Technical Considerations for Sampling and Sample Preparation of Biomedical Samples for Trace Element Analysis

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Sampling and sample preparation procedures are to a large extent determined by the analytical method used since different methods vary in the amount of material required for analysis and in how this is pre-treated before being introduced into the measuring instrument. Judging from intercomparison studies conducted by the International Atomic Energy Agency (IAEA), the most widely applicable methods now in use are Neutron Activation Analysis, Atomic Absorption Spectrometry, and Inductively Coupled Plasma Atomic Emission Spectrometry, though the latter still seems to have insufficient sensitivity for many trace elements of biomedical interest. Common to all these methods is the problem of contaminating the sample before or during analysis. For many elements (e.g., As, Cd, Co, Cr, Mn, Mo, Ni, Pb, Sb, and V) sufficient control over contamination can only be achieved by the use of special tools and reagents, and by working in a controlled (dust-free) environment. Several important elements (e.g., As, Hg, Sb, and I) are subject to losses on drying or ashing, but can be recovered reliably if wet-ashed in a closed container such as a PTFE “bomb.” For representative sampling it is almost always necessary to start with several grams of material, and to homogenize this, if the effects of sample heterogeneity are to be reduced to an acceptable level. Quality assurance procedures covering all these aspects are difficult both to define and to apply. However, much can be learned from the statistical evaluation of results for duplicate samples, and from a determination of the limit of quantitation of the analytical procedure.

Key words: analysis; analyte losses; biomedical samples; contamination; quality assurance; sample handling; sampling; trace elements.

1. Introduction

This paper discusses some of the technical considerations underlying sampling and sample preparation of biomedical materials for trace element analysis, leaving aside medical, legal, ethical and financial aspects. The two main classes of problems to be considered are 1) the avoidance of contamination (and its inverse, the loss of the element of interest from the specimen), and 2) the requirement to obtain an analytical sub-sample that is representative of the specimen to be analyzed. Quality assurance aspects are also discussed.

Technical solutions for many of the problems that arise have been available for several years, but unfortunately still appear to be ignored by many analysts working in this field judging by the poor agreement between the results reported by different laboratories for the same or similar materials [1,2]. Recent efforts to improve this situation are exemplified by the actions of official bodies such as the International Union of Pure and Applied Chemistry [3], the American Chemical So-

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1 Figures in brackets indicate literature references.
ciety [4,5], and the International Atomic Energy Agency (IAEA) [6], which have developed relevant definitions and guidelines for data acquisition and quality assurance. If followed conscientiously, these would do much to help analysts identify and minimize some of the errors affecting their work.

What follows is the author's own personal assessment of some of the more important factors that analysts should consider when sampling and preparing biomedical materials for trace element analysis. The references quoted are not intended to be an exhaustive list but rather to be illustrative of the problems being discussed.

2. Choice of Analytical Method

Procedures for sampling and sample preparation are to a large extent determined by the analytical method used since different methods vary in the amount of material required for analysis and in how this is pre-treated before being introduced into the measuring instrument. The main problem, that of contamination, can generally be reduced by keeping the number and complexity of sample handling operations to a minimum. In this respect, Neutron Activation Analysis (NAA) is regarded by its proponents as an ideal method since sample preparation may involve nothing more than placing the specimen in an irradiation vial, and exposing it to neutrons; after this, contamination (unless with radio-
nuclides) has no effect.

Other common trace analysis methods such as Atomic Absorption Spectrometry (AAS) and Inductively Coupled Plasma Atomic Emission Spectrometry (ICP-AES) may also sometimes be used directly without sample preparation, particularly for the analysis of biological fluids. In general, however, other steps are also involved, each of which should be considered as a potential source of error, particularly of contamination. Examples include drying, ashing, grinding, dissolution, mixing with internal standards or spikes, and/or addition of reagents to effect a chemical separation or to reduce interferences. Each step involves its own special problems. Of fundamental importance for the analyst is that he should have a thorough understanding of the whole procedure and an awareness of the analytical errors that may be introduced at each step.

Although the number and complexity of sample handling operations is an important factor in evaluating an analytical technique, the most important criterion has to do with whether or not it is appropriate for the element and matrix of interest, i.e., whether it can deliver results of acceptable accuracy and precision. Most analysts prefer to draw their own conclusions on this point, though useful guidance is offered in the literature [7-10]. Table 1 identifies methods recommended by a working group sponsored by the American Institute of Nutrition [9]. Similar guidance (table 2) has been offered by an Advisory Group of the IAEA [10]. Experimental confirmation of the latter's predictions is provided by the results of several recent intercomparisons organized by the IAEA [11]. However, the following exceptions should be noted. In practice, NAA is rarely, if ever, used for the determination of F, Ni, or P; AAS is rarely used for Sb, Se, or Si; ICP-AES is rarely used for Si; and mass spectrometry is rarely used for Cd, P, or Sb.

Summing up, it would appear that the most widely applicable method for trace element research is NAA, which is commonly used for 23 of the 26 elements listed in Table 1. Then follows AAS, which is widely used for 19 of these elements. ICP-AES is applicable to only nine elements, most of which, in biomedical materials, occur at "minor" rather than at "trace" levels. Mass spec-

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Table 1. Methods recommended for various elements [9].

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* May not be acceptable for those elements by that technique in all types of samples.
Table 2. Analytical methods applicable to four biological materials (blood serum, muscle, liver, and a plant material, kale) with precisions better than 10% relative standard deviation (ref. [10], p. 367).

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* A-1: atomic absorption spectroscopy (AAS)—flame atomization with direct nebulization of aqueous sample solutions
* A-2: AAS—flame atomization using special sample techniques, or after pre-concentration and separation of the analyte
* A-3: AAS—electrothermal atomization in graphite furnace
* C-1: chemical methods
* C-2: electrochemical methods
* E: emission spectroscopy—inductively coupled plasma source
* M: mass spectrometry—spark source
* N-1: neutron activation analysis (NAA)—instrumental methods
* N-2: NAA with single-element separation
* N-3: NAA with group separation (simple scheme involving removal of alkali metals, halogens and phosphorus)
* X: X-ray analysis—PIXE

Analytical method

Atomic spectrometry is also applicable to a fairly wide range of trace elements, but only a few research centres appear to have access to it.

A word of warning. Not only is it necessary to choose an appropriate analytical method, but also to use an appropriate version of the method. For example, with some analyses can only be performed reliably if the radionuclide of interest is separated radiochemically before the activity measurement. Similarly, with AAS, a chemical separation may be necessary to overcome matrix effects reliably.

3. Reduction and Control of Contamination

For most biomedical materials, significant contamination can be introduced right from the very moment of taking the sample. This is not usually a problem for elements occurring at concentrations of a few parts per million or more, such as Cu, Fe, and Zn in liver. However, many trace elements of biomedical interest, such as As, Cd, Co, Cr, Mn, Mo, Ni, Pb, Sb, and V, often occur at much lower levels, and their values are therefore more easily disturbed by contamination. For such elements it may be essential to work in dust-free conditions and with ultra-pure reagents, and to use non-contaminating tools and containers such as titanium knives, and PE, PTFE, or quartz specimen vials, which should be rigorously cleaned before use. All of these aspects of the subject have been discussed extensively in the scientific literature [12-27].

The use of class 100 laminar flow clean air benches, or rooms, is now becoming the norm in trace element work [25]. Whether or not such conditions are essential is, however, open to question. Lieve et al. [28] measured dust fallout in a normal laboratory and found values for many elements below 1 ng cm⁻² day⁻¹ (for As, Co, Cu, I, Mn, Sb, and V even below 0.1 ng cm⁻² day⁻¹). At such low levels, contamination from dust can hardly be a significant risk factor except possibly for the determination of Mn in blood serum [29] and Pb in many biomedical materials [13]. Even for such difficult analyses, normal clean conditions with a filtered air supply (but not necessarily class 100) and an overpressure of 2-4 mm water column are almost certainly adequate [13].

The availability of class 100 conditions may even lull the analyst into a feeling of false security if the analyst is not aware that the placement of equipment, and activities of laboratory personnel, can cause turbulences which drastically affect the performance of clean air installations. Dust carried into or created in the laboratory by personnel may be a much more potent source of contamination than the background levels in the laboratory itself [19]. An important feature of good laboratory design is therefore not just that clean air be provided but also that the pattern of air flows in the laboratory be arranged so as to protect the sample from cross contamination arising from other samples or from the laboratory personnel [23].
Most biomedical specimens are collected, not in a clean laboratory, but in a normal room for treating patients or conducting autopsies. Obviously, such rooms should be of a reasonable standard of cleanliness. However, there is no real need to demand class 100 or similar conditions, particularly if a sufficient amount of material is taken to permit removal of the possibly-contaminated surfaces at a later stage.

Whether tissue specimens should be treated before analysis to remove residual blood is a question that has so far not received much attention. Most workers consider it is sufficient just to remove excess blood, for example by blotting with ashless filter paper [30].

The contamination problems encountered in collecting tissue specimens or biological fluids using stainless steel tools such as surgical blades and blood collection needles are now well recognized [24,27,31] particularly for elements such as Cr, Co, Mn, Mo, and Ni. This is the principal reason why analysts have been recommended to use alternative materials such as titanium for knives and polypropylene catheters instead of metal needles. For some kinds of sample, however, conventional tools appear to present no particular hazard [32], and may even be acceptable for “problem analyses” such as chromium in blood serum if they are appropriately treated before use such as by siliconing [33].

In any case the careful analyst does not permit himself the luxury of assuming contamination to be insignificant unless good evidence exists for this. If necessary, exhaustive tests should be made of every sample handling operation, and of every tool and reagent used. Such investigations are all the more necessary if complex sample preparation procedures are used, as for example in biochemical fractionation studies [31,34].

4. Representative Sampling

Biological aspects of this problem are discussed in detail in the companion paper by Hopps [35]. Here the author would only like to draw attention to the fact that the problem of obtaining a representative sub-sample is also dependent on the analytical method chosen since different methods vary in their requirements regarding sample size. This may typically be 0.5–2 g (dry matter) for ICP-AES, 0.1–1 g for flame AAS, 0.1–0.5 g for NAA and 0.01–0.05 g for electrothermal AAS. X-ray methods such as PIXE may only require a few mg or less. Very few biological materials, however, are homogeneous for sample sizes as small as these.

The mathematical basis of sampling theory is discussed in many publications [5,36–38]. An important concept is that of the sampling constant, \( K_w \), which is the mass (in grams) of material needed to reduce sample heterogeneity to 1%. This is related to \( R \), the relative standard deviation (%) of the measurement, and \( m \), the mass (in grams) of sample taken for the measurement, by the relation \( m = K/R^2 \).

Very little information is available from the literature on sampling constants for different tissues. According to Heydorn [8] it is around 200 g for trace elements such as Fe, Se, and Zn in human liver and kidney medulla, though much less than this (<10 g) for heart muscle. For Na in human kidney it is about 35 g [37]. The implication of these figures is that, taking \( K_w = 200 \) g as an example, one would need a sample size of 8 g to reduce sample heterogeneity to 5% RSD, and much more if one wanted the heterogeneity to be better than this. Obviously, these are much larger amounts than are normally used for a single analysis. It therefore follows that, for representative sampling, the analyst should start with a large amount of material, such as 8 g, and homogenize this to produce a suitable sub-sample for analysis.

Fortunately, suitable methods are available for performing such homogenization without at the same time introducing significant contamination. For small amounts of material (up to a few g), the brittle fracture technique applied at LN2 temperature is effective even for difficult-to-homogenize materials such as hair and bone [39]. For larger amounts (up to a few 100 g) the same principle can be applied using a PTFE disc mill [40].

5. Analyte Losses

Much of the foregoing is concerned with inadvertent addition of elements to the sample. The inverse of this problem is the loss of analytes due to inappropriate storage or sample handling operations. Sample storage before analysis presents special problems as discussed in the companion paper by Kemper [41]. Among the operations most likely to result in a loss of the analyte are ashing and drying.

This subject has been reviewed extensively by Iyengar and Sansoni [16], and more recent data are available in the work of Pietra et al. [42]. Many of the investigations to test for losses on drying or ashing have, however, been done with radioisotopes and are therefore of somewhat uncertain value since there is no guarantee that the tracer will behave in exactly the same way as the non-radioactive forms of the element, which may be quite different chemical species. Nevertheless, there is good evidence that naturally occurring forms of elements such as As, Sb, Hg, and I may be lost in significant amounts from some matrices not only when the sample is ashed at a high temperature (>400 °C) but also under the milder conditions of oven-drying or even freeze-drying.
The latter method, however, has in recent years emerged as the way preferred by most analysts to pre-concentrate their samples before analysis, and is probably safe for most elements. Even for "problem elements" such as mercury, it may be safe for many kinds of specimen [43]. Prudence requires, however, that if there is any possibility of losing an element during a drying or ashing operation, then these steps should either be avoided or should be carried out in a closed system that prevents any loss from occurring. A solution to this problem can be found in the use of PTFE "bombs" which have come into widespread use in recent years. These appear to offer a very convenient and reliable means for wet ashing biological materials without losses of trace elements [42]. Mercury, however, may still be a problem due to adsorption on PTFE surfaces, but can be reliably recovered if a suitable closed quartz digestion vessel is used instead [44].

6. Quality Assurance

Quality assurance procedures for sampling and sample preparation are difficult both to define and to apply. The main requirement is simply to follow the rules of good laboratory practice, which can be summarized as: 1) work in a clean environment, 2) use specially purified reagents, 3) select tools and containers with the lowest possible impurities, and 4) be constantly aware of your own effect on the blank.

As regards quantitative measures of analytical quality, much can be learned by the statistical evaluation of results for duplicate samples together with a detailed investigation of the individual sources of error in the whole analytical procedure. This technique has been developed primarily by Heydorn, who defines a test statistic $T$, with a $\chi^2$ distribution, which is derived from the results of duplicate analyses and their respective errors [8,45-46]. Results from successive duplicates can be accumulated. Departures from acceptability only show that something is wrong, and that some unknown source of variability is operating. However, Heydorn has shown that this is a sensitive test, which can be very helpful in identifying problems such as unexpected contamination [29,47].

Current rules of good laboratory practice [5] place emphasis on the study of the analytical blank, in particular its standard deviation, since this is the primary determinant of the limit of detection of the analytical procedure (defined as three times the standard deviation of the blank) and the limit of quantitation (10 times the standard deviation of the blank). If actual measured values in samples are less than the limit of quantitation, reliable results cannot be obtained until the analytical blank has been reduced further. The determination of the limit of quantitation (to the extent that this can be done realistically) is thus an important means for investigating whether sample preparation has been performed satisfactorily.

There are, however, some problems in applying this concept. For example, in NAA, the analyst normally just takes an empty vial, and defines the blank as the amount of the analyte that can subsequently be extracted from it. Alternatively, some analysts just report the spectrum blank, based on the background under the photopeak of interest. Both of these, however, are only components of the total blank. They ignore, for example, the contamination arising from other sample preparation steps such as drying and homogenization.

In principle, there is a simple way to test for such errors, namely be preparing and analyzing samples of different weights. If the blank is zero, then the regression line for the plot of measured amount of analyte versus weight of sample should go through the origin [48]. Alternatively, if the blank is different from zero, it can be estimated from the intercept of the regression line at zero sample weight.

7. Conclusions

Technical solutions are now available for most of the problems that arise during sampling and sample preparation of biological materials for trace element analysis. Perhaps better solutions can still be found. The lack of them, however, is certainly not the main reason for the large discrepancies that can still be found in the scientific literature between results reported by different analysts for the same or similar materials. Reliable data can only be obtained if the analyst is made to be aware that serious errors can be introduced at almost every step in the analytical procedure. Quality assurance is therefore, in the first place, mainly an attitude of mind. In helping to draw attention to these problems, and offer practical solutions to them, the organizers of this workshop have taken an important initiative, and it is hoped that their efforts will be rewarded with success.

References

[1] Parr, R. M., On the Need for Improved Quality Assurance in Biomedical Neutron Activation Analysis as Revealed by the Results of Some Recent IAEA Intercomparisons, ref. [5], 53-70.


[11] Dybczynski, R., Relative Accuracy, Precision and Frequency of Use of Neutron Activation Analysis and Other Techniques as Revealed by the Results of Some Recent IAEA Intercomparisons, in ref. [6], 39–52.


[13] Patterson, C. C., and D. M. Settle, The Reduction of Orders of Magnitude Errors in Lead Analyses of Biological Materials and Natural Waters by Evaluating and Controlling the Extent and Sources of Industrial Lead Contamination Introduced During Sample Collecting, Handling, and Analysis, in ref. [12], 321–351.


[27] Versieck, J., Collection and Manipulation of Samples for Trace Element Analysis: Quality Assurance Considerations, in ref. [6], 71–82.


[47] Heydorn, K., Detection of Systematic Errors by the Analysis of Precision, in ref. [12], 127–139.