Cyclotron-based production of ^{68}Ga,[^{68}Ga]$GaCl_3$, and [^{68}Ga]Ga-PSMA-11 from a liquid target -V 1.0 03/12/2024-TKI-GA01

1. Scope

This method aims to separate ^{68}Ga from liquid Zn targets in order to obtain a pure isotope suitable for labelling.

2. Summary

The reported method is based on the publication of Rodnick et al. (Rodnick et al., 2020). The main goal was to extract ^{68}Ga from liquid Zn targets. Moreover, the main focus was not only to obtain an interference-free Ga product but also a product suitable for radiolabelling reactions (e.g. with PSMA-11). For the chemical separation of Ga from matrix elements, a cassette-based approach using two different cartridges sequentially, ZR Resin (TrisKem International, 2016) and TK200 Resin (TrisKem International, 2018), was employed. By using this approach, the on-line cartridge conditioning, the use of smaller amounts of acid and the exclusion of organic solvents and/or base-mediated pH adjustments was achieved. The complete radiochemical separation procedure led to chemical yields ranging from 87% to 93%. The final product was obtained in around 1-2 mL water plus dilute HCl to achieve desired formulation, suitable for further radiolabelling.

3. Significance of use

This is a fast and automated method to obtain highly pure ^{68}Ga from liquid Zn targets using a cassette-based approach. The same cartridge combination (ZR Resin and TK200 Resin) may also be used for solid Zn targets, however conditions need to be optimized accordingly.

4. Interferences

Since Zn is the target element which will be irradiated to produce ^{68}Ga, Zn was the main interference investigated. Additionally, enriched Zn liquid targets may contain some iron (1-3 ppm) which have also to be considered in regards of the chemical separation.

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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 employed
- Peristaltic pump
- Cassette reagent vials
- Cassette collection vials
- N_2 gas
- 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.

- 2 mL ZR column (50-100 µm) (TrisKem International, France)
- 2 mL TK200 column (50-100 µm) (TrisKem International, France)
- 69% HNO_3
- 37% HCl
- NaCl salt
- Milli-Q water

b. Preparation of solutions

- 0.1 M HNO_3: For 100 mL solution add around 70 mL deionized water at the bottom of the 100 mL flask and add slowly 625 µL concentrated HNO_3 (70% HNO_3). Then, add water to the volumetric flask until the total volume. Mix thoroughly.
- 1.75 M HCl: For 100 mL solution add around 50 mL deionized water at the bottom of the 100 mL flask and add slowly 14.58 mL concentrated HCl (37% HCl). Then, add water to the volumetric flask until the total volume. Mix thoroughly.
- 2 M NaCl/0.13 M HCl: For 100 mL solution add around 60 mL deionized water at the bottom of the 100 mL flask. Then, add 17.53 g NaCl and stir until NaCl has been completely dissolved. Finally, add water to the volumetric flask until the total volume. Mix thoroughly.

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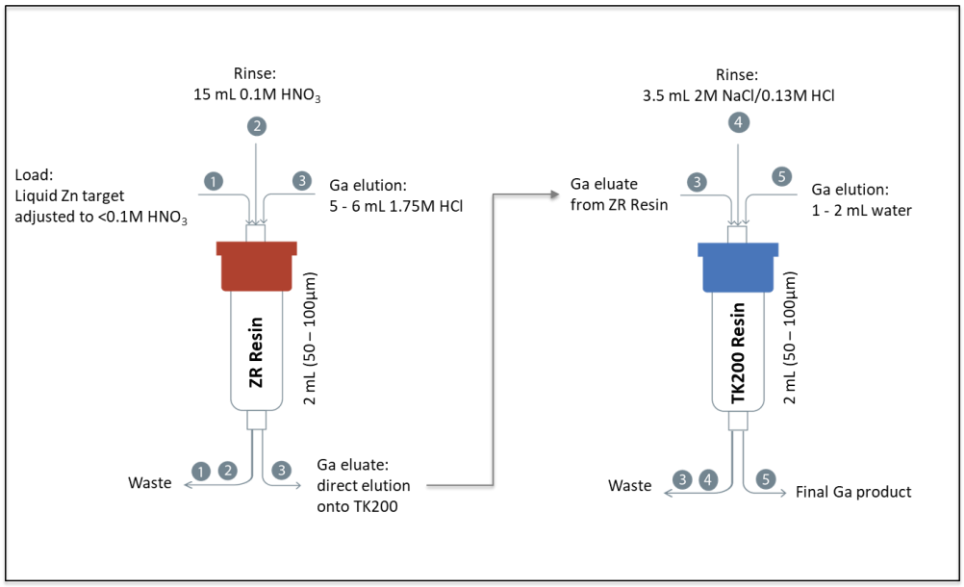
7. Procedure

a. Graphical scheme



b. Sample preparation

1. Liquid Zn target irradiation on a cyclotron
2. Transfer the liquid Zn target solution into a 10 mL V-vial which is directly connected to the synthesizer
3. Dilution of the Zn target solution with water to <0.1 M HNO_3
4. Load diluted Zn target onto the synthesizer cassette using nitrogen overpressure

c. Radiochemical separation

1. Conditioning of the two different cartridges:
    a. Add 7 mL 0.1 M HNO_3 to ZR Resin
    b. Add 7 mL water and 4 mL 1.75 M HCl to TK200 Resin
2. Use nitrogen overpressure to load the target solution onto the cassette (ZR Resin cartridge)
3. Add 15 mL 0.1 M HNO_3 onto ZR Resin in order to remove any possible interference
4. Add 5-6 mL 1.75 M HCl to elute Ga and directly load it onto the already preconditioned TK200 Resin
5. Add 3.5 mL 2 M NaCl in 0.13 M HCl onto the TK200 Resin
6. Finally, to elute Ga add 1-2 mL water followed by a few mL diluted HCl to yield desired formulation (e.g. 5 mL 0.1 M HCl)
7. Solution may be prepared e.g. for PSMA-11 labelling

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8. References

Rodnick, M. E., Sollert, C., Stark, D., Clark, M., Katsifis, A., Hockley, B. G., Parr, D. C., Frigell, J., Henderson, B. D., Abghari-Gerst, M., Piert, M. R., Fulham, M. J., Eberl, S., Gagnon, K., & Scott, P. J. H. (2020). Cyclotron-based production of 68Ga, [68Ga]GaCl3, and [68Ga]Ga-PSMA-11 from a liquid target. *EJNMMI Radiopharmacy and Chemistry*, *5*(1). https://doi.org/10.1186/s41181-020-00106-9

TrisKem International. (2016). *Product sheet ZR Resin*. https://www.triskem-international.com/catalog/products/resins-and-accessories/zr-resin/bl,product,424,0

TrisKem International. (2018). *Product sheet TK200 Resin*. https://www.triskem-international.com/catalog/products/resins-and-accessories/tk200-resin/bl,product,423,0

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