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The production of ^{82}Sr using larger format RbCl targets

N.P. van der Meulen, T.N. van der Walt, G.F. Steyn, H.G. Raubenheimer

[a] *iThemba LABS, PO Box 722, Somerset West 7129, South Africa*
[b] *Cape Peninsula University of Technology, Faculty of Applied Sciences, PO Box1906, Bellville 7535, South Africa*
[c] *University of Stellenbosch, Department of Chemistry, Private Bag X1, Matieland 7602, South Africa*

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^{82}Sr is produced by the proton bombardment of a larger RbCl target using a 66 MeV beam at 250 mA.
^{82}Sr is separated from the target material using chromatographic methods on Purolite S950.
A further purification step is performed using AG MP-50 macroporous cation exchange resin.
The final product has a high radionuclidic purity and negligible Rb and Fe impurity content.

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a b s t r a c t

The production of ^{82}Sr at iThemba LABS is performed by the proton bombardment of a RbCl target using the facility's Vertical-Beam Target Station (VBTS). ^{82}Sr is separated from the target material using a method based on target dissolution, using dilute ammonium chloride solution, and the use of chromatographic methods on Purolite S950 ion exchange resin. After performing a further purification step using AG MP-50 macroporous cation exchange resin, the result is a product with a high radionuclidic purity and negligible Rb and Fe impurity content.

1. Introduction

^{82}Sr ($t_{1/2}$ ¼ 25.55 d), which can be produced by means of a cyclotron, is currently a sought after commodity for use in medical generators, with a growing world demand driven, particularly, by cardiologists in North America. It decays purely by electron capture (Qaim et al., 2007) into its daughter, ^{82}Rb ($t_{1/2}$ ¼ 75 s), which behaves physiologically like potassium and is effective for myocardial infusion imaging studies of patients with the use of Positron Emission Tomography (PET) (Mullani et al., 1983; Saha et al., 1990). PET can be used as a technique to monitor coronary disease patients, particularly as it has better image resolution and image contrast than its Single Photon Emission Computed Tomography (SPECT) counterpart (Sylvester et al., 2004). ^{82}Rb is also used in the measurement of blood–brain barrier permeability (Brooks et al. 1984).

Due to the fact that ^{82}Rb has such a short half-life, it can be injected into the patient at 10 min intervals, with a minimum amount of damage to the patient, as well as hospital staff treating the patient (Fabbender et al. 2004; Vereshchagin et al., 1993). It justifies the use of a generator, where ^{82}Sr is loaded on to an ion exchange resin and the daughter ^{82}Rb is milked from it when required. A number of different ion exchange resins have been used for this type of generator over the years. Grant et al. (1975) reported using Chelex 100 when developing a ^{82}Sr/^{82}Rb generator, while (Yano et al., 1977,1979) performed comparisons between Chelex 100 and Bio-Rex 70 ion exchange resins. The use of tin oxide as an exchanger for this type of system appears to be the most popular type available these days; Brihaye et al. (1987), Alvarez-Diez et al. (1999) and Klein et al. (2007) being just three of many to report the use of such a generator. Sylvester et al., (2004), however, reported the use of sodium nonatitanate as a replacement for tin oxide as substrate for the ^{82}Sr/^{82}Rb generator.

The ^{82}Sr product has been obtained from various routes, namely, spallation reactions on molybdenum metal targets (Phillips et al., 2000), enriched ^{85}Rb metal targets (Cackette et al., 1993; Qaim et al., 2007) and natural Rb salts in the form

[n] Corresponding author at: iThemba LABS, PO Box 722, Somerset West 7129, South Africa. Tel.: þ27 21 8431295; fax: þ27 21 8433901.
E-mail address: nick@tlabs.ac.za (N.P.v.d. Meulen).

of RbCl (Mausner et al., 1987; Vereshchagin et al., 1993; Aardaneh et al., 2006). While the use of enriched Rb is the more popular choice of material, it is expensive and the recovery of target material for further production use is cumbersome.

A recommended excitation function for the production of ^{82}Sr via proton-induced reactions on ^{nat}Rb was published in 2001 by the Nuclear Data Section (NDS) of the IAEA (Gul et al., 2001, IAEA-TECDOC-1211). In that publication, the NDS recommended that new data for this reaction ought to be measured. An updated evaluation was posted on the NDS web site (http://www-nds.iaea.org/medportal) in 2003, including all data available up to the end of 2002. This is the only evaluation for that reaction on the NDS web site. A later evaluation was, however, performed by Qaim et al. (2007) which also included the data of Kastleiner et al. (2002) and Buthelezi et al. (2006). This latter recommended excitation function has a maximum of approximately 10% higher than the 2003 recommendation currently available on the NDS web site.

As the impurity ^{85}Sr is a bone of contention with the production of ^{82}Sr, it can be noted that the impurity can be kept to 12% when using ^{85}Sr as target material in a 70 MeV cyclotron, while the impurity can be kept below 20% when using ^{nat}Rb and a cyclotron greater than 60 MeV. It is important to have the ratio of ^{85}Sr/^{82}Sr less than 5, as a generator cannot be used for medical purposes if the ratio is greater than specified above (Cackette et al. 1993).

Ironically, the requirement for the production of ^{82}Sr is similar to that of the generator requirements, that is, for the Sr to be retained by the resin and the Rb to be easily eluted. As a result, many productions have been reported using Chelex 100 chelating resin (Qaim et al., 2007; Phillips et al., 2000; Mausner et al., 1987; Cackette et al. 1993). Sylvester et al. (2006) recently reported a separation method of ^{82}Sr from its target material using sodium nonatitanate resin, following their report of using the same material as resin for a ^{82}Sr/^{82}Rb generator. Vereshchagin et al. (1993) performed their production using Dowex-1 anion exchange resin, while Van der Walt and Vermeulen (2004) and Aardaneh et al. (2006) produced papers indicating the use of Purolite S950 as their resin of choice.

iThemba LABS makes use of a 66 MeV primary proton beam for all its routine radionuclide productions. With the Vertical Beam Target Station (VBTS) having been put into service for the production of longer-lived radionuclides, considerably higher beam intensities can be utilised, nominally 250 mA over extended periods of bombardment, in contrast to a maximum of 100 mA previously. The main advantage of higher beam intensity is, of course, a higher production rate. Unfortunately, higher beam intensity also results in more energy dissipated in the target volume in the form of heat. The removal of the heat requires a larger surface in contact with a cooling medium (in this case fast flowing water). In practice, the RbCl salt is contained in a suitable metal capsule to prevent direct contact with the cooling water. Since the target thickness is determined by the required production energy window, it is not a parameter which can be adjusted to increase the contact surface. Instead, the target diameter has to be increased. This results in larger targets and consequently more target material to be processed. The different sizes of the old target and a new VBTS target are shown in Fig. 1.

2. Experimental

Analytical grade reagents were used throughout this work and were obtained from Merck (SA) Pty. Ltd. or Sigma Aldrich GmbH, which included Sigma, Aldrich, Fluka and Riedel de Haen products. The Purolite S950 chelating resin used in this work was obtained from Purolite International, United Kingdom.

Fig. 1. Encapsulated RbCl targets for ^{82}Sr production. Both targets have nominally the same thickness but different diameters (outer diameters of 23 and 40 mm respectively). RIGHT: these capsules, made of aluminium, were used for many years at iThemba LABS to irradiate RbCl with a 66 MeV proton beam, up to a maximum beam current of 100 mA. LEFT: the new VBTS targets utilise stainless steel capsules, which are irradiated with a 66 MeV beam of nominally 250 mA. The increased surface area is necessary to effectively dissipate the increased heat load generated by the beam (see text).

Wherever water is referred to in the experimental descriptions, de-ionised water was used. This was obtained by de-ionising tap water using a Millipore MilliQ Reagent Grade Water System to a conductivity of greater than 10 MO cm ^{1}.

All radioactive determinations were performed using a standard calibrated HPGe detector, with a relative efficiency of 8% (relative to three inch NaI), connected to a multichannel analyser. 10 g (Experiment 1), 20 g (Experiment 2) and 32 g (Experiment 3) of RbCl salt was weighed out. Each aliquot was treated in the following manner: the salt was dissolved in 200 mL 0.5 M ammonium chloride, containing 5% methanol and 0.1 g o-phenanthroline monohydrate (to increase the distribution coefficient of Sr for a more effective separation). Tracer activity was added to the solution in the form of ^{85}Sr and ^{84}Rb and the solution activity measured.

The resultant solution was loaded through a column (1.0 cm internal diameter) filled to 9 cm^3 with Purolite S950, lightly crushed to increase the mesh size, and equilibrated with 50 mL 0.5 M ammonium chloride at a pH of 8. The elements in the solution were washed onto the resin using a further 50 mL 0.5 M ammonium chloride.

The Rb was eluted from the resin column using 150 mL 0.5 M ammonium chloride, before the column was rinsed with 100 mL water to remove any traces of ammonium chloride. The final product was eluted with 50 mL 2 M HCl. Two production runs were performed using bombarded RbCl targets once the experimental runs were completed, the first being a 8 g target and the second a 30 g target with 12000 mAh beam time placed on it.

3. Results and discussion

Each of the three experiments performed were done so with success. The results of the experiments, as well as that of two production yield studies, are listed below in Table 1.

The Purolite S950 resin was lightly crushed to increase the mesh size, as well as increase the number of exchange sites while allowing the solution to take longer to run through the column. While lightly crushed, it was separated using a molecular sieve to obtain a pore size between 100 and 200 mesh. Previous experiments using the 50 mesh size resin produced undesirable results. The separation results with the ''manipulated'' resin were reproducible.

Table 1
Percentage impurity removal and percentage product yield using Purolite S950 resin.

|	Tracer experiment 1	Tracer experiment 2	Tracer experiment 3	Production yield run 1	Production yield run 2
Sr removal in load step (%)	0	0	0	0	5.662
Rb removal in load step (%)	96.993	94.495	95.178	96.532	95.566
Sr removal in intial rinse step (%)	0	0	0	0	0
Rb removal in initial rinse step (%)	3.007	5.505	4.822	3.468	4.434
Sr removal in wash steps (%)	0	0	0	0	0
Rb removal in washsteps (%)	0	0	0	0	0
^{82}Sr yield (%)	100	100	100	100	94.338
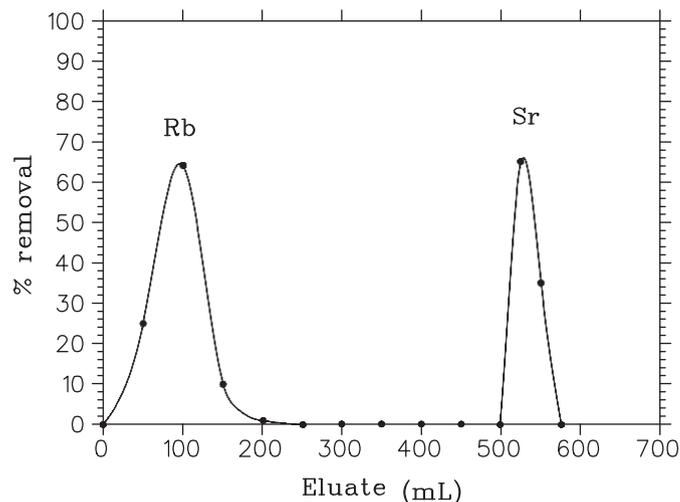
Fig. 2. Elution curves of ^{82}Sr and ^{84}Rb from Purolite S950 using 0.5 M NH$_4$Cl and 2.0 M HCl.

The difference in results between the two production runs is due to the types of encapsulation used for the target material. The first production run was performed using a 8 g RbCl target encapsulated in aluminium, bombarded using the routine production bombardment station, while the second production run was performed using a 30 g RbCl target encapsulated in stainless steel, bombarded using the Vertical Beam Target Station at iThembaLABS.

The aluminium target capsule was removed when cut open, while facilities prevented the larger stainless steel capsule to be cut open successfully and it had to be punctured such that the target could be dissolved. As a result, the dissolution of the target material in Production Yield Study 2 turned a shade of orange, due to the o-phenanthroline monohydrate binding with iron and other impurities and, when loading the solution on to the Purolite S950 resin, the impurities may have interfered with the ^{82}Sr being retained by the resin, resulting in the loss of 5.6% in the load step. The remainder of the product was successfully retained by the resin and eluted using the 2.0 M HCl. Although much of the colour was removed in the rinse steps of the production, there was still some colour in the final product, even when it was evaporated to dryness and picked up in 5 mL 0.1 M HCl.

Phillips et al. (2000) reported a similar tendency in their separations. In this work, it may also have been due to the o-phenanthroline monohydrate increasing the iron distribution coefficient for the chemical separation (Iyer and Venkateswarlu, 1976), and the following method was employed to overcome this. The ^{82}Sr product was evaporated to dryness and the salts dissolved in 100 mL 2.0 M HCl-70% methanol. The solution was pumped through a column containing 10 mL AG MP-50 macroporous cation exchange resin (equilibrated with 50 mL 2.0 M HCl-70% methanol). The elements were washed onto the resin using a further 50 mL 2.0 M HCl-70% methanol.

The impurities (Fe, Mn, Ni, Al and Cr) were eluted from the resin column using 50 mL 3.0 M HCl-45% methanol, before the ^{82}Sr final product was eluted from the column with 50 mL 4.0 M HNO$_3$. This was evaporated to dryness, before the final product was picked up in 0.1 M HCl.

The activity of ^{82}Sr was determined using the 776.5 keV g-ray peak, of the ^{82}Rb daughter which is in equilibrium with the parent after about three days after EOB. It was determined that the final product, other than the initial loss in the load step, was intact and devoid of impurities (A sample of the product was allowed to decay, before it was tested utilising a JY Ultima Inductively Coupled Plasma instrument). The two Production Yield Runs produced 25 mCi and 40 mCi, which were in agreement with the thick target yield excitation function (Qaim et al., 2007).

From the tracer experiments and production yield runs performed elution curves of Rb and ^{82}Sr were plotted (Fig. 2).

Aardaneh et al. (2006) briefly described a method to produce ^{82}Sr comparing Chelex 100 and Purolite S950 chelating resins. While the authors determined Purolite S950 to be the resin of choice for their work, it differs from this work in that a 7 g target was used, while this work involved the use of a 30 g RbCl target. The main difference, however, was the fact that they used an ''open'' system using their ion exchange method, that is, applying gravity flow use of the column by dripping the solution into the column from the top at a pump rate of 2 mL/min maximum. This work uses a ''closed'' system use of ion exchange, in that the column was sealed using a sinter on either end of the column and a Teflon plunger on one side. This allowed the resin to remain wet at all times, while being able to increase the pump speed up to 5 mL/min without any side effects. The use of a ''closed'' system is also regarded as a safer method of performing a production, as any losses due to a broken tap or burst line can be kept to a minimum, while there is a danger of losing all of one's activity that happens when using an open gravitational system.

Cackette et al. (1993) described a method using Rb metal as target material over RbCl, due to the salt target having a tendency of failing. The hot cell production method of processing the target involved dissolving the target in n-butanol after piercing it in the processing hot cell, all taking place in a glass vessel purged with argon, before being processed further by means of ion exchange. It has been determined that this method is not favourable for use at iThemba LABS, due to budgetary constraints, and the method used in this work is preferred.

4. Conclusion

A method was developed to effectively separate ^{82}Sr from the RbCl target material, producing a yield of over 94% of ^{82}Sr. While the purification step is rather time-consuming, a second column setup was relatively easily addressed. The final evaporation step had to be addressed in a separate hot cell, but logistics can address the issue should be the production commence as a commercial entity.

The production method utilised in this work was more effective, being a closed system, with the column being sealed and the flow rate being determined by pump speed (up to 5 mL/min) instead of gravity flow using an open system.

The final product was determined to be of high purity, with only ^{85}Sr/^{82}Sr found in the product, making it radiochemically pure, with the ratio of ^{85}Sr/^{82}Sr found to be less than 4. The purification step ensures that there is no iron contamination, making the product ideal for use in ^{82}Sr/^{82}Rb generators.