Development of Aluminium-26 as a Tracer for Biological Research

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Abstract

The tandem accelerator at Daresbury Laboratory has been used in the development of accelerator mass spectrometry for aluminium absorption experiments in humans. By fully stripping the final ions, the method avoids the problem of background from the intense flux of the isobar ^{26}Mg. Also, the use of ultrathin ion source preparations minimises the ^{26}Al dose and the amount of biological material needed for a measurement. Currently, the ^{26}Al detection limit is about 10^{-18} gram and the ratio $^{26}Al/^{27}Al \sim 10^{-13}$. Preliminary biological studies include measurement of the uptake and identification of aluminium carrier proteins in blood, and the rate of aluminium elimination in humans.

1 INTRODUCTION

The ultrasensitive analysis technique of accelerator mass spectrometry (AMS) has been developed at Daresbury Laboratory using the Nuclear Structure Facility (NSF) tandem accelerator and is being applied to the detection of the radioisotope ^{26}Al for use as a tracer in biological investigations.

The toxicity of aluminium to living organisms is now generally recognised. It is implicated as a cause of serious conditions in renal patients and there is a suggestive correlation between aluminium accumulation in the brain and Alzheimer's disease. It is detrimental to plants and aquatic life and is mobilised from soils by acid rain with serious environmental consequences.

As yet, not enough is known about the way organisms respond to aluminium in its many forms and how it is transported and accumulated. An effective tracer is needed in order to carry out this basic research. Unfortunately, naturally occurring aluminium is so widespread in the environment that sensitive measurements are generally masked by a large background. Aluminium-26 is the only suitable radio nuclide, but it is expensive and its half life is 0.7My, which means that it must be used in substantial quantities if counting techniques are to be used. However, a much more attractive alternative is to use ^{26}Al coupled with AMS. The isotope's extremely low natural abundance means that backgrounds are low and the sensitivity of the method allows doses to be reduced to a level at which the radiological hazard is negligible. Also, the use of the NSF tandem effectively eliminates the potentially serious problem of interference from the isobar ^{26}Mg, which is also commonly found in biological and environmental samples.

2 THE METHOD

2.1 What is it?

AMS is an application of techniques developed for low-energy nuclear physics to the sensitive detection of minute amounts of isotopic tracers. Most frequently it is used to determine fractional concentrations of cosmogenic isotopes, eg: ^{10}Be, ^{14}C, ^{26}Al, ^{36}Cl, ^{41}Ca and ^{129}I. For the longer-lived radioisotopes in particular, measurements can be made with a sample which is 10^{-3} to 10^{-4} of that needed for decay counting and this is one of the main advantages of the technique. Traces of stable isotopes, Pt, Ir and Os have also been measured.

There is a large and growing number of areas of science which have advanced through the application of AMS. These include archeology, geology, astrophysics, oceanography, environmental science, biology and medicine, materials science and nuclear physics. Perhaps the best known example to the layman is its use to date a fragment of Turin shroud by measuring the isotopic concentration of ^{14}C.

2.2 How does it Work?

As its name implies, AMS employs established methods of mass spectrometry but in addition, accelerates ions to energies where all molecules are dissociated and charged-particle detectors can be used to record and uniquely identify individual ions thus providing an additional and necessary stage of isobar selection.

A schematic diagram illustrating the application of the method at Daresbury (1) is shown in Figure 1. A sample, generally solid, is deposited onto a small pellet or pill and mounted in the NSF ion source where it is sputtered by a caesium beam. The resulting negative ions are extracted and mass analysed in the first 90° magnet before being injected into the tandem. At the centre of the machine, the ions pass through a thin foil. A number of electrons are removed and any molecular species dissociate at this point. The positive ions now receive a further boost of acceleration to the bottom of the machine where they undergo a second 90° bend in a magnet which is set to transmit the ions of interest (eg ^{26}Al). Other ions can be transmitted, most notably the isobar (^{26}Mg), which often is very prolific. In adapting the method to the NSF, the accelerator is stabilized from an error signal obtained by sensing the position of the intense ($>10^3$-$10^5 s^{-1}$) flux

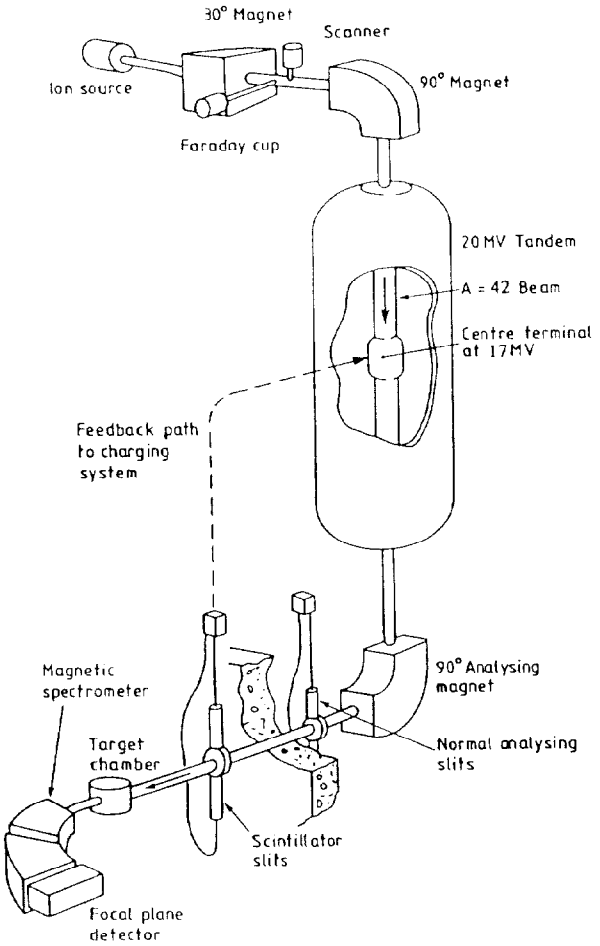

Figure 1: Use of NSF as an Accelerator Mass Spectrometer

of the ^{26}Mg isobar with a pair of scintillator slits positioned after the second 90° magnet at the bottom of the accelerator.

A second foil followed by the selection of the fully-stripped component $^{26}Al^{13+}$) in a magnetic spectrometer serves to remove all but a trace of the background ions. Finally, a multi-element, gas ionization detector at the spectrometer focal plane identifies the ions of interest from all the other different particles which have managed to reach the end of the system.

There are many factors which influence the probability of transmission of a given ion species and the isotopic ratio of an unknown sample is determined by comparing it with that of a sample for which the ratio is known. Work with prepared standards and blanks has demonstrated the expected linearity of the method over three orders of magnitude. A 1 hour run on a blank sample gave a detection limit of approximately 3 x $10^{-4}s^{-1}$ corresponding to a $^{26}Al/^{27}Al$ ratio of 7 x 10^{-14} or about 4 x 10^{-18}g of ^{26}Al.

3 ION BEAM DEVELOPMENT

In principle, AMS can be applied to the measurement of virtually all elemental species. In practice some (e.g. ^{14}C) are easy, but most require a certain amount of technical development. In the present case, a good deal of work was done to develop a procedure for preparing a sample from a biological specimen which optimised the source output and also minimized the amount of material used (1).

The best samples were those composed of a mixture of alumina and either silver or copper powder. Greater beams could be obtained using metallic aluminium but this benefit is more than offset by the difficulty in preparing a metallic sample from an organic matrix.

Sample deposits down to a mass of 0.5 - 5$\mu g/mm^2$ were prepared. Although the current obtained from these very thin sources was lower and for a shorter duration than that obtained from a standard pill (~10mg/mm^2), the reduction in source mass by over 10,000 fold greatly improves the limit of detectability and, hence, the sensitivity of the technique. There appeared to be no significant long-term memory effects or cross contamination (at the 10^{-4} level) within the source. This is an important result since normally measurements are made on a set of up to 24 pills of varying strengths which are installed in the ion source together and then run sequentially.

4 APPLICATIONS

We have made two applications of the use of AMS to trace ^{26}Al in biological systems. In both experiments, the ^{26}Al was introduced into healthy human volunteers.

4.1 Aluminium Uptake and Speciation

The aim of the first study was to obtain a limit for the gastrointestinal absorption (GIA) of aluminium and to characterise the particular proteins in blood which carry it. The isotope was orally administered in sodium citrate. Blood specimens were taken at six hourly intervals, red blood cells were separated by centrifuge and the plasma further fragmented by column chromatography. Total aluminium in each fraction was determined by conventional means. Then a standard amount of ^{27}Al was added to the material which was processed, transferred to AMS source pills and measured. The results of the measurements on the set of high molecular weight plasma protein fractions are summarised in figure 2. The top part of the figure shows the ultra violet absorption spectrum, on which two of the main proteins, transferrin (Tf) and albumin (Alb) are identified. Next are shown the relative ^{26}Al concentrations determined by AMS. The lower two spectra show the analyses of ^{27}Al and ^{56}Fe by gas furnace, atomic absorption spectroscopy (GFAAS). Both the ^{26}Al and Fe correlate well, and the latter, as expected, is identified with transferrin. It is interesting to note how contamination invalidates any possible ^{27}Al analysis and thus confirms AMS as the only practical technique for this kind of tracer work. Assuming a dispersal volume in the plasma of about 3 litres, the estimated total amount of ^{26}Al circulating in the system after 6 hours was about 1% of intake and must be considered to be a lower limit for the GIA factor. This result is to be compared with 0.01% derived previously using normal aluminium. However,

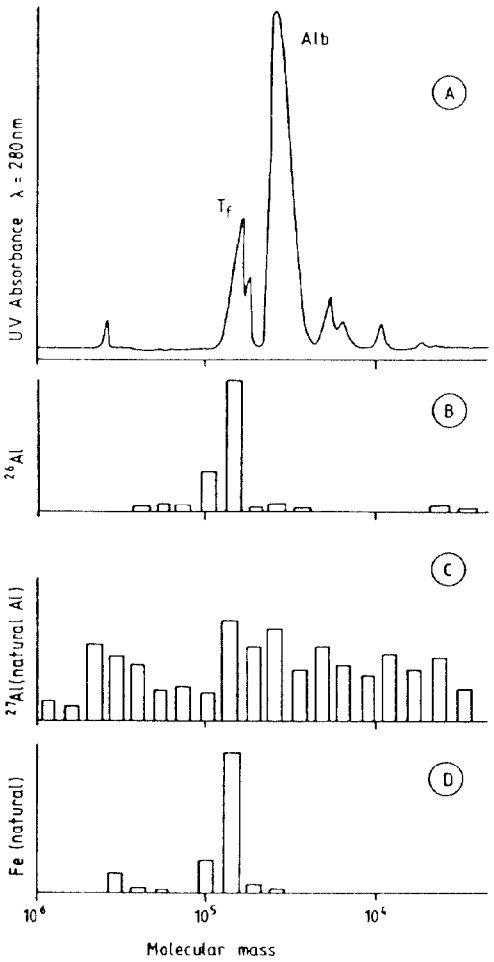

Figure 2: Analyses of high Mol Wt blood plasma fractions

in these earlier experiments, the uptake could have been inhibited by the large amount of aluminium hydoxide which was ingested. Also, it is suspected that citrate, which was used as a carrier in the ^{26}Al experiment, may enhance aluminium absorption significantly.

4.2 Aluminium Biokinetics

In the second study, a considerably larger amount of ^{26}Al was injected intravenously into a human subject. Blood samples were taken both prior to and sequentially after administration for up to 106 days. Quantities of these whole samples were processed, and AMS measurements made. The results, which are summarised in figure 3 show that the injected ^{26}Al is lost very rapidly from the blood stream initially, but later reaches a much slower decline. After 106 days, the concentration of ^{26}Al was about 10^{-4} of that present at the beginning of the experiment. This is in contrast to a parallel experiment

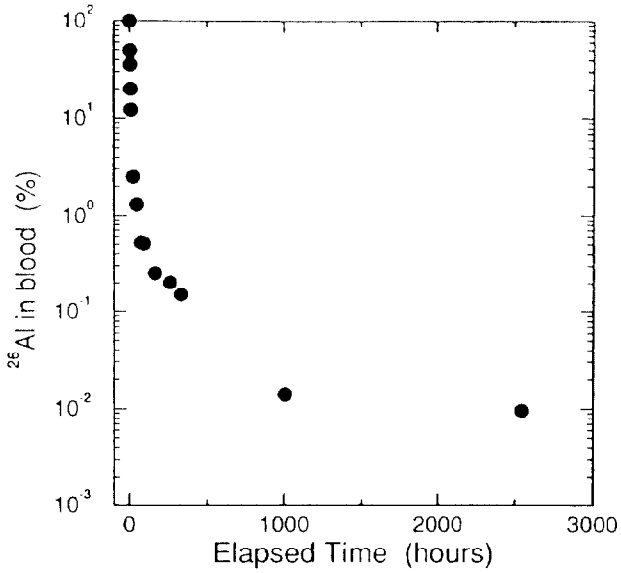

Figure 3: Retention of Al–26 in whole blood

(2) carried out using radioactive ^{67}Ga, which appears to be retained by the body much longer and expelled more slowly.

The biological implications of this experiment form part of a larger study of the retention of aluminium in blood and further work will be done. The important point which this work has established is the ability of AMS to determine ^{26}Al in the residues over the four orders of magnitude spanned by the experiment. Thus while the first sample in the sequence contained just enough radioisotope to be determined by direct counting, AMS was able to extend this range downwards by a factor of at least 10^4.

5 FUTURE WORK

Other areas in which we are applying ^{26}Al as a tracer are in experiments to study the uptake of aluminium in human neuroblastoma cells in culture and in investigations of aluminium species taken in natural water. The latter application is of importance in understanding the toxicity of aqueous aluminium to fish and is related to investigations of the effects of acid rain. Experiments also are being prepared and preliminary measurements carried out, to study possible abnormalities in aluminium absorption in Alzheimer and renal patients.

Supported by the Science and Engineering Research Council.

6 REFERENCES

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