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TRENDS AND DEMANDS IN AND ON TRACE ELEMENT ANALYSIS IN THE BIOMEDICAL AND ENVIRONMENTAL FIELD

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Problems in trace element analysis in the biomedical and environmental field are discussed, especially for the most interesting elements, as well as adequate analytical techniques for their analysis. The "state of the art" for the relevant elements, the recommended methods as well as the new "speciation" analysis are briefly described. Besides these points, quality control, becoming more and more important to improve the reliability of analytical data, is discussed.

Introduction

Trace element analysis in the biomedical and environmental field shows a steady increase in importance. This is mainly due to our increasing knowledge on the role of trace elements for the living organism. However, the mere concentration values are no longer in the center of interest. The chemical form or the oxidation state are now focussed on, because only the "species" defines the function or the effect. Therefore, "speciation analysis" is becoming more and more important and today represents the great new challenge for analytical chemists.

Classification of elements

It is well known that the elements are divided into different groups (of interest and/or of knowledge):

(a) Mineral elements

main constituents of the living organism elements like C, O, N, Ca, K, Mg, Na, P, S

(b) Trace elements

The trace elements are again divided into 3 different groups (of knowledge):

(1) Essential: of known biological importance

(2) Toxic: of known toxic effect at low doses

(3) Effects unknown

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Table 1

Relevant trace elements

for which different analytical techniques are necessary:

in the biomedical field
Co, Cr, Cu, F, Fe, I, Mn, Mo, Ni, Se, Si, Sn, V, Zn,
in the environmental field
As*, Cd*, Hg, Pb*, Tl

*These elements are under discussion as having essential effects

Table 2

Relevant concentration ranges of some elements in biological matrices

Element	Body Fluids (Serum)	Tissue (Liver)
Co	< 1 μg/l	< 1 μg/g
Cr	< 1 μg/l	< 1 μg/g
Cu	1 mg/l	20 μg/g
Fe	1 mg/l	500 μg/g
Mn	< 1 μg/l	3 μg/g
Mo	< 1 μg/l	3 μg/g
Ni	< 1 μg/l	< 1 μg/g
Se	50 μg/l	2 μg/g
Si	< 10 μg/l	?
Sn	< 1 μg/l	< 1 μg/g
V	< 1 μg/l	?
Zn	1 mg/l	100 μg/g

Here there is a need for different analytical techniques with respect concentration.

This classification is not fixed. It corresponds only to our present knowledge.

When one is talking of trace element analysis in the biomedical field, one is mostly thinking of the analysis of the 14 known essential trace elements in all kinds of body fluids and tissues of man and animal. In the environmental field, main interest is focussed on the different relevant heavy metals ("toxic" trace elements) in plants, soils, sludges, water, air, foodstuffs, etc. The concentration ranges of relevant elements (and of matrices) is bigger than in the biomedical field (Table 1).

Not only the elements themselves are important for the correct choice of the analytical method, but also the expected concentration range. Table 2 shows very roughly the conditions in body fluids and tissues. In the environmental field, the range is very wide and may cover the lower ppb- up to the %-range, depending on many factors which will be discussed here.

Analytical methods

Looking at the methods commonly available for these tasks, one must distinguish between routine and scientific work. On the purely scientific level it usually suffices to analyze a few samples, but often by highly sophisticated techniques. Sometimes such analyses are purley works undertaken to show that they can be done, and for the purpose of writing a publication. On the routine level, there is need of a high sample throughput and the possibility to perform the analysis in many different laboratories, because similar samples have to be analyzed at several places and the results must be comparable. The most commonly used analytical techniques are shown in Table 3.

It is well known that there is no universal analytical technique able to detect all the relevant elements in the frequently highly varying concentration ranges and in completely different matrices. (Only final measurements will be regarded here not the entire analytical procedures as this would render the discussion too complex).

Different analytical methods are necessary to solve given problems. In general, it is impossible to discuss the capacity of a technique without simultaneously discussing the problem in question. The techniques are to be seen as complementing each other, rather than being competitive.

The simplest question concerns the field of application, with respect to the great differences between routine- and research investigation. In the biomedical field, the trace element status is still used as an additional diagnostic tool in some few diseases, like, e.g., Morbus Wilson (a Cu accumulation in the liver), certain skin diseases, malnutrition states, etc. Here one is still really only at the very begnning and an increasing and better knowledge concerning the biochemical functions of trace elements in the living organism is necessary. Good analytical techniques are a step in the right direction. But the main demand, besides accuracy and precision, on an analytical technique is a short response time. The physician and the patient

Table 3

Analytical techniques (final measurements)

Not complete; a wide range of highly sophisticated methods is available but normally not used for routine - work! Commonly used: AAS- and AES-techniques

NAA	INAA RNAA
RFA	
AAS	FES/AAS GFAAS HAAS (CVAAS)
AES	ICP different plasma sources
MS - ICP	

Note: INAA - instrumental neutron activation analysis, RNAA = radiochemical neutron activation analysis, FES/AAS = flame emission spectrophotometry and atomic absorption spectrophotometry, GFAAS = graphite furnace atomization atomic absorption spectrometry, ICP-AES = inductively coupled plasma atomic emission spectrophotometry, HAAS = hydride-generation atomic absorption spectrophotometry, and ECA = electrochemical analysis, MS = mass spectrometry

are waiting for the answer and the result should be available within hours. This demand can scarcely be met by NAA, apart from other reasons, because of the bad availability of facilities for this method. In pure research, one practically always has enough time to wait for the analytical answer. Mere NAA has some advantages and can deliver important contributions for some relevant trace elements.

The same points apply to a discussion of environmental analysis. In the different scopes of environmental control (for example limits of tolerance of threshold values in air, water, soil, sludges, foodstuffs, etc.) a short response time is again necessary and may be essential in case of economic consequences. A lot of other factors may strongly influence the decision for or against a given technique and must be seen strictly in connection with the given problem.

Knowing that it is nearly impossible to discuss the capacity of an analytical technique without regarding the investigated problem at the same

Table 4
Methods recommended for various elements

INAA	RNAA	FES/AAS	GFAAS	ICP-AES	HAAS	ECA
Ca	As	Al	Al	Cd	As	Cd
Cl	Cr	Ca	Cd	Cu	Hg	Cu
Co	I	Co	Cr	Fe	Se	Pb
Fe	Fe	Fe	Cu	Pb		
Se	Mn	Li	Fe	Mg		
Zn	Hg	Mg	Pb	Mn		
	Mo	K	Mn	Ni		
	V	Na	Ni	P		
		Zn		K		
				Na		

Table 5
State of the art of analysis*

Status	Element
Satisfactory	Cu, Fe, Mn, Zn
Borderline	Hg, Se
Unsatisfactory	Sb, As, Cd, Cr, Co, Pb, Ni, Mo

*Highly dependent on the concentration and on the matrices

time, some methods for the analysis of specific trace elements may be recommended (Table 4).

Let us look at the most commonly used analytical techniques. NAA is usually not regarded as one of them. Regarding this picture, one sees, that for As for example, only RNAA and HAAS (HICP) can be used. Excluding NAA, only HAAS remains. Another example is Cd, which can be analyzed by ETAAS, ICP-AES, ECA and of course by ICP-MS.

Taking into account the very different concentrations in the different matrices, it may be observed that ETAAS and ICP-AES are sufficient for most of the environmental samples, but in the biomedical field (excepting analyses of kidney and liver), especially in body fluids ECA (DPASV) or ICP-MS must be used. Formally, elements of interest can be discussed in the same way. Therefore the term "recommended" does not always mean generally applicable owing to insufficient limits of determination. The detection limits are not practicable in this connection.

The "state of the art" for some relevant elements in the biomedical and environmental field is briefly outlined in Table 5.

It can be seen and is nearly daily shown in many round robins or certification analyses that a satisfactory status is only being achieved for very few elements like Cu, Fe, Mn and Zn (but for example Mn in serum with a "normal" reference value below 1 ppb is in the unsatisfactory group!).

Most of the relevant trace elements have up to now an unsatisfactory status in the analysis of biological samples. This may be also the main reason for the big gaps in the knowledge concerning the biochemical functions of most of the trace elements. This is also true for interesting elements like Si, Sn and V or Tl classed as toxic elements, for which only very few reliable data are available.

This picture is reflected also by the scanty results in the certification of standard reference materials for these fields, where normally the most promising methods and laboratories are involved. Therefore, there is still a considerable need for the development and improvement of sufficient analytical techniques to generally improve the quality of analytical results on the one hand and to enable us to obtain reliable data for all elements on the other hand. Today, a considerable number of political and economic decisions are based on analytical data and thus faulty data may be very expensive.

Speciation

As mentioned in the beginning, inspite of the problems in the pure elemental analysis, the concentration alone, in both biomedical and environmental samples, is no longer in the foreground. For a better understanding of the effects of elements (essential and toxic ones) and their biochemical functions, one has to know the "species" (oxidation-, bonding state, macro-molecule, etc.) in which the element of interest has its characteristic function.

Therefore "speciation" analysis is the new challenge for analytical chemistry. Entirely new problems arise and all the old excellent working techniques (now regarding all the steps in the analytical procedure, from sampling up to the final measurements) are going to be unsuitable. New demands require reorientation in nearly all the analytical steps, such as, e.g. the coupling of organic (like HPLC or GC) and inorganic techniques.

Here again, the given problem defines the analytical strategy.

Conclusion

At the end of these brief comments on the trends and demands in and on trace element analysis, the main topics of the 6th International Workshop on Trace Element Analytical Chemistry in Medicine and Biology held in

April 1991 in the GSF/Neuherberg may serve to illustrate the points that have been discussed.

The points discussed were as follows:

Development and improvement of analytical procedures (all steps) including the preanalytical problems.

Quality control to improve the reliability of analytical data.

Speciation of trace elements.

Use of trace element status as a diagnostic tool (biomedical and environmental).

Clearing up the mystery of all the biological and biochemical functions of trace elements (includes also research on new essential trace elements).

Where does NAA stand in these wide fields of applications?:

There are only few contributions by this classical method today. The main reason is the poor availability of the technique. But NAA has its place as really independent technique with some advantages (for example free of blanks, no chemical interferences) and can be used for the verification of other techniques and whole analytical procedures and for the certification of SRMs.

The analytical strategy and the analytical procedure are defined by the problem in question.