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A Biomedical Application Of ^{32}Si Using Accelerator Mass Spectrometry

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Radioactive isotopic tracers are widely used in biomedical research, but for some elements of much current interest such as aluminium, silicon and plutonium, suitable isotopes for radioactive decay counting are not available. Each of these elements, however, possesses a long-lived isotope which could in principle be used if a suitable atom-counting detection technique were available. Accelerator Mass Spectrometry (AMS) is such a technique.

A significant challenge to the AMS detection of ^{32}Si ($T_{½}$ = 150 a) is posed by the ubiquity of the stable isobar ^{32}S which leads to prohibitively-high counting rates in a conventional AMS detector. Consequently, we have recently developed a gas-filled magnet technique for measuring ^{32}Si which allows a spatial separation of ^{32}S from ^{32}Si and hence a reduction in the counting rate entering the detector by a factor of 10^6. The ion-identification capability of the detector then provides an additional factor of 10^6 discrimination against residual ^{32}S ions, and permits measurements of the $^{32}Si/Si$ ratio down to 10^{-15}.

As a first application of this technique to a biomedical project, the first measurement of silicon uptake by a human subject has been carried out. The motivation for this study arose from the proposition that silicate may be important in human physiology in protecting against aluminium toxicity. Indeed, in an earlier study of aluminium uptake, using the isotopic tracer, ^{26}Al, it had been shown that blood-Al levels following Al dosing were lower when the dose was accompanied by dissolved silicate than when it was not [1], and in a recent study we concluded that this effect was largely due to enhanced Al excretion when silicate was present [2]. Specifically, in the two subjects studied, the renal clearance of Al was enhanced nearly twofold for the first 12-24 hours following the Al dose in the case where the dose was accompanied by silicate, although after this period Al clearance fell to the normal (i.e. non-silicate) level. It was suggested that the concurrent presence of aluminium and silicate in the blood plasma could lead to an increase in low molecular-weight Al species, more readily eliminated by the kidney than the transferrin-bound Al, of high molecular weight, known to be the dominant plasma-Al species under normal circumstances.

There is very little quantitative information on the uptake, elimination and retention of silicate. However, the credibility of the above Al-silicate binding hypothesis would be greatly enhanced if the kinetics of silicate uptake and elimination were shown to occur on

the same time scale as the enhanced Al elimination, i.e. if it were demonstrated that the enhanced levels of plasma silicate following uptake persisted for no more than 12-24 hours. Thus, we set out to determine directly the fraction of silicate absorbed from the gastrointestinal tract, and to quantify the kinetics of renal elimination, using the silicon isotopic tracer, ^{32}Si.

A healthy male volunteer ingested the dose solution which consisted of 53pg of ^{32}Si and 1 mg of stable silicon in a form which was expected to be monomeric silicic acid $Si(OH)_4$. Urine collections were made for extending intervals from 2 to 12 hours over 2 days following ingestion. Silicon was isolated as SiO_2 by first co-precipitating calcium silicate and calcium phosphate from the urine samples, and then distilling SiF_4 into a solution of dilute nitric acid where it precipitated as silica gel. After firing and mixing with silver powder, the ^{32}Si content of the resulting samples was determined by AMS.

The results are shown in figure 1, from which the following can be deduced:

a) Uptake appears to have been essentially complete within 2 hours of ingestion, and the gastrointestinal uptake factor was an unexpectedly large 36%.
b) Excretion occurred by two simultaneous first-order processes with half-lives of 2.0 and 8.6 hours, representing 90 and 10%, respectively, of the total output.
c) The main body reservoir appears to be the extracellular fluid volume, and there was no evidence for any specific binding or retention of silicate under these conditions. The 10% component may represent intracellular silicate absorption, or may reflect the presence of a component of oligomeric silicate.

Note that these results for silicon absorption and excretion are in marked contrast to those obtained for aluminium, where the uptake factor is typically 0.1%, excretion is an order of magnitude slower, and there is good evidence for long-term retention of some of the absorbed aluminium. Nevertheless, the results of this study are consistent with the hypothesis advanced in our earlier study [2], that the simultaneous ingestion of aluminium and silicate enhances the rate of aluminium excretion for a period of 12-24 hours, because this is just the period when silicate would be present and during which a silicate interaction would be possible.

1.) J.A. Edwardson, P.B. Moore, I.N. Ferrier, J.S. Lilley, G.W.A. Newton, J. Barker, J. Templar and J.P. Day, *Lancet* **342** 211-212 (1993).
2.) S.J. King, J.P. Day, C. Oldham, J.F. Popplewell, P. Ackrill, P.B. Moore, G.A. Taylor, J.A. Edwardson, L.K. Fifield, K. Liu and R.G. Cresswell, *Nuclear Instruments and Methods in Physics Research B* **123** 254 - 258 (1997).

Figure 1. Urinary ^{32}Si excretion following a single dose: (a) the ordinate is expressed as the fraction (%) of the ingested dose excreted in each urine collection, or cumulatively (times are recorded as the mid-point of the relevant intervals); (b) the ordinate is the logarithm (base 10) of the cumulative excretion subtracted from the limiting value estimated from the cumulative plot in graph (a).