoless double beta decay (0νββ) to demonstrate the mysterious of neutrinos, such as lepton non-conservation number, and absolute mass of neutrino [3, 4]. $^{48}$Ca is a double beta decay nuclide with the highest Q-value of 4.27 MeV, greater than natural radioactivity background. However, to study an ultra-rare event of neutrinoless double beta decay, a large amount of $^{48}$Ca nuclide is required. The enrichment of $^{48}$Ca isotope is mandatory. Nonetheless, because calcium has no gaseous compound, industrial-scale methods of isotope enrichment such as gas diffusion or gas centrifuge are inapplicable. Electromagnetic separators are commercially available and offer a promising method. However, this separation method has a low production yield and is a time-consuming and expensive procedure.

Crown-ether is a host-guest molecule used in various cation extraction methods due to the electrostatic attraction between the ion and the oxygen atom in crown-ether [5]. Jepson and DeWitt [6] were the first to report the isotope effect of lighter calcium isotopes using liquid-liquid extraction (LLE) with DC18C6 and DB18C6 crown-ether. The following reaction occurs in the isotope exchange:

$$^{40}\text{Ca}_{(\text{aq})}^{2+} + ^{48}\text{CaL}_{(\text{org})}^{2+} \rightarrow ^{48}\text{Ca}_{(\text{aq})}^{2+} + ^{40}\text{CaL}_{(\text{org})}^{2+}$$

(1)

where L represent macrocyclic crown-ether. The subscripts (aq) and (org) denote the aqueous and organic phases, respectively. Crown-ether absorbs the lighter isotope of calcium more than the heavier isotope. Recently, separation methods that have the potential for $^{48}$Ca enrichment, such as resin chromatographic and laser isotope separation, have been studied and improved [7 – 10]. However, the yield of those methods is low. LLE allows for high calcium concentrations in feed solutions, increasing isotope enrichment and mass production feasibility. [11].

This research examined the effect of different initial feed concentrations and acidity solvents (HCl) on liquid-liquid extraction using DC18C6 crown-ether to obtain the appropriate conditions for $^{48}$Ca enrichment. Furthermore, by skipping the phase separation procedure, the use of filter separation could improve enrichment progress. As a result, filter separation of LLE was also performed in comparison to a conventional LLE. A preliminary experiment on multi-stage iteration was also discussed to demonstrate the enrichment feasibility.

2. Methods

2.1. Liquid-liquid extraction (LLE)

Calcium was extracted using a liquid-liquid extraction (LLE) system between an aqueous phase and an organic phase containing DC18C6 crown-ether. As an organic phase, 0.07M DC18C6 (98% purity, Sigma Aldrich (Germany)) was dissolved in chloroform (CHCl$_3$, FUJIFILM Wako Pure Chemical Industries, Ltd.). The aqueous phase of CaCl$_2$ solution (calcium chloride dihydrate: CaCl$_2$·2H$_2$O, FUJIFILM Wako Pure Chemical Industries, Ltd.) was mixed with various concentrations with an

![Figure 1. liquid-liquid extraction using crown-ether.](image-url)
organic phase by the volume ratio of 1/10 (aqueous/organic). The mixing solution was stirred in an Erlenmeyer flask with a magnetic stirrer by the variety mixing time and allowed to keep standing in the separation funnel for 10 minutes to complete phase separation. After each phase was separated into its container, the organic phase was mixed with pure water (Milli-Q water purification system (Merck Millipore, USA.)) in the same volume ratio to retrieve the calcium from the organic phase (back extraction). The extraction process was completed at room temperature (22 ± 0.5°C). Figure 1 shows the mechanism of isotope separation by crown-ether liquid-liquid extraction.

This study aims to determine the various fundamental factors of LLE to find an appropriate condition for isotope separation and enrichment feasibility. The factors investigated in the study include the time required for equilibria the chemical exchange reaction (1 second to 60 minutes), the initial feed concentration of CaCl2 solution (1.0 – 4.8 M (10 % – 40 % w/w)), the absence of a crown-ether system, the acidity solvent effect (12 M HCl acid solvent (37% w/w HCl, FUJIFILM Wako Pure Chemical Industries)), and the use of filter separation to shorten the time requirement of the extraction progress.

2.2. Determination of calcium concentration and isotopes composition

Feed, extracted, and back-extracted samples were diluted with the appropriate concentration by pure water. The calcium concentration was measured by atomic absorption spectroscopy (AAS: AA-6800, Shimadzu Japan). Inductively coupled plasma mass spectrometry (ICP-MS: Agilent 7900, Agilent technologies, USA) was used for isotopic analysis.

The quantitative analysis of calcium concentration was carried out using standard calcium solution (Ca 1000, Fujifilm Wako Pure Chemical Industries, Ltd.) of various concentrations, ranging from 0.5 to 10 ppm [Figure 2]. The calcium concentration was determined using flame AAS with a lumina hollow cathode lamp at a wavelength of 422.7 nm and a deuterium lamp for real-time background correction. The isotopic analysis was performed using a reaction cell ICP-MS (Agilent 7900) with additional H2 gas. Because of the isobaric interference of argon charge, the measurement of calcium isotopes by ICP-MS is difficult [12]. The reaction gas could significantly reduce the isobaric interference by charge transfer and chemical reaction between H2 gas and argon, resulting in more negligible interference. [13, 14] To avoid mass bias caused by different calcium concentrations, the preparation for calcium isotopic analysis was constant at 1 ppm calcium concentration. The H2 gas reduced the background signal approximately 4,525, 15, 117, and 23 times when compared to no gas mode, resulting in an improvement of signal-to-noise ratio (S/N) for 141.0, 1.7, 15.3, and 4.0 times for 42Ca, 43Ca, 44Ca, and 48Ca, respectively. To eliminate the matrix effect, additional nitric acid (15 M HNO3, (Tama Chemicals Co., Ltd (Japan)) was added at 1.5 % w/w. The tuning solution was a 2% HNO3 matrix (ICP-MS tuning solution, Agilent technologies, U.S.). 5% w/w nitric acid was used to eliminate memory effect or unwanted interference in the ICP-MS cleanup procedure after the measurement of each sample. To ensure that the memory effect was insignificant, the measurement sequence was included pure water (background) before and after the measurements. Furthermore, the signal-to-noise ratio (S/N) between 1 ppm calcium concentration and background count (pure water) was kept above 100 to ensure that no background correction was required. Following the sample measurement, the standard calcium solutions were measured again to ensure the measurement stability. The uncertainty in the isotope ratio measurement is approximately 0.2 – 0.3% RSD. Moreover, it is well known that the mass bias is time dependent [15]. The mass bias in the recession direction was revealed by our measurement setup. The feed bracketing sequence techniques were measured every two measurements to ensure measurement reliability. The obtained isotope ratio was assured by the interval feed samples, which determined that the mass bias during measurement was in an uncertainty period of the interval samples, resulting in a reliable outcome. Nonetheless, the measurement of the 40Ca isotope had a higher mass bias, resulting in an inaccurate
result that cannot be reported. It was necessary to improve the measurement reliability in order to measure the isotope composition of $^{40}\text{Ca}$.

Following the equations (2), (3), and (4), two essential factors, distribution coefficient (D) and single-stage separation factor ($\alpha$), were determined. D is a distribution of calcium concentration between two immiscible phases. The calcium isotope ratio in extracted organic phase compared to feed was determined by the single-stage separation factor ($\alpha$).

$$D = \frac{[\text{Ca}]_{\text{org}}}{[\text{Ca}]_{\text{aq}}}$$

$$\alpha = \frac{C_{\text{org}}}{C_{\text{feed}}}$$

where $C$ denotes the isotope counting ratio obtained from the subscript phase. The x superscript indicates the calcium isotope, which includes $^{42}\text{Ca}$, $^{43}\text{Ca}$, and $^{44}\text{Ca}$.

3. Results

3.1. Reaction time equilibrium

Various mixing times ranging from 1 second to 1 minute, 10 minutes, 30 minutes, and 60 minutes were studied to investigate the time requirement in the chemical exchange between calcium ion and crown-ether. The finding had the potential to shorten the production time required. The mixing time effect of LLE was investigated using 3.3 M CaCl$_2$ (aq) (30% w/w) as a feed solution. The volume ratio between the aqueous/organic phase, 0.07 M DC18C6, was maintained at 1/10 (20/200 mL). The phase separation time was 10 minutes in the separation funnel. The initial volume ratio corresponded to the amount of pure water used for back-extraction. The extraction process was completed at room temperature ($22\pm0.5^\circ\text{C}$), noted that 1 second mixing time system was carried out by shaking in the separation funnel.

Figure 3 shows the obtained distribution coefficient (D). The results indicate that 1 second system has a lower distribution coefficient (D = 0.0064±0.0008) than the other longer mixing time systems (1 minute to 60 minutes). The results of 1 minute to 60 minutes system were 0.0156±0.0001 to 0.0182±0.0001, indicating that the chemical reaction took at least 1 minute to reach equilibria.

| Mixing time | D (±σ) | $^{48}\text{Ca}/^{42}\text{Ca}$ (±σ) | $^{48}\text{Ca}/^{43}\text{Ca}$ (±σ) | $^{48}\text{Ca}/^{44}\text{Ca}$ (±σ) |
|-------------|--------|---------------------------------|---------------------------------|---------------------------------|
| 1 sec       | 0.0064±0.0001 | 0.991±0.004 | 0.992±0.003 | 0.995±0.003 |
| 1 min       | 0.0182±0.0001 | 0.995±0.005 | 0.994±0.004 | 0.996±0.005 |
| 10 mins     | 0.0165±0.0001 | 0.995±0.004 | 0.993±0.004 | 0.995±0.003 |
| 30 mins     | 0.0167±0.0006 | 0.993±0.003 | 0.992±0.003 | 0.994±0.002 |
| 60 mins     | 0.0156±0.0001 | 0.993±0.005 | 0.993±0.004 | 0.994±0.003 |
single-stage separation ($\alpha$) factor is shown in table 1. In the organic phase, the isotope effect of the depleted in heavier isotope was observed. The effect of different mixing times on the separation factor ($\alpha$) result was not statistically significant.

3.2. Feed concentration dependency and acidity solvent contribution

One of the essential factors in establishing isotope enrichment and mass production by LLE was the appropriate calcium feed concentration. The initial feed concentrations were studied, ranging from 1.0 to 4.8 M CaCl$_2$ (aq) (10% – 40% w/w). In the organic phase, the crown-ether concentration was 0.07 M DC18C6. The mixture solutions were stirred in an Erlenmeyer flask for 1 minute with a magnetic stirrer and then put in a separation funnel for 10 minutes to complete the phase separation. Pure water was used for the back extraction with the same initial volume ratio. Simultaneously, the acidity solvent effect was studied using a system of 12 M HCl acid (37% w/w) as a solvent at 1.1 – 3.9 M CaCl$_2$ (HCl) (10%, 20%, and 30% w/w). The additional experiment was carried out in the absence of the DC18C6 crown-ether system at 3.3 M CaCl$_2$ (aq) (30% w/w) and 3.6 M CaCl$_2$ (HCl) (30% w/w) to ensure that crown-ether plays the role.

The effect of different feed concentrations, acidity solvent concentrations, and the absence of crown-ether were studied. The feed concentration directly corresponded to the distribution coefficient ($D$). Nevertheless, the acidity solvent of 12 M HCl had a significantly higher distribution coefficient, indicating that the HCl solvent increased and maintained the distribution coefficient even at lower feed concentrations (Figure 4). The cross marks indicate the absence of a crown-ether system. The distribution coefficient was found to be much lower in the absence of a crown-ether extraction system than in the presence of crown-ether ([Ca]$_{org} < 0.5$ ppm). It was discovered that the calcium extracted is delivered via the formation of an ion-crown complex. Despite this, the absence of a crown-ether system resulted in a slightly higher distribution coefficient in the 12 M HCl solvent. However, the obtained value was still lower than the aqueous solvent system at an initial feed concentration of 2.7 M CaCl$_2$ (aq) (25% w/w) system. The results were consistent with resin chromatographic methods investigated by Umehara et al., Hayasaka et al., and Nemoto et al. [7–9]. It was discovered that calcium absorption to crown-ether resin increased in the presence of HCl acid. Moreover, it was reported that the higher HCl concentration, the more calcium was absorbed by the crown-ether. In the case of LLE, further research into HCl concentration dependency was still lacking. However, our findings indicated that LLE at high concentrations was also possible without the addition of a problematic handling reagent such as HCl acid. This advantage enabled the extraction to be completed more quickly and safely.

The current setup for calcium isotopic analysis by ICP-MS was only appropriate for the samples that had been diluted more than 100 folds. The organic contaminant caused signal interference, resulting in insufficient nebulization and plasma extinguishment. Therefore, in the low dilution ratio sample, the obtained data was unreliable. One-hundred-fold dilution ratio by pure water was required to reduce the contamination interference, and the target concentration was 1 ppm. Therefore, the samples with initial concentrations less than 100 ppm were ineligible. Back extraction concentrations were ranged from 263
to 24,588 ppm from a 2.7 to 4.8 M CaCl₂ (aq) feed concentration system (25%, 30%, and 40% w/w). Simultaneously, at 1.9 M CaCl₂ (aq) (20% w/w), the calcium concentration in the back-extraction sample was found to be 26 ppm, preventing it from being prepared in the appropriate dilution ratio for ICP-MS measurement at 1 ppm. As a result, only 25% w/w to 40% w/w of the aqueous solvent system could reveal the isotopic composition. On the other hand, the HCl solvent increased calcium absorption to the organic phase. Hence, even at low feed concentrations, the back-extraction samples from the HCl system were suitable for ICP-MS isotopic analysis. The single-stage separation factor (α) of an aqueous system with various feed concentrations and 12 M HCl solvent are shown in Table 2. The results show that there was no significant dependency on the acidity solvent in terms of separation factor, and the single-stage separation factor was found to be 0.992±0.003, 0.994±0.003, and 0.996±0.004 for ⁴⁸Ca/⁴²Ca, ⁴⁸Ca/⁴³Ca, and ⁴⁸Ca/⁴⁴Ca under 3.3 M CaCl₂ (aq) extraction system, respectively.

**Table 2.** The distribution coefficient (D) and single-stage separation factor (α) of feed concentration dependency in aqueous and HCl solvent.

| Feed [Ca] (M) | %CaCl₂ (w/w) | Solvent       | D            | ⁴⁸Ca/⁴²Ca α ± σ | ⁴⁸Ca/⁴³Ca α ± σ | ⁴⁸Ca/⁴⁴Ca α ± σ |
|--------------|---------------|---------------|--------------|----------------|----------------|----------------|
| 2.7          | 25%           | Aqueous       | 0.0025±0.0001| 0.993±0.005    | 0.990±0.004    | 0.993±0.004    |
| 3.3          | 30%           | Aqueous       | 0.0200±0.0003| 0.992±0.003    | 0.994±0.003    | 0.996±0.004    |
| 4.8          | 40%           | Aqueous       | 0.1480±0.0012| 0.993±0.005    | 0.995±0.003    | 0.996±0.004    |
| 1.1          | 10%           | Aqueous + 12 M| 0.1863±0.0028| 0.995±0.006    | 0.995±0.004    | 0.997±0.003    |
| 2.5          | 20%           | HCl           | 0.0768±0.0004| 0.993±0.004    | 0.995±0.005    | 0.995±0.005    |
| 3.9          | 30%           | HCl           | 0.0546±0.0012| 0.995±0.005    | 0.996±0.004    | 0.996±0.003    |

Nemoto et al. [8] used the molecular orbital calculation (MO calculation) to determine the isotope effect of calcium in the resin chromatographic method. It was discovered that increasing the concentration of HCl acid resulted in a lower value of isotope fractionation. Under 9 M HCl acid, the fractionation coefficient (ε = α – 1) of the ⁴⁸Ca/⁴⁰Ca system with B18C6 crown-ether resin was reported to be 0.0060±0.0010. It was discovered to be 0.0028±0.0002 at a higher concentration of the HCl system (12 M). According to our findings, a high concentration of HCl acid increased calcium absorption to crown-ether, which is consistent with the chromatographic method and could improve absorption even at low concentrations. The isotope effect was confirmed in the organic phase. The isotope effect of the HCl system was found to be the same as the aqueous system. However, the aqueous phase could not yet be observed the enrichment via the single-stage separation. Because the ICP-MS had an enormous uncertainty value (σ) of separation factor (σ = 0.003 – 0.006). The isotope fractionation in the aqueous phase, where the heavier was enriched, was still negligible to be observed. The multi-stage iteration was required to demonstrate the enrichment and needed to be measured by other isotopic analyzers, such as TIMS, for comparison. Because the contribution of calcium content in the liquid-liquid extraction was much higher than that of the resin chromatographic method, a large amount of calcium was distributed to the crown-ether. This could explain why the isotope effect did not significantly differ in the presence or absence of an acidic solvent. Nonetheless, our results show that HCl kept the calcium content attached to crown-ether even at lower feed concentrations. More research on liquid-liquid extraction with various HCl concentrations was needed to determine the optimal HCl concentration, maintain the ion-crown complex, and study the enrichment feasibility.
Filter separation was applied to skip the phase separation time and reduce the time required for isotope separation and mass production. The filter used in this experiment was a Phase Separating Filter No.2S (Advantech Co., Ltd.) that could separate the aqueous and organic phases. Furthermore, the purpose of this study could be used to investigate the effect of different extraction system volumes on economically expensive materials like crown-ether. As an organic phase, 100 mL of 0.07 M DC18C6 dissolved in chloroform was used. The aqueous phase was 1.0 – 4.8 M CaCl2 (aq) (10% – 40% w/w), with the same volume ratio (1/10) as a conventional LLE. The solutions were mixed for 1 minute by a magnetic stirrer before being separated using a glass funnel with the filter. The organic phase was collected in the container after passing through the filter. The organic solution was mixed with 10 mL of pure water using a magnetic stirrer for 1 minute to recover the calcium. The mixing solution was separated by the filter as well. The distribution coefficient could not be compared because the filter LLE conditions differed from conventional LLE. To investigate extraction efficiency, the mole ratio (η) represented the ratio of extracted calcium to the total crown-ether using the following equation (5).

\[
\eta = \frac{\text{mole of } Ca_{\text{org}}}{\text{mole of Crown–Ether}}
\]  (5)

Figure 5 shows the mole ratio (η) of filter LLE compared to a conventional LLE. It was discovered that the filter LLE posed a comparable result to a conventional LLE, even though the volume of the organic phase and aqueous phase was less than the conventional LLE. The 1.0 – 1.6 M CaCl2 (aq) (10% – 15% system) filter LLE system did not exhibit the same behavior as conventional LLE. Because the total substance of crown-ether in the organic phase of filter LLE was less than in conventional LLE, resulting in a low extracted calcium concentration (less than 0.5 ppm). Even at the highest feed concentration system, the η was less than unity, indicating that the chemical formation of the ion-crown complex was less than a one-to-one ratio. It also implied that the crown-ether contribution was still not fully activated.

Table 3 shows the single-stage separation factor of filter LLE compared to conventional LLE. It was noted that the back extraction sample at 2.8 M CaCl2 (aq) (25% w/w) of filter LLE system was lower than 100 ppm, resulting in the inappropriate preparation for 100 folds dilution ratio and only a higher concentration system (30%, and 40% w/w) could be revealed. The single-stage separation factor of filter LLE showed the same trend as conventional LLE as well. At 3.5 M CaCl2 (aq) (30% w/w), it was found to be 0.995±0.005, 0.993±0.002, 0.996±0.003 for 48Ca/42Ca, 48Ca/43Ca, and 48Ca/44Ca, respectively.
These findings demonstrated the superiority of filter LLE in that the extraction conditions could be reduced to a more cost-effective use of crown-ether, which is an expensive material. Simultaneously, this behavior demonstrated that higher volume extraction, which was applicable to scale up to mass production, could also provide the same behavior. Furthermore, without the phase separation time, single-stage extraction could be completed in less than 10 minutes. Compared to conventional LLE, which has a phase separation time of 10 minutes, those procedures would take approximately 1 hour for a single-stage separation. This superior filter separation is applicable for reducing the time required for mass production of isotope enrichment.

3.4. Multi-stage iteration for enrichment feasibility

Multi-stage iteration has explored the feasibility of enrichment using a liquid-liquid extraction (LLE) system with DC18C6 crown-ether. A preliminary experiment on filter LLE iteration was carried out using 2 mL of 3.5 M CaCl$_2$ (aq) (30% w/w) system as a feed solution mixed with 20 mL of 0.07 M DC18C6 dissolved in chloroform as a feed solution. Additional low-level vacuum filtration was used to separate the organic and aqueous phases. Because only a small amount of calcium was used, the number of iterations was limited to the fourth iteration. The isotopic compositions of the extracted phase were measured to demonstrate the $^{48}$Ca isotope enrichment. The aqueous phase separation factor ($\alpha_{aq}$) at the fourth iteration was 1.004±0.004, 1.002±0.003, and 1.002±0.004 for $^{48}$Ca/$^{42}$Ca, $^{48}$Ca/$^{43}$Ca, and $^{48}$Ca/$^{44}$Ca, respectively (figure 6). The results showed that the heavier isotope was enriched in the extracted aqueous phase. However, the separation factor at the fourth iteration remains within the measured uncertainty, necessitating a precise measurement of the isotope composition. The correlation between iteration stage (x) and aqueous phase separation factor (aq) is denoted in equations (6), (7), and (8), which represent $^{48}$Ca/$^{42}$Ca, $^{48}$Ca/$^{43}$Ca, and $^{48}$Ca/$^{44}$Ca, respectively.

$$\alpha_{aq}^{48/42} = 0.9983e^{0.0016x}$$

$$\alpha_{aq}^{48/43} = 0.9985e^{0.0010x}$$

$$\alpha_{aq}^{48/44} = 0.9992e^{0.0006x}$$

| Feed [Ca] (M) | %CaCl$_2$ (w/w) | Separation method | $\eta$ | $\alpha \pm \sigma$ | $\alpha \pm \sigma$ | $\alpha \pm \sigma$ |
|---------------|-----------------|------------------|-------|------------------|------------------|------------------|
| 2.7           | 25%             |                  | 0.009 | 0.993±0.005      | 0.990±0.004      | 0.993±0.004      |
| 3.3           | 30%             | Separation funnel| 0.089 | 0.992±0.003      | 0.994±0.003      | 0.996±0.004      |
| 4.8           | 40%             |                  | 0.897 | 0.993±0.005      | 0.995±0.003      | 0.996±0.004      |
| 3.5           | 30%             |                  | 0.065 | 0.995±0.005      | 0.993±0.002      | 0.996±0.003      |
| 5.1           | 40%             | Filter           | 0.896 | 0.995±0.003      | 0.995±0.003      | 0.997±0.003      |
Regardless of calcium recovery in the extracted aqueous phase, preliminary calculations show that the number of required iterations to achieve ten times enrichment of $^{48}\text{Ca}$ were 1,440, 2,304, and 3,839 iteration stages for $^{48}\text{Ca}/^{42}\text{Ca}$, $^{48}\text{Ca}/^{43}\text{Ca}$, and $^{48}\text{Ca}/^{44}\text{Ca}$, respectively.

4. Conclusion

The liquid-liquid extraction method was used to demonstrate the isotope effect and the feasibility of isotope enrichment and mass production. The conclusions and future improvements are as follows.

- The mixing time effect revealed that the time required for the chemical exchange reaction to reach equilibrium was at least 1 minute. Even with a 1 second mixing time, the single-stage separation factor ($\alpha$) was found to be the same. Further research on the mixing time between 1 second and 1 minute was required to optimize the time requirement.

- The distribution coefficient demonstrated the dependency of feed concentration in the case of the aqueous solvent. The absence of a crown-ether system was found to be much lower than the presence of a crown-ether system, indicating that the calcium was extracted via an ion-crown complex formation. On the other hand, the HCl acid solvent increased and maintained the distribution coefficient. The results agreed well with the resin chromatographic method, which required HCl acid to make calcium absorption to crown-ether. To establish mass production, the presence of hard handling reagents such as HCl acid was problematic. Our findings indicated that LLE has the advantage of not requiring an acidity substance. However, because the crown-ether was still not fully activated, more research on the concentration of HCl acid is required to find an optimal condition to maintain calcium content attached to the crown-ether. If the crown-ether was fully activated, the chemical exchange of calcium isotopes should increase, resulting in the more significant isotope fractionation.

- Filter LLE was used to reduce the time required and consume expensive materials such as DC18C6 crown-ether. The mole ratio ($\eta$) was comparable with conventional LLE, indicating that the extraction efficiency was relatively similar. The advantage of the LLE filter was that it allowed the extraction procedures to be completed with much less time.

- A preliminary experiment on filter LLE for the multi-stage iteration was carried out and found the enrichment of heavier isotope on the extracted aqueous phase.

- Additionally, a precise measurement method of calcium isotopic analysis, such as TIMS, was required to compare and investigate the $^{40}\text{Ca}$ isotope abundance, which is the most naturally occurring isotope abundance.

- In order to find the most cost-effective method for enriching $^{48}\text{Ca}$, studies on the use of other side chain crown-ethers, such as 18C6 or DB18C6, are required.

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