RAPID NEUTRON ACTIVATION OF BROMINE USING 6.1-MINUTE BROMINE-82M: APPLICATION TO THE DETERMINATION OF BROMINE IN BLOOD PLASMA.

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SUMMARY

A rapid method is described for the determination of bromine in blood plasma using neutron activation analysis. By measuring bromine-82m with X-ray spectrometry, analyses of $10\mu\ell$ aliquots of plasma can be carried out within 10 minutes. Bromine sensitivity, in the presence of the large concentrations of sodium and chlorine normally found in plasma, is about 5 ng. Apart from statistical errors, the experimental error introduces a relative precision uncertainty of about ± 2%. The use of different detectors is compared.

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INTRODUCTION

A rapid determination of bromine by neutron activation analysis is possible through the use of 6.1-minute bromine-82m. This nuclide is produced from the stable bromine-81 isotope, which has an abundance of 49,96 atom % in natural bromine. The cross section for the formation of the radio-isotope by neutron capture with thermal neutrons is about 3 barns, so that reactors providing neutron fluxes between 10^{12} and $10^{15} cm^{-2} sec^{-1}$ can produce sufficient activities from relatively short irradiations to enable microgram

and nanogram quantities of bromine to be determined.

The sensitivity of determining bromine-82m activities can be enhanced by the appropriate choice of detector. With the use of low energy gamma-ray or X-ray detectors, the energy spectrum covered during a measurement can be restricted to radiation not exceeding 100 keV in energy. Under such conditions, the radiation measured from neutron activation of natural bromine is restricted to 37 and 49 keV gamma-rays from 4.4 hour bromine 80-m and 46 keV gamma-rays from 6.1-minute bromine-82m. These radiations are all internally converted to produce bromine X-rays[1]. The 37-keV gamma-ray has a conversion coefficient α_k = 1 so that only about half these radiations will contribute to the measured K X-rays of 11,9 keV, in contrast with the other two aforementioned gamma-rays which are virtually entirely internally converted: the values of the respective conversion coefficients for X-ray production from the 49 keV gamma-ray of Br-80 m and the 46-keV gamma-ray of Br-82 m are about 400 and 382 and over 70% of the decays result in K X-rays. In addition to these radiations, there is a small intensity of selenium K-rays of 11.2 keV produced from the electron capture mode of decay of 17.6 min bromine-80 having a relative probability of about 5%. It thus follows that X-rays generated from the radio-bromine isotopes will consist almost entirely of those originating from bromine-82m decaying with a half-life of 6.1 minutes together with a small contribution of a 4.4 hour component originating from bromine-80m and a 17.6 minute component from bromine-80.

To enable the analyses to be carried out as quickly as possible, but without loss of precision, the counting period should be extended until most of the bromine-82m had decayed. Correction factors from the above three-component decay system were obtained from pre-computed tables using measured intensities of the components.

The sensitivity limit attainable with gamma-ray spectroscopy is determined by the relative intensities of the gamma-rays of interest and interfering radiation which arise from other causes viz., bremsstrahlung effects resulting from the production of a radiation continuum caused by energetic beta-particles from the sample, backscatter effects resulting from the detection of usually low energy gamma-rays scattered from the sample to the detector by extraneous matter and Compton effects caused from the detection of electrons from gamma-rays scattered in the detector. These effects cannot be eliminated entirely, even from samples which contain only radio-bromine isotopes, but their effects can be decreased by using detectors with comparatively small sensitive volumes in which the probability of interaction is small for energetic gamma-rays, and by removing material of large atomic number from the vicinity of the detector, thereby decreasing the intensity of bremsstrahlung.

Blood plasma contains both sodium and chlorine at a concentration level of about 3 mg/ml, whereas the bromine concentration is about 3 p.p.m. in normal plasma. Thermal neutron activation of plasma thus produces relatively large yields of chlorine-38 and sodium-24, the effect of which will be to reduce the sensitivity for determining bromine.

This work reports the results of studies carried out with two different detecting systems to develop a suitable technique for the rapid determination of bromine in blood plasma and for evaluating the precision, accuracy and sensitivity of the technique.

EXPERIMENTAL

Materials

Dilute aqueous solutions of ammonium bromide were used to establish the conditions for analysis and to collect physical data.

Synthetic plasma solutions were prepared containing 5.77g NaCl and 2.74g

Na_2CO_3 per liter.

This corresponded to concentrations of 3.30 g/l of sodium and 3.50 g/l of

chlorine as found in average blood plasma.   Varying quantities of ammonium

bromide were added to these solutions as required.

Liquid blood plasmas were analysed as received.

Preparation of samples for counting

Pipetted volumes from 5 to 20 μl were deposited on discs of filter

paper.   The average thickness of paper was 7.2 ± 0.2 mg/cm^2 and the pipetted

droplets were spread over a circular area of about 8 to 15 mm diameter.   The

resulting samples had an effective thickness between 18 and 32 mg/cm^2.   Over

this range of thicknesses, no change in count rate, due to self-absorption,

could be observed, in agreement with previously reported results[2].   In cases

where relatively old samples of liquid plasma were irradiated, undispersed

solid material sometimes obstructed the action of the automatic pipette.

In such cases, and all samples where there was doubt about the correct volume

pipetted, bromine activity was expressed relative to the activity of sodium-24

in the sample, determined later with a Ge(Li) spectrometer.

Two different modifications of the procedure were used.   In the first,

liquid plasma measuring about 200μl was sealed in a polyethylene vial for

irradiation, and samples for counting were prepared from the activated liquid.

The disadvantage of this procedure lay in the loss of time, and hence loss of

activity of bromine-82m, during pipetting and preparation of the sample. The

second modification involved the deposition of the required volume of plasma

onto filter paper before activation and then counting the paper directly

after its return from the reactor.   Although counting could start much sooner

the disadvantage of this technique lay in the possibility of contamination

before activation and possible interference from fluctuations in the bromine

content of the paper.

Irradiation

Samples were irradiated in aluminium or polyethylene containers for

periods varying from to 10 sec to 5 min. Three reactor facilities were used

viz:

OSIRIS,   Saclay, France, thermal neutron flux $2,5 \times 10^{14}$ neutrons
$$cm^{-2}Sec^{-1}$$

EL 3   Saclay, France, thermal neutron flux 6.6×10^{12}

SAFARI I   Pelindaba, South Africa, thermal neutron flux 1.3×10^{13}

Measurement

Bromine activities were recorded with two different spectrometers,

using either a NaI(Tℓ) scintillator 3 cm diameter x 3 mm thick having a re-

solution of about 6,3 keV at 12 keV, or a Si(Li) detector of 30 mm^2 area and

3 mm thick having a resolution of 262 ev at 6.4 keV. Both detectors had

thin beryllium windows, the latter being 0.025 mm thick.

Because the scintillator had a very much higher efficiency, count rates

were appreciably higher than with the Si(Li) detector, due to the activities

from chlorine and sodium. To avoid excessive errors due to dead-time

correction, samples were mounted about 25 to 40 mm away from the crystal face.

In contrast to this, paper discs counted with the Si(Li) detector were mounted

as close to the detector window as possible, typically about 4 mm from the

window. For routine analysis samples were counted for a fixed live time

of the measuring system, but because of the high activities the added decay

of bromine-82m caused by the dead-time of the measuring system could not be

neglected, hence real time was recorded at the start and end of each count.

Under fixed conditions and using the pre-irradiation pipetting technique, it was found that the difference between live time and clock time was surprisingly constant. Accordingly extended counting periods of up to 500 sec could be used and tables calculated from accurately determined decay curves were used to correct the measured nett count to corrected undecayed activity at the end of the irradiation. (see Table I)

RESULTS AND DISCUSSION

Gamma-ray spectrometry

Typical spectra obtained with the NaI(Tℓ) scintillator and the Si(Li) detector may be compared in Figure 1. The much improved resolution of the latter makes it possible to observe the presence of selemium X-rays and both the $K\alpha$ and $K\beta$ X-rays of bromine. However, the spectra from the NaI scintillator were recorded with a much greater count rate, so that despite the better resolution of the semi-conductor diode, the precision of the results are about equal.

As the decay proceeds, the intensity of the X-rays decreases and it becomes possible to observe[3] the peak from the unconverted 37 keV gamma-ray of bromine-80m.

Comparison of the two curves obtained from a sample with about 8 ng bromine clearly illustrates the gain in sensitivity effected by the Si(Li) detector. Using the criterion of sensitivity as being the weight of bromine which gives an integrated count equal to three times the standard deviation of the background, the sensitivity limit in a blood plasma sample is about 5 ng bromine.

Calculations

The blank sample gave the shape of the spectral continuum under the combined peaks corresponding to Se K and Br $K\alpha$ and $K\beta$ X-rays. This shape was
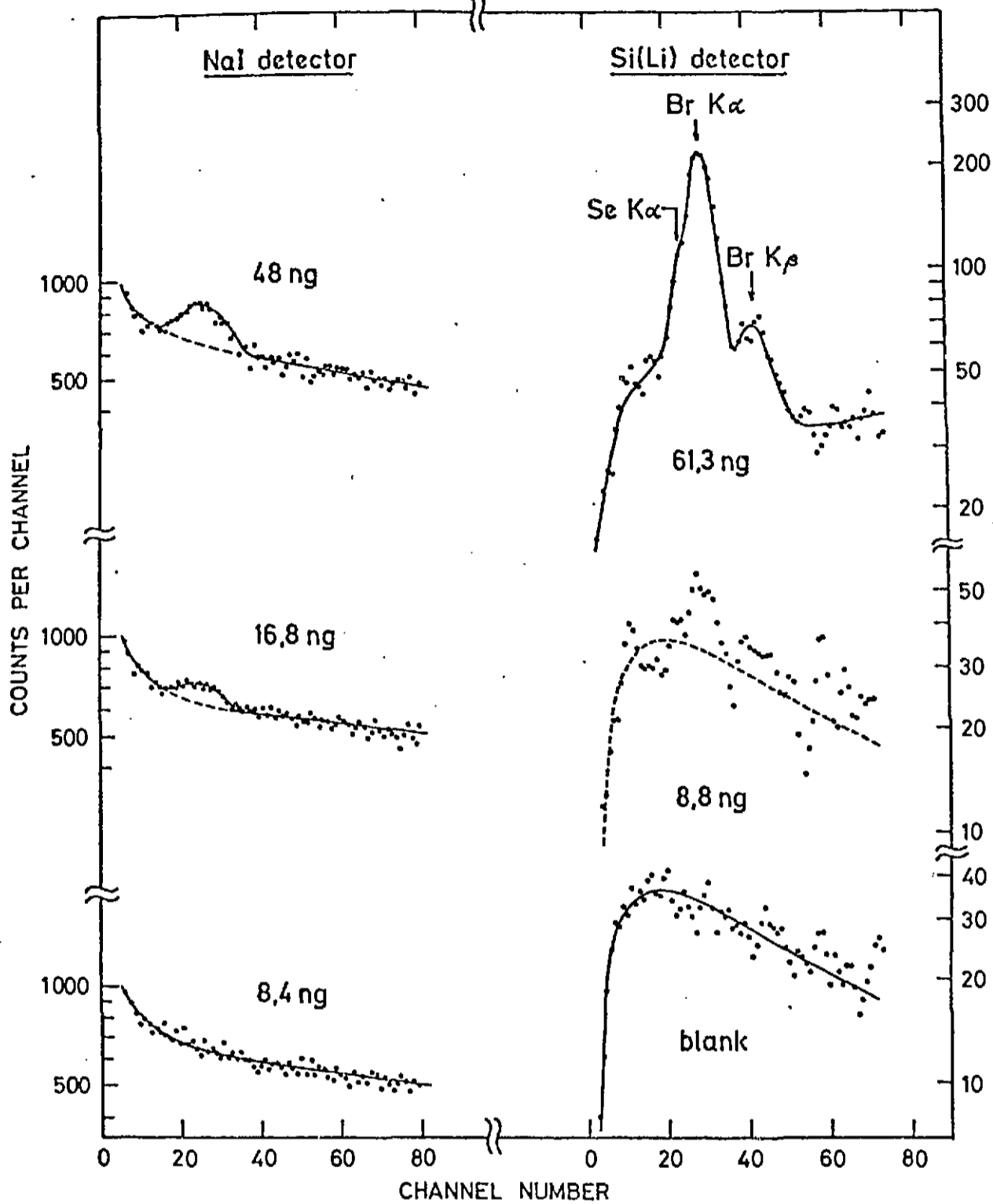
Figure 1: Portions of gamma-ray spectra from different weights bromine in
10μℓ aliquots of plasma.

fitted to the low energy edge of the peaks and the corresponding background

was subtracted.   Using tables such as Table I computed from decay curves

the activity at the end of the irradiation was calculated and converted to

bromine content by comparison with synthetic standards.

Precision and Accuracy

Precision was determined by repeated analysis of a single sample. Some

replicate analyses of a series of 16 analyses are shown in the upper portion

of Table II, and analyses of known samples in the lower part. The relative precision is ±   %, the root mean square error is   ng bromine and the results do not show bias within the precision of the method.

CONCLUSION

The method using Si(Li) detectors is suited for routine use.   If the usual statistical errors of counting are acceptable, single irradiations followed by a single relatively long counting period enables results to be obtained with a relative precision of about ± 6% within 10 minutes.   Analyses are non-destructive and repeat irradiations can be carried out to improve precision.

ACKNOWLEDGEMENTS

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TABLE I

EXTRACT FROM DECAY CORRECTION CALCULATIONS

Time at start of count (minutes)	count duration (minutes)				
	3	4	5	6	8
1	1.2903	1.3536	1.4183	1.4844	1.6207
2	1.4290	1.4984	1.5693	1.6417	1.7907
3	1.5810	1.6570	1.7345	1.8136	1.9762
4	1.7473	1.8302	1.9149	2.0011	2.1782
5	1.9288	2.0192	2.1113	2.2052	2.3975
6	2.1264	2.2247	2.3249	2.4267	2.6352
7	2.3412	2.4479	2.5564	2.6667	3.0465
8	2.5741	2.6895	2.8068	2.9258	3.0465
9	2.8258	2.9503	3.0768	3.2050	3.4659

These data are dependent on the relative yields of radiobromine isotopes as affected by the neutron energy distribution at the activation facility used.

TABLE II

SOME RESULTS OF ANALYSES

Known Br Content ng	Nett Integrated count at t = 0 Ao	Found Br Content ng	Error ng

(a) Replicate analyses. Precision test.   Si(Li) detector

Known Br Content ng	Nett Integrated count at t = 0 Ao	Found Br Content ng	Error ng
35.0	265.1	31.1	- 3.9
35.0	303.3	35.6	+ 0.6
35.0	295.4	34.6	- 0.4
35.0	315.0	36.9	+ 1.9
35.0	297.1	34.8	- 0.2
35.0	283.6	33.3	- 1.7

No. of test analyses = 16

Mean value of Ao = 298,8 ± 18,2

Overall relative precision = 6.1% due to statistical errors (5.8%) and added experimental errors (2.0%).

(b) Test analyses. Accuracy test. Both detectors.

Known Br Content ng	Nett Integrated count at t = 0 Ao	Found Br Content ng	Error ng
8.8	109.1	12.8	+ 4.0
8.9	46.2	5.4	- 3.5
21.9	202.1	23.7	+ 1.8
30.7	274.5	32.2	+ 1.5
35.0	295.9	34.7	- 0.3
43.5	350.4	41.1	- 2.4
48.2	433.1	50.8	+ 2.6
61.3	491.9	57.7	- 3.6

37 test analyses on 22 samples prepared

Root mean square error (all analyses) = ± 2.8 ng bromine