Automated, cassette-based isolation and formulation of high-purity [^{61}Cu]$CuCl_2$ from solid Ni targets -V 1.0 03/12/2024-TKI-CU01

1. Scope

This method aims to separate ^{61}Cu, as well as ^{64}Cu, from solid Ni targets to obtain a pure isotope suitable for radiolabelling.

2. Summary

The reported method is based on the publication of Svedjehed et al. (Svedjehed et al., 2020). The main goal was to separate ^{61}Cu from Ni targets, which might also contain other metals such as Fe or Co. Moreover, the main focus was not only to obtain an interference-free Cu product but also a product suitable for radiolabelling reactions. For the chemical separation of Cu from matrix elements, a cassette-based approach using two different resins sequentially, TBP Resin (TrisKem International, 2015) and TK201 Resin (TrisKem International, 2019), was employed. The complete radiochemical separation procedure led to chemical yields ranging from 87% to 93%. The final product was recovered in around 2 mL of 0.06 M HCl, of suitable purity for further use in radiolabelling.

3. Significance of use

This is a fast and automated method to obtain highly pure ^{61}Cu using a cassette-based approach. It could also be applied to ^{64}Cu production via ^{64}Ni targets. This method allows for routine production of the isotope ^{61}Cu with highly repeatable results from ^{nat}Ni solid targets.

4. Interferences

Since Ni is the target element which will be irradiated to produce ^{61}Cu, Ni was the main interference investigated. Additionally, other metals such as Fe and Co (Co isotopes might be also produced during target irradiation), were also considered since they might also be present in the dissolved solid target. Using sequentially different specific resins helped to remove and avoid the presence of this interferences in the final product.

5. Apparatus

- Analytical balance -0.0001 g sensitivity
- Cassette-based synthesizer (in the publication this method is based on a FASTlab system is used, however other systems (AiO, Alceo,... may also be used)
- Peristaltic pump
- Cassette reagent vials

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- Cassette collection vials
- ICP-AES or other measurement equipment to quantify the different metal concentrations

6. Reagents

a. Reagents

Unless otherwise indicated, all references to water should be understood to mean deionized distilled water. All reagents should be at least of analytical grade.

- 1 mL TBP column (50-100 µm) (TrisKem International, France)
- 2 mL TK201 column (50-100 µm) (TrisKem International, France)
- NaCl salt
- Milli-Q water
- 37% HCl
- Optional: trace metal standards (1000 mg/L) for calibration or optimisation tests
    - Co
    - Cu
    - Fe
    - Ni
    - Zn

b. Preparation of solutions

- 11.1 M HCl: For 100 mL solution add around 5 mL deionized water at the bottom of the 100 mL flask and add slowly 91.74 mL concentrated HCl (37% HCl). Then, add water to the volumetric flask until the total volume. Mix thoroughly.
- 6 M HCl: For 100 mL solution add around 40 mL deionized water at the bottom of the 100 mL flask and add slowly 49.67 mL concentrated HCl (37% HCl). Then, add water to the volumetric flask until the total volume. Mix thoroughly.
- 4.5 M HCl: For 100 mL solution add around 50 mL deionized water at the bottom of the 100 mL flask and add slowly 37.19 mL concentrated HCl (37% HCl). Then, add water to the volumetric flask until the total volume. Mix thoroughly.
- 0.05 M HCl: For 100 mL solution add around 60 mL deionized water at the bottom of the 100 mL flask and add slowly 413 µL concentrated HCl (37% HCl). Then, add water to the volumetric flask until the total volume. Mix thoroughly.
- 5 M NaCl in 0.05 M HCl: For 100 mL solution add around 60 mL deionized water at the bottom of the 100 mL flask and add slowly 413 µL concentrated HCl (37% HCl).

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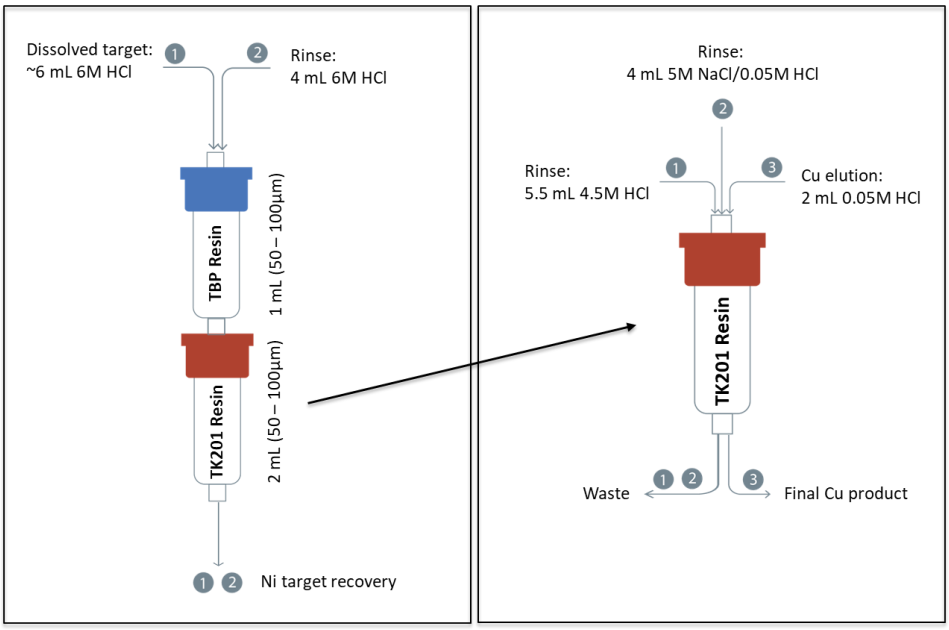
Then, add 29.22 g NaCl and stir until NaCl has been completely dissolved. Finally, add water to the volumetric flask until the total volume. Mix thoroughly.

7. Procedure

a. Graphical scheme



b. Sample preparation

1. Ni target irradiation on a cyclotron
2. Dissolution Ni target:
3. Add 3 mL 1:1 7 M HCl: 30% H_2O_2 over the Ni target surface at a temperature around 60°C.
4. Add 3 mL 11.1 M HCl while bubbling with air to ensure dissolution
5. Transfer the dissolved Ni target to the synthesizer using a peristaltic pump at 1 mL/min

c. Radiochemical separation

1. Add 7 mL H_2O and 6 mL 11.1 M HCl to condition the stacked columns
2. Load the ~ 6mL Ni dissolved target onto the stacked columns. The solution collected after loading is placed in a Ni recovery vial
3. Rinse with 4 mL 6 M HCl to enhance Ni recovery. The solution collected after rinsing is placed in a Ni recovery vial
4. Separate both TBP and TK201 Resins columns to proceed with Cu separation

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5. In the TK201 column, add 5.5 mL 4.5 M HCl to elute most of Co that might be present. The solution collected after rinsing is placed in a waste vial
6. Add 4 mL 5 M NaCl in 0.05 M HCl to reduce the amount of residual acid on the resin and remove remaining Co. The solution collected after rinsing is placed in a waste vial.
7. Add 2 mL 0.05 M HCl to elute quantitatively Cu. The solution collected after adding the diluted HCl is the final product which will be further used for radiolabelling.

d. Sample measurement

1. For the optimization of this method, trace metal standards were used and measured with ICP-AES (other techniques might also be used for their quantification).
2. Gamma-ray spectrometry was used to quantify the activity of ^{61}Cu and ^{58}Co produced by irradiating Ni targets.
3. Chemical recovery evaluation: the chemical yield reported in Svedjehed et al. (Svedjehed et al., 2020) was 90.4 ± 3.2% (*N*=5) in regards of the chemical separation. The total time reported for the Ni target dissolution together with the chemical separation was 65 ± 3 min. The presence of potential 58Co produced during the irradiation was evaluated after separation, reporting a ratio of (8.3± 0.6)x10^{-5}%, which means a factor of 500 times more Cu than Co.

⚠ **Note**: CU Sheets (Svedjehed et al., 2022; TrisKem International, 2024) may be used for the quantification of free Cu isotopes vs labelled Cu isotopes using a TLC scanner.

8. References

Svedjehed, J., Bas, M., Happel, S., & Gagnon, K. (2022). *New extractant-impregnated iTLC-SG paper facilitates improved TLC analysis for Cu radiolabelled peptides*. https://www.triskem-international.com/posters-and-presentations.php

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