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RESEARCH ESTABLISHMENT

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AN IMPROVED DISTILLATION SEPARATION FOR THE PRODUCTION OF FLUORINE-18 FROM REACTOR IRRADIATED LITHIUM CARBONATE

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ABSTRACT

A process is described whereby ^{18}F of pharmaceutical quality can be rapidly isolated from irradiated lithium carbonate by distillation under controlled conditions. By this method a consistent, high yield of ^{18}F can be obtained in a solution containing reproducible concentrations of sodium sulphate and carbonate.

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Figure 1 ^{18}F Distillation Apparatus

1. INTRODUCTION

Fluorine-18, which has the longest half life ($T_{½}$ 110 min.) of the nuclides of fluorine, is commonly produced in particle accelerators by the reactions:

^{16}O (^{3}He,p) ^{18}F

^{16}O (^{4}He,pn) ^{18}F

or ^{16}O (^{4}He,d) ^{18}F

where oxygen or its compounds such as water are used as the target material. Multicurie quantities of ^{18}F free from contaminating nuclides can be produced readily in this way and may be isolated by simple chemical procedures.

However at nuclear centres where a cyclotron or other suitable particle accelerator is not available there must be recourse to the neutron irradiation in a reactor of compounds containing ^{6}Li and ^{16}O to produce ^{18}F by the following sequence of reactions:

^{6}Li (n, ^{4}He) ^{3}H

^{16}O (^{3}H, n) ^{18}F

The disadvantages of this method lie in the low yield of ^{18}F from the secondary reaction and the production of tritium in the irradiated target. For pharmaceutical applications it is particularly important that ^{18}F be separated from tritium. Fluorine-18 produced in this manner has been isolated either by distillation from an acid solution, by absorption on a bed of the hydrous oxides of aluminium, magnesium or zirconium, by coprecipitation on compounds such as lead chloride (Banks 1955), calcium hydroxide (Banks 1955) or lithium hydroxide (Dworkin and La Fleur 1966) or by solvent extraction (Bowen and Rood 1966).

The problems encountered in the production of ^{18}F by absorption on hydrous zirconium oxide and by distillation are reported here. This work also describes experiments leading to the development of the optimum condition for the isolation of ^{18}F by distillation.

1.1 Problems Arising in the Separation on Hydrous Zirconium Oxide

Fluorine-18 had been produced at the AAEC Research Establishment by adsorption on hydrous zirconium oxide from an acid lithium chloride solution prepared from irradiated lithium carbonate. Whilst at the low activity level this process had advantages of speed and consistency of yield, problems arose on scaling up to 100 mCi per batch. The principal problems were:

(i) Difficulty was experienced frequently in removing the target material (lithium carbonate enriched to 40% ^{6}Li) from the irradiation capsule of welded titanium because the considerable nuclear heating occurring during the irradiation had sintered the original free flowing powder into a hard mass.

(ii) Scaling up by increasing the target mass resulted in a larger volume of lithium chloride solution to be passed through the hydrous zirconia column. There was a proportionate increase in the time required to absorb the ^{18}F in the column and consequently losses due to radioactive decay increased with the scale of the operation. Attempts to reduce the time taken by this step by using a smaller volume of a higher concentration of lithium chloride with an increase in the size of the bed of hydrous zirconia were only partially successful and the yield of ^{18}F became variable from batch to batch.

Since the very desirable properties of speed and reproducibility on which the process of ^{18}F absorption on hydrous zirconia had been preferred were no longer applicable a reappraisal was made of the isolation of ^{18}F by distillation.

1.2 Fluorine-18 Separation by Distillation

Fluorine-18 has been isolated from irradiated lithium compounds by distillation from acid solution either as fluosilicic acid in glass apparatus (Thomas et al. 1965; Dunsen et al. 1971) or as hydrofluoric acid in teflon apparatus (Meier-Borst and Sin 1968). In previous work at the AAEC Research Establishment (Robson 1968) it had already been shown that distillation was the more suitable process to isolate ^{18}F from larger quantities of irradiated lithium compounds because the rate of distillation from sulphuric acid solutions increased with the concentration of lithium salts. However the major difficulty had been to regulate the process to give a distillate containing a reproducible minimum quantity of sulphuric acid and a ^{18}F product of consistent quality. The experiments reported here were conducted to establish the optimum conditions for a simple and reliably efficient process by which the distillation method could be applied to the large scale separation of ^{18}F.

2. EXPERIMENTAL

2.1 Lithium Carbonate Irradiations

Titanium capsules, sealed by welding and each completely full and containing 0.75 g of lithium carbonate (^6Li abundance 40%), were irradiated in the X-33 facility in HIFAR at a thermal neutron flux of about 5×10^{13} neutrons cm^{-2} s^{-1} for 6 hours.

2.2 Distillation Apparatus (Figure 1)

A 100 ml round bottom glass flask was constructed with an integral still head leading directly into a receiver: the receiver had a capacity of 20 ml and was designed for efficient scrubbing of the vapour stream issuing from the still. Access to the flask for the addition of target capsules (opened at one end) was provided through a spherical joint. The corresponding ball joint which functioned as a stopper was fitted with a gas inlet tube extending to below the liquid level of the flask. The temperature of the flask contents was monitored by an iron-constantan thermocouple placed in a thermometer pocket in the flask wall.

2.3 Fluorine-18 Separation Procedure

A minimum of 2 ml of 1 M sodium bicarbonate solution was added to the receiver and was sufficient to cover the end of the outlet from the still flask. Irradiated lithium carbonate was added to the still flask followed by the particular acid selected for the experiment (see Sections 3.2.1 and 3.2.3(a)). The flask was immediately stoppered, a steady stream of nitrogen passed through the contents then the flask was heated by an infra red heater. Distillation was carried out until the contents of the flask had reached the maximum temperature selected for the experiment (see Section 3.2.3(b)). The receiver contents were then evaporated to dryness to remove any tritium and the residue was dissolved in water. This solution was removed for measurement of the ^{18}F content in a 4π gamma ionisation chamber.

3. RESULTS AND DISCUSSION

3.1 Fluorine-18 Produced in Target Material

The irradiation of each capsule of lithium carbonate resulted in the formation of 60–75 mCi of ^{18}F per g of target material at the time of removal from the reactor. The amount of ^{18}F produced in each capsule could not be increased by using a higher abundance of ^6Li because first sintering took place, then at > 60% ^6Li abundance the target material melted due to the intense nuclear heating effect. Consequently the production of ^{18}F could be increased only by the irradiation of more lithium carbonate, up to the limit of reactor space available.

3.2 Fluorine-18 Separation by Distillation

In Australia pharmaceutical preparations of ^{18}F have been shipped frequently by air over long distances to the medical centres where they were to be used. Consequently the production schedule for this short lived nuclide was linked to the airline timetables and the isolation and preparation of ^{18}F in a form suitable for intravenous injection had to be completed within a predetermined period.

Because of the exigencies involved in the supply of ^{18}F the process by which it is prepared must consistently yield the maximum activity at the time of shipment. The achievement of the highest separation efficiency does not necessarily result in the highest yield of ^{18}F if the time required for the process leads to losses by radioactive decay. In this work it was found that approaching 100% of ^{18}F could be isolated by distillation from sulphuric acid solution and this was a more efficient separation than obtained by the chromotographic method on hydrous zirconium oxide. However, although a major portion of the ^{18}F was rapidly distilled, it was clear that the additional time required to isolate more than 80–85% of the ^{18}F resulted in a lower activity due to losses by radioactive decay.

The optimum conditions leading to a maximum ^{18}F activity were therefore selected as a compromise where a less than 100% efficiency for the distribution separation was compensated by smaller decay losses occurring in the more rapid isolation. Where possible the experimental technique was refined to reduce delays between steps in the process, e.g. by preheating all electrical heaters so they were ready for immediate use. The experimental results of an examination of a number of the factors involved in the distillation method are considered individually below.

3.2.1 Choice of Acid for Distillation

Only acids with low vapour pressures and non toxic salts were considered suitable for distilling ^{18}F because, although it was expected that some acid would be distilled, it was desirable that this should be a minimum to avoid the excessive accumulation of salts in the receiver.

Initially distillation from sulphuric and orthophosphoric acids was examined. However, it was found that considerably more acid reached the receiver when distilling from phosphoric than from sulphuric acid solutions. As orthophosphoric acid is known to be partially converted to the more volatile pyro and metaphosphoric acids at temperatures exceeding 200 °C (Bolineff 1910, 1917) the appearance of significant quantities of acid in the distillate can be attributed to the formation of some condensed phosphoric acids. Consequently all distillations were carried out from sulphuric acid solution in further work.

3.2.2 Addition of Lithium Carbonate to the Still

It was discovered that the presence of titanium did not reduce the efficiency of ^{18}F distillation so that it was possible to add the open capsules of irradiated lithium carbonate directly to the still. Although the time previously required to remove the irradiated target material from the capsules had been eliminated it was necessary to extend the distillation period over 15 minutes to allow sufficient time for the still acid to react with the contents of the capsule.

3.2.3 Distillation

(a) Still Acid Concentration

When 5.25 g of irradiated lithium carbonate (7 capsules) dissolved in 30 ml of 50 vol.% sulphuric acid was distilled, 62% of the ^{18}F was separated in 20 minutes (increasing to 77% after 40 minutes); the volume in the receiver exceeded 12 ml and tended to overflow with the gas stream through the apparatus. However, when the distillation was carried out from 40 ml of 75 vol.% sulphuric acid then 75% of the ^{18}F was distilled in 20 minutes, rising to 87% after a further 10 minutes.

Under the latter conditions the yields were found to be reproducible and the volume of liquid remaining in the receiver at the end of the distillation was less than 7 ml.

(b) Control of Distillation

An additional expedient adopted to reduce the distillation time was the separate addition to the still of the required volumes of water and concentrated sulphuric acid. This achieved an immediate temperature rise to 120–150 °C and by positioning an infra red heater under the flask, distillation was started with the minimum delay.

When distillation was continued until the still temperature reached 230 °C, the amount of acid distilled had neutralised 3 ml of 1 M sodium bicarbonate solution in the receiver and about 80% of the ^{18}F had been distilled. By distilling only up to 220 °C and with 4 ml of 1 M sodium bicarbonate solution in the receiver a consistent yield of 75–80% of the ^{18}F could be obtained in 15 minutes and the receiver contents remained alkaline.

Occasionally traces of sulphuric acid from the still would adventitiously reach the receiver in quantities sufficient to acidify the contents. Therefore, 0.1 ml of 0.1% bromothymol blue indicator was added to the receiver before distilling to provide a means of pH monitoring. Additional sodium bicarbonate solution could thus be added if the receiver solution approached neutralisation.

3.2.4 Processing of the Distillate

Provided the receiver contents remained alkaline, ^{18}F was efficiently absorbed from the gas stream out of the still. However, because the still was not followed by a condenser before the receiver and also because the temperature of distillation and consequently the gas stream from the still exceeded 150 °C, the temperature of the receiver contents rose to close to boiling during the isolation of ^{18}F. Under these conditions there was evaporation of water from the receiver without the loss of ^{18}F and the volume remaining at the end of the distillation was 5–6 ml. Although much of the water removed from the still flask during distillation was evaporated from the receiver some of the tritium originating from the nuclear reaction of ^{6}Li was found to remain in the receiver contents. By transferring the receiver contents to a small beaker and evaporating to dryness a residue containing only about 50 μCi of tritium per 350 mCi of ^{18}F (ex reactor) resulted.

The residue from the evaporation consisted of ^{18}F, sodium sulphate and sodium carbonate with bromothymol blue indicator. To prepare a solution of ^{18}F for pharmaceutical use the residue was dissolved in water, at the rate of 4.2 ml per ml of 1 M sodium bicarbonate used in the receiver, to obtain an isotonic solution which was finally passed through a Millipore filter before dispensing.

3.3 Routine Production of Fluorine-18 by Distillation

The distillation process was employed for routine daily production of ^{18}F and consistent 70% yields were obtained by distilling until a still temperature of 210 °C had been reached. Under these conditions only 30 minutes was required from receiving seven capsules of irradiated lithium carbonate to dispensing the ^{18}F product. After completing the process the still flask was placed in storage for a few days to allow the residual radioactivity of the irradiation capsules to decay and a replacement still flask was substituted for each new preparation.

4. REFERENCES

Banks, H.O. (1955). – Nucleonics 13, 62.

Bolineff, D. (1910). – Zeit Inorg. Chem. 67, 234.

Bolineff, D. (1917). – Zeit Inorg. Chem. 102, 34.

Bowen, L.H. and Rood, R.T. (1966). – J. Inorg. Nucl. Chem. 28, 1985.

Dunsen, G.L., Crofford, W.C., Hosain, F., Jones, A.E. and Mellor, M.K. (1971). – Nucl. Med. 10, 256.

Dworkin, H.J. and La Fleur, P.D. (1966). – J. Am. Med. Assoc., 198, 985.

Meier-Borst, W. and Sin, H. (1968). – Nucl. Med. 7, 396

Robson, J. (1968). – AAEC/TM435.

Thomas, C.C. Jr., Sondel, J.A., Kerns, R.C. (1965). – Intern. J. Appl. Rad. Isot. 16, 71.

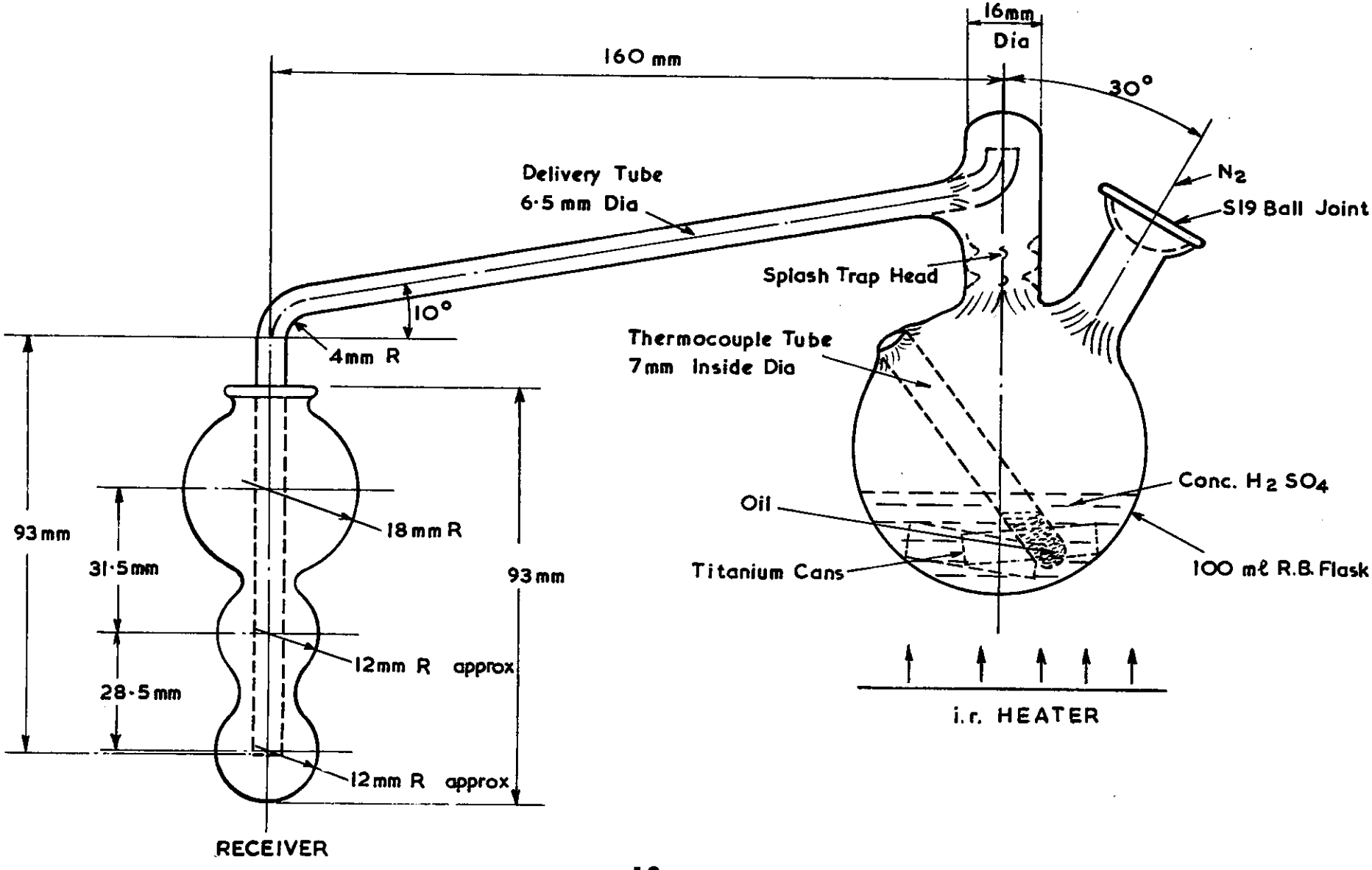

FIGURE 1. ^{18}F DISTILLATION APPARATUS