JAAS

Cite this: *J. Anal. At. Spectrom.*, 2012, **27**, 537

www.rsc.org/jaas

ASU REVIEW

Atomic spectrometry update. Clinical and biological materials, foods and beverages

Andrew Taylor,*[a] Martin P. Day,[b] John Marshall,[c] Marina Patriarca[d] and Mark White[e]

Received 23rd January 2012, Accepted 23rd January 2012
DOI: 10.1039/c2ja90005j

[a]*Supra-regional Assay Service, Trace Element Laboratory, Faculty of Health and Medical Sciences, University of Surrey, Guildford, Surrey, GU2 7XH, UK. E-mail: A.Taylor@surrey.ac.uk*
[b]*The Australian Wine Research Institute, PO Box 197, Glen Osmond, SA 5064, Australia*
[c]*Glasgow Caledonian University, Cowcaddens Road, Glasgow, G4 0BA, UK*
[d]*Istituto Superiore di Sanità, Viale Regina Elena 299, 00161 Roma, Italy*
[e]*Health and Safety Laboratory, Harpur Hill, Buxton, Derbyshire, SK17 9JN, UK*

Amid the traditional development and applications work reported during the period covered by this review, the most obvious identifiable trend is that of downsizing. This is seen with techniques requiring smaller sample sizes or more effective analyte pre-concentration, and with new instrumentation. Procedures for extraction included the use of nanoparticles in various ways and the single-drop methodology with one example exploiting 1-dodecanol, a material that shifts between liquid and

solid states at around room temperature. Hand held instrumentation is commonplace in some application areas but less so within the sector covered by this Update. However an XRF device was used to carry out limit tests for harmful metals in pharmaceutical agents. The potential for expansion of in vivo *testing is now on the horizon with the development of a portable XRF instrument. Other features to mention are the larger than usual number of topics reviewed and the publication of several reference ranges for trace elements in biological fluids and also results from market-basket surveys. Application areas that were mentioned more than usual were studies involving the brain, CSF and neural function, and measurements of iodine including one method that involved vapour generation for ICP-AES. New approaches to establishing the authenticity of foods and food labelling were reported and examples of discrepancies between amounts measured and the stated contents were identified. A new writer, John Marshall, is welcomed to the team with primary responsibility for preparing the foods and beverages table.*

1. Reviews

This latest Update adds to that from last year[1] and complements other *reviews of instrumental techniques* in the series of Atomic Spectrometry Updates from the last year[2–6] together with our Perspective Review which discusses developments throughout the first 25 years of JAAS.[7] An unusually large number of relevant reviews were published during this year. These include those that concentrate on analytical topics, some that discuss the implication of results while others include both aspects. Because of the number, only a simple listing is all that can be given here for information and reference:

- Atomic spectrometry methods in general as applied to analysis of brain,[8] pharmaceuticals[9,10] and wine[11]
- Mass spectrometry techniques as applied to investigations of interactions between metallo-drugs and bio-molecules[12] and for investigations of food safety[13]
- Imaging techniques[14–16]
- *In vivo* XRF[17]
- Arsenic, metabolism and biological effects of As and its species in seafoods[18]
- Iodine, methods for sample preparation and measurement[19]
- Mercury, extraction procedures[20]
- Selenium, measurement in sperm[21] and selenoproteins,[22] variation of isotopic ratios in yeasts[23]
- Cerebrospinal fluid, metal speciation[24]
- Hair, analytical techniques and validity of results[25,26]
- Proteins. Analysis using CE[27]

2 Metrology, interlaboratory studies, reference ranges

Carioni *et al.*[28] describe a feasibility study undertaken prior to the preparation of a tuna fish RM for total As. Procedures to collect, lyophilise, homogenise and evaluate the material were presented. Concentrations of iAs and Hg species were determined in total diet and caprine blood *CRMs*, respectively, to extend the usefulness of these two materials. The Typical Japanese Diet (NIES CRM No. 27) was shown to contain 17 As^{III} and 43 As^{V} ng g^{-1}.[29] The whole blood SRM 955c Toxic Elements in Caprine Blood was further analysed at NIST to determine concentrations of MeHg, EtHg and iHg by triple spiked GC speciated ID-ICP-MS. Certified values ± expanded uncertainties were 4.5 ± 1.0, 5.1 ± 0.5, 9.0 ± 1.3 and 17.8 ± 1.6 μg L^{-1} for MeHg, EtHg, iHg and total Hg, respectively.[30]

The Eurachem/Citac Guide to estimation of *estimation of uncertainty of analytical measurement* using method validation data was applied to measurements of As, Co, Cr, Mn, Mo, Ni, Sn and V in human serum by ICP-SF-MS.[31] Results were reported for linearity, LOQs, trueness by analysis of a CRM, repeatability and reproducibility. The expanded uncertainties at concentrations in the range 0.1–2.0 μg L^{-1} were from 14.7% for Mn to 27.9% for Cr.

In previous years, these Updates have regularly featured studies involving *in vivo* XRF measurements of Pb in bone. The Updates have also included reports of measurement error inherent in the technique and the sample matrix. Lamadrid *et al.*[32] reported on yet another protocol designed to *correct for measurement bias* using what they describe as 'errors-in-variables regression', claiming this to be superior to ordinary least squares regression models.

Two *interlaboratory studies* were reported during the last year. One, with 142 participants in 42 countries assessed performance for measurement of Cd and Pb in herbal material. The between laboratory RSDs were 18.7% and 19.8% for Cd and Pb, respectively. Of the total number of participants, 22 gave one or more unsatisfactory results.[33] Four laboratories participated in an exercise to compare performance in measuring As species (As^{III}, As^{V}, MMA, DMA, AB) in whole blood. Results for five species were returned by the participants and the agreement was deemed to be good by the scheme organizer, particularly as the concentrations were at typical environmental levels. However many of the results were reported as below the LOD, which is a comment on the methods available for analysis of environmental samples, and the study did not really challenge the performance of methods at levels for which they may be used.[34]

Compared with previous years, the number of reports of *reference ranges or normal values* is much increased. The concentrations of five metals were determined in blood samples from 1420 Japanese adult women living in non-industrialised areas. The geometric mean concentrations as μg L^{-1} were: Cd 0.23, Cr 0.55, Mn 13.2, Ni 1.81 and Pb 15.8.[35] Blood samples from 215 adults living in Sardinia were analysed for six elements and the geometric means as μg L^{-1} were: Cd 0.53, Cu 1036, Mn 8.91, Pb 33.4, Se 140 and Zn 6481.[36,37] The blood Pb concentrations of Polish children were determined in 1995 and in 2007.[38] The mean concentrations fell over that time from 7.52 μg dL^{-1} to 4.8 μg dL^{-1}. Using 4276 urine samples from the 2003-06 USA National Health Nutrition and Examination Survey, Navas-Acien *et al.* determined the total As, DMA and AB concentrations and related the results to intake of seafood. Subjects who had eaten seafood within 24 h prior to the sample collection had geometric mean concentrations of 24.5, 6.0 and 10.2 μg L^{-1}, for total As, DMA and AB. As the interval between seafood intake and sample collection increased, so the As concentrations were reduced.[39] Morton *et al.*[40] measured Be concentrations in urine from 167 workers in the aluminium smelting industry and in 62

unexposed controls. The mean and 90th percentiles for the control group were 11.6 and 20.0 ng L^{-1} compared with 19.5 and 42.0 ng L^{-1} for the exposed group. Baxter *et al.* reported the first reference range for MeHg in serum when they used ID-GC-ICP-MS to analyse samples from 50 subjects.[41] The median, mean and range of results were 0.081, 0.091 and <0.03–0.19 μg L^{-1}, respectively. Results for Al, As, Cd, Hg, Pb and Sb in the 2nd French *Total Diet Study*, of 2006, were presented and were generally low and comparable with other studies in Europe. Values for Cd, Hg and Pb were below the maximum permitted levels.[42] From a similar project in Sweden in 1999, 15 essential and non-essential elements were measured. Most were at similar concentrations compared with a 1987 study but Fe and Pb were lower by 40% and 50%, respectively, while Se was 30% higher.[43]

3 Sample collection and preparation

3.1 Collection and storage

The *stability of Sb and Se species* at various temperatures and times was investigated by two groups. At −70 °C oxidation of Sb^{III} occurred and there was also loss of analyte, due possibly to co-precipitation or to the formation of species retained on the HPLC column. Addition of EDTA solved these problems.[44] To maintain volatile Se species in urine without loss, it was found that samples should be kept in the dark and, if not analysed on the day of collection, stored at −20 °C or −80 °C with NaN_3 added.[45]

In previous reviews, we have discussed the *effect of formalin fixation* on elements in tissue samples. Schrag *et al.*[46] measured concentrations of Cu, Fe and Zn in paired specimens of brain. Compared with fresh frozen samples, the concentrations of Fe and Zn were decreased by 40% and 77%, respectively in formalin fixed counterparts, while the concentrations of Cu were increased by 37%. The authors rightly concluded that care is necessary when interpreting data obtained from fixed samples.

3.2 Extraction and digestion

Almost all innovative work is focussed on *extraction methodologies* rather than digestion. This trend is related to the requirement to preserve structures for speciation studies and also to the shorter preparation times afforded. Many of the procedures reported involved ultrasound-assisted extraction into, usually, acidic solutions and the reports, of several sample types and analytes determined, include optimization of the conditions employed.[47–50] Nevertheless, Costas *et al.*[47] still found it necessary to include a further clean-up of the extracts in their work to measure concentrations of REEs in marine biological samples. Although complete breakdown of the sample matrix is deemed unnecessary, some microwave heating may be employed to increase efficiency and further shorten the analysis time. Extraction under pressure was first described a few years ago but has not become a popular approach. It was, however, used by Moreda-Pineiro *et al.*,[51] in conjunction with enzymatic hydrolysis, to release As species from seafood samples prior to measurement by ICP-MS. The effectiveness of this procedure was indicated by the results reported for CRMs with certified concentrations for AB and DMA. Without sonication or a specific pressure device, Khajeh and Ghanbari followed a Box-Behn design to optimize conditions to extract Cu, Fe, Mn, Ni, Pb and Zn from Snow trout, finding 685 W, 116 °C, HNO_3 at 2.5 mol L^{-1} for 38 min provided the best results.[52] To preserve labile Mn and Fe species in brain and liver tissue, Diederich and Michalke developed a cryogenic extraction at the temperature of liquid N_2 and under an inert gas. Comparison with the results of total digestion, showed that this extraction process recovered up to 44% Fe and 26% Mn in brain and 74% Fe and 44% Mn in liver, more than with a non-cryogenic process.[53] A device developed by Luftmann was used to extract iodinated X-ray contrast agents in urine samples from TLC spots.[54] This device provided a direct connection between the plate and an ICP-mass spectrometer for the measurement of I. The device was fixed to the plate over a spot and an eluant containing CH_3OH and CH_3OONH_4 was pumped through at a rate of 0.3 mL min^{-1} to extract the contrast agents and transport them to the nebulizer.

Sample digestion does feature in some work, however, with Hg species in whole blood separated and measured by GC-ICP-MS after closed vessel microwave heating with TMAH.[55] This procedure was reported to require no further clean-up and to be faster than other GC-based methods. Mesko *et al.*[56] mindful of problems associated with sample preparation for the measurement of I concentrations, elected to use microwave-induced combustion to prepare 500 mg samples of liver, corn starch, milk powder and wheat flour. A small amount of NH_4NO_3 was added as an ignition aid with the vessels charged with 15 bar O_2. The released I was absorbed into a H_2O–H_2O_2,–$(NH_4)_2CO_3$–TMAH solution which was then refluxed for 5 min. Low blanks and no memory effects were seen, good results were obtained for CRMs and the LOQ was 0.002 μg g^{-1}.

3.3 Preconcentration

Miniaturization best describes the key work taking place in sample preparation in general and in preconcentration in particular. Miniaturization, applied to sample size and to the resources employed. Nanomaterials, with capacities to be loaded with large sample volumes, featured in several publications. Nano-alumina coated with SDS and functionalized by addition of 2,4-dinitrophenylhydrazine, was used to trap Cr and Pb from water, urine and food samples. A maximum enhancement factor of 267 was achieved from an 800 mL sample and LODs for Cr and Pb of 0.55 and 0.45 μg L^{-1}, by FAAS, were reported.[57] Baytak *et al.*[58] prepared a minicolumn of yeast immobilized TiO_2 nanoparticles to preconcentrate six elements from water for measurement by ICP-AES and afforded 250-fold enrichment factors. A minicolumn packed with ME-3 chelating resin was used by Jin *et al.* in an on-line arrangement for measuring the concentrations of 24 elements in green tea leaves and their extract, by ICP-AES. Flow rates of 50, 70 and 35 μL min^{-1} were applied for conditioning the column, loading and eluting analytes, respectively. Enrichment factors of 40- to 74-fold were reported.[59]

Examples of *single drop microextraction*, in which analytes are extracted from sample solution into a 1–10 μL acceptor drop which is then taken for analysis, have featured in our recent Updates. The technique has now been reviewed by Choi *et al.*[60] who described systems used and a range of biological applications including analysis of urine, blood and saliva. A specific

example of the technique was reported by Wu *et al.*[61] for the measurement of Cu in cereals by FAAS. These workers described their procedure as "dispersive liquid liquid microextraction based on solidification of floating organic drop". The Cu was complexed with 8-hydroxyquinoline and extracted into 1-dodecanol, a low density material with a melting point of 22–26 °C which may be used, therefore as a liquid or solid. The enrichment factor was 122-fold and gave an LOD of 0.1 ng mL^{-1}.

In a couple of interesting reports, more *conventional procedures* were used in combination with more uncommon measurements. Cloud point extraction involving pyridyl-azo-naphthol was used to chelate Cd in soft drinks into micelles of Triton X-114, followed by measurement using TS-FF-AAS.[62] Hexavalent Cr in drinking water was trapped onto Aliquat 336-AC in a solid state and the concentration then measured by XRF.[63]

4 Progress with analytical techniques

4.1 Inductively coupled plasma-mass spectrometry

Husakova *et al.*[64] reported the simultaneous determination of more than 50 elements in urine using *ICP-orthogonal acceleration-TOF-MS*. While this technique was said to be suitable for certain elements for which ICP-QMS is difficult, polyatomic interferences cause problems for elements such as As, Cr, Fe, Se and V, requiring mathematical corrections.

The use of *LA-ICP-MS* for imaging structures and distribution in tissues is further discussed in section 5.2. Elsewhere, this technique is usefully applied to the distribution of elements along strands of hair. Two papers have addressed the issue of calibration for such assays. Dressler *et al.*[65] noted that use of CRMs for calibration limits the range of elements that may be determined. These workers devised a strategy to compensate for differing sensitivities between ICP-MS and LA-ICP-MS and to overcome limitations with CRMs for calibration. The LA products were transported in an Ar gas flow while a parallel flow carried aqueous calibration solutions *via* a pneumatic nebulizer. The sample and the desolvated calibrant gas streams entered an injection tube through separate apertures and were mixed in the torch. The ^{34}S in hair was used as the internal standard. Cheajesadagul *et al.*[66] adopted what is possibly a simpler approach, preparing Pb-doped keratin film standards by precipitating hair protein solution in Pb standard solutions. Transferrin, the Fe-binding protein in blood plasma was measured by LA-ICP-MS following separation from other proteins by gel electrophoresis.[67] Calibration was achieved using an isotopically enriched [^{57}Fe] transferrin prepared by these workers and analysis of a serum CRM gave results that were within the acceptable range.

As illustrated in the previous paragraph, measurement of *individual proteins* by determination of specific metal co-factors is of growing interest. This topic, in relation to proteomic research, was discussed in general by Zheng *et al.*[68] who referred to various complementary techniques including ICP-MS, ESI-MS and MALDI-MS. As seen in previous ASU reviews, much of the metalloprotein interest relates to Se. Letsiou *et al.*[69] reported the quantification of Se in selenoprotein P, GPx and selenoalbumin, by HPLC-ICP-MS, in serum samples from 399 healthy human subjects. They found concentrations for these three proteins of 49 ± 15, 23 ± 10 and 11 ± 4 ng mL^{-1},respectively.

Electrothermal vaporization-ICP-MS has not been used extensively for clinical or nutritional work. Two reports from the same department demonstrate the potential for this approach. Huanh and Jiang[70] prepared slurries of cereals and used a chemical modifier, 8-hydroxyquinoline-5-sulfonic acid, to both increase the volatility of the ten elements studied and to give similar sensitivities between slurries and aqueous solutions. Methane was used as the reaction gas to reduce background interference at *m/z* 52 and 80. In the second paper, Lin and Jiang[71] used a mixed chemical modifier of APDC and 8-hydroxyquinoline in measuring six elements in slurries of anti-hypertensive drug tablets. Interferences at *m/z* 52 and 53 were reduced by NH_3 as the reaction gas. Chen *et al.*[72] showed that theonyltrifluoroacetone forms a chelate with Cr^{III} which vaporizes at 900 °C and can thus be separated from Cr^{VI}. The method was successfully applied to the determination of these species in water.

As for ETV-ICP-MS, *MC-ICP-MS* has few applications relevant to this ASU. The Se isotopic ratios in Se-rich yeast were determined by Far *et al.*[23] The ratios ^{82}Se:^{77}Se, ^{82}Se:^{76}Se and ^{82}Se:^{74}Se were measured as the hydrides after acid digestion, and significant variations were seen among nine different yeast supplements, suggesting an approach to authentication. Measurement of the isotopic ratios of O and Sr in coffee was shown to also be useful for authentication.[73] Several examples in which likely sources of exposure have been identified in cases of Pb poisoning, on the basis of their Pb isotopic ratios, are known. Takagi *et al.*[74] suggested that accurate results are compromised by Al, Ca, Fe and Na at concentrations greater than 10 mg kg^{-1} and proposed that Pb must be separated from the sample matrix, for which purpose they used bromine complexation and anion exchange.

Some interferences in the more widely used ICP-QMS should be mentioned. The $^{156}Gd^{2+}$ ion has the same *m/z* ratio as $^{78}Se^{+}$ and examples of inappropriate serum Se results in patients following NMR investigations have been noted.[75] Analyses of urine samples from subjects given a Ga-containing anti-cancer drug[76] were subject to interferences from $^{36}Ar^{35}Cl^{+}$ and $^{36}Ar^{31}P^{+}$. The effects of Mo on the determination of Cd was further investigated by Vrijens *et al.*[77] who, curiously, found that the interference was greater with SF-ICP-MS than with ICP-QMS.

4.2 Atomic absorption spectrometry

A few *interesting applications* were reported involving measurements by AAS. There is some concern over the possible toxicity of fish-based baby foods due to the presence of As. Lopez-Garcia *et al.*[78] developed an approach to speciate samples with different ETAAS chemical modifiers. Samples were prepared as suspensions in TMAH and total As determined using a Pd modifier. When a Ce^{IV} modifier was employed, As^{III}, As^{V} and MMA were measured. No signal with this modifier indicates the presence of DMA and AB, which were differentiated by use of a Zr-coated atomiser, when only the DMA is atomised. Guerra *et al.*[79] enhanced an HGAAS procedure for determination of As and Sb in mineral water by adopting a fast-sequential option with measurement times of 3 s per element. Concentrations of HCl

and $NaBH_4$ and the delay and read times were optimized following which the LODs were 0.15 and 0.14 μg L^{-1} for As and Sb, respectively. The method was applied to analyses of commercial bottled mineral waters.

Variations of established approaches were seen for several applications. A crude slurry was prepared by weighing meat sample into analyser cups and adding TMAH, for determination of Cd and Pb by ETAAS.[80] Calibration was achieved using aqueous standards and results were in agreement with those obtained after digestion. Concentrations of Mn and Pb were measured by FAAS in shrimp powder, seasoning and river sediment CRMs as slurries of 0.1 g powder in 0.3% w/v HNO_3.[81] Cooking oils and fats were analysed for 13 elements, using both FAAS and ETAAS, following emulsification with Tween 80 and Triton X-100.[82] Cloud point extraction and TS-FF-AAS for measurement of Cd in soft drinks, and the method to determine Cu in cereals involving solid floating drop FAAS were mentioned in section 3.3.[61,62]

4.3 Atomic emission spectrometry and laser induced breakdown spectroscopy

Innovations involving AES techniques, now supplemented by applications of LIBS to the clinical and foods arenas, were evident during the last year. Matusiewick and Slachcinski[83] made use of a coupled continuous-microflow USN triple-mode capillary system to deliver I_2 vapour to the ICP-AE spectrometer. With an LOD of 1.6 ng mL^{-1} and RSDs of 2–4%, performance was superior to that of a conventional pneumatic nebulizer. Using a high temperature LC system coupled to an ICP-AE spectrometer, Terol *et al.*[84] reported the measurement of both organic and inorganic analytes in various foodstuffs. Aerosol formation from the column eluent was facilitated by the high temperature which allowed direct entry to the spray chamber without passing through a nebulizer and also reduced the plasma cooling effects associated with the solvents. Organic constituents such as different sugars were separated by LC and detected by the C emission signals. Metals were determined by separately injecting a small sample volume between the column and the spectrometer. The advantages of this approach, compared to evaporative light scattering detection, were an increased dynamic range and the determination of organic and inorganic analytes in the same measurement.

Other applications to note included a platinum wire loop to introduce 3 μL of sample into an air–CH_4 flame to determine Rb in beverages and juices by FAES. The LOQ was 4.3 pg and there was good agreement with measurements made by continuous nebulization[85] In a comparison of CV-AAS and ICP-AES to measure concentrations of Hg in mushrooms, the latter technique, with readings at 194.163 nm, gave inaccurate and imprecise results[86] leading the authors to conclude that reports of high Hg concentrations in wild-grown mushrooms, using this procedure, were probably inaccurate.

In a joint Chinese-French study in which K and Mg were measured in milk powders by *LIBS*, Lei *et al.*[87] noted a matrix effect which influenced the physical parameters of the plasma and the quantitative results. The effect was eliminated by using Ca as an internal reference for calibration rather than external calibrants and results were then comparable with the expected concentrations and with measurements by ICP-AES. The analysis of fingernails by LIBS was reported by Hussainimakarem and Tavassoli[88] who measured 13 elements and the CN molecule. The results include an observation of high K and Na concentrations in samples from patients with hyperthyroidism.

4.4 Atomic fluorescence spectrometry and vapour generation procedures

Most of the reports of interest during the year involved *the determination of Hg*. In response to concerns around the possible adverse effects of EtHg from thiomersal used as a preservative in vaccines, methods to monitor concentrations in such products are required. A simple photochemical vapour generation procedure was employed by dos Santos *et al.*[89] with an LOD of 0.3 μg L^{-1} of Hg. Analysis of vaccine products confirmed the manufacturers' content except for one in which none was detected. Dorea *et al.*[90] measured concentrations of MeHg, EtHg and iHg in hair samples from infants living in Amazonian riverine communities. These infants are potentially exposed to EtHg from vaccines and, *via* breast milk, to MeHg from fish and iHg from dental amalgam. Hair leachates were concentrated on a polymeric resin for analysis by Hg-thiourea LC-CV-AFS. The LODs, based on a 20 mg sample were 0.05, 0.10 and 0.10 for MeHg, EtHg and iHg, respectively. Of the six analysed samples from infants, five contained detectable EtHg and, in four, the major proportion of the total Hg was in the inorganic form. In a second paper, these workers used GC-CV-AFS to analyse 20 hair samples finding EtHg in 15 (at 3.7–65 ng g^{-1}) and MeHg in 18 (at 10.3–668 ng g^{-1}).[91] Gao *et al.*[92] also measured MeHg in single hair samples, using headspace GC-AFS. Following acid extraction, recovery of MeHg was 103% with an RSD of 7%, which was slightly better than with alkaline extraction although either procedure could be used as similar results were obtained for the CRM IAEA-086. The LOD, from 20 mg samples was 0.04 ng g^{-1}. Measurements on real samples indicated that MeHg accounted for 70% of the total Hg (by combustion CV-AAS, see 93).

A method *to vaporise I* for measurement by AES at 183.038 nm was developed by Matusiewick and Slachcinski.[83] Samples were solubilised using TMAH and the I_2 vapour formed during passage through a microflow USN triple-mode micro-capillary system. Mixing with H_2SO_4, H_2O_2 and $NaNO_2$ at the quartz oscillator oxidised the sample solution and allowed formation of the I_2 vapour. The method LOD was 1.6 ng mL^{-1} with RSDs of 2–4%. Analyses of CRMs (NIST 1549 and NIST 1566b) gave satisfactory results.

Simultaneous determination of Cd, Pb and Sn in biological samples by chemical vapour generation coupled with non-dispersive AFS was reported by Li *et al.*[94] The system consisted of two peristaltic pumps, two gas-liquid separators and an AF detector. In the first gas-liquid separator system, the main Cd vapour and some SnH_4 were formed with reductant solution I (HCl–$CoCl_2$–thiourea–KBH_4). In the second gas-liquid separator system, the main PbH_4 and some SnH_4 were produced using reductant solution II (HCl–KBH_4–$K_3[Fe(CN)_6]$). Under optimized experimental conditions LODs of 0.002, 0.071 and 0.058 ng mL^{-1} for Cd, Pb, and Sn, respectively, were obtained. The RSDs were, respectively, 2.9, 1.3 and 3.4% for 2 ng mL^{-1} of Cd and 10 ng mL^{-1} of Pb and Sn. The method was successfully used for the

simultaneous determination of Cd, Pb and Sn in a series of Chinese biological CRMs using aqueous calibration, and results were in good agreement with the certified values.

4.5 X-ray fluorescence

4.5.1 ***In vivo*** **XRF.** A review by Chettle[17] described the technique of *in vivo* XRF and its limitations, referred to the range of elements for which applications are available and described in more detail the measurement of *Pb and Sr in bone*. A bone Pb survey among 497 smelter workers, by his own group, was reported during the year.[95] For this work, their 'clover-leaf' design of detector was used, providing a three-fold increase in sensitivity and improved precision compared with systems used in previous surveys at the same establishment in 1994 and 1999.

That *the technique continues to experience challenges and requires further development* was demonstrated by Nie *et al.*[96] and Lamadrid-Figuero *et al.*[32] This latter group addressed the bias introduced into measurements by the various estimates and assumptions that have to be made. As an alternative to the 'Ordinary Least Square' regression model used to take account of these features they proposed 'Errors-in-variables' regression, suggesting that this is a better approach to the correction.[32] Nie *et al.*[96] reported on work to develop portable equipment for measuring Pb in bone. Parameters such as voltage, current, filter combination, radiation dose, were optimized for this one application. Measurement of soft tissue thickness from the XRF spectrum was included as part of the operating features. Comparison of the purpose-built portable XRF and KXRF technologies gave significant correlation between the measured bone Pb concentrations and similar sensitivities (LOD for the portable instrument was 8.4 ppm with 2 mm soft tissue thickness). The total body radiation dose of 1.5 μSv represents minimal radiation risk.

4.5.2 Quantitative analysis. A role for *XRF measurements in rapid, inexpensive monitoring of the content of medical materials, pharmaceuticals, dietary supplements and basic food items* was demonstrated in a number of papers. Using a hand held XRF spectrometer, it was shown to be possible to rapidly perform limit tests for harmful metals in pharmaceutical agents.[97] The spectra formed were analysed by continuous wavelet transformation filters to pick out the signal and noise components and transform readings to quantitative values. The LODs for As, Cr, Hg and Pb were 8, 150, 20 and 14 μg g^{-1}, respectively. Al-Omari[98] analysed ten ayurvedic medicines by EDXRF to determine the concentrations of 19 elements. All contained Ca, Fe, K and Sr and the amounts present were below the recommended dietary allowance for most elements although high concentrations of Hg were found in some samples. Stosnach[99] recommended TXRF to measure concentrations of Se in a range of medical and food items. Depending on the preparative procedure, LODs, although not as impressive as possible with other techniques, were deemed suitable for monitoring purposes. The limits were 7–10 μg L^{-1} for medical materials and 0.1–0.2 mg kg^{-1} for basic food items and dietary supplements. L-shell XRF was used to measure traces of Cd in rice.

Investigation of specific food types showed important difficulties and advantages associated with XRF. L-shell XRF was used to measure traces of Cd in rice and, in order to avoid signal from K, the excitation energy had to be set below the K absorption edge, at 3580 eV. It was also necessary to identify a suitable sample support material and a 6 pm film of polypropylene with polyvinyl acetate was found to be suitable. With these conditions, the LOD was 0.34 ppm.[100] The region in which coffee beans are grown is relevant to presumed quality and brand naming. To determine if measurement of trace element concentrations is an effective way to authenticate products, Akamine *et al.* analysed samples of coffee beans from Brazil, Colombia, Guatemala, Indonesia, Tanzania and Vietnam by XRF with 3D polarization optics. Using PCA analysis of the results for Ba, Fe, Mn, Ni, Rb and Sr, successful definition of the production areas was possible.[101]

Two similar papers show how *Cr^{VI} may be determined in drinking waters*. After adjusting the sample pH to 3, Inui *et al.*[102] passed the water through an anion exchange resin disc placed on top of a cation exchange resin disc. The Cr^{VI} was retained on the upper disc with Cr^{III} trapped on the lower. The discs were oven dried, coated with a laminate film and taken for measurement of Cr by WDXRF. The LODs were 0.17 and 0.16 μg g^{-1} for Cr^{III} and Cr^{VI}, respectively. Aranda *et al.*[63] used discs of Aliquat 336-AC, 16.7 mm diameter and 0.64 mm thick to trap Cr^{VI} which was then measured by XRF.

5 Applications: Clinical and biological materials

5.1 Metallomics

Developments in *metallomics and speciation is extensively reviewed in a separate Update* appearing in the August issues of JAAS.[6] This section is intended to give an indication of the range of work relevant to clinical, biological interests, foods and beverages from the last year. As in the past, the major topics of interest involve As, Hg and Se but work in other areas is evident too.

Picking up on *applications aside from the three main elements*, Al in plasma is almost exclusively bound to transferrin with a small fraction associated with low *Mr* species. To study Al metabolism and the effectiveness of chelation treatments, a rapid procedure for speciation was developed by Murko *et al.*[103] using a HiTrap desalting size exclusion column, with ICP-MS to show the elution profile. Free Ca^{2+} and eight Ca-containing species with *Mr* ranging from <15 kDa to >100 kDa were identified in human erythrocytes following ultrasonic-assisted dialysis and separation by CE-ICP-MS.[104] Iodinated X-ray contrast agents were separated using TLC. In this work, by Meerman *et al.*[54] an extraction device coupled the thin layer plate to an ICP-mass spectrometer (section3.2). Quiroz *et al.*[44] used HPLC-ICP-MS to determine concentrations of Sb^{III}, Sb^{V} and $(CH_3)_3Sb^{V}Cl_2$ in urine from occupationally exposed subjects. Good separation was achieved in less than 4 min and the LODs were <0.2 μg L^{-1}. As mentioned above, the speciation of metals in CSF was reviewed[24] as also were techniques such as FAB-, ESI- and MALDI-MS to investigate mechanisms of interactions between metallodrugs and biomolecules.[12] Methods for separating Cr^{III} and Cr^{VI} in water[72,102,105] are described elsewhere in this review. For similar speciation of Cr in serum, Wu *et al.*[106] used silica-coated Fe_3O_4 magnetic nanoparticles modified with

Table 1 Clinical and biological materials

Element	Matrix	Technique:atomisation: presentation	Sample treatment/comments	Ref.
Al	Serum	MS;ICP;SEC	The separation of the high and low *Mr* Al species present in human serum (spiked and unspiked) was achieved in 10 min, by means of HiTrap desalting size exclusion columns with tris-HCl buffer (pH 7.4)	103
As	Urine	MS;ICP;HPLC	The determination of five As species (AB, DMA^{V}, As^{III}, MMA^{V} and As^{V}) in urine in less than 3 min was achieved using HPLC-ICP-MS and a reaction cell. The chromatographic separation was performed on an IC-PAK HR anion exchange column, with a mobile phase of 0.012 mol L^{-1} $(NH_4)_2CO_3$, pH 9.8, followed, after 0.5 min, by 0.025 mol L^{-1} $(NH_4)_2CO_3$, pH 7.5. The polyatomic species $ArCl^{+}$ coeluted with MMA^{V} and As^{V} was eliminated using H_2 as the reaction gas. LODs were between 0.003 and 0.007 μmol L^{-1} for 1 : 10 diluted urine samples	108
As	Urine	MS;ICP;HPLC	The impact of a rice based diet on urinary As was investigated comparing the urinary levels of total As and As species (DMA, MMA, iAs) of Bangladeshi and white Caucasian volunteers, living in the UK	111
As	Chinese medicines	MS;ICP;HPLC	Traditional Chinese medicines (*Cordyceps*, *Radix Astragali*, *Radix et Rhizoma Rhei*, *Radix Scutellariae*, *Radix Polygoni Multiflori* and *Radix Rehmanniae*) were analysed by HPLC-ICP-MS for the simultaneous determination of As^{III}, As^{V}, MMA and DMA. Analytical performance data were as follows: LOQs ranged from 0.8 to 1.0 μg L^{-1}; RSDs were <10%; recoveries of spikes ranged from 82.40% to 119.5%. The main form of As present was iAs (As^{III}, As^{V})	168
As	Urine	MS;ICP;HPLC	A procedure for the determination of five (AB, As^{III}, As^{V}, MMA^{V} and DMA^{V}) As species in urine in just 6 min was reported. The method, based on micro-LC coupled to ICP-MS, used a low-pressure delivery six-port valve with a 5 cm anion exchange column, and was applied to the routine biological monitoring of 65 workers in a semiconductor factory	109
As	Urine	MS;ICP;L MS;ICP;HPLC	The association between seafood intake and the concentration of As species (DMA and AB) in spot urine was assessed as part of the 2003–2006 US National Health Nutrition and Examination Survey on a sample of 4276 subjects. Total As was measured by DRC-ICP-MS and As species were measured by HPLC-ICP-MS	39
As	Serum, urine	MS;ICP;HPLC	The concentrations of As species (As^{III}, As^{V}, DMA and MMA) were monitored in serum and urine of a man working at a recycling factory, taken to hospital following acute arsine poisoning. The results provided insight of arsine metabolism in humans	132
As	Urine	MS;ICP;HPLC	Six As species were determined in human urine with LODs of 0.06 μg L^{-1} (AB), 0.11 μg L^{-1} (As^{III}), 0.08 μg L^{-1} (DMA^{V}), 0.12 μg L^{-1} (MMA^{V}) and 0.15 μg L^{-1} (As^{V}). Results for a sample of 387 individuals with chronic, low level, exposure to As from drinking water were reported	110
As	Tobacco products	MS;ICP;HPLC XANES;-;-	An investigation of the concentrations and speciation of As in cut tobacco was carried out using a sequential extraction procedure (leaching with water followed by extraction with driselase and SDS) and anion-exchange HPLC-ICP-MS. In the water soluble fraction, 89% of As was found to be iAs. Total As concentration in a homogenate of cut tobacco was determined by microwave-assisted acid digestion followed by DRC-ICP-MS and found to be 318 ± 9 ng g⁻1 ($n = 3$)	172
As	Blood	MS;ICP;HPLC	The results of an interlaboratory comparison for the determination of As species in whole blood were reported	34
As	Cardiovascular tissue	AA;-;HG MS;ICP;HPLC	Total As and As species concentrations were determined by HG-AAS and HPLC-ICP-MS, respectively, in cardiovascular tissues of patients with coronary heart disease, exposed or not exposed to As	131
Be	Urine	MS;ICP;L	A procedure, with an LOD (3 SD) of 6 ng L^{-1}, was set-up and applied to demonstrate low level exposure to Be at an aluminium smelter. The mean and 90th percentiles of urinary Be were 19.5 ng L^{-1} and 42.0 ng L^{-1} for workers, compared with 11.6 ng L^{-1} and 20.0 ng L^{-1} for controls	40

Table 1 (*Contd.*)

Element	Matrix	Technique:atomisation: presentation	Sample treatment/comments	Ref.
Ca	Erythrocytes	AE;ICP;CE	Eight Ca-containing species were identified in two-fold diluted erythrocyte lysates, using a procedure based on ultrasound-assisted dialysis and CE coupled with ICP-AES. The separation was achieved using a 20 kV voltage and 40 mmol L^{-1} Tris-HCl buffer (pH 7.40). Only five species and free Ca^{2+} were observed in the erythrocyte cytoplasm analysed by the same method. The LOD for free Ca^{2+} in erythrocyte cytoplasm was 12 nmol L^{-1}, RSD was 2% and recovery for spiked samples ranged from 96.0% to 103%. For the species observed in erythrocytes, RSD were <2% and recovery was estimated as 94.71% by comparison of the sum of the concentrations of the species and the total Ca concentration measured in the same sample by ICP-AES	104
Cd	Water, urine, CRMs	AA;F;L	A new material with chelating properties was synthesised, characterised and applied to the separation and preconcentration of Cd, Cu and Zn from CRMs, tap water and human urine. The metals were eluted with 0.1 mol L^{-1} HNO_3 prior to analysis by FAAS. A 100-fold concentration factor and an LOD as low as 0.013 μg mL^{-1} were reported	214
Cd	Urine	MS;ICP;L	In a study of 191 premenopausal women, consumption of specific foods, notably tofu, was associated with increased urine Cd concentration among non-smokers	134
Cd	Chinese medicines	MS;ICP;L	In an international proficiency testing program (APLAC T065) on the Cd and Pb content of a sample of *Herba Desmodii Styracifolii*, with assigned values determined by ID-ICP-MS, RSDs of 18.7% (Cd) and 19.8% (Pb) were observed for the results provided by 109 laboratories from 42 countries	33
Cd	Blood	AA;ETA;L MS;ICP;L	Cd concentrations were measured in 1,159 blood samples by both ETAAS and ICP-MS. The geometric mean and maximum concentration observed were 1.22 μg L^{-1} and 6.90 μg L^{-1} by ICP-MS *vs.* 1.47 μg L^{-1} and 7.40 μg L^{-1} by ETAAS	135
Cd	Biological samples, CRMs	AF;-;VG	The simultaneous determination of Cd, Pb and Sn in biological samples was achieved by means of a chemical vapour generation dual gas-liquid separator system coupled with a non-dispersive AF spectrometer. Calibration was based on aqueous standards. LODs of 0.002 ng mL^{-1} (Cd), 0.071 ng mL^{-1} (Pb) and 0.058 ng mL^{-1} (Sn) were achieved. The RSD ($n = 7$) was 2.9% at 2 ng mL^{-1} Cd, 1.3% (Pb) and 3.4% (Sn) at 10 ng mL^{-1}. The procedure was applied to the analysis of Chinese CRMs	94
Cd	Blood	MS;ICP;L	A study of the interferences in ICP-QMS, DRC-ICP-MS and SF-ICP-MS, performed on blood samples spiked with K, Na_2EDTA and Mo, highlighted significant interferences with all the techniques at *m/z* 111, especially in K spiked blood samples, whereas overlaps with ^{114}Sn and $^{98}Mo^{16}O$ were successfully overcome by mathematical corrections	77
Co	Serum, urine	AA;-;-	In a prospective study, serum and urine concentrations of Co and Cr were monitored, before and up to 24 months after surgery, in Chinese patients given hybrid resurfacing arthroplasty. Both metal concentrations increased to a peak at 6 months, followed by a gradual decline	136
Cr	Water, food, industrial effluents, urine	AA;F;L	A new sorbent, based on modified nano-alumina, was applied for the preconcentration of Pb^{2+} and Cr^{3+} ions from aqueous solutions prior to their determination by FAAS. Elution was achieved with a mixture of HNO_3–MeOH. With an 800 mL sample, a preconcentration factor of 267 was obtained. The LODs (3 s, N = 10) were 0.55 (Cr) and 0.43 (Pb) μg L^{-1}	57
Cr	Transferrin	AE;ICP;L AE;PB-HC;-	Three analytical techniques (UV-VIS spectrophotometry, ICP-AES and PB-HC-AES) were compared for the investigation of Cr^{3+} upload into transferrin	137
Cr	Water, serum	AA;F;L	The determination of Cr^{III} and Cr^{VI} in water and human serum samples by FAAS was achieved using a new adsorbent, based on silica-coated Fe_3O_4 magnetic nanoparticles modified with N-(2-aminoethyl)-3-amino-propyltrimethoxy-silane. At pH 5.0–9.0, Cr^{III} was retained on the adsorbent and subsequently eluted with 1.0 mL of 1.0 mol L^{-1} HNO_3, followed by magnetic decantation. Cr^{VI} was determined by difference, after reduction with ascorbic acid and measurement of total Cr. The adsorption capacity was 22.6 mg g^{-1} and, with an enrichment factor of 100, the LOD was 0.66 ng mL^{-1}	106
Cr	Serum, urine	AA;-;-	See Co, ref. 136	136

Table 1 (*Contd.*)

Element	Matrix	Technique:atomisation: presentation	Sample treatment/comments	Ref.
Cu	Water, urine, CRMs	AA;F;L	See Cd, ref. 214	214
Cu	Brain	AA;-;-	Cu, Fe and Zn concentrations were measured by AAS in paired autopsy brain specimens, either conserved by formalin fixation or rapidly frozen. The results indicated significant lower (Fe, Zn) or higher (Cu) concentrations in the formalin fixed samples	46
Fe	Brain	MS;ICP;L	The potential of MRI for *in vivo* quantitative imaging of the distribution of Fe in brain was demonstrated by comparison with ICP-MS data. Measured Fe concentrations in prespecified gray and white matter regions from seven human post-mortem brains were compared to the transverse relaxation rates R2 and R2*, measured *in situ*, as surrogate markers for Fe in brain tissue, by using linear regression analysis and paired t tests for hemispheric differences. The results indicated an overall strong linear correlation for both parameters ($r^2 = 0.67$ for R2, $r^2 = 0.90$ for R2*; $P < .001$), but only for R2* in white matter structures. Significant differences in Fe concentrations between the two hemispheres were not reflected in the relaxation rates	142
Fe	Brain	AA;-;-	See Cu, ref. 46	46
Fe	Brain, liver	AE;ICP;L MS;ICP;SEC	A procedure for the extraction of Fe and Mn labile species from fresh tissues was developed, based on the use of cryogenic conditions under inert gas atmosphere. Fresh brain and liver tissues were stored either 1 day or 1 month in liquid N_2. Mn and Fe concentrations in extracts and pellets were determined by ICP-AES and the results compared with acid digests of the same sample, indicating that longer storage increased the extraction efficiency. SEC-ICP-MS was applied to quantify Fe and Mn species in extracts	53
Fe	Serum	MS;ICP;HPLC	To overcome difficulties in the quantification of transferrin (Tf) glycoforms in blood of harbour seals, a new approach was developed, based on the measurement of the Fe content of the relevant protein fractions by HPLC-ICP-MS. Analysis of a human serum CRM (ERM-DA470K/IFCC) with a Tf concentration of 2.35 ± 0.08 g L^{-1} gave a result of 2.33 ± 0.03 g L^{-1} as the sum of all quantified Tf glycoforms. Reference ranges for male (1.42–2.35 g L^{-1}) and female German North Sea seals (1.93–2.74 g L^{-1}) were established	144
Fe	Serum	MS;ICP;LA	Transferrin in human serum was quantified in less than 15 min by means of nondenaturing gel electrophoresis followed by LA-ICP-MS. Calibration was based on species-specific ID, using an isotopically enriched ^{57}Fe-transferrin complex, prepared in-house and characterised for its stoichiometry and stability	67
Fe	Cancer cells	XRF;-;- XANES;-;-	Qualitative and semiquantitative information on the elemental composition of human cancer cells, as well on the oxidation status of Fe, was obtained simultaneously by means of XANES combined with SR-TXRF. The cell suspension was pipetted directly onto the quartz reflectors	143
Ga	Serum	MS;ICP;L	The pharmacokinetics of gallium maltolate in 6 adult horses was determined by measuring the Ga concentration in timed (0–120 h) serum samples, after intragastric administration	138
Ga	Urine	MS;ICP;L	To monitor the renal elimination of a novel anticancer drug (tris(8-quinolinolato)gallium(III)), a procedure was developed for the determination of Ga in human urine by ICP-MS, after sample dilution with 1% v/v HNO_3. Recovery of Ga from urine samples spiked with the drug ranged from 95% to 102% and the LOQ was 0.2 μg L^{-1}	76
Gd	MRI contrast agents	MS;ICP;L	Two chromatographic procedures were reported for the speciation of Gd in nanoemulsion-based contrast agent formulations: one using RP-HPLC with fluorescence detection and post-column online ID-ICP-MS, the other based on high-pressure SEC and online ID-ICP-MS or species-specific ID-ICP-MS. The results indicated that the species-specific ID was critical for accurate determination of Gd species	156
Gd	Skin, serum	MS;ICP;L	In patients with nephrogenic systemic fibrosis, Gd concentrations in affected skin were higher than in the unaffected tissue and Gd levels in serum were higher than those of controls	157
Gd	Liposomes	AE;ICP;L	The cellular uptake of Gd in liposomes to be used for cancer therapy was determined	215

Table 1 (*Contd.*)

Element	Matrix	Technique:atomisation: presentation	Sample treatment/comments	Ref.
Gd	Plasma, skin and bone	MS;ICP;L MS;ICP;LC	In an investigation of the *in vivo* dissociation of Gd chelates, used as contrast agents, ionic macrocyclic or nonionic linear Gd chelates were administered to renally impaired Wistar rats for 5 consecutive days. On day 11, total Gd concentrations were measured in skin, femur epiphysis and plasma by ICP-MS and dissociated Gd^{3+} levels were determined in plasma by LC-ICP-MS	158
Hg	Urine, serum	MS;ICP;HPLC	Hg and Se species (SeMetCys, SeO_3^{2-}, SeO_4^{2-}, L-SeMet, D-SeMet, MeHg and iHg) were determined simultaneously, in about 27 min, in samples of urine and serum, by means of HPLC-ICP-MS, using column switching and two mobile phases. LODs were between 0.30 and 2.46 ng and recovery (for all species) ranged from 93% to 110%. RSDs ($n = 10$, 80 μg L^{-1}) were between 4.5% and 9.2%	113
Hg	Vaccines	AES;ICP;VG	The content of thimerosal in vaccines was determined as Hg. Samples were 1 : 100 diluted with 10% v/v formic acid and analysed by photochemical VG coupled to axial view ICP-AES, at 253.652 nm. Aqueous standard solutions of Hg^{2+} containing 10% v/v formic acid were used for calibration. The LOD (3 s, $n = 10$) was 0.3 μg L^{-1} of Hg, which corresponds to 60.0 μg L^{-1} of thimerosal in the original vaccine solution. Recovery ranged from 93% to 102% and RSDs were 2.9% (repeatability) and 4.4% (reproducibility). The analysis of anti-rabies, diphtheria/tetanus, hepatitis B and influenza vaccines, sourced from two producers, confirmed the product information, except for one (Hg level below the LOD)	89
Hg	Hair, CRM	AF;GC;- AA;-;-	The concentration of total Hg and MeHg were determined in human hair by combustion AAS, using the AMA analyzer (Advanced Mercury Analyzer 254), and headspace GC-AFS, respectively. Analytical performance was assessed by analysis of the IAEA 086 CRM. For total Hg, recovery was 97.5%, RSD was 3.2% and LOD ($n = 10$) was 1.5 ng g^{-1} for a 20 mg sample of human hair. For MeHg, similar performances were obtained with either acid or alkaline extraction: recovery was 103% *vs.* 110% and RSD was 7% *vs.* 9%. The LOD was 0.04 ng g^{-1} for a 20 mg sample	92
Hg	Tissues (brain, heart, kidney and liver), blood	MS;ICP;L MS;ICP;LC	In an experimental study, the distribution of Hg species (MeHg, EtHg and iHg) in rat tissues (brain, heart, kidney and liver) and blood, following administration of 0.5 mg Hg kg^{-1} day^{-1} as either thimerosal or MeHg, was compared, indicating different toxicokinetics for the two substances	150
Hg	Blood	MS;ICP;L	The results of an investigation of the levels of blood MeHg, by means of ID-ICP-MS, and the corresponding food consumption data, in a group of 299 fishermen and their families indicated positive associations mainly with fish consumption, but with other foods as well. Mean (range) blood MeHg concentration was 4.6 (0.21–22) μg L^{-1} among men and 2.8 (<0.15–20) μg L^{-1} among women	151
Hg	Blood	MS;ICP;L	The certification of the content of MeHg, EtHg, and iHg in a whole blood CRM (NIST SRM 955) was carried out by triple spike speciated ID-ICP-MS. The certified values (±expanded uncertainty) were 4.5 ± 1.0 μg L^{-1} (MeHg), 5.1 ± 0.5 μg L^{-1} (EtHg), 9.0 ± 1.3 μg L^{-1} (iHg) and 17.8 ± 1.6 μg L^{-1} (total Hg)	30
Hg	Tissues and subcellular fractions	MS;ICP;HPLC	The distribution of Hg species (MeHg and iHg) and Hg-binding proteins in brain, liver and kidney and the subcellular fractions (nucleus, mitochondrion, lysosome, microsome and cytosol) of maternal and infant rats after *in utero* and lactational exposure to MeHg was determined by means of HPLC-ICP-MS (Hg species), ID-HPLC-ICP-MS (Hg binding proteins). In addition, SDS-PAGE and MALDI-TOF-MS were used for protein identification	107
Hg	Blood	MS;ICP;GC	Hg species (MeHg, EtHg and iHg) in whole blood were separated and quantified by GC-ICP-MS, after derivatization and closed-vessel microwave-assisted digestion with TMAH. LODs for all species were <0.5 μg L^{-1} blood. The procedure was validated by analysis of a CRM (NIST SRM 966) and comparison of results with a previously reported LC-ICP-MS method	55

Table 1 (*Contd.*)

Element	Matrix	Technique:atomisation: presentation	Sample treatment/comments	Ref.
Hg	Hair	AF;CV;L AF;CV;GC	A procedure for the speciation of EtHg, in addition to MeHg and iHg, in hair was reported. Hair samples were leached with an acidic thiourea solution and leachates were concentrated on a polymeric resin prior to analysis by CV-AFS. The reported LODs, based on a 20 mg sample, were 0.050 ng g^{-1} (MeHg), 0.10 ng g^{-1} (iHg), and 0.10 ng g^{-1} (EtHg), respectively. In a second paper, the simultaneous determination of MeHg and EtHg in hair was achieved by coupling isothermal GC to CV-AFS. Both procedures were applied to the analysis of Hg species in hair of breastfed infants who received vaccines containing thimerosal	90,91
Hg	Urine, hair and toenails	AA;-;CV-	Hg levels were measured in urine, hair and toenail samples from 182 children aged 5–15 years in association with dental amalgam fillings	149
Hg	Blood	AA;-;CV	The direct determination of Hg concentration in whole blood was performed by means of a mercury analyzer (Model SMS 100), with a combustion step carried out at 650 °C for 60 s. Sample throughput was 7 h^{-1}. An LOD of 0.02 ng was achieved and RSDs were between 1.1% and 3.2%	93
Hg	Serum, plasma	MS;ICP;GC	The MeHg concentrations in human serum or plasma samples were determined for the first time using a newly developed procedure based on GC-ICP-MS and ID with MeHg labelled with ^{198}Hg. The LOQ (10 SD) was 0.03 μg L^{-1}, RSDs were <10% in the range of added concentrations of 0.14–2.8 μg L^{-1} and recoveries ranged from 82% to 110%. The median, mean and range of the concentrations measured in 50 plasma/serum samples were 0.081 μg L^{-1}, 0.091 μg L^{-1} and <0.03–0.19 μg L^{-1}	41
I	Urine	MS;ICP;L	The performance of an analytical method for the determination of I in urine by ICP-MS met the requirements of the FDA guidelines for bioanalytical method validation. The method was applied to assess I concentrations in random urine samples from 120 thyroid cancer patients, given a low I diet for 1 week prior to treatment with radioactive I, and 80 controls (median 38.7 μg L^{-1} *vs.* 238.8 μg L^{-1})	140
I	X-ray contrast agents, urine	MS;ICP;TLC	A procedure was developed for the quantitative determination of iodinated X-ray contrast agents in urine by TLC coupled with ICP-MS. A specifically designed extraction device assured the quantitative transfer of TLC spots to the plasma *via* the nebulizer. Recovery from spiked urine samples ranged from 3.2% to 16.6%	54
I	Edible salts, urine	MS;ICP;IC	The speciation of I^- and IO_3^- in edible salts and human urine samples was achieved by separation in only 170 s on a short (50 mm) anionic column coupled to ICP–MS, using 8 mmol L^{-1} $(NH_4)_2CO_3$ as the mobile phase. LODs were 0.015 μg L^{-1} and 0.081 μg L^{-1} for IO_3^- and I^-, respectively. Recovery on spiked samples and CRMs ranged between 89.5% and 101.1% for IO_3^- and from 97% and 106% for I^-	141
I	Biological sample, CRMs	AE;ICP;VG	I was determined in biological samples by *in situ* VG-ICP-AES at the emission line of 183.038 nm using a coupled continuous-microflow USN triple-mode micro-capillary system. After sample solubilisation with TMAH, I_2 vapours were generated by mixing the sample, H_2SO_4, H_2O_2, and the $NaNO_2$ solution at the quartz oscillator, converting liquids into aerosol at the entrance to the spray chamber. Improved performance, as compared to pneumatic nebulization, were (at a 15 μL min^{-1} flow rate): LOD (3 SD, based on peak height) of 1.6 ng mL^{-1} and RSD ranging from 2% to 4%	83
Mn	Brain, liver	AE;ICP;L MS;ICP;SEC	See Fe, ref. 53	53
Mn	Biological samples, sediments, CRMs	AA;F;Sl	Slurries were prepared by adding 0.30% w/v HNO_3 to 0.10 g of powdered sample, homogenised in an ultrasonic bath for 15 min and analysed by FAAS with a slotted tube atom trap for the content of Mn and Pb. Calibration was performed using acidified aqueous standards. LODs and LOQs were, respectively: 0.5 μg g^{-1} and 1.6 μg g^{-1} for Mn; 0.8 μg g^{-1} and 2.61 μg g^{-1} for Pb. The RSD was <6%. The procedure was applied for the analysis of CRMs (ERM-CE 278 Mussel tissue; CRM 397 Human hair; SRM 1646a Estuarine sediment) and 6 samples of shrimp powder, seasoning, and river sediment	81

Table 1 (*Contd.*)

Element	Matrix	Technique:atomisation: presentation	Sample treatment/comments	Ref.
Mn	Blood, urine	AA;ETA;L MS;ICP;L	The performances of atomic spectrometry techniques (ETAAS, ICP-QMS, DRC-ICP-MS and SF-ICP-MS) were compared. In blood, LODs (3 SD) ranged from 0.6 μg L^{-1} for SF-ICP-MS to 6.4 μg L^{-1} for ICP-QMS, whereas in urine they varied from 0.5 μg L^{-1} for SF-ICP-MS and DRC-ICP-MS to 2.1 μg L^{-1} for ETAAS. The RSD was typically between 3% and 4%, except for blood Mn by ICP-QMS (11%) and urine Mn by ETAAS (7%). Analysis of RMs indicated that, in contrast with other techniques, ICP-QMS is prone to positive bias for both matrices	148
Ni	Hair	AE;ICP;L	In an investigation of the Ni content in cats' hair, no significant difference was associated with their living conditions, sex or age, but the lowest Ni content was observed in white hair, followed by tortoiseshell hair and black hair, with the highest content in brownish grey hair	216
P	Polythymidylic acids	MS;ICP;HILIC	Oligonucleotides (10, 15, 20 and 30 nucleotides) were separated and detected by means of HILIC coupled with ICP-MS. Reaction with O_2 was used to convert P into $^{31}P^{16}O^+$ (m/z 47) and avoid the interferences at m/z 31. LODs, based on amount loaded on column, ranged from 1.69 pmol to 0.55 pmol	152
Pb	Bone	AA;ETA;L	The concentration of Pb in bones was determined by ETAAS, with 1% v/v $NH_4H_2PO_4$ as modifier, after microwave-aided digestion. Analytical performance was reported as linearity: 1–100 μg L^{-1}; LOD: 2.3 μg L^{-1}; LOQ: 7.0 μg L^{-1} and repeatability RSD: <5%. The authors reported the use of a software-aided methodology (Surface Response Methodology) to optimize ashing and atomization temperatures at 522 °C and 2146 °C, respectively, but such careful setting does not take into account the effect of furnace wear on the actual temperatures reached. The Pb concentrations in rib bone autopsy samples from 121 subjects, aged between 18 and 86 years, were reported with significant figures exceeding by far the method repeatability (range: 24.48–4459.96 μg kg^{-1}; mean ± SD 437.17 ± 75.66 μg kg^{-1})	145
Pb	Blood, serum	MS;ICP;L	The concentration of Pb was measured in blood and serum samples from 120 healthy pregnant women (more than 38 weeks of gestation) and their respective umbilical cord samples. Both blood and serum Pb concentrations were higher in the women than in the respective umbilical cord samples, whereas the ratio between serum and blood Pb concentrations were similar in both types of samples	146
Pb	Bone	XRF;-;-	In a survey of 497 smelter employees, bone Pb levels were measured *in vivo* using a four-element 'clover-leaf' geometry detector system. The results also provided information to validate the detector system, showing that both the minimum detection limit and the precision were improved in comparison with previous surveys on the same population, when a conventional system was used	95
Pb	Hair	MS;ICP;LA	Calibration of LA-ICP-MS for the determination of Pb in a single hair strand was achieved using a Pb doped keratin film standard, using S as an internal standard. Longitudinal analysis of single hair strands from workers in a battery manufacturing factory was carried out	66
Pb	Bone	XRF;-;-	A mathematical method (errors-in-variables regression) was applied to improve the reliability and the uncertainties of *in vivo* measurements of Pb in bone by KXRF	32
Pb	Bone	XRF;-;-	With a newly developed portable XRF device, an LOD of about 8.4 ppm with 2 mm soft tissue thickness was obtained. Measurement results were compared with those obtained with conventional KXRF	96
Pb	Blood, environmental samples	MS;ICP;L	An extraction procedure, based on Pb complexation with Br^-, followed by AEC, was developed to improve the accuracy of measurements of Pb isotopic ratios in blood and environmental samples by MC-ICP-MS	74
Pb	Teeth, blood, serum, saliva	MS;ICP;L	In a study of 444 Brazilian children, aged 6 to 8 years, the association of Pb concentrations in tooth enamel with those in blood, serum and/or saliva was investigated	147
Pb	Chinese medicines	MS;ICP;L	See Cd, ref. 33	33

Table 1 (*Contd.*)

Element	Matrix	Technique:atomisation: presentation	Sample treatment/comments	Ref.
Pb	Antacids	AA;ETA;L	Pb concentrations were determined in aluminum and magnesium based antacids by ETAAS, using pyrolysis and atomization temperatures of 700 °C and 2200 °C, respectively, PO_4^{3-} as the chemical modifier and calibration with aqueous standards. The characteristic mass was 25 pg, LOD and LOQ were 0.40 and 1.35 μg L^{-1}, respectively, and an RSD of 4.03% was obtained on an antacid sample containing 284.5 μg g^{-1} Pb. The Pb content measured in five antacid samples ranged from 87 to 943 μg g^{-1} and was confirmed by ICP-MS analysis	167
Pb	Biological samples, sediments, CRMs	AA;F;Sl	See Mn, ref. 81	81
Pb	Blood	AA;ETA;L	The results of surveys of blood Pb levels in children, carried out in 1995 and 2007, respectively, were compared	38
Pb	Biological samples	AF;-;VG	See Cd, ref. 94	94
Pb	Hair	XRF;-;-	Insight into prenatal exposure to Pb was obtained by longitudinal analysis of foetal hair by SR Micro XRF	217
Pt	Blood, amniotic fluid, urine and tissues	AA;-;-	An experimental study investigated the transplacental transport of commonly used anticancer agents (paclitaxel, docetaxel, carboplatin, and trastuzumab) in a pregnant baboon model. The appearance of the drugs was monitored in serial foetal and maternal blood samples, amniotic fluid, maternal urine, and foetal and maternal tissue samples, collected for 76 h after drug infusion. Levels of carboplatin were determined by AAS, docetaxel and paclitaxel by HPLC, and trastuzumab by ELISA	218
Pt	Cell	MS;ICP;HPLC	The concentration of intact, free cisplatin in a cell model was quantified by means of two, complementary, HPLC-ICP-MS procedures	154
Pt	Proteins	MS;ICP;L	A 2D electrophoretic separation procedure, based on sequential OFFGEL isoelectric focussing and PAGE, followed by enzymatic digestion of gel fractions and ICP-MS analysis, was developed to study Pt-binding proteins. The integrity of Pt-protein bonds throughout the procedure was assessed using standard proteins incubated with cisplatin. LODs were between 2.4 and 13.9 pg Pt	155
Pt	Plasma	AA;-;L	The pharmacokinetics and potential adverse effects of a new liposomal cisplatin form, after intrapleural administration, were assessed in a rat model	219
Ra	Urine	MS;ICP;L	A purification procedure for the extraction of ^{226}Ra from urine prior to determination by ICP-QMS was reported, which gave an LOD of 6.3 mBq L^{-1}	220
Rare earth elements	Marine biological tissues, seafood, CRM	MS;ICP;L	Ultrasound-assisted extraction was evaluated as the sample pre-treatment step for the determination of REEs in marine biological tissues by ICP-MS. Extraction conditions were: 5 mL of 3% v/v HNO_3–2% v/v HCl; particle size <200 μm; sonication time 3 min; sonication amplitude 50%. Extracts were purified on a C_{18} cartridge for non-polar SPE prior to analysis. Between batches RSD ($n = 3$) ranged from 0.9 to 7.7% and LODs were improved by a factor of 5 in comparison with those obtained after microwave-assisted digestion	47
Sb	Urine	AFS;HG;HPLC	A procedure based on HPLC-HG-AFS was developed for the determination of Sb species (Sb^V, Sb^{III} and $(CH_3)_3SbCl_2$) in urine of occupationally exposed subjects. The retention times were 0.88, 2.00 and 3.61 min, respectively, and LODs of 0.18, 0.19 and 0.12 μg L^{-1} were obtained with a 100 μL injection. The stability of Sb species at 4 °C and −70 °C was investigated	44
Se	Urine, serum	MS;ICP;HPLC	See Hg, ref. 113	113
Se	Serum proteins	MS;ICP;HPLC	A procedure was developed for the determination of selenoproteins (selenoprotein P, GPx, and selenoalbumin) in human serum, based on combined affinity chromatography and SEC, coupled to ICP-MS. Post-column ID with ^{77}Se in 25% MeOH was used for quantitation, while also enhancing sensitivity. The procedure was applied to determine selenoproteins concentrations in serum samples from 399 healthy Greek volunteers	69
Se	Plasma, erythrocytes, Brazilian nuts	AA;HG;L	Significantly increased ($P < 0.0001$) concentrations of Se in plasma (from18.8 ± 17.4 μg L^{-1} to 104.0 ± 65.0 μg L^{-1}) and erythrocyte (from 72.4 ± 37.9 μg L^{-1} to 244.1 ± 119.5 μg L^{-1}) were observed in 81 patients on haemodialysis after	162

Table 1 (*Contd.*)

Element	Matrix	Technique:atomisation: presentation	Sample treatment/comments	Ref.
			supplementation with one Brazilian nut (*ca.* 58.1 μg Se g^{-1}) a day for 3 months. GPx activity also increased from 46.6 ± 14.9 to 55.9 ± 23.6 U g^{-1} Hb ($P < 0.0001$)	
Se	Clinical samples, staple food and dietary supplements	XRF;-;-	The suitability of TXRF for rapid, on-site (or near-to-site) determination of the Se content in clinical samples (blood, serum and urine), staple foods and dietary supplements was investigated. The LODs ranged from 7 to 12 μg L^{-1} for clinical samples and from 0.1 to 0.2 mg kg^{-1} for food basics and dietary supplements	99
Se	Serum	MS;ICP;L	The relationship between serum Se concentration and major food groups and beverages consumed by Greek adults was investigated in a cohort of 506 participants in the ATTICA study (296 men, 210 women, aged from 18 to 75 years). Serum Se concentrations were positively correlated with consumption of red meat but not of other Se-containing foods	159
Se	Biological samples	MS;ICP;HPLC	The quantification of two volatile Se species (DMeSe, and dimethyl diselenide, DMeDSe) in biological samples was achieved, after separation on a short RP column using 40% MeOH as eluent, by DRC-ICP-MS, at *m*/*z* 80. The LOD was 8 nM for both species (corresponding to 0.6 and 1.3 μg Se L^{-1} for DMeDSe and DMeSe, respectively), linearity was in the range 0.1–1 μM and RSD was <3%	120
Se	Blood, serum, kidneys, urine	MS;ICP;L	The distribution and metabolism of selenohomolanthionine—found in Japanese radish—were investigated in rats given the compound labelled with ^{77}Se (25 μg kg^{-1} body weight). Samples of tissues, serum or urine were acid digested with 1 mL of a 1 : 1 mixture of conc. HNO_3–30% H_2O_2 at room temperature for more than 1 day, then at 160–180 °C until digestion was complete. Se isotopes were determined by ICP-MS equipped with an octopole reaction system, using 2 mL min^{-1} D_2 as the reaction gas	174
Se	Urine	MS;ICP;GC	An investigation of the stability of volatile Se species (DMeSe and dimethyl selenenyl sulfide) in urine from non-supplemented human volunteers provided recommendations to store urine samples in the dark immediately after collection and analyse them on the same day. Short term storage should be at 4 °C, after addition of 0.05% NaN_3. In addition, urine samples can be stored at −20 °C for up to 2 weeks or −80 °C for at least 4 weeks	45
Se	Serum	MS;ICP;HPLC	Two procedures for Se speciation in human serum were reported by the same group. Low *Mr* species (Se^{IV}, Se^{VI}, SeCys and SeMet) were separated in 7.5 min by AEC, with an NH_4 citrate–MeOH mobile phase, coupled with ICP-MS. LODs (3 SD) were 0.34 μg L^{-1} (SeCys), 0.67 μg L^{-1} Se^{IV}, 1.38 μg L^{-1} SeMet and 0.63 μg L^{-1} Se^{VI}, respectively, and RSDs were <9% ($n = 3$). The separation of Se species including Se^{IV}, Se^{VI}, $SeCys_2$, SeMet, selenoprotein P, selenoalbumin and GPx was carried out by RP and affinity chromatography, coupled with ICP-QMS, using a collision cell and post-column ID. LODs were 0.1 μg Se L^{-1} for GPx and other non-retained Se compounds and ranged from 1.0 μg Se L^{-1} to 1.3 μg Se L^{-1} for the other Se species. The RSD (repeatability, $n = 10$) was <6%. Both methods were applied to the analysis of serum samples from subjects with long-term Hg exposure given Se supplementation as Se-enriched yeast	119,161
Se	CSF	MS;ICP;HPLC	The distribution of Se species in CSF samples from 15 neurologically healthy subjects was determined using ICP-MS coupled with chromatographic methods. The separation of selenoproteins from low M*r* Se species was achieved by SEC coupled with DRC-ICP-MS, at *m*/*z* 80. Additional investigations, carried out using a strong anion exchange (SAX) column, allowed to separate and quantitate 6 Se species, among which Se^{VI}, thioredoxinreductase, selenoprotein P and selenoalbumin were identified. The other two species did not correspond to either SeMet, $SeCys_2$, GPx or Se^{IV}	128
Se	Urine, blood	MS;ICP;HPLC	A novel Se metabolite, Se-methylselenoneine, was identified in human urine and blood, after SPE, by parallel coupling of 2D RP/HILIC chromatography with ICP-MS and ESI- hybrid linear ion trap-orbital ion trap MS	117
Sn	Biological samples	AF;-;VG	See Cd, ref. 94	94

Table 1 (*Contd.*)

Element	Matrix	Technique:atomisation: presentation	Sample treatment/comments	Ref.
Ti	Skin	SIMS;-;-	*In vitro* studies were performed using pig skin to assess the safety of sunscreens containing TiO_2 and ZnO nanoparticles, using light microscopy, scanning and transmission electron microscopy, TOF-SIMS and ICP-MS. The results showed no evidence of transdermal absorption	221
U	Bones	MS;ICP;LA	The distribution of U isotopes in a fossilised horse tooth was investigated by means of LA-ICP-MS to support possible approaches to direct dating of human bones and teeth older than 500,000 years	222
U	Bone ashes	MS;ICP;L	As a follow-up of a previous study, the absorption fractions for U ingestion were estimated, according to an internationally agreed biokinetic model, from the analysis of bone-ash samples from 69 Canadian subjects, aged 7 to 25 years	163
V	Pharmaceutical formulations, dialysate and parenteral solutions	AA;ETA;L	Levels of V were determined in pharmaceutical formulations (10.5–15.2 μg L^{-1}), dialysate (0.65–1.32 μg L^{-1}) and parenteral solutions (1.76–6.93 μg L^{-1}), using a procedure based on cloud point extraction of the V complex with 8-hydroxyquinoline in the presence of Triton X-114. After separation, the surfactant-rich phase was diluted with a solution of HNO_3 in EtOH, prior to analysis by ETAAS. Using a 50 mL sample, an enrichment factor of 125-fold and an LOD of 42 ng L^{-1} were obtained	164
V	Blood	MS;ICP;L	In a case of fatal poisoning by self administration of ammonium vanadate, V blood levels of 6.22 mg L^{-1} (6000 times the concentration observed in the general population) were observed	223
W	Kidney, liver, colon, bone, brain, and spleen tissues	MS;ICP;L	The W concentrations, determined by SF-ICP-MS, in kidney, liver, colon, bone, brain, and spleen of mice, given different oral doses of sodium tungstate, increased with increasing dose of exposure, with the highest concentration found in the bones and the lowest concentration found in brain tissue	224
Zn	Water, urine, CRMs	AA;F;L	See Cd, ref. 214	214
Zn	Brain	AA;-;-	See Cu, ref. 46	46
Zn	Sputum	AA;-;L	To assess sputum Zn concentration as a potential biomarker for airway inflammation, total and labile Zn levels were measured, by AAS and complexation with a Zn specific fluorescent probe (Zinquin), respectively, in a sample of 163 subjects (114 with asthma). The median (±interquartile range) of total Zn concentrations observed in patients was 31.8 (±117) μg L^{-1} *vs.* 50 (±188.5) μg L^{-1} in controls ($p = 0.02$); for labile Zn levels, the median (±interquartile range) was 0 (±48) μg L^{-1} in patients *vs.* 26 (±84.5) μg L^{-1} in controls ($p = 0.05$)	165
Zn	Skin	SIMS;-;-	See Ti, ref. 221	221
Various	Exhaled breath condensate	MS;ICP;L	The elemental composition of exhaled breath condensate from patients with interstitial lung diseases of unknown etiology and controls was compared. Only the pattern of Co, Cu, Ni, Si, Se and Zn allowed to distinguish patients from healthy non-smokers with relatively high diagnostic sensitivity (96.4%) and specificity (90.9%)	129
Various	Brain, hair	MS;ICP;LA	A calibration method for the quantification by LA-ICP-MS of chemical elements in biological samples (brain tissue, single hair strands) without the need of CRMs was reported. This strategy is based on the separate introduction of the aerosol of the laser ablated solid sample (brain tissue, hair) and that of the nebulized aqueous standard into a special ICP torch	122,65
Various	Urine	MS;ICP;L	The performance of the NexION 300 ICP-MS was demonstrated using the determination of trace elements in a group of UTAK (R) freeze-dried urine SRMs as an example	225
Various	Urine	MS;ICP;L	The performance of ICP- orthogonal acceleration TOF-MS for the simultaneous determination of over 50 chemical elements in 10-fold diluted urine were reported, based on the analysis of commercially available urine RMs and/or spiked samples and isotope ratio evaluation	64
Various	Tumour tissue	MS;ICP;LA	LA-ICP-MS was applied to mapping the spatial distribution of Gd-doped iron oxide nanoparticles and other chemical elements in a tumour slice	123
Various	Hair	XRF;-;-	XRF and other techniques were applied to the analysis of mammoth's hair to gain insight of biological rhythms and seasonal food intake variations associated with trace element composition	226

Table 1 (*Contd.*)

Element	Matrix	Technique:atomisation: presentation	Sample treatment/comments	Ref.
Various	Biological tissues	MS;ICP;LA	A new technique for the imaging of small areas of biological tissues was developed, consisting of a laser microdissection apparatus combined with ICP-QMS	121
Various (4)	Pharmaceutical materials	XRF;-;-	A new procedure, based on continuous wavelet transform filters, allowed to improve the analysis of XRF spectra. The LODs were estimated as 8 (As), 14 (Pb), 20 (Hg), and 150 (Cr) μg g^{-1}	97
Various (4)	Cord blood, cord serum	MS;ICP;L	The body burdens of Cu, Hg, Pb and Se in a sample of 300 newborns in Baltimore was assessed by measuring the concentrations of these elements in umbilical cord blood or serum. Factors associated with the elemental levels were assessed by multivariate analyses	227
Various (4)	Teeth	MS;ICP;LA	2D maps of the distribution of Cd, Pb, Sr and Zn in teeth were obtained by LA-ICP-MS, using custom-built software. Teeth were sectioned longitudinally, embedded in resin and polished to a smooth surface, prior to laser ablation of the entire sectioned tooth surface and ICP-MS analysis. Quantification was based on single-point calibration against a CRM (NIST SRM 1486 Bone Meal)	124
Various (5)	Blood	MS;ICP;L	Reference values for the concentrations of Cd, Cr, Mn, Ni and Pb in blood of Japanese women were reported. Blood samples were collected from 1,420 adult women and analysed using ICP-SF-MS after wet digestion with HNO_3. Checks on phlebotomy devices indicated possible contamination of blood samples for Cr, Mn and Ni. The reported geometric means were 1.23 μg L^{-1} (Cd), 0.55 μg L^{-1} (Cr), 13.2 μg L^{-1} (Mn), 1.81 μg L^{-1} (Ni) and 15.8 μg L^{-1} (Pb)	35
Various (5)	CSF	MS;ICP;L	The assessment of the concentrations of Cu, Fe, Mg, Mn and Zn in CSF from patients with neurodegenerative diseases (amyotrophic lateral sclerosis, Alzheimer's disease and Parkinson's disease) suggested a possible role, in particular for Cu and Zn, in the onset and/or progression of these diseases	126
Various (6)	Hair	AE;ICP;L	Hair samples obtained from 22 European bisons from the Bialowieza Primeval Forest were analysed by ICP-AES, after microwave aided digestion with HNO_3. The observed mean content (SD) of Fe, Mg, P and Ti was 119.48 (83.31) mg kg^{-1}, 97.32 (33.16) mg kg^{-1}, 245.14 (65.00) mg kg^{-1} and 2.368 (2.097) mg kg^{-1}, respectively, with no significant difference associated with gender or age. On the contrary, both S and V levels were higher in mature bisons compared to calves	228
Various (6)	Blood	MS;ICP;L	In a study of a population sample of 215 non-occupationally exposed adults living on the Italian island of Sardinia, Nuoro province, the concentrations of Cd, Cu, Mn, Pb, Se and Zn in blood were determined by SF-ICP-MS, after microwave-assisted acid digestion. Reference ranges and possible determinants were reported	36,37
Various (6)	Drug tablets	MS;ICP;ETV	The concentration of Cd, Cr, Mo, Pb, Pd and Pt were determined in drug tablets using ultrasound-assisted slurry sampling and ETV-DRC-ICP-MS. The chemical modifier was a mixture of APDC and 8-hydroxyquinoline and NH_3 was used as the reaction gas. The LODs were in the range 0.1–0.9 ng g^{-1} of tablet and RSD was <5%, except for Pt (25%). The results obtained on antihypertensive drug tablets were confirmed by pneumatic nebulization ICP-MS analysis performed on dissolved tablets	71
Various (8)	Serum	MS;ICP;L	The analytical performances of a procedure for the determination of As, Co, Cr, Mn, Mo, Ni, Sn and V in human serum were reported as follows: LODs ranging from 0.05 μg L^{-1} (Cr, Mn) to 0.49 μg L^{-1} (As); mean trueness, estimated from the analysis of a CRM, between 95.4% (As) and 107.7% (Ni); RSD <10.2% (repeatability) and <12.0% (reproducibility) over the range 0.1–2.0 μg L^{-1}. The expanded uncertainty estimated from these data was between 14.7% (Mn) and 27.9% (Cr)	31
Various (11)	Saliva	MS;ICP;L	Ten-fold dilution with 1% v/v HNO_3 was chosen as the preferred method for the pretreatment of saliva samples (as compared with microwave-assisted acid digestion and dilution with distilled water) prior to ICP-MS analysis. The concentrations of 11 trace elements (Al, Cd, Cu, Mg, Mn, Mo, Pb, Rb, Sr, Tl and Zn) were determined in unstimulated whole saliva samples, collected from male volunteers (10 non-smokers, 30 smokers).	130

Table 1 (*Contd.*)

Element	Matrix	Technique:atomisation: presentation	Sample treatment/comments	Ref.
			Recoveries of spiked amounts of 5 and 10 μg L^{-1} ranged from 86.1% to 117.7%. Results showed large day-to-day variation. Blood contamination was shown to artificially increase the trace element content in saliva, whereas the number of metal restorations had no influence. Only the concentration of cotinine and Al were significantly increased in smokers	
Various (13)	Nails	LIBS;-;-	Thirteen elements and the CN molecule were identified in 45 nail samples analysed by LIBS	88
Various (15)	Herbal medicines	AE;ICP;L	A mathematical procedure (spectroscopic fingerprint), based on MATLAB and Excel software, was developed, aimed to combine the information from the ICP-AES analysis of herbal medicines to improve their quality control	169
Various (18)	CSF, plasma	MS;ICP;L	The ratios between the concentrations of 18 chemical elements in plasma and CSF were determined in paired samples from 264 patients with Alzheimer's disease and 54 controls, to investigate possible alterations of the blood-brain barrier associated with the duration and severity of the disease	127
Various (19)	Herbal medicines	XRF;-;-	The elemental concentration of ten ayurvedic drugs was determined by EDXRF. Only Ca, Fe, K and Sr were present in all samples. Hg concentration was above the maximum allowed limit in some specimens	98

N-(2-aminoethyl)-3-amino-propyltrimethoxy-silane, for magnetic solid phase adsorption. At pH 5.0–9.0, Cr^{III} was retained, to be eluted with HNO_3 followed by magnetic decantation. Total Cr was determined after reduction of Cr^{VI} to Cr^{III} by ascorbic acid and the Cr^{VI} concentration reported by calculation of the difference

The same techniques mentioned in the review of interactions between metallodrugs and biomolecules were also featured in a review on quantitative proteomics by Zheng *et al.*,[68] where the interest is in isotopic tagging as a means to identify biomarkers of disease and to study protein-based therapeutic agents. To investigate metabolism of MeHg to iHg in samples from maternal and infant rats, HPLC-ID-ICP-MS, SDS-PAGE and MALDI-TOF-MS were used to track Hg-binding *proteins* in tissue and cell fractions. The distributions of MeHg and iHg were quite different between mothers and offspring reflecting the different sensitivities to toxic mechanisms of Hg.[107] Similar approaches and techniques were discussed by Heras *et al.*[22] in a review on selenoproteins and Se metabolism.

Three almost identical procedures for *As speciation* from urine samples, using anion exchange HPLC-ICP-MS, have appeared. Two[108,109] specifically emphasised the rapid separation (<3 and <6 min) that is possible with virtually no sample preparation, and both resolved As^{III}, As^{V}, MMA^{V}, DMA^{V} and AB. The third paper[110] went one better and separated MMA^{III} from MMA^{V} but, when analysing samples from subjects with exposure to As in drinking water, no MMA^{III} was detected. Cascio *et al.*[111] monitored the urinary excretion of As species in subjects consuming mainly rice-based diets. The MMA and iAs concentrations were high compared to non-rice eating subjects and the authors suggested that this reflected the DMA and iAs in the rice. However, when incorporation of As into the roots of rice plants and its speciation were investigated by Seyfferth *et al.*,[112] they found As^{III} and As^{V} with only very small amounts of DMA and trisglutathione ($Asglut_3$) in the plant roots. This implied that any methylation must have occurred elsewhere in the plant. D'Amato *et al.*[49] extracted As from wheat and wheat-based foods and found around 95% as iAs with most of the remainder as DMA. In all of these investigations the analytical work involved anion exchange HPLC-ICP-MS.

To facilitate study of Hg-Se interactions in human metabolism, Moreno *et al.*[113] developed an HPLC-ICP-MS method for the simultaneous determination of iHg, MeHg, Se^{IV}, Se^{VI}, SeMetCys, L-SeMet and D-SeMet that was applicable to both urine and serum and afforded LODs of 0.30 to 2.46 ng. The concerns raised over the possible toxicity from EtHg in vaccines were mentioned in an earlier section. Consequently, methods are being developed for *Hg speciation* of EtHg, MeHg and iHg in blood. Rodrigues *et al.*[55] used TMAH digestion with microwave heating, followed by ethylation or propylation for GC-ICP-MS to establish a rapid, sensitive and accurate procedure. A more elaborate procedure was applied by Davis and Long,[30] involving triple spike speciated ID-GC/ICP-MS to certify a blood CRM (SRM 955c). Speciation of mercury extracted from samples of hair using AFS was described in section 4.4.[90–92] As the main environmental source of exposure to MeHg is from foods, particularly fish, methods for monitoring are important. A relatively fast procedure was reported by Ghanthimathi *et al.*[114] with a simple extraction step and RP-HPLC-ICP-MS using 0.1% L-cysteine as the mobile phase. The LOD for MeHg was 0.5 μg kg^{-1} and accurate results were given for two marine CRMs. Applicable to various food types, as demonstrated by the analysis of several fish and other CRMs, is a method developed by Chung and Chan.[115] Samples were digested with pancreatin and then by HCl. The MeHg and EtHg were derivatized with sodium tetraphenylborate, separated from the aqueous phase and taken for GC-ICP-MS, with PrHgCl used as the internal standard. The LOD for both species was 0.3 μg kg^{-1}.

The complex picture of *selenium metabolism* is growing ever more complex. In last year's review, we reported that a new metabolite, given the name selenoneine, had been identified in muscle tissue of several fish species. The same workers,

Yamashita *et al.* followed up their observations with analyses of many other fish some of whom had much lower concentrations of selenoneine or none at all.[116] Meanwhile, another group provided evidence for Se-methylselenoneine which they detected and characterised in human urine and blood.[117] The original identification was achieved using SPE and parallel coupling of RP-HILIC chromatography with ICP-MS and ESI-linear ion trap-orbital ion trap MS. To confirm the authenticity of this species, further ESI-MS work on Se-methylselenoneine was carried out, together with selenoneine, and their S-analogues. All four metabolites were independently detected in blood and urine samples and different methylated/nonmethylated ratios were seen between blood and urine suggesting involvement in Se metabolism. Given this ever increasing complexity, the formidable task set for themselves by Rao *et al.*[118] is worth mentioning even though no atomic spectrometric techniques were applied. These workers aim to map the Se metabolic pathway in yeast and have reported the detection and identification of at least 12 organo-Se species using a method that involves adding iodoacetic acid to stabilize selenols for LC-orbitrap-MS. In a complementary piece of work, Li *et al.*[119] attempted to quantify all the Se species in serum of Hg-exposed subjects who had consumed Se-enriched yeast. Combined ion-pair RP chromatography and affinity chromatography was employed to achieve separation, with detection by post-column ID-ICP-MS. This allowed detection and quantification of Se^{IV}, Se^{VI}, $SeCys_2$, SeMet, selenoprotein P, selenoalbumin and GXp. By contrast, the work of Lunoe *et al.*[120] would seem to be quite straightforward. They treated cancer cell lines with SeMet, SeMetCys, Se^{IV} and methylseleninic acid and sought to determine the formation of the volatile species DMSe and dimethyl diselenide (DMDSe). This was achieved with a short RP column by LC-ICP-MS. The latter species was detected in some samples.

5.2 Imaging: LA-ICP-MS and XRF

Becker and a number of colleagues have continued to describe techniques for *quantitative imaging of metal distribution in tissues*. Particular attention was given to the mouse brain and how LA-ICP-MS could provide structural information relevant to disease and damage.[14,15,65,121,122] Emphasis was placed on improving the spatial resolution that might be achieved, looking to the low-μm and nm scale using the near field effect at the tip of fine silver needle[14] and a laser micro-dissection apparatus.[14,121] The challenge of quantification of elements detected by LA-ICP-MS has been met by developing the dual gas flow sample introduction device described by Dressler *et al.*[65,122] Becker, together with a number of colleagues reviewed LA-ICP-MS and other techniques available for high spatial resolution imaging, such as SR-XRF and SIMS, and several applications.[15] Hsieh *et al.*[123] used LA-ICP-MS to map the spatial distribution of Gd-doped iron oxide nanoparticles in a tumour slice that had been subjected to magnetic fluid hyperthermia. The Gd was highly correlated with the Fe and an observed enrichment of Cu atoms after magnetic field hyperthermia was thought to be due to inflammation in the tumour. An abnormal distribution of Ni suggested a probable biochemical reaction in the tumour. Distribution of Cd, Pb, Si and Zn in longitudinal sections of teeth, using LA-ICP-MS, was shown by Hare *et al.*[124] Higher concentrations were found in the dentine, especially adjacent to the pulp. Cazares *et al.*,[16] with an interest in biomarkers that may be useful in diagnosis of prostate disorders, discussed how MALDI tissue imaging might be used, not only to look at the endogenous distribution of elements but also to detect molecular tags on antibodies, aptamers and other affinity molecules.

The distribution of Cu, Fe and Zn in breast, prostate and lung was shown, using XRF micro-tomography, to be different from each other and unrelated to the pathological changes that were observed by *X-ray transmission micro-tomography*.[125] As a non-clinical application, the localization of As in rice plants was studied by Seyfferth *et al.*[112] to help understand why As does not accumulate in the plant. It was noted that As and Fe were co-located in the roots and suggested that Fe has a scavenging action and restricts transfer of As to other parts of the plant.

5.3 Multielement applications

5.3.1 Biological fluids. Some reference to analyses of biological fluids has been made in the earlier sections on Reviews and Reference Ranges and there is further discussion in the section 5.6 on individual elements. With an increasing number of elderly people within many populations, interest in *brain dysfunction and neurodegenerative disease* is expanding. Two observational studies reported on the measurement of trace elements in *CSF*. Hozumi *et al.*[126] measured concentrations of Cu, Fe, Mg, Mn and Zn in samples from patients with Alzheimer's disease, Parkinson's disease and amytropic lateral sclerosis, by ICP-MS, finding higher concentrations than in control samples. Although they presented no evidence that these changes were causative they suggested that chelating agents might help in the treatment of patients. Gerhardson *et al.*[127] obtained CSF and plasma samples from 264 patients with Alzheimer's disease and from 54 control subjects and measured the concentrations of 18 elements. Significant differences in the CSF:plasma ratios were observed for Hg, Mn, Pb, Rb, and Sb. A review featuring available techniques for investigating trace element biochemistry in CSF was prepared by Michelke and Nischwitz.[24] This focused on metal speciation studies and included some data in addition to the analytical aspects. In a separate paper they reported the speciation of Se in CSF.[128] While not a multi-element application, their finding of six Se species illustrated the relevance of CSF studies to understanding the pathways of trace element metabolism.

In a follow-up to work which we mentioned in our last Update,[1] Corradi *et al.* have extended their investigations using *exhaled breath condensate*.[129] A number of elements were determined as part of a study on the pathogenesis of interstitial lung disease and concentrations of Co, Cu, Ni, Se, Si and Zn were significantly different compared with samples from healthy non-smokers, with high degrees of sensitivity and specificity.

The effects of smoking and of dental restorations on the concentrations of trace elements in *saliva* were investigated by Kim *et al.*[130] It was found that blood contamination had a profound effect on results and that other published data appeared to be inaccurate for failing to account for this feature. From suitable samples, wide daily variations in concentrations were seen and there was no association with the number of

restorations. However concentrations of Al were increased in the smokers.

5.3.2 Tissue, hair and nails. Surprisingly few reports dealing with *tissue samples* were seen during the last year. The work on the effects of formalin fixation[46] was mentioned in section 3.1. Kosanovic and Jokanovic[26] returned to the topic of hair analysis and whether the results give any useful information. In this extensive review, they discussed the many factors that influence the results and concluded that it is not really a valid approach. Kempson and Lombi[25] discussed the chemistry of incorporation of elements into hair and also referred to the factors leading to variation of results and the minimal usefulness of hair analysis. They did note, however, that such work can be of value in some circumstances such as population studies. The same conclusions, for the same reasons, were expressed by this reviewer in 1986 (Annals of Clinical Biochemistry 1986; 23: 364–378). The trend nowadays is towards the use of nail samples instead of hair although whether the same factors that influence hair analysis will prove to be relevant remains to be determined. Hosseinimakarem and Tavassoli[88] have shown that with LIBS it is possible to generate huge amounts of data, they analysed 45 nail samples, detected 14 analytes and monitored 63 emission lines, requiring a discriminant function analysis to give any meaning to the results. But it was not clear whether this provided any relevant information on the subjects whose nails had been analysed.

5.4 Progress for individual elements

5.4.1 Aluminium. Murko *et al.*[103] described a method for *the rapid fractionation and quantitative determination of Al in human serum* by combining desalting SEC with ICP-MS. Separation of high *Mr* Al species from low *Mr* Al species was achieved in 10 min using commercial HiTrap™ desalting columns packed with Sephadex G-25 and a tris-HCl buffer (pH 7.4). Quantitative determination of Al in the eluted fractions revealed that 94% of serum Al was found in the HMM fraction bound to transferrin. The authors considered the method to be a promising tool for investigating the kinetics of Al binding to transferrin and in studies on the effectiveness of chelation therapies for patients overloaded with Al.

5.4.2 Antimony. A Chilean group[44] described a method for *the determination of Sb species in human urine using HPLC coupled with HG-AFS*. With optimized chromatographic conditions, three Sb species, Sb^{V}, Sb^{III} and $(CH_3)_3SbCl_2$ were separated with LODs of 0.18 μg L^{-1}, 0.19 μg L^{-1} and 0.12 μg L^{-1}, respectively, for a 100 μL injection volume. The authors considered these LODs to be satisfactory for monitoring occupational exposures to Sb. The researchers investigated the stability of the three Sb species in preserved urine samples and made the observation that Sb species were unstable at a storage temperature of −70 °C, which they hypothesised was due to co-precipitation. They noted that the stability could be improved by the addition of EDTA to the urine samples.

5.4.3 Arsenic. A large proportion of the papers on As determination considered in this review period relate to the impact of diet on *As speciation in human biological fluids*. A comprehensive review on the identification and determination of As compounds in seafoods and seafood products was undertaken by Miyashita and Kaise.[18] The reviewers also summarised recent findings on the metabolism and biological effects of these As species in animals and humans. Within the 2003–2006 US National Health Nutrition and Examination Survey (NHANES) Navas-Acien *et al.*[39] evaluated the association between the concentration of As species in spot urine samples and dietary seafood intake. Total urinary As was measured using ICP-MS and the As species DMA and AB using HPLC-ICP-MS. They reported that individuals consuming seafood in the 24 h period before urine collection had higher urine concentrations of total As (24.5 *vs.* 7.3 μg L^{-1}), DMA (6.0 *vs.* 3.5 μg L^{-1}) and AB (10.2 *vs.* 0.9 μg L^{-1}). They concluded that seafood intake was a major determinant of increased urinary As species and argued that epidemiological studies that use urine As speciation as a marker of iAs exposure need to take account of dietary seafood consumption. Morton and Leese[109] described a rapid method for the quantitative determination of As species in urine using micro-LC-ICP-MS. The authors used a low-pressure delivery system with a 5 cm anion-exchange column to obtain fully resolved separation of five As species: AB, As^{III}, As^{V}, MMA and DMA. They used the method to monitor As species in urine samples collected from a group of 65 semiconductor industry workers. They also highlighted the need to consider dietary influences on urine As speciation. Belanger and Dumas[108] also reported a 'fast' method for the determination of As species in urine using HPLC-ICP-MS. With gradient elution chromatography coupled to ICP-MS, with a collision cell and H_2 as the reaction gas to eliminate the $ArCl^{+}$ interference on As, the researchers reported quantitative determination of the same five As species within a three minute analysis cycle. Rivera-Nunez *et al.*[110] presented a method for the quantitative determination of six As species; As^{III}, As^{V}, MMA^{III}, MMA^{V}, DMA^{V} and AB. The authors used the method to monitor As species in urine collected from 387 individuals chronically exposed to low levels of As in drinking water. They detected DMA in 99.2% of samples, AB in 98.2%, MMA^{V} in 73.4%, As^{III} in 45% and As^{V} in 27.1%. They did not detect MMA^{III} in any of the samples analysed and raised the doubt as to whether this species is a significant metabolite in humans exposed to low levels of iAs.

Ito *et al.*[34] reported on an inter-laboratory study on the determination of *As species in whole blood*, which was undertaken in conjunction with the NY State Department of Health proficiency testing programme for total As in blood. They reported that good agreement between the participants was observed for most of the five As species for which values were reported, despite the very low concentrations in the proficiency testing samples distributed. However, it was noted by the review team that many of the values were reported as being below the LOD for the method employed and clearly demonstrated the difficulty in making quantitative measurements of some As species in complex biological matrices. Roman and colleagues[131] determined *total As and As^{III} in cardiovascular tissue biopsies* from a group of patients with cardiovascular disease living in the Atofagusta region of Chile, who were environmentally exposed to As. The concentration of total As was determined using HG-AFS and the concentration of As^{III} species determined using HPLC-ICP-MS. The workers reported elevated levels of both

species in auricle and mammary artery biopsies compared with a control group of cardiovascular disease patients who were not exposed to environmental As. Auricle tissue was also reported to be a target tissue for As^{III}.

Cascio *et al.*[111] investigated *the impact of a high rice diet on urinary As levels* in a group of Bangladeshi volunteers living in the UK. The researchers determined total urine As and MMA, DMA and iAs species. They reported higher levels of DMA and iAs in the volunteers compared with a white Caucasian group. They concluded that the higher DMA intake from rice significantly altered the DMA:MMA ratio in urine.

Finally, it is now very uncommon for this review to report on *cases of acute occupational metal intoxication*. Yoshimura *et al.*[132] confirmed a case of acute arsine poisoning in a worker from a semiconductor recycling plant. Urine and serum As species were determined using HPLC-ICP-MS. On admission, serum total As was 244.8 μg L^{-1}, which declined over the five days of hospitalisation to 97.1 μg L^{-1}. Speciation analysis identified four species derived from arsine in both serum and urine. Concentrations of the four species at admission were: As^{III} 45.8 μg L^{-1}, As^{V} 5.2 μg L^{-1}, MMA 17.9 μg L^{-1} and DMA 9.3 μg L^{-1}. Levels of As^{III}, As^{V} and MMA declined during hospitalisation whilst DMA increased towards the time of discharge. After discharge, urine concentrations of all four species decreased with a calculated half-life of 15 days. The authors considered that arsine is rapidly metabolised to As^{III} and then *via* MMA to DMA.

5.4.4 Beryllium. *To monitor workers exposure to Be* at an aluminium smelter, Morton and colleagues[40] developed a sensitive method for the quantitative determination of Be in urine using ICP-MS. Urine samples were simply diluted 1 + 9 v/v with 1% HNO_3 containing Ge and Y as internal standards, and introduced to the plasma by direct nebulization. With optimized sampler and skimmer cone assemblies, a 25-fold enhancement in signal sensitivity was obtained giving a reported LOD of 6 ng L^{-1}. The mean and 90th percentile values reported for a group of 167 exposed workers were 19.5 ng L^{-1} and 42 ng L^{-1}, respectively compared to 11.6 ng L^{-1} and 20 ng L^{-1} in a control population. The authors noted that workers had 47% higher levels of urine Be at the end of a work week and also that smokers had significantly higher levels than non-smokers.

5.4.5 Cadmium. It is encouraging to see yet again the small number of papers concerned with the determination of this element in biological matrices compared with the situation over 10 years ago, reaffirming its rapidly declining industrial use. Lemos and deCarvalho[133] presented a review of spectrometric methods for *the determination of Cd and Pb in human biological samples*. The authors paid particular attention to sample preparation procedures for the determination of both elements in hair, nails, blood and urine. Adams and colleagues[134] investigated sources of environmental Cd exposure in a group of healthy women. The concentration of Cd in spot urine samples was determined using ICP-MS and normalised to urine creatinine concentration. The environmental factors contributing to the urine Cd concentration were evaluated using multivariate linear regression. Smoking was the main contributory factor to urine Cd levels. A mean urine Cd concentration of 0.43 μg g^{-1} creatinine was reported for women with any history of cigarette smoking compared with a mean of 0.3 μg g^{-1} for women who had never smoked. The most important dietary source of Cd was identified as tofu and the authors estimated that urine Cd was 0.11 μg g^{-1} creatinine higher in women who consumed tofu.

Two groups described method comparison studies for *the quantitative determination of Cd in blood*. Vrijens *et al.*[77] presented a comparison of HR-ICP-MS and ICP-QMS. To investigate the interference effects in detail, blood samples were spiked with K, Na_2EDTA and Mo. The researchers observed significant interferences on the ^{111}Cd isotope especially in samples spiked with K and that the interferences were more pronounced with HR-ICP-MS. The authors considered that accurate analysis could be achieved using the ^{114}Cd isotope and applying a mathematical correction for ^{114}Sn and $^{98}Mo^{16}O$ interferences. Fukui and colleagues[135] compared ETAAS and ICP-MS for the determination of Cd in blood by analysing 1159 samples collected from women throughout Japan. The regression line between the methods showed a slope close to one and an intercept near to zero from which the authors concluded the methods could be employed inter-convertibly when blood Cd levels were above 2 μg L^{-1}. Finally, reference intervals for Cd and Pb in blood were reported by Forte *et al.*[37] for the general population of Sardinia (Italy). Blood samples were acid digested with microwave heating and both elements quantitatively determined using SF-ICP-MS. The reference ranges, expressed as the 5th to 95th percentile were 0.24 to 1.82 μg L^{-1} for Cd and 13.2 to 87.3 μg L^{-1} for Pb.

5.4.6 Calcium. Deng *et al.*[104] developed a method for the identification and determination of Ca species in erythrocytes using ultrasonic dialysis and capillary electrophoresis with ICP-AES. Optimum separation of Ca species was achieved at 20 kV with a 40 mM Tris–HCl buffer. Eight Ca-containing species were identified and the concentration of free Ca^{2+} in red blood cells was reported to be 112 nM. The researchers noted that the Ca species with the highest mobility was not free Ca^{2+} but a Ca-erythrocyte membrane species.

5.4.7 Chromium. Afkhami *et al.*[57] investigated a new solid-phase sorbent, 2,4 dinitrophenylhydrazine immobilised on nano-alumina, for *the pre-concentration of Cr^{III} and Pb^{II} from biological matrices* for quantitative determination using FAAS. Adsorbed ions were eluted from the sorbent column with HNO_3–CH_3OH. A maximum pre-concentration factor of 267 was reported giving LODs of 0.55 μg L^{-1} and 0.43 μg L^{-1} for Cr and Pb, respectively. The method was evaluated by analysing a range of water, food and clinical samples. A Chinese group[106] also described a method for pre-concentration of Cr species from biological samples onto a nanoparticulate sorbent for quantitative determination using FAAS. In their approach, Cr was extracted onto a magnetic solid-phase adsorbent (Fe_3O_4 nanoparticles modified with N-(2-aminoethyl)-3-aminopropyltrimethoxysilane). Within the pH range 5–9, the adsorbent was selective for Cr^{III}. Total Cr was determined following reduction of Cr^{VI} to Cr^{III} with ascorbic acid. The researchers reported an adsorption capacity of 22.6 mg g^{-1} for Cr^{III} giving an enrichment factor of 100 and an LOD of 0.66 ng ml^{-1}. The method was applied to the determination of Cr species in environmental waters and serum samples.

Previous reviews in this ASU series have regularly reported on studies to measure *the concentrations of trace elements in body*

tissues and fluids of patients fitted with metal implants. Yang *et al.*[136] monitored the serum and urine concentrations of Co and Cr in younger (<50 years) active individuals who had undergone metal-on-metal resurfacing arthoplasty. Concentrations of the two metals were monitored over a two-year period using ETAAS. The authors noted peak concentrations at six months post-surgery followed by a gradual reduction. They observed no evidence of renal impairment over the monitoring period.

Quarles *et al.*[137] investigated the merits of UV-VIS, ICP-AES and PB-HC-AES for the qualitative and quantitative determination of *Cr binding to human transferrin*. Whilst both AE methods gave comparable and reliable results, and were considered by the authors to be equally suitable for investigating metal-protein interactions, the UV-VIS method suffered from spectral interferences and overlapping charge transfer bands which gave inaccurate determinations.

5.4.8 Gallium. American veterinary surgeons have investigated the merit of gallium maltolate (GaM) as a novel antimicrobial agent. As part of these studies, Arnold *et al.*[138] examined the pharmacokinetics of GaM in adult horses. Following a single nasogastric administration of GaM (20 mg kg^{-1}), blood samples were regularly taken over a 120 h period and serum *Ga concentrations determined using ICP-MS*. The measured concentrations were best described by a one-compartment model with first order kinetics from which the researchers calculated a maximum serum Ga concentration of 0.29 μg mL^{-1} and an elimination half-life of 48.82 h. Filatova *et al.*[76] used ICP-MS to determine Ga in human urine following administration of a novel anti-cancer drug tris(8-quinolinolato)gallium(III). Urine samples were simply diluted with 1% v/v HNO_3. An LOQ of 0.2 μg L^{-1} was reported together with spike recoveries of 95–102%, from which the authors considered that the method had practical merit in monitoring urinary excretion of Ga in clinical trials of the drug.

5.4.9 Gold. *Investigations on the interaction between novel nanomaterials and biological systems continue to be reported*. A therapeutic application for Au and Fe nanoparticles was presented by Kim and colleagues.[139] The authors exploited the phenomenon of a localised PIXE effect when nanoparticles are activated with a high-energy proton beam for therapeutic irradiation of tumours. PIXE directed at CT26 tumour cells *in vitro* increased when cells were incubated with Au or Fe nanoparticle suspensions over the concentration range 0.1–2 mg mL^{-1}. In an *in vivo* study, mice with CT26 tumours showed a tumour volume reduction of 75–90% when treated with proton beam therapy coupled with metal nanoparticle injections compared with only 18% reduction in tumour volume for proton beam therapy alone.

5.4.10 Iodine. Each review period sees a flurry of new activity on an individual trace element. In this review period, there has been increased attention on I with five papers meriting comment. Oliveira and colleagues[19] presented a critical review of ICP-MS and ICP-AES methods for *the determination of I in a wide range of biological matrices*. The authors paid considerable attention to the merits and limitations of sample preparation for quantitative analysis by either technique. They reported that the best figures of merit were obtained with sample preparation in alkaline media with determination of I using ICP-MS. An alkaline solubilisation treatment was used by Matusiewicz and Slachcinski[83] for the quantitative determination of I in biological matrices using VG-ICP-AES. Following solubilisation with TMAH, the sample solution was reacted with H_2SO_4–H_2O_2–$NaNO_3$ in a triple-mode microflow USN to generate I_2 vapour for quantitative determination of I by ICP-AES at the 183.038 nm emission line. A univariate approach was used to establish optimum conditions for I_2 VG to give a reported LOD of 1.6 ng mL^{-1} and RSDs of 2–4%, which the authors considered to be superior to those obtained with pneumatic nebulization. The method was validated using CRMs with a simple external calibration approach.

Lee *et al.*[140] developed a method *to quantitatively determine I in urine* using ICP-MS, which met the FDA guidelines for the validation of bio-analytical methods. The researchers used the method to determine urinary I in patients with thyroid cancer who were on a low I diet. The mean concentration of urine I in the patient group was 38.7 μg L^{-1} compared with the mean level of 238.8 μg L^{-1} in a healthy control group. They considered the method to be very useful for monitoring I status in patients on low I diets. A method for the fast speciation of I in edible salts and human urine was described by Zhang *et al.*[141] using short-column IC coupled with ICP-MS. With a commercial anionic column of 50 mm and a mobile phase of 8 mM $(NH_4)_2CO_3$, I^- and IO_3^- were separated in 170 s with LODs of 0.015 and 0.081 μg L^{-1} for IO_3^- and I^-, respectively. The method was validated by analysing CRMs.

5.4.11 Iron. Two papers reported *studies on the determination of Fe in brain*. Langkammer *et al.*[142] examined the correlation between brain Fe concentrations determined by ICP-MS and the results from MRI (R_2 and R_{2*} transverse relaxation rates). Quantitative MRI was performed on seven post-mortem brains *in situ*. The brains were extracted and Fe concentrations determined in pre-selected regions of grey and white matter using ICP-MS. Mean concentrations of Fe were determined in the following brain regions: globus pallidus (205 mg kg^{-1}), putamen (153 mg kg^{-1}), caudate nucleus (92 mg kg^{-1}) and thalamus (49 mg kg^{-1}). The concentration of Fe in the selected regions was correlated with the MRI data using linear regression analysis. Relaxation rates showed a strong linear correlation with Fe concentrations throughout the brain ($r^2 = 0.67$ for R_2 rates and $r^2 = 0.9$ for R_{2*} rates). Significantly higher concentrations of Fe were determined in the left hemisphere but this was not reflected in the relaxation rates. The researchers recommended that R_{2*} be the preferred parameter for assessment of brain Fe levels owing to its greater sensitivity to variations in brain Fe concentration. Diederich and Michalke[53] described a method for the extraction of Fe and Mn species from brain and liver tissues using cryogenic conditions under an inert gas atmosphere. Concentrations of Fe and Mn in extracts and residue pellets were determined using ICP-AES and the results compared with those for acid digestion of the same samples. When compared with a previous extraction method, that did not employ an inert atmosphere, extraction efficiency for Mn was increased from 17% to 26% in brain and from 28% to 44% in liver, whilst for Fe, extraction efficiency increased from 40% to 44% in brain and from 64% to 70% in liver. The researchers also combined SEC with ICP-AES to examine the Fe and Mn species in the extracts. Extracted Mn was associated with organic species from the 0.7–4 kDa fraction in brain and the

70–80 kDa fraction in liver. Extracted Fe from liver was associated with the 140–160 kDa fraction.

A novel study was reported by Polgari *et al.*[143] in which *Fe speciation in cancer cells* was investigated using SR-TXRF and XANES. Cell suspensions were pipetted onto the quartz reflectors for spectral measurements and the collected spectra compared with spectra from analysis of pure organic and inorganic Fe compounds. The XANES spectra from cell lines were very similar to that of ferritin, irrespective of the cell type and phase of growth. When cells were subjected to oxidative stress by administration of 5-fluorouracil, the XANES spectra shifted towards higher energies indicative of a higher oxidation state for Fe.

The concentration of transferrin (Tf) can be used as a diagnostic marker of the health status of seals. Grebe *et al.*[144] highlighted the limitations of quantitative methods for Tf based on immunoassay and described a method for the *absolute quantification of Tf* in seal serum using HPLC coupled with ICP-MS. The method was validated by analysing a human serum CRM. The authors used the method to determine reference values for Tf in serum of German North Sea seals. The reported ranges were 1.42–2.35 g L^{-1} for males and 1.93–2.74 g L^{-1} for females. The Spanish group of Konz *et al.*[67] also reported a method for determining the absolute amount of Tf in human serum using ID-LA-ICP-MS after gel electrophoresis under non-denaturing conditions to separate the serum metalloproteins. Their method was also validated by analysing a human serum CRM.

5.4.12 Lead. As with Cd, the number of papers reporting on *the determination of Pb in biological matrices* continues to decline year on year. Furthermore, many of this year's papers relate to investigations of body-burden from past exposures rather than current exposure. Mergen and Soylemezoglu[145] used surface response methodology to optimize the temperature programme for the quantitative determination of Pb in microwave-digested autopsy bone samples using ETAAS. With a 1% $NH_4H_2PO_4$ chemical modifier, the optimum ashing and atomization temperatures were 522 °C and 2144 °C respectively. An LOD of 2.3 μg L^{-1} was reported and the method was validated by analysing NIST SRM 1400 Human bone ash. The prolific research group of Chettle and co-workers[95] presented the results of a bone Pb survey of 497 exposed smelter workers using XRF with a novel clover leaf detector system to determine bone Pb *in vivo*. They reported that the clover-leaf geometry gave improved precision and a 3.1 fold improvement in LODs for tibia and calcaneous bone compared with the conventional one-detector system used in earlier surveys of the same population. Nie *et al.*[96] examined the feasibility of a portable XRF system for the quantitative determination of bone Pb *in vivo*. The researchers used Monte-Carlo simulation to determine the minimum radiation dose delivered to the subjects. Soft tissue thickness measurements were initially made using ultrasound, from which an alternative method to assess soft tissue thickness was developed using data from the XRF spectrum. Data obtained with the portable system correlated well with that obtained using standard K shell XRF technology (interclass correlation coefficient = 0.65). An LOD of 8.4 ppm was reported at a soft tissue thickness of 2 mm. The authors considered the method to be comparable with K XRF technology. The lack of suitable calibration materials for quantitative determination of Pb in hair led Cheajesadagul *et al.*[66] to develop a lead-doped keratin film as a calibration standard for the determination of Pb in hair strands using LA-ICP-MS. The standard was prepared by trichloracetic acid precipitation of a hair protein solution, containing a known amount of Pb, onto the keratin film. The S content of the precipitated protein was used as an internal standard to correct for variations in ablation efficiency. The calibration method was used to determine Pb in hair strands from workers at a battery manufacturing plant in Thailand.

The ongoing concern over *foetal and infant exposure to Pb* continues to be represented by the number of studies reported in each ASU review. Amaral *et al.*[146] investigated the relationship between maternal blood, serum and umbilical cord blood and serum Pb concentrations in a group of 120 healthy pregnant women. The concentration of Pb in the samples was determined using ICP-MS. Although levels of Pb in both blood and serum were higher than the corresponding umbilical cord samples, significant positive correlations were noted between blood Pb and cord blood Pb ($r^2 = 0.57$) and between serum Pb and cord serum Pb ($r^2 = 0.39$) from which the authors concluded that the assessment of blood Pb levels in pregnant women can provide relevant indices of foetal exposure to Pb. A Japanese group[74] described a method for the quantitative determination of Pb isotopes in blood using MC-ICP-MS. To eliminate matrix interferences, Pb was separated from the matrix by Br complexation and AEC. The authors used the method to investigate sources of Pb exposure in young Japanese children. A significant contribution from indoor dust was reported. de Almeida *et al.*[147] investigated the relationship between the Pb content of tooth enamel and Pb levels in blood, serum and saliva in a group of schoolchildren from Sao Paulo State, Brazil. Successive micro-biopsies of primary and permanent tooth enamel were taken from each child. Blood, serum and saliva samples were collected in 'trace-element free' tubes. Concentrations of Pb in the different sample types were determined using ICP-MS. The authors reported a significant correlation between Pb levels in primary and permanent teeth, but no correlation between enamel Pb and blood or saliva Pb. There was a correlation between enamel Pb and serum Pb but only in subjects with the highest 10th percentile of enamel Pb concentrations. A Polish group[38] reported the results of a study comparing the levels of blood Pb in children, from a copper mining district of Southern Poland, which were determined in 1995 and again in 2007. Blood Pb was determined using ETAAS with the same analytical protocol in both study years. The authors reported that blood Pb levels declined significantly over the 12-year interval between the surveys, with mean blood Pb falling from 7.5 μg dL^{-1} in 1995 to 4.8 μg dL^{-1} in 2007. In both studies, blood Pb was higher in boys than girls.

5.4.13 Manganese. Praamsma *et al.*[148] *compared ETAAS and ICP-MS for the determination of Mn in whole blood and urine*. The authors paid particular attention to the polyatomic interferences that affect Mn determinations in these matrices by ICP-MS. The reported method LODs for blood (and urine) were 1.5 (2.1) μg L^{-1} using ETAAS, 0.6 (0.5) μg L^{-1} using SF-ICP-MS, 1.0 (0.5) μg L^{-1} using DRC-ICP-MS and 6.4 (0.6) μg L^{-1} using ICP-QMS. The authors concluded that results determined using

ETAAS, SF-ICP-MS and DRC-ICP-MS showed good agreement and were suitable for monitoring Mn in both matrices. However, ICP-QMS showed a positive bias equating to 1 μg L^{-1} for urine and 4 μg L^{-1} for blood compared with the other methods.

5.4.14 Mercury. Mercury is again one of the main elements of interest in this review period. Although the primary focus is again on speciation of Hg, papers have also been presented on *the determination of total Hg in a variety of biological matrices*. Reyes *et al.*[20] presented a comprehensive critical review of microwave assisted digestion procedures for the quantitative determination of Hg in biological matrices. In their review, the authors considered the main factors influencing the extraction process, statistical optimization approaches and strategies for method validation. Herbello-Hermelo *et al.*[93] described a method for the direct determination of Hg in whole blood using a specific Hg analyser. Blood samples were combusted in an O_2-rich furnace, the Hg amalgamated with gold and then released and transported in an O_2 stream to the measurement cell for quantitative determination by AAS. The authors recorded that combustion temperature and timing were critical to avoid spluttering of the sample. Optimized conditions were 650 °C for 60 s.

The debate over *the risks and benefits of Hg dental amalgams* is still ongoing. Al-Saleh and Al-Sedairi[149] investigated the body-burden of Hg and its relationship with dental amalgam fillings in a group of children living in Taif City, Saudi Arabia. Mercury concentrations were determined in urine, hair and toe nail samples using CV-AAS with a vapour generation system. The authors reported a higher mean urine Hg level in children with amalgam fillings (3.76 μg g^{-1} creatinine) compared with children without (3.457 μg g^{-1} creatinine). Similarly, higher values of Hg were reported for hair and nails. They also reported evidence of a relationship between amalgam Hg and symptoms of poor oral health. They concluded that the potential detrimental effect of increased Hg levels in children with amalgam fillings should be a cause for concern and required further investigation.

Dorea and colleagues[91] highlighted a risk of early post-natal infant exposure to *EtHg from vaccines containing thimerosal*, which continue to be used in many countries. The group evaluated a method for the quantitative determination of MeHg and EtHg in hair samples taken from breast-fed infants who had received a course of vaccinations. The group coupled isothermal GC with CV-AFS to determine both MeHg and EtHg. They reported concentrations between 3.7 and 65 ng g^{-1} for EtHg in 10 mg hair samples and observed a significant inverse relationship between hair EtHg concentration and time elapsed since the last vaccination. Rodrigues *et al.*[150] examined the distribution of Hg species in tissues of rats following administration of thimerosal or MeHg by gavage. Total blood Hg was determined using ICP-MS and mercury species (MeHg, EtHg and iHg) using LC-ICP-MS. The researchers reported that Hg remained longer in the blood of rats treated with MeHg compared with thimerosal. They noted that Hg in tissues and blood following administration was predominantly iHg but a significant amount of EtHg was also detected in liver and brain. They concluded that the toxicokinetics of thimerosal is different to that of MeHg and that further studies are required to evaluate thimerosal toxicity.

Baxter *et al.*[41] developed a method for *the quantitative determination of Hg species in plasma and serum*. Samples were spiked with ^{198}Hg labelled MeHg, extracted into CH_2Cl_2 and back extracted into H_2O. The extracted MeHg was ethylated, separated on a GC column and quantitatively determined using ID-ICP-MS. Spiking a 2 mL sample with 1.2 ng of labelled Hg enabled accurate determination in the concentration range 0.007–2.9 μg L^{-1}. The researchers determined MeHg concentrations in 50 plasma and serum samples and reported a median value of 0.081 μg L^{-1} and range of <0.03–0.19 μg L^{-1}. A Spanish group[55] reported a rapid, simple method for the determination of MeHg, EtHg and iHg in blood using capillary GC-ICP-MS. Samples were digested with TMAH and the researchers compared ethylation and propylation procedures for derivatization of the species for chromatographic separation. With propylation the reported absolute LODs were 50 fg, 20 fg and 50 fg for MeHg, EtHg and iHg respectively. The method was validated by analysing NIST SRM 966 Toxic Metals in Bovine Blood. They considered the method to be an improvement on previous GC separation methods, as no clean-up steps were required and the speed of analysis was considerably improved. Meanwhile, a team at NIST[30] characterised a caprine whole blood SRM (SRM 955c) for the content of MeHg, EtHg and iHg. Certification of the values was achieved using triple spike speciation ID-ICP-MS. The certified values were 4.5 ± 1 μg L^{-1}, 5.1 ± 0.5 μg L^{-1}, 9.0 ± 1.3 μg L^{-1} and 17.8 μg L^{-1} ± 1.6 μg L^{-1} for MeHg, EtHg, Hg_i and total Hg, respectively.

A Chinese group[107] determined *MeHg and Hg-containing proteins in subcellular fractions of tissues* from maternal and infant rats following pre- and post- natal exposure to MeHg. Methylmercury was extracted and pre-concentrated for quantitative determination using HPLC-ICP-MS. Mercury-containing proteins were identified using SDS-PAGE combined with MALDI-TOF-MS and quantitatively determined using HPLC-ID-ICP-MS. The authors noted that the subcellular distribution patterns of Hg species were significantly different between mothers and their offspring, which they hypothesised was due to different metabolism and transport behaviour between adult and infant rats.

A Finnish group[151] investigated *dietary sources of MeHg exposure* in a Finnish population. Blood concentrations of MeHg were quantitatively determined using HR-ID-ICP-MS. Reported mean blood MeHg concentrations were 4.6 μg L^{-1} in men and 2.8 μg L^{-1} in women. The researchers reported that fish consumption was most strongly positively correlated with blood MeHg but positive associations were also found with fruit, vegetable, wheat and wine for the male study group and with vegetables and game in the female study group. They concluded that a thorough exposure assessment is recommended in the general Finnish population due to the high concentrations observed in this study group.

Finally Gao *et al.*[92] determined total *Hg and MeHg in hair* using combustion AAS for total Hg and headspace GC-AFS for MeHg. The method was validated by analysing IAEA 086 CRM. An LOD of 0.15 ng g^{-1} was reported for total Hg based on a 20 mg sample, whilst the LOD for MeHg ws 0.04 ng g^{-1}.

5.4.15 Phosphorus. This review includes a paper by Easter *et al.*[152] describing *the identification of oligonucleotides by*

hydrophilic interaction LC coupled with ICP-MS. Polythymidylic nucleotide chains of 10–30 nucleotides were separated under gradient LC conditions and detected by measuring $^{31}P^{16}O^+$ at *m*/*z* 47 using DRC-ICP-MS. Oxygen was used as the reaction gas to generate PO^+ and thereby overcome the interferences on P at *m*/*z* 31. Reported LODs ranged from 1.69 pmol for 10 nucleotide chains to 0.53 pmol for 30 nucleotide chains.

5.4.16 Platinum. The three papers concerning Pt determinations discussed in this review period are all concerned with *the interaction of Pt anticancer agents with intracellular proteins and peptides*. Moller and colleagues[153] compared various mass spectrometric techniques to investigate the binding of oxaliplatin to insulin, selected as a model protein for binding studies. The group highlighted the relative advantages and disadvantages of ESI or MALDI-Q-TOF-MS approaches. Using both techniques, the researchers identified five peptides with bound Pt, the major binding site being identified as histidine 5 on the β chain on the insulin protein. Falta *et al.*[154] determined concentrations of intact 'free' cisplatin in model cancer cell lines using two complementary LC-ICP-MS methods. Following centrifugal filtration of cell lysates to remove excess proteins, separation of 'free' cisplatin from cisplatin-peptide adducts was achieved using a pentafluorophenylpropylsiloxane or porous graphite (Hydrocarb™) stationary phase. Free cisplatin concentrations in cells administered 5 μM cisplatin for 24 h ranged from 0.2 to 1.5 μg g^{-1} protein. Mena *et al.*[155] described a 2D electrophoretic procedure for the separation of Pt-containing proteins. A sequential procedure of isoelectric focusing and PAGE was optimized with respect to reagents and post separation treatments. Separated Pt species were determined using ICP-MS. To preserve the integrity of Pt species during electrophoresis, the authors avoided the use of β-mercaptoethanol or dithiothreitol reagents in the procedure. Under non-reducing conditions, Pt species were separated on polyacrylamide gels in very narrow bands and were quantitatively recovered by mineralization of the gel matrix. Reported absolute LODs for a mixture of proteins incubated with cisplatin ranged from 2.4 to 13.9 pg.

5.4.17 Rare earth elements. Costas and colleagues[47] investigated the suitability of ultrasound assisted extraction as a sample pre-treatment for *the quantitative determination of REEs from biological tissues using ICP-MS*. The researchers focused their attention on optimizing the conditions for quantitative extraction of REEs including the composition of the extraction reagents and both sonication amplitude and time. Quantitative extraction was achieved with an extraction solution of 3% v/v HNO_3–2% v/v HCl and a sonication time of 3 min at 50% amplitude. The researchers reported that the LODs were 5 times better than those obtained with a microwave assisted digestion method.

Papers continue to be presented on the determination of Gd in *MRI contrast agent formulations*. An American group[156] described two robust methods for the separation and quantitative determination of Gd species from nanoemulsion-based contrast agents using either RP-HPLC or high pressure SEC coupled with ID-ICP-MS. Three Gd species were identified in the formulations examined; free Gd, Gd chelated with diethylenetriamine pentaacetic acid and Gd chelated with 1,2-dimyristoyl-sn-*glycero*-3-phosphoethanolamine-*N*-diethylenetriamine pentaacetic acid. The group considered that species-specific ID-ICP-MS provided the most accurate measurements but that ID-ICP-MS could be used for rapid quantitative screening for the presence of free Gd. A second American group[157] determined Gd in skin and serum samples from patients with nephrogenic systemic fibrosis (NSF), a potentially fatal disorder associated with renal insufficiency following exposure to Gd-based contrast agents. The researchers determined Gd in fresh skin biopsy samples and serum using ICP-MS. The mean serum Gd concentration in patients with the disease was 4.8 ng mL^{-1}, which was more than a factor of ten times the concentration in healthy controls. In patients with NSF, the mean ratio of Gd in lesioned skin to healthy skin was 23.1 (range 1.2–88.1). The researchers concluded from these differences that free Gd deposition from Gd-based contrast media has a role in the pathogenesis of NSF. On a very similar topic, Fretellier *et al.*[158] investigated the dissociation of 'free' Gd from Gd-based contrast media administered to nephrectomized rats. The rats were given daily injections of either Dotarem, Omniscan or gadodiamide contrast media over a five day treatment period. On completion of the study (day 11), concentrations of total Gd were determined in skin, femur epiphysis and plasma using ICP-MS and dissociated Gd^{3+} was determined in plasma using LC-ICP-MS. The researchers reported comprehensive data on the concentrations of total and dissociated Gd in the different samples analysed. They noted that higher concentrations of total Gd were found in tissues of animals administered Omniscan and gadodiamide compared with Dotarem and concluded that this was due to the gradual release of dissociated Gd^{3+} from these contrast media whereas Dotarem remained relatively stable over the study period.

5.4.18 Selenium. As has been the case for many of the recent reviews in this ASU series, Se has emerged as the primary element of interest based on numbers of papers appearing in the literature. Stosnach[99] investigated the suitability of TXRF for *quantitative determination of Se in a range of clinical, food and biological matrices*. The author determined LODs for a range of sample matrices and reported values between 7 and 12 μg L^{-1}, which although not as good as those reported for ETAAS or ICP-MS were considered to be sufficient for measuring physiological concentrations of Se in the samples investigated. Letsiou *et al.*[159] investigated the relationship between serum Se and dietary habits in a group of 506 Greek adults. Total serum Se was determined using ICP-MS and food consumption was evaluated using a validated food frequency questionnaire. Serum Se was positively correlated with consumption of red meat but consumption of other Se-rich foods did not show such a relationship. The same group[69] also described a method for speciation of Se in human serum in which dual column affinity chromatography was coupled with ID-ICP-MS. Eicher and Mestek[160] described a method for the quantitative determination of total Se in urine using ICP-MS. Suppression of the $^{40}Ar^{40}Ar^+$ interference on the $^{80}Se^+$ isotope was achieved with a DRC and CH_4 as reaction gas. By coupling HPLC with ICP-MS, the authors determined Se^{IV}, Se^{VI}, SeMet, SeCys and selenourea in urine samples. They reported good separation of all species except Se^{IV} and SeCys,

which had very similar retention times under the chromatographic conditions used.

The majority of published papers were concerned with *the determination of Se species in a wide spectrum of clinical and biological matrices*. Heras *et al.*[22] presented a comprehensive review of the major contributions of analytical chemistry to the identification and determination of selenoproteins and selenium-containing proteins in biological matrices. The review highlighted the challenges of combining elemental and molecular MS to Se speciation studies. A Chinese group[119,161] described methods for the full quantitative determination of Se species in serum using RP and affinity chromatography hyphenated with ID-ICP-MS with a DRC. Inorganic Se^{IV}, Se^{VI} and organic SeCys, SeMet, selenoprotein P, selenoalbumin and GPx were quantitatively determined. The authors used the methods to study the dynamic distribution of Se species in human serum samples from subjects living in a mercury-contaminated area and who were receiving Se supplementation. Reported LODs for SeCys, Se^{VI}, SeMet, and Se^{IV} were 0.34 μg L^{-1}, 0.67 μg L^{-1}, 1.38 μg L^{-1} and 0.63 μg L^{-1}, respectively.

Lunoe *et al.*[120] developed a fast, simple method for the quantitative determination of DMSe and DMDSe using HPLC-ICP-MS with a DRC. The two species were separated on a short RP column with a 40% v/v CH_3OH eluent. An LOD of 8 nM was reported for both species. The method was used to measure both Se species in samples of a cancer cell line incubated with different selenium compounds. Michalke and Berthele[128] reported a method for the *speciation of Se* in CSF samples from neurologically healthy subjects. The researchers initially used SEC coupled with ICP-DRC-MS to separate and quantitatively determine low *Mr* Se compounds and selenoproteins. They reported improved speciation data with a method based on strong AEC. With this approach, six Se-containing species were distinguished in CSF of which three were identified as Se^{VI}, thioredoxinreductase and selenoalbumin. Bertelsmann and colleagues[21] presented a review of methods used for the identification and quantitative determination of Se species in human spermatozoa. They reported that the quantitative determination of every Se species present in sperm requires analytical approaches with necessary sensitivity such as fs LA-ICP-MS or INAA, which can be used to determine Se species separated on polyacrylamide gels. Klein *et al.*[45] established suitable sample handling and storage conditions for urine to ensure reliable measurements of Se-containing volatile metabolites. They established that urine samples should be kept in darkness immediately after collection and preferably analysed within a day. However, if stored at −20 °C or lower, no measurable changes in Se species were observed over a 4-week period. This same group[117] also applied a similar 2D RP and affinity chromatography method to that described by the Chinese group[119] for the identification and characterization of a new Se metabolite, Se-methylselenoneine, in both human blood and urine. Coupling the chromatographic columns in parallel with ICP-MS and ESI- linear ion trap MS allowed the researchers to confirm its presence in non-preconcentrated urine and blood matrices and to discard the possibility that the metabolite was an artefact of sample pre-treatment.

It has been hypothesised that Se may exert an anti-arthrogenic effect by reducing oxidative stress caused by reactive O_2 species and, therefore, *Se supplementation may be beneficial in prevention of cardiovascular disease*. Apparently the richest natural source of Se is the Brazil nut and Stockier-Pinto and colleagues[162] investigated the benefits of supplementation with these nuts on the plasma and erythrocyte concentrations of Se in a group of haemodialysis patients. Patients were given a single Brazil nut daily for three months. Plasma and erythrocyte Se was determined using HG-AAS and GPx was determined using a commercial Randox kit. The researchers noted that both plasma Se (18.8 μg L^{-1}) and erythrocyte Se (72.4 μg L^{-1}) in the haemodialysis patients were well below the normal reference ranges prior to the start of supplementation but increased to 104 μg L^{-1} and 244 μg L^{-1}, respectively after completion of the course of supplementation. They concluded that haemodialysis patients presented Se deficiency and that consumption of only one Brazil nut daily significantly improved Se status and GPx activity.

5.4.19 Uranium. Chen *et al.*[163] measured *U in 69 bone ash samples*, collected in the Health Canada survey, and selected to represent infants and adults from 7 to 21 years in a region with elevated U in the drinking water supply. Total U was determined using ICP-MS. From the data, the authors estimated a GI tract absorption fraction of 0.03 for children and 0.021 for adults, which was in good agreement with the International Commission of Radiological Protection recommended value.

5.4.20 Vanadium. *Cloud-point extraction continues to be a favoured methodology for extraction and enrichment of trace elements from complex matrices*. Kahn *et al.*[164] described such a method to extract V from pharmaceutical formulations and parenteral solutions. They extracted V from the matrix using complexation with 8-hydroxyquinoline and Triton X-114 non-ionic surfactant. The surfactant-rich phase was diluted with HNO_3–CH_3CH_2OH for quantitative determination of V using ETAAS. With optimized conditions for extraction, an enrichment factor of 125 was reported for a 50 mL sample volume. The authors reported an LOD of 42 ng L^{-1} and concentration ranges of 10.5–15.2, 0.6–1.32 and 1.76–6.93 μg L^{-1} for V in pharmaceutical preparations, dialysates and parenteral solutions, respectively.

5.4.21 Zinc. Examination of induced sputum is an established procedure for assessing airway inflammation. Jayaram and colleagues[165] determined total and rapidly exchangeable (labile) Zn in induced sputum to investigate any correlation between *sputum Zn and symptoms of asthma*, including lung function and airway hyper-responsiveness. Sputum samples were collected from 114 patients with asthma symptoms and a control group. Labile and total Zn were determined using Zinquin fluorescence and AAS respectively. The researchers reported that both total Zn levels (31.8 μg L^{-1} *vs.* 50 μg L^{-1}) and labile Zn (0 μg L^{-1} *vs.* 26 μg L^{-1}) were lower in the asthmatic group compared with controls. They considered that the findings demonstrated a potential role of sputum Zn as a biomarker for asthma.

Lech and Sadlik[166] used FAAS to determine Zn concentrations in human tissues and body fluids from 203 autopsy cases, none of which were associated with metal intoxication. The authors used the data to present *reference ranges for Zn in a wide range of tissues and body fluids*.

Table 2 Foods and beverages

ELEMENT	MATRIX	TECATMNPRES	SAMPLETREATMT	REFERENCE
As	Edible seaweed	MS;ICP;L	Evaluation of the bioaccessibility of As in edible seaweed. An *in vitro* digestion method based on piperazine-*NN-bis* (2-ethane-sulfonic acid) disodium buffer solution at pH 7.0 was used with dialysis membranes of 10 kDa *Mr* cut-off to assess bioavailability	173
As	Tuna fish	AA;ETA;S AA;HG;S	Samples were freeze dried and either (1) ground in a cutting mill and separated in different particle sizes or (2) ground in a cryogenic mill, prior to determination of total As mass fraction by analysis of slurries of these materials. The trueness of the procedures was checked with tuna fish CRM(BCR 627) with recoveries of 102 and 94% for ETAAS and HG-AAS, respectively	28
As	Fish based baby foods	AA;ETA;L	Samples were prepared as suspensions in a 0.01 mol L^{-1} TMAH solution. As species were determined selectively using either a palladium or cerium matrix modifier for inorganic species or by using a zirconium-treated atomiser tube for organic species	78
As	Seafood	MS;ICP;HPLC	As species were released from dried seafood tissues using pressurized conditions to assist pepsin protease enzymatic hydrolysis. Trueness was confirmed by analysis of CRMs (DORM-2 and BCR 627). RSD was reported to be better than 6%	51
As	Rice flour and seafood SRMs.	MS;ICP;IC	Ultrasound-assisted enzymatic extraction was used to improve the efficiency and speed (5 min.) of sample preparation prior to As speciation by IC-ICP-MS. The method was applied to the determination of As^{III}, As^{V}, MMA, DMA, and AB. Recoveries were reported in the range 93–122%	50
As	Wheat and wheat products	MS;ICP;IC	Ultrasound-and microwave-assisted extraction of samples containing As was achieved using different solvents or enzymes. As species were separated on an anion exchange PRP-X100 column with $NH_4H_2PO_4$–NH_4NO_3–CH_3OH at pH 5.5 as the mobile phase. Total As was reported in the range 8.6 to 29.8 ng g^{-1} dw and LODs were between 0.35 and 0.46 ng g^{-1} dw	49
As	Rice roots	XRF;-;S XANES	Study of the effect of Fe plaques on As absorption in rice plants using imaging techniques	112
As	Total diet matrix	MS;ICP;HPLC	As in NIES CRM No.27 Typical Japanese Diet was determined by extraction using 0.07 mol L^{-1} HCl and pepsin, followed by HLPC-ICP-MS detection with or without HG. The reference value was estimated to be 43 and 17 ng $g^{-1}$for As^{V} and As^{III}, respectively	29
As	Tobacco	MS;ICP;HPLC	Samples were leached with water (by ultrasound- or microwave-assisted extraction) followed by sequential extraction with driselase and SDS. Complementary cation-exchange HPLC-ICP-MS showed the presence of As^{V}, DMA and MMA	172
As	Edible oils	MS;ICP;IC	Microwave-assisted extraction of As species which were then separated by IC using a rapid gradient elution with $(NH_4)_2CO_3$ at pH 8. Spiked sample recoveries were reported in the range 92–110%, and LODs were given as 0.08–0.24 ng g^{-1} in the original oil sample and the precision obtained using the method was typically 8% RSD	194
As	Wine	AE:ICP;L	Use of V as an internal standard and automated sample spiking to eliminate the need for sample dilution. Recoveries of As spikes were reported in the range 95–103%	212
As	Mineral waters	AA;HG;L	Determination by rapid sequential AAS combined with CF-HG. LODs reported for As and Sb were 0.15 and 0.14 μg L^{-1}, respectively. The method gave accurate results for CRMs Trace elements in water (NIST 1643e) and Trace metals in drinking water (HPS TMDW)	79
Be	Natural and flavoured mineral waters	AA;F;L	Pre-concentration method based on the complexation of Be^{2+} with a mixture of acetylacetone (pentane-2,4-dione) plus morin (3,5,7,2',4'-pentaoxyflavone) and adsorption on activated carbon. Be was subsequently eluted in 2 mol L^{-1} HNO_3 prior to determination. The LOD reported was 0.01 ng mL^{-1} Be	206
Br	Edible seaweed	MS;ICP;L	Samples were prepared using a microwave-assisted alkaline digestion. Internal standards Te and Y were used for the determination of I and Br respectively. Trueness of the method (total Br and I determinations) was assessed by analysing a NIES-09 CRM	177
Br	Drinking water	MS;ICP;IC	An ICS-A23 IC column was used for anion separation with a mobile phase of 0.03 mol L^{-1} $(NH_4)_2CO_3$ at a flow rate of 0.8 mL min^{-1}. The LODs reported for BrO_3^-, Br^-, IO_3^- and I^- were 0.032, 0.063, 0.008 and 0.012 μg L^{-1}, respectively	205

Table 2 (*Contd.*)

ELEMENT	MATRIX	TECATMNPRES	SAMPLETREATMT	REFERENCE
Cd	Tap water	AA;F:L	A new chelating sorbent synthesised by the covalent condensation of alizarin complexone to polyurethane foam was used to separate and preconcentrate the metals (Cd, Cu, Zn) 100-fold	214
Cd	Soft drinks	AA;F;L	The sample was treated with pyridyl-azo-naphthol to form hydrophobic chelates, then extracted into Triton X-114 in a solution buffered at pH 9. NaCl was used for the phase separation prior to analysis by TS-FF AAS. An LOD for Cd of 0.0178 μg L^{-1} was reported with an RSD of 4.1% ($n = 8$)	62
Cd	Rice flour	XRF;-;S	Samples were fixed onto a film of 6 pm thick polypropylene with polyvinyl acetate and analysed directly using L-shell excitation. It was reported that LOD for Cd in rice was 0.34 ppm using this method	100
Cd	Fresh meat	AA;ETA;Sl	A slurry was prepared using TMAH in an autosampler cup containing the weighed sample and Triton X-100 as a modifier. The results obtained were consistent with certified values for two CRMs at the 95% confidence level	80
Cr	Water	XRF;-;S	The sample was adjusted to pH 3 and passed through an anion-exchange resin disc placed on top of a cation-exchange resin disc to separate Cr^{III} and Cr^{VI}. The discs were dried and coated with laminate film prior to XRF measurement. A spike test for 50 μg L^{-1} Cr^{III} and Cr^{VI} in tap water showed quantitative recoveries (94–114%) and LODs were reported as 0.17 and 0.16 μg L^{-1}, respectively	102
Cr	Water	MS;ICP; ETV	Thenoyltrifluoroacetone (TTA) was used as chemical modifier to form a volatile Cr^{III}–TTA chelate that was transported at low temperature into the ICP while Cr^{VI} was retained in the graphite furnace allowing sequential determination. The method was applied to water samples with a recovery of 93.5–104%. The LOD was reported as 0.008 ng mL^{-1} for Cr^{III} and the RSD was 4.6%	72
Cr	Water	AA;ETA;L	Selective extraction method for speciation of Cr^{III} and Cr^{VI} using pyrrolidinedithiocarbamic acid in xylene; RSDs ($n = 10$) of 1.8% and 3.4% were obtained using the method for 0.16 μg L^{-1} of Cr^{VI} and Cr^{III} and LODs of 0.75 ng L^{-1} and 0.64 ng L^{-1}, respectively, were reported	105
Cr	Drinking water	XRF;-;S	Pre-concentration of Cr^{VI} on Aliquat 336-AC followed by detection directly on the solid. A pre-concentration factor of 71-fold was reported	63
Cu	Tap water	AA;F;L	See Cd, ref. 214	214
Cu	Cereals	AA;F;L	Dispersive liquid–liquid micro-extraction of Cu using 8-hydroxy quinoline complexing agent concentrated into a small volume of l-dodecanol. The enrichment factor was reported as 122 and the LOD was given as 0.1 ng mL^{-1}	61
Fe	Rice roots	XRF;-;S XANES	See As, ref. 112	112
K	Milk powder	AE;ICP;L LIBS	Comparison of LIBS in a "calibration free" mode and ICP-AES for the determination of K and Mg in milk powder. The LIBS system used Ca present in the sample as an internal reference element	87
Hg	Canned tuna fish	AA;CV;L	Samples were subjected to microwave digestion prior to Hg determination *via* CV generation. Hg levels in 5 commercial products were found to be in the range 0.19 (±0.07) μg g^{-1} to 3.60 (±0.17) μg g^{-1}	198
Hg	Fish muscle	MS;ICP;L	Hg contents in samples were reported in the range 0.01–5.12 nmol g^{-1} tissue See also Se, ref. 116	116
Hg	Fish	MS;ICP;HPLC	Rapid separation of Hg species by HPLC using a RP column with 0.1% of L-cysteine as the mobile phase. The reported LOD for this method was 0.5 μg kg^{-1} and trueness was confirmed by analysis of marine biological CRMs (TORT-2 and DORM-2)	114
Hg	Predatory fish	AA;CV;L	Canadian fish tissues (188 samples) were digested using HNO_3–HCl–H_2O_2 and diluted prior to analysis. Recoveries were reported as averaging 97 and 101% for spiked blanks and samples respectively. Solution LODs averaged 0.045 ng mL^{-1} and sample LODs averaged 1.9 ng g^{-1}	197
Hg	Seafood	MS;ICP;HPLC	Hg species were extracted by sonication with mercaptoethanol, L-cysteine and HCl for 15 min. A C8 RP column with mercaptoethanol–cysteine–CH_3COONH_3 mobile phase was used for separation. LODs were 0.25, 0.20 and 0.1 ng g^{-1} for iHg, EtHg and MeHg, respectively	48

Table 2 (*Contd.*)

ELEMENT	MATRIX	TECATMNPRES	SAMPLETREATMT	REFERENCE
Hg	Dietary intake material	AF;-;-	The daily Hg intakes were reported for children and adults in the Jinju area of China (median and range. Results were significantly lower when fish or shellfish was not consumed, for both children and adults	182
Hg	Food SRMs	MS;ICP;GC	Samples were digested with pancreatin and then HCl. MeHg and EtHg in the extract were derivatized in an aqueous buffer with sodium tetraphenylborate. After phase separation, the extract was analysed directly	115
Hg	Mushrooms	AES;ICP;L AA;CV;L	Comparison of CV-AAS using prior sample pyrolysis into a gold trap as a reference method and an ICP-AES method using microwave-assisted digestion. It was reported that the ICP-AES method using the 194.163 nm line was unreliable as assessed by analysis of several CRMs	86
I	Bovine liver, corn starch, milk powder, wheat flour SRMs	MS;ICP;L	Samples were decomposed in a microwave induced O_2 combustion system using NH_4NO_3 as an ignition aid. Recoveries of >99% were obtained when either $(NH_4)_2CO_3$ or TMAH were used as absorbing solutions. Results for the determination of I in SRMs were in agreement with certificate values (>97%)	56
I	Edible seaweed	MS;ICP;L	See Br, ref. 177	177
I	Edible salts	MS;ICP;IC	A commercial anionic column of 50 mm length was chosen for the rapid separation (170 s) of I species using $(NH_4)_2CO_3$ as the mobile phase. LODs of 0.015 and 0.081 μg L^{-1} for IO_3^- and I^- were reported	141
I	Drinking water	MS;ICP;IC	See Br, ref. 205	205
Mg	Milk powder	AE;ICP;L LIBS	See K, ref. 87	87
Mo	Milk and infant foods	AA;ETA;S	Slurries were prepared in ultrapure water with 5 to 20 min of sonication in concentrations of 10% w/v. The injection of 5.0 μL of 0.1% (v/v) cetyl trimethyl ammonium chloride reduced the effect of build-up of carbonaceous residues within the atomizer. Powdered sample concentrations were between 39 and 1,570 μg kg^{-1}	185
Ni	Fast food products	AA;ETA;L	Ni was determined in 170 samples of 43 different convenience and fast foods widely consumed in Spain. Ni levels ranged from 18.5 to 95.0 ng g^{-1}. It was reported that the mean Ni dialysable fraction estimated by *in vitro* assays ranged from 4.50 to 7.75%	178
O	Green coffee beans	MS;ICP;L	O and Sr isotope data were used to provide proof of authenticity of geographical origin of coffee	73
Pb	Dietary intake	AE;ICP;-	A survey of Pb contamination in 104 of the representative food items in the Saudi diet	183
Pb	Fresh meat	AA;ETA;S	See Cd, ref. 80	80
Rb	Beer, wine, vegetable and fruit juices	AE;F, CH_4–air;L	The sample was atomized directly from a Pt-wire inserted into the flame. The LOQ(6 sigma) obtained was 4.3 ± 1.8 pg	85
Sb	Mineral waters	AA;F;L	See As, ref. [32/4276	79
Se	Wheat flour	MS;ICP;L MS;ICP;HPLC	Microwave-assisted acid digestion prior to ICP-MS allowed the determination of total Se content. A multiple-step enzymatic hydrolysis and hydrolysis with methanesulfonic acid followed by ID-HPLC-ICP-MS were used for the specific detection of SeMet	191
Se	Flour and bread	MS;ICP;HPLC	SeMet accounted for 65–87% of total extractable Se species in Se-enriched flour and bread. The Se concentration of flour ranged from 30 ng g^{-1} in white flour and 35 ng g^{-1} in wholemeal flour from untreated plots up to >1800 ng g^{-1} in white and >2200 ng g^{-1} in wholemeal flour processed from grain treated with Se (as Se^{VI})	190
Se	Yeast	MS;ICP;L	Samples were digested and reduced to Se^{IV} *via* HG. The Se isotope ratios in nine Se-rich yeast supplements were subsequently determined using a MC- ICP-MS instrument. Results suggest that the method could be used in determining yeast provenance	23
Se	Rice	MS;ICP;CE	Enzyme-assisted extraction was used to prepare samples prior to detection of Se species separated by CE. The method was used to determine trace Se^{VI}, Se^{IV}, $SeCys_2$ and SeMet in rice directly without any derivatisation or pre-concentration. An LOD of 0.1–0.9 ng mL^{-1} was reported	193
Se	Food supplements	AF;HG;L MS;ICP;IC	Detection of total Se by digestion and AFS detection and Se species by enzymatic hydrolysis followed by analysis using IC-ICP-MS. The method was used to detect Se^{IV} and $SeCys_2$. In one sample, the total Se content was over 6 times that quoted on the product label	170
Se	Food and dietary supplements	TXRF;-;S	Se LODs reported in the range 0.1 to 0.2 mg kg^{-1} for food basics and dietary supplements	99

Table 2 (*Contd.*)

ELEMENT	MATRIX	TECATMNPRES	SAMPLETREATMT	REFERENCE
Se	Greek diets: the ATTICA study	MS;ICP;L	Study of relationship between Se dietary intake and health status. PCA was used to show a correlation between serum Se data and red meat consumption whereas a vegetarian diet was inversely correlated	159
Se	Se-enriched fermented milk	MS;ICP;HPLC	Total Se was quantified after *in vitro* gastrointestinal digestion. Results indicated that 76 ± 3% Se was extracted after gastrointestinal digestion and 24 ± 6% remained in the insoluble residue. Bioaccessible Se species $SeCys_2$ and SeMetCys were found to predominate	187
Se	Se enriched eggs	AF;HG;L	Organic and iSe were separated by precipitating albumin with trichloroacetic acid. Se was measured by HG-AFS. The LOD for Se was 0.07 μg L^{-1}. Recoveries were reported in the range 90.1–112% and the RSD ($n = 5$) was given as 0.6–3.4%	175
Se	Fish muscle	MS;ICP;HLPC	Speciation of selenoneine and overall organic Se using a gel filtration column. Total Se and Hg content were also measured by ICP-MS. Se contents were found in the range 1.4–19.1 nmol g^{-1} tissue. The Se:Hg molar ratio varied from species to species, ranging from 1 for swordfish to 217 for marbled sole	116
Sn	Canned foodstuffs	MS;ICP:L AES;ICP-L and HG AA:ETA;L	Analytical comparison of four atomic spectrometry methods for the determination of Sn in canned foodstuffs. Wet digestion, sequentially, with HNO_3 and H_2O_2 was reported as best for sample preparation	176
Sr	Green coffee beans	MS;ICP;L	See O, ref. 73	73
Zn	Tap water	AA;F;L	See Cd, ref. 214	214
Various (63)	Bottled mineral water	MS;ICP;L AE;ICP;L AF;CV;L	Comparison of analytical methods for the determination of trace elements in 1785 samples of bottled mineral water from 40 European countries	204
Various (71)	Bottled mineral water	MS;ICP;L AE;ICP;L	Report of a study of 908 German bottled water samples for major and trace element content. Only 42 of these samples were found to exceed German or EU action levels for particular minerals. Ten of the bottled water samples contained U concentrations above the 10 μg L^{-1} recommended limit	203
Various (6)	Water samples	AE;ICP;L	Preconcentration using a minicolumn of yeast-immobilized TiO_2 nanoparticles followed by elution in HNO_3. LODs for Cr, Cu, Fe, Mn, Ni and Zn were reported as 0.17, 0.45, 0.25, 0.15, 0.33 and 0.10 μg L^{-1}, respectively. The RSD ($n = 5$) was better than 5% for the method	58
Various (6)	Milk, cream, candy, isotonic beverage and beer	AE;ICP; LC	High temperature LC was combined with ICP-AES without a nebulizer to determine metals (B, Ca, K, Mg, Na and Zn) and organic compounds (glucose, sucrose, maltose and lactose) in foodstuffs. Alternative ELSD provided comparable data	84
Various (5)	Milk	AA;ETA;L	Raw milk samples (157) from Croatia were analysed for As, Cd, Cu, Hg and Pb. Samples were digested using HNO_3 in a closed microwave digestion vessel at 800 W for 15 min, and diluted prior to analysis. The amount of each metal was different in samples from northern and southern regions of Croatia	189
Various (40)	Milk and feeds	MS;ICP;L	Comparison of three different digestion procedures and two different calibration approaches for multi-element determination by SF-ICP-MS. Results obtained were found to be in agreement with certified values for two milk and three feed CRMs	188
Various (8)	Infant foods	AE;ICP;L MS;ICP;L	Quantitative analyses for 8 major and trace elements were conducted on 8 different products representing four popular brands of infant food on the UK market in order to ascertain their suitability relative to dietary guidelines for the 6–9 months age group Ca, Cu, Fe, K, Mg, Na, Se and Zn	186
Various (12)	Infant formulae	AE;ICP;L	Method for the determination of mineral nutrients (Ca, Cu, Fe, Mg, Mn, P, Zn) and trace elements in products such as milk powders. B, Ba and Sr were reported in these products up to 104, 117 and 221 μg per 100 g, respectively	184
Various (10)	Cereals	MS;ICP;Sl	Samples were slurried ultrasonically and vaporised into the ICP by ETV. The method was applied to the determination of Cd, Co, Cr, Cu, Hg, Ni, Pb, Se, V, and Zn in NIST SRM 1568a Rice Flour and SRM 1567a Wheat Flour CRMs, and two cereal samples	70
Various (13)	Rice	MS;ICP;L	Rice samples from Brazil (4 parboiled brown, 17 white and 6 parboiled white) were analysed for trace element content	181
Various (21)	Bread, cheese, fruit and vegetables	MS;ICP;L	Samples were digested with a mixture of concentrated HNO_3 and H_2O_2 and analysed by double-focusing SF-ICP-MS to remove spectral interferences. The method was validated by the analysis of CRMs: wheat flour (NIST 1567a), non-fat milk powder (NIST 1549) and brown bread (BCR-IRMM 191)	229

Table 2 (*Contd.*)

ELEMENT	MATRIX	TECATMNPRES	SAMPLETREATMT	REFERENCE
Various (46)	Tomatoes and tomato products	MS;ICP;L	Use of ICP-MS, IC and IDMS for characterizing Italian tomato products for the purposes of assessing geographical provenance	213
Various (6)	Total diet	MS;ICP;L	Samples (1319 in total, from the second French total diet study) were subjected to microwave-assisted digestion prior to analysis. Contamination data for Al, As, Cd, Hg, Pb and Sb were reported	42
Various (21)	Total diet	MS;ICP;L	Closed-vessel microwave-assisted digestion was used to prepare samples for the simultaneous determination of 21 metals in foods by ICP-MS. The work was part of the second French Total Diet Study by the National Reference Laboratory of the French Food Safety Agency	179
Various (14)	Swedish market basket diets	AA;F;L AA;ETA;L AE;ICP;L	Samples were dry ashed and dissolved in HNO_3. Cd, Co, Cr, Ni and Pb were then determined by Zeeman-effect ETAAS using the method of standard additions. Cu, Fe, Mn and Zn were determined by FAAS. For Ca, K, Mg, Na and Se, samples were subjected to a mixed acid digestion and measured by ICP-AES	43
Various (6)	Total diet	MS;ICP;L	An estimate was made of dietary exposures of main minerals and trace elements from 1319 samples of foods habitually consumed by the French population. The foodstuffs were analysed for Al, As, Cd, Hg, Pb and Sb levels by ICP-MS after microwave-assisted digestion	180
Various (6)	Snow Trout	AA;F;L	A response surface methodology was used to optimize parameters in a microwave-assisted HNO_3 extraction sample preparation procedure for the determination of Cu, Fe, Mn, Ni, Pb, and Zn	52
Various(5)	Wild and farmed bluefin Tuna	AA;-;L	Determination of Cu, Fe, Mn, Ni, and Zn in dorsal muscle tissue of tuna. The NRCC-DORM-2 Dogfish Muscle SRM was used to check the bias of the method	199
Various (20)	Fish and seafood products	MS;ICP;L	Determination of 20 essential or toxic elements in 159 samples of fish or other seafood. Samples were prepared using microwave-assisted digestion in HNO_3 prior to determination	200
Various (24)	Tea leaves and extracts	AE;ICP;L	Use of an online ME-3 chelating resin minicolumn for preconcentration of metals from hot water extracts of tea leaves. Elements were eluted with 2.5 mL of 2 M HNO_3 at 35 μL min^{-1}. Enrichment factors for the method ranged from 40 to 74, and the LODs reported were in the range 0.01 to 0.20 ppb	59
Various (6)	Coffee beans	XRF;-;S	Rapid method for the determination of Ba, Fe, Mn, Ni, Rb and Sr in coffee beans. PCA was used to classify the geographical origin of the samples	101
Various (3)	Chocolate	AA;ETA;L	Samples were prepared in a microemulsion using Tween-80 surfactant, heated and mixed for 15 min and analysed directly by ETAAS. Recoveries for Cu and Mn were reported as 98 and 108% respectively for a baking chocolate sample (SRM 2384)	196
Various (18)	Vegetable oils	MS;ICP;L	Samples were prepared by microwave-assisted digestion in HNO_3 prior to determination of metals in virgin olive, olive, pomace-olive, sunflower, soybean and corn oils	195
Various (13)	Vegetable oils, margarine and butter	AA;F;L AA;ETA;L	Samples were prepared by emulsification, heating and mixing with surfactant (Triton X-100 and Tween-80) for 15 min and directly introduced to the flame (for major elements) and furnace (for trace elements). Recoveries were reported in the range 90–112% for FAAS and 83–121% for ETAAS methods, respectively	82
Various (5)	Wines	TXRF;-;S	A portable TXRF instrument was used for the direct determination of Fe, K, Mn, Rb and S in wine in the sub ppm to high ppm range. Co was used as internal standard. It was reported that a high spectral background from dried organic residue affected the precision of the method for which the RSD was reported to be 4–28%	211
Various (15)	Turkish wine	AE;ICP;L AE;ICP;HG	Commercially available red and white wines (10 samples each) were analysed by HG-ICP-AES. The trueness of the method employed was verified using the CRM NRC SLRS-4 (River Water)	210
Various (24)	Wines	MS;ICP;L	Samples were diluted 10-fold and matrix matched standards were used for the quantitative and semi-quantitative determination of trace metals using a HR-ICP-MS system	209

6 Applications: Drugs and pharmaceuticals, traditional medicines and supplements

With the shift of Pharmacopoeial testing from classical wet chemistry to atomic spectrometry over the last decade, Lewen[9] has made a short review of appropriate applications for the analysis of drug products including APIs, raw materials and intermediates. Lin and Jiang[71] used slurry sampling of hypertensive drug tablets to introduce a dry aerosol for ETV-ICP-MS measurement of Cd, Cr, Mo, Pb, Pd and Pt. They unusually chose to use APDC and 8-hydroxyquinoline as matrix modifiers to enhance ion signals and the use of NH_3 in

the DRC reduced isobaric interferences for Cr (*m*/*z* 52 and 53). The method precision was better than 5% RSD (25% for Pt) and compared favourably with that on a fully dissolved and pneumatically nebulized sample. A more traditional ETAAS method was used by Portugal *et al.*[167] to determine Pb in aluminium and magnesium antacid preparations, using PO_4^- as modifier, giving results with no statistical difference from those by ICP-MS. They reported Pb levels in five commercial products, obtained locally in Brazil, as being between 87 and 943 μg g^{-1}. The powderised form of many pharmaceutical products is suited to the use of XRF and Arzhantsev *et al.*[97] applied continuous wavelet transform to a hand-held instrument measurement for As, Cr, Hg and Pb. Their limit test format eliminated the need for external calibration but system suitability was still required; LODs were 8, 150, 20 and 14 μg g^{-1}, respectively.

Non-conventional medicines are relied on by 70–80% of the world population but this poses the risk of exposing many to toxic heavy metals. Yuan *et al.*[10] used this as a focus to examine and review the literature for the wealth of methodologies used in assays of herbal medicine. An international proficiency testing programme on Cd and Pb in a herbal preparation (*Herba Desmodii stryacifolii*), encompassing 109 laboratories in 42 countries, was reported by Hon *et al.*[33] The between-laboratory RSDs were 18.7% and 19.8%, respectively, and the performance was reported as generally good although 20% of the laboratories had at least one unsatisfactory z-score. Speciation of As in traditional Chinese medicine preparations was undertaken by Jin *et al.*[168] using HPLC-ICP-MS. They concluded that As^{III} and As^{V} were the dominating species and found no evidence of DMA or MMA in preparations of the Radix family although MMA was found in Cordyceps; they also found that iAs concentrations increased after processing. Al-Omari[98] showed EDXRF is a simple way of analysing a large number of elements in Ayurvedic drugs. Only Ca, K, Fe and Sr were found in all ten products with very high reported concentrations, although with the dosage required this would not exceed recommended daily amounts. Alarmingly three preparations had As levels between 15,900 and 30,000 mg kg^{-1} which were not commented on and two with Hg levels between 12,850 and 19,000 mg kg^{-1} which did elicit a mention. As a new approach to QC, Liu and Zheng[169] proposed an ICP-AES finger-printing technique based on their measurement of 15 metals in 16 herbal medicines.

Isotope ratios of Se were determined by Far *et al.*[23] in *selenised yeasts* by HG-MC-ICP-MS after complete digestion and reduction to Se^{IV}. Interestingly, variation in the isotope ratios showed differences based on manufacturer and the authors suggested this may be an "attractive" parameter for ascertaining the provenance of a yeast supplement. The safety of a few Se-containing food supplements (also containing coenzyme Q10 and various vitamins) available in Slovenia was verified by Cuderman and Stibilj[170] by investigation of Se species (HPLC-ICP-MS) and total Se (HG-AFS). One sample exceeded the declared level seven times and was mainly $SeCys_2$ rather than the declared Se^{IV}; one sample had 60% as Se^{IV} although no one species was declared on the label and another had 75% as SeMet.

7 Applications: Foods and beverages

7.1 Progress for individual elements

7.1.1 Arsenic. The toxicokinetic behaviour of arsenosugars was reviewed by Feldmann and Krupp.[171] In terms of metabolite formation and tissue accumulation, the authors concluded that arsenosugars are similar to iAs and further suggested that As species should be reported in three part-speciated groups: toxic iAs as As^{V} after oxidation; non-toxic AB and potentially toxic As including arsenosugars and organoarsenicals. *Quantitative As speciation* in cut tobacco and smoke was investigated by Taebunpakul *et al.*[172] using sequential extraction and anion exchange-HPLC-ICP-MS. The extraction, which involved water leaching assisted by sonication (2 h) or microwave (10 min at 50 W power) followed by extraction with driselase and SDS, yielded 42% of total As, of which 89% was reported as iAs for the first time; the major species was AsV, and minor species were identified as DMA and MMA. Instrumental LODs were 10 and 50 ng kg^{-1} for As^{III} and As^{V}, respectively. The total As content of the CRM 3R4F Kentucky Reference Cigarette was reported as 319 ± 9 ng kg^{-1} and water extracts of the smoke were found to contain both As^{III} and As^{V}. The effect of cooking on total and assimilable As was determined by DRC-ICP-MS in edible seaweeds (Kombu, Wakame, Non and Sea Lettuce).[173] Simulated *in vitro* digestion was carried out before and after cooking with disodium piperazine-*N*,*N*′-bis(2-ethanesulfonic acid)(PIPES) as buffer at pH 7.0 in a 10 kDa dialysis membrane. Cooking was shown to extract all As into the water and digestibility of raw and cooked seaweeds were similar, except for Sea Lettuce which was less digestible after cooking.

7.1.2 Mercury. Sources other than fish were shown to contribute to *MeHg exposure*, although fish consumption was considered the main source.[151] The mean concentration of blood MeHg from 299 professional Finnish fishermen and their families, determined by ID-ICP-MS was 4.6 μg L^{-1} (range: 0.21–0.22) for men and 2.8 μg L^{-1} (<0.15–20) in women. Despite fish consumption showing the strongest correlation with blood MeHg, fruit, vegetables, wheat and wine consumption also showed positive correlation in the male diet and root vegetables, legumes and game for women, none of which are usually considered as dietary contributors. The simultaneous determination of MeHg and EtHg with GC-ICP-MS in several food matrices was developed and validated by Chung and Chan.[115] Sequential digestion with pancreatin and HCl was employed followed by derivatization with tetraphenylborate; PrHgCl was used as internal standard. The precision was quoted as less than 15%, LOD was 0.3 μg Hg kg^{-1} and recovery was 87–117%; trueness based on analysis of three SRMs was between 3.8% and 9% which improved with the use of ID-MS. With microwave-assisted extraction being widely accepted as a standard preparative technique, Reyes *et al.*[20] discussed the theoretical background involved, examined inherent advantages and disadvantages and critically reviewed applications to Hg speciation with comparison to other established techniques.

7.1.3 Selenium. The distribution and metabolism of a new selenoamino acid, selenohomolanthionine (SeHLan:

4,4′-selenobis[2-aminobutanoic acid][174]), isolated from Se-enriched Japanese pungent radish, was studied in rats using the ^{77}Se homologue.[174] Intact SeHLan was detected in the kidney supernatant, showing a differing accumulation to SeMet and SeMetCys which occurs in the pancreas thus potentially providing a different route to supplementation. Heras *et al.*[22] reviewed the diverse analytical techniques employed to elucidate the structures of *Se-containing proteins* and presented the best characterized proteins, highlighting the many challenges involved. The relative proportion of organic Se and iSe in enriched eggs was determined using a new HG-AFS method developed by Sun and Feng[175] giving an LOD of 0.07 μg L^{-1}. The amount of organic Se was 3 to 7 times that of iSe. Although not directly involving analysis by atomic spectrometry, Rao *et al.*[118] proposed the addition of iodoacetic acid to stabilize selenols in order to identify a wide range of Se metabolites in enriched yeast by Orbitrap HR-MS. Derivatizing with p-hydroxymercurybenzoate confirmed identification of the selenol since the isotope patterns of Hg and Se overlapped.

7.1.4 Other elements. A new SPE sorbent for the preconcentration and subsequent *measurement of Pb and Cr* by FAAS was proposed by Afkhami *et al.*[57] for the analysis of water and foods. The sorbent material, 2,4-dinitrophenylhydrazine immobilised on nano-alumina coated with SDS was characterised by N_2 adsorption and FTIR. Analytes were desorbed using HNO_3 and MeOH achieving a concentration factor of 267. For an 800 mL sample, linearity was between 1.2 and 350 μg L^{-1} for Pb and between 2.4 and 520 μg L^{-1} for Cr with LODs of 0.43 and 0.55 μg L^{-1}, respectively. Thenoyltrifluoroacetone (TTA) was proposed as a matrix modifier for the separation and quantification of Cr^{III} and Cr^{VI} in water when using low temperature ETV-ICP-MS.[72] Formation of the volatile Cr^{III}–TTA chelate allowed the vaporization of Cr^{III} at 900 °C while Cr^{VI} remained in the graphite tube permitting subsequent determination. The LOD for Cr^{III} was 0.008 ng mL^{-1}, the precision was 4.6% at 1.0 ng mL^{-1} and the recovery range was 93.5–104%. The same analytes were similarly determined in water using two layered ion-exchange resin discs for analysis with WDXRF.[102] The pH adjusted sample (100 mL) was passed through the discs containing anionic and cationic exchange resins with a flow rate of 1 mL min^{-1} during which Cr^{VI} was concentrated in the upper layer and Cr^{III} in the lower; drying at 100 °C was required for 30 min. The LODs for Cr^{III} and Cr^{VI} were 0.17 and 0.16 μg L^{-1} and recovery was between 94% and 114% although this was mitigated in mineral water samples because of overlap of V Kβ and Cr Kα energy bands.

Trace determination of *Cd in rice* using L-shell excitation XRF was optimized to reduce the influence of K in the matrix (the optimized energy was 3580 eV).[100] The rice flour was fixed to a 6 pm-thick film sample support of polypropylene with polyvinyl acetate; an LOD of 0.34 ppm was achieved.

Determination of *Sn in canned beverages and foods* by different techniques (ETAAS, HG-ICP-AES, ICP-AES, ICP-MS) was compared in terms of linearity, precision, recovery, LOD, decision limit and detection capability by Boutakhrit *et al.*[176] Precisions across the different techniques were between 1.6% and 4.9%. The best sample preparation was found to be sequential wet digestion with HNO_3 followed by H_2O_2 and no matrix interferences were observed. Limits of detection were determined as 0.01 μg L^{-1} (ICP-MS), 0.05 μg L^{-1} (HG-ICP-AES), 2.0 μg L^{-1} (ETAAS) and 200 μg L^{-1} (ICP-AES). In view of EU maximum levels for canned baby foods and infant foods being 50 mg kg^{-1} and 200 mg kg^{-1} respectively, ICP-AES was deemed the most appropriate technique because of its precision, reliability and ease of use.

The determination of I is considered "non-trivial" and it has elicited a lot of interest this year. Oliveira *et al.*[19] reviewed interference issues with the use of ICP-MS and ICP-AES and the memory effects encountered with nebulization. The authors reviewed sample preparation of many and various sample types and concluded preparation in alkaline conditions followed by measurement with ICP-MS obtained the best analytical figures of merit. Microwave-induced combustion was successfully employed for the preparation of various food matrices (bovine liver, corn starch, milk powder, wheat flour) for the determination of I by ICP-MS.[56] An ignition aid (50 μL, 6 M NH_4NO_3) was added to the combustion vessel with O_2 at 15 bar. Recoveries of 99% were achieved when an absorbing solution (50 mM $(NH_4)_2CO_3$ or 56 mM TMAH) and a 5 min reflux step were added; recovery was 97% and the LOQ was 0.002 μg g^{-1}. A micro-USN coupled with VG-ICP-MS was evaluated for the determination of I using a short oxidation reaction time.[83] Mixing of sample (solubilised in TMAH) and oxidant (H_2SO_4–H_2O_2–$NaNO_2$) at the quartz oscillator resulted in rapid delivery of the reaction products to the spray chamber entrance and, at a flow rate of 15 μL min^{-1}, the LOD was 1.6 ng mL^{-1} and the RSD was between 2 and 4%. The trueness was reported as being satisfactory, as was the determination of I in a variety of samples.

The in vitro bioavailability of Br and I in various edible seaweed samples was determined by ICP-MS.[177] Sample preparation for total I and Br in the whole sample and the non-dialysable fractions was by microwave-assisted digestion with TMAH; internal standards were Te and Y. *In vitro* intestinal digestion was carried out in PIPES buffer solution at pH 7.0 with a 10 kDa *Mr* cut-off dialysis membrane. Two red seaweed species (Dulse and Non) were found to have the highest Br digestibility (36 ± 0.7% and 47 ± 3.0%, respectively) while the highest I dialysibility was for brown seaweed (Kombu) at 17 ± 0.7%. A similar study looked at Ni in convenience food.[178] Total Ni concentrations were 18.50–95.00 ng g^{-1} but with a dialysable fraction determined at 4.50–7.75% the overall risk of exposure was low. It should be noted that *in vitro* dialysibility is a surrogate for human digestibility. Egg and pork-based foods contained the highest Ni levels and these levels increased when spices, herbs, whole cereals, dried fruits, cheese and mushrooms were added ingredients.

7.2 Single and multielement applications in food and beverages

7.2.1 Dietary intake studies. *This year has seen the reporting of several country-specific single and multi-element dietary intake surveys* (undertaken in France, Sweden and Brazil). Millour *et al.*[42,179,180] reported on the Second French Total Diet Study of 2006 which estimated the dietary exposure to toxic elements arising from 1319 habitually-consumed foodstuffs in France. Observed levels were low and consistent with other European countries. Fish products and a food group comprising sweeteners, honey and confectionery presented the highest values of Al, As, Cd, Hg, Pb and Sb although, for the elements with stated

European maximum permitted levels (Cd, Hg and Pb), the concentrations were still acceptable. Exposure to a range of toxic and essential elements was investigated on "market baskets" purchased in four Swedish cities, representing major geographical regions and covering 90% of food types consumed.[43] Only minor changes in intake of Ca, Cd, Cu, Mg, Mn and Zn have occurred since a previous study in 1987. The average consumption of essential mineral elements was close to or above the recommended daily adult intake except for Mg and Fe, the latter being 40% lower since flour fortification no longer took place, whereas Se intake was up 30%; the elimination of Pb from petroleum products has reduced exposure by 50%. Dietary intake by Brazilian consumers of various elements from rice was highlighted by Batista *et al.*[181] as representing a considerable contribution to dietary reference intakes and PTWI of toxic elements (estimated daily intake through rice consumption: As 9.5 μg; Cd 2.4 μg; Co 3.1 μg; Cu; 0.2 μg; Mg 85.6 mg; Mn 1.9 mg; P 333 mg; Se 3.0 μg; Rb 0.9 μg; Sb 0.029 μg; U 0.013 μg; V 0.3 μg; Zn 1.6 mg). This conclusion was reached through the ICP-MS analysis of 27 rice samples of three different types. Duplicate diet studies of Hg intake in China (Jinhu area) found exposure in children was higher than for adults although these were below the PTWI and therefore considered safe.[182] Levels of Hg in 176 duplicate diets from 60 people were analysed by AFS. On days without consumption of fish/seafood, median Hg intake was 0.13 μg kg^{-1} day^{-1} (range: 0.05–0.78) and 0.07 μg kg^{-1} day-1 (0.04–0.18) for children and adults respectively, whereas when fish/seafood were consumed, Hg intake was 0.16 μg kg^{-1} day^{-1} (0.11–0.84) and 0.09 μg kg^{-1} day^{-1} (0.05–0.46).

Mass spectrometry-based metabolomic studies are currently emerging in the area of food safety but given the complexities involved in this powerful approach, Antignac *et al.*[13] reviewed the current state of the art, listing short-comings and highlighting future challenges. Focusing on individual elements, the gastrointestinal tract absorption fraction, f(1), of U was found by Chen *et al.*[163] to be above values agreed by the International Commission on Radiological Protection for children up to the age of 18 (f(1) < 0.02). Using ICP-MS to measure U in bone ash of children (7–18 years old) and young adults (18–25 years old) living in a Canadian district known for elevated U levels, f(1) values were reported as 0.030 ± 0.022 and 0.021 ± 0.015. The correlation between dietary intake (from food frequency diaries) and serum Se (measured by ICP-MS) was found by Letsiou *et al.*[159] to hold for only a few specific food types. Among 506 participants in Greece (296 men, 210 women) aged 18–75 years, consumption of red meat was highly correlated whereas none was seen for other Se-containing foods (fish, cereals, dairy and vegetables); adoption of a vegetarian diet led to a negative correlation with serum Se. The Saudi diet was assessed for Pb intake by inhabitants of Riyadh city and was found to be comparable with that of other countries.[183] Vegetables and cereal products accounted for 50% of food consumed, and using food frequency diaries completed by 300 families, the total daily intake was estimated at 22.7–24.5 μg day^{-1}, depending on the calculation method used.

7.2.2 Human milk, infant formula and food. Mineral contents of *commercially available infant formulae* in Poland were surveyed using ICP-AES.[184] Comparison with values declared on the label (Ca, Cu, Fe, Mg, Mn, P and Zn) showed good agreement, while undeclared values for B, Ba and Sr were 104, 117 and 221 μg g^{-1}, with Al and Ni being below the LOD. A slurry ETAAS technique for the determination of Mo in infant formula was developed by de Amorim *et al.*[185] using a judicious choice of modifiers. A pre-injection of 5 μL of 0.1% (v/v) cetyl trimethylammonium chloride was used to reduce carbon build up in the atomizer while Eu (5 μg) and Nb (500 μg) were found to be optimum chemical and permanent modifiers with an atomization temperature of 2700 °C and pyrolysis temperature of 2,000 °C. The LOD achieved was 1.1 ± 0.1 μg L^{-1} with a linear range up to 100 μg L^{-1}. The concentrations of Mo in infant formulae ranged from 39 to 1570 μg kg^{-1}. Once an infant is weaned, there is a plethora of commercial infant foods, however, little data are available for the nutritional content of complementary infant foods.[186] Eight meat and vegetable products from four popular UK brands were analysed by ICP-AES and ICP-MS for Ca, Cu, Fe, K, Mg, Na, Se and Zn. With the exception of K, all samples presented micronutrient levels below the Recommended Nutrient Intake (EU Directive 2006/125/EC).

7.2.3 Milk and dairy products. The suitability and bioaccessibility of selenised fermented milk was studied using HPLC-ICP-MS following *in vitro* gastrointestinal digestion by Alzate *et al.*[187] Solubilised Se accounted for 76 ± 3% with Se-species smaller than 1.5 kDa comprising mainly SeCys2 and SeMetCys. A multi-element screening of cattle feed and resulting milk showed a correlation between the elemental composition of the milk and feed.[188] Significant differences in Br, Co, Cu, I, Li, Mn, P, Rb and Sr (measured by SF-ICP-MS) were found between the two farms studied. A survey of *heavy metals in milk* collected from Croatian producers suggested that Pb levels exceeded European maximum allowed levels.[189] Mean Pb concentrations were 58.7 and 36.2 μg L^{-1} while As levels ranged up to 283 and 1019 μg L^{-1} for northern and southern regions respectively. A significant difference ($p < 0.001$) was observed between Cd and Hg levels in those regions (northern: 1.76 and 1.59 μg L^{-1}; southern: 3.4 and 7.1 μg L^{-1} respectively). Levels of Cu were similar in both regions at 931.9 and 848.4 μg L^{-1} respectively.

7.2.4 Cereals, flour and rice. Field trials of a Se-biofortified fertiliser in a high-yielding UK wheat crop have shown that the level of Se species in *flour and bread* was approximately linearly related to the field application rate.[190] At an application rate of 100 g Se ha^{-1} (as Se^{VI}), total Se was 60 times higher than the control in both white flour (30 ng g^{-1}) and wholemeal flour (35 ng g^{-1}) while at 10 g Se ha^{-1}, levels in bread were 155 and 185 ng g^{-1}, respectively. The major Se species was SeMet (65–87%) while other species found were SeCys, SeMetCys, Se^{IV} and Se^{VI}. Given that wheat appears to provide the major intake of iAs in countries where rice is not the diet staple, D'Amato *et al.*[49] assessed different extraction processes for As speciation. They used AEC-ICP-MS with a PRPX-100-filled column and 10 mM $NH_4H_2PO_4$–1 mM NH_4NO_3–2% MeOH at pH 5.5 as mobile phase. Ultrasound- and microwave-assisted extraction procedures were compared, with the latter being most effective in releasing As species; the LODs ranged from 0.35 to 0.46 ng g^{-1} dw. Total As in wheat and wheat products was 8.6–29.8 ng g^{-1}

dw; iAs was the most abundant (95%) species, As^{III} was the next most abundant species followed by DMA. Ultrasonic slurry sampling was used by Huang and Jiang[70] to introduce cereal samples into ETV-ICP-MS for a multi-element method using 8-hydroxyquinoline-5-sulfonic acid as modifier to increase volatility. A DRC with CH_4 (flow rate 1.0 mL min^{-1}) was used to reduce the background ions of *m*/*z* 52 and 80 for Cr, Cu, Se and Zn while Cd, Co, Ni, Hg, Ni, V and Zn were determined in standard mode. Good agreement was obtained with wheat and rice flour SRMs and LODs in ng g^{-1} dw were 0.6 (Cd), 3.6 (Co), 2.1 (Cr), 6.8 (Cu), 0.8 (Hg), 4.3 (Ni), 2.6 (Pb), 1.7 (Se), 1.3 (V) and 16 (Zn). Wu *et al.*[61] described the use of dispersive liquid–liquid micro-extraction prior to FAAS for the determination of Cu in rice and millet samples. The analyte was complexed with 8-hydroxyquinoline and extracted into a small volume of dodecanol. The method, which achieved a preconcentration factor of 122, was linear over three orders of magnitude up to 500 ng mL^{-1}, with an LOD of 0.1 ng mL^{-1} and precision of 3.9–5.7% RSD. A key comparison performance assessment programme for national measurement institutes (NMI) (CCQM-K60) under the auspices of the Comité Consultatif pour la Quantité de Matière (CCQM) reported on the quantification of total Se and SeMet in selenised wheat flour.[191] Total Se was determined by ICP-MS with external calibration following microwave-assisted acid digestion and SeMet by multi-step enzymatic hydrolysis or hydrolysis with methanesulfonic acid, followed by ID-HPLC-ICP-MS. Eight of the nine NMIs reported total Se within a 3.5% deviation of the key comparison reference value (KCRV) and all participating NMIs reported SeMet values within 3.2% of the KCRV.

The influence of Fe plaque on the ability of root systems of *rice* (*Oryza sativ L.*) to take up As was investigated by Seyfferth *et al.*[112] Using a combination of XRF imaging, μ-XANES, transmission X-ray microscopy and tomography, the authors elucidated the co-localisation of As and Fe on rice rhizomes. Fine roots were shown to be dominated by As^{V} and As^{III} with smaller amounts of DMA and arsenic triglutathione. Although Fe and As were strongly co-located in roots with Fe-plaque, these do not intercept As uptake but serve as "a bulk scavenger". With high levels of As and Cd contamination in Bangladeshi tube wells, Khan *et al.*[192] studied the effect of washing rice prior to cooking (samples from 13 households). Washing rice with water before cooking reduced the concentration of As in uncooked rice by 13–15%, but this had little effect on Cd concentrations. A simple enzyme-assisted extraction of Se species from rice, which did not alter the species, was proposed by Zhao *et al.*[193] This sensitive method, based on CE-ICP-MS, allowed determination of Se^{IV}, Se^{VI}, $SeCys_2$ SeMet with LODs of 0.1–0.9 ng Se mL^{-1}. Enriched rice was shown to contain only SeMet at concentrations from 0.136 to 0.143 μg Se g^{-1} dw.

7.2.5 Vegetables, vegetable oils, fruits and nuts. Speciation of As in fresh and used *vegetable oils* using HPLC-ICP-MS was undertaken by Chu and Jiang[194] who used $(NH_4)_2CO_3$ and MeOH as eluents. The achieved LODs ranged from 0.08 to 0.24 ng g^{-1} in the oil sample. Major As species in the used oil depended on the food cooked. A method for the elemental profiling of edible vegetable oils (corn, olive, olive pomace, virgin olive, soybean and sunflower) was developed by Llorent-Martinez *et al.*[195] using HNO_3 digestion followed by ICP-MS; the short-term repeatability was less than 10%. Grouping by sample types (virgin olive oil, olive oil, olive-pomace oil, sunflower oil, corn oil and soybean oil) was possible using PCA which accounted for 75.3% of total variance over two factors.

Discrepancies in the determination of total Hg in wild *mushrooms* using ICP-AES at 194.163 nm was highlighted by Jarzynska and Falandysz.[86] The authors used pyrolysis followed by a gold wool trap prior to CV-AAS as a reference method to analyse several species of mushroom growing in Poland. They concluded the ICP-AES method was biased to higher values and was imprecise.

Microemulsification of *chocolate* enabled Ieggli *et al.*[196] to determine Cu and Mn using ETAAS with minimal sample handling. They used Tween 80 as surfactant, stirred with heat for 15 min to stabilise the emulsion and were able to use aqueous calibrants, obtaining adequate trueness. The same research group used a similar technique for the determination of a range of elements in various edible oils.[82]

7.2.6 Fish and seafood. As in previous years it is *As, Hg and Se in fish* that have been particularly investigated. The influence of seafood consumption in the US on human As intake was evaluated over six years.[39] Subjects reporting consumption within 24 h prior to urine collection presented considerably higher levels of total As, DMA, AB and the difference between total As and AB (median *vs.* control: 24.5 *vs.* 7.3 μg L^{-1}; 6.0 *vs.* 3.5 μg L^{-1}, 10.2 *vs.* 0.9 μg L^{-1} and 11.0 *vs.* 5.5 μg L^{-1}), as measured by HPLC-ICP-MS. The authors of the report recommended that epidemiological studies should take seafood consumption into account when estimating dietary As species. Selenoneine, a Se-containing imidazole compound, along with total organic Se was determined in a variety of fish species in Japan.[116] A gel filtration column was used with monitoring of ^{82}Se by ICP-MS. Most of the organic Se (9–42%) comprised selenoneine. Fish were grouped as those with high levels, ranging from 1.3 to 2.8 nmol g^{-1} (Swordfish, Bigeye tuna, Pacific bluefin tuna, Albacore, Yellowfin tuna and Alfonsino), those with intermediate levels, with 3–34% organic Se, at concentrations of 0.1–1.4 nmol g^{-1} (Pacific sardine, greeneye, Pacific mackerel, horse mackerel, red sea bream and Japanese barracuda), and those with selenoneine levels below the LOD of 0.05 nmol g^{-1} (Japanese conger, Anchovy, Chum salmon, Pacific saury, White croaker and Marbled sole). The levels of total Hg measured by Dabeka *et al.*[197] in predatory fish sold in Canada was found to exceed national limits in many cases. The authors analysed 188 fish samples of ten species taken from retail supply in 2005; mean Hg concentrations and ranges were quoted for each species and those exceeding set levels were identified. Total Hg in five brands of canned tuna purchased in Pennsylvania, USA was determined by CV-AAS.[198] The lowest Hg concentration was 0.19 ± 0.07 μg g^{-1} and the highest was 3.6 ± 0.17 μg g^{-1}. Minimal or no loss of Hg was observed during the microwave digestion. A rapid HPLC-ICP-MS method for Hg speciation in fish was described and validated by Batista *et al.*[48] using sonication for 15 min with mercaptoethanol, L-cysteine and HCl prior to separation on a C8 RP column. This method permitted a considerable reduction in time with LODs of 0.25, 0.20 and 0.1 ng g^{-1} for iHg, EtHg and MeHg, respectively. In a survey of Hg species in Brazilian fish was given (iHg: < 0.25–13.8 ng g^{-1}; MeHg: 3.8–160 ng g^{-1}; EtHg:

< 0.2 ng g^{-1}) and the highest values were found in canned tuna. A similar method[114] for MeHg in fish was described achieving an LOD of 0.5 μg kg^{-1}.

Differences in the concentration of several elements in *wild and farmed bluefin tuna* collected in Turkey were observed by AAS.[199] All elements except Mn were higher in wild fish and the rear dorsal ordinary muscle showed higher values except for Cu. The authors found that values agreed with the literature. A multi-element survey of fish and seafood on the French market was conducted in 2005 by Guerin *et al.*[200] using ICP-MS. Concentrations of Co, Cu, Fe, Li, Mn, Pb, Se and Zn were similar or lower than those found in previous surveys although the authors pointed out that levels of Ag were considerably higher.

Some *interesting analytical developments* were reported. Using a judicial selection of matrix modifiers, non-chromatographic speciation of As in fish-based baby foods was demonstrated by Lopez-Garcia *et al.*[78] Slurry injection was used with TMAH suspensions and ETAAS with standard additions. Total As concentration was determined with Pd modifier, Ce^{IV} modifier gave rise only to signals from iAs + MMA while a Zr-coated atomizer produced only signals from DMA; other species were deduced by subtraction from total As. Concentration of total As from locally made products was 108–275 ng g^{-1} with DMA at 30–45 ng g^{-1} for three food types. Pressure assisted enzymatic hydrolysis, prior to As speciation of dried fish muscle by anion exchange-HPLC-ICP-MS, was optimized and evaluated by Moreda-Pineiro *et al.*[51] The amount of pepsin used, pH and ionic strength conditions were optimized along with a short three-step thermal cycle which resulted in a process in which the temperature reached a maximum of 50 °C and lasted 7 min. Complete solubilisation was not achieved but good agreement (within certified ranges for DORM-2), precision (RSD: 3% for AB and <6% for As^{III}, DMA, As^{V}; LOQ: 18.1 ng g^{-1} As^{III}, 362 ng g^{-1} MMA, 357 ng g^{-1} DMA, 28.6 ng g^{-1} As^{V}, 20.6 ng g^{-1} AB and 22.5 ng g^{-1} AC) and sensitivity, were attained. Response surface methodology (Box-Behnken design) was used to optimize a microwave digestion technique prior to FAAS determination of several elements (Cu, Fe, Mn, Ni, Pb and Zn) in Snow trout found in Iran.[52] Optimized parameters were: 2.5 M HNO_3, 685 W synchrotron power to achieve a temperature of 116 °C with a digestion time of 38 min.

7.2.7 Meat and poultry. There is little to report relating to *analysis of meat*. A slurry sampling technique using TMAH was optimized by Damin *et al.*[80] for the determination of Cd and Pb in fresh meat by ETAAS. A common matrix modifier (0.05% Pd–0.03%–0.05% Triton X-100) was used and trueness was shown to be identical to that of a digestion method. A validated method for determination of ultra-trace amounts (0.004–0.55 ng) of Be in dried bovine liver was made possible by Lui *et al.*[201] using ETAAS after microwave-assisted digestion at 85 °C for 10 min with acetylacetone as chelating agent in the presence of acetate buffer at pH 6.0. Figures of merit for this method were LOD of 0.18 ng g^{-1} and LOQ 0.60 ng g^{-1}, calibration linearity up to 27 ng g^{-1}, RSD <3%, recoveries from eight spiked samples (four liver and four muscle, of which two were CRMs) were 96–103%.

7.2.8 Drinking water and non-alcoholic beverages. *Undue concentrations of elements in drinking water* arise from various sources. The presence of corrosion by-products of cast iron water mains and service pipes that contribute to increased V contamination of municipal drinking water was highlighted by Gerke *et al.*[202] Synchrotron μ-XRF and μ-XANES confirmed the presence of discrete grains of $Pb_5(VO_4)_3Cl$ (vanadinite) with bulk concentration between 35 and 899 mg kg^{-1} which might lead to V concentrations exceeding limits set in some administrations. With bottled water being a popular alternative to such drinking water, Birke *et al.*[203,204] undertook a comprehensive survey across Europe. Only 70% of samples fulfilled the European requirements for tap water, nearly 5% did not meet European standards for mineral and table water, exceeding limits for one or more of As, Ba, NO_3^-, NO_2^-, Mn or Ni, and 1% had U concentrations >10 μg L^{-1}. The authors went on to present element distribution maps for Germany and remarked on a conspicuous geochemical influence, indeed a serendipitous occurrence which is exploited in food and beverage authentication techniques. Using IC-ICP-MS (ICS-A23 column, 0.03 M $(NH_4)_2CO_3$ mobile phase), Liu *et al.*[205] surveyed 22 retailed bottled waters for BrO_3^-, Br^-, IO_3^- and I^- and found that 36.4% had BrO_3^- concentrations which exceeded the Chinese limit of 10 μg L^{-1}.

Much effort has been made over the past year in developing *new methodologies for preconcentrating water samples*, which represents the majority of papers for this matrix type. A strong enhancement in analytical throughout for the determination of As and Sb in bottled mineral waters was detailed by Guerra *et al.*[79] Complexation on pentane-2,4-dione and 3,5,7,2′-pentaoxyflavone adsorbed onto activated carbon permitted a 500-fold preconcentration of Be.[206] On-line preconcentration of U was achieved using a mini-column of Amberlite XAD-4 resin functionalized with β-nitroso-α-naphthol.[207] The batch-wise adsorption of Cr^{VI} onto Aliquat 336-AC before XRF circumvented the need for elution.[63] The *in situ* formation of pyrrolidinedithiocarbamic acid allowed the preconcentration and separation of Cr^{III} and Cr^{VI}.[105] A yeast (*Yamadazyma spartinae*), immobilised onto TiO_2 nanoparticles, was used in a mini-column for preconcentration of several transition elements.[58]

The performance of an automated lab-made ICP-AES collection and concentration system for the determination of elements in *tea leaves* was reported by Jin *et al.*[59] Analytes (16 REEs, seven transition elements and Pb) were measured after microwave-assisted extraction of tea leaves without HF and in hot water infusions. Use of an in-line mini-column packed with ME-3 chelating resin (conditioned with 0.5 M CH_3COONH_4 (pH 5.5) and eluted with 2 M HNO_3) allowed concentration factors of 40 to 74 with LODs from 0.01 to 0.2 ppb and RSD values <9%. The tea plant (*Camelia sinensis*)—from which a widely-consumed and studied beverage is made—is often shown capable of accumulating non-essential elements and to potentially exceed permissible levels. With elemental content reported over large ranges, Karak and Bhagat[208] reviewed levels and have updated knowledge in this area. They reported concentration ranges in tea: Al 0.06–16.82 mg L^{-1}, As trace–1.53 μg L^{-1}, Cd trace–0.79 μg L^{-1}, Cr <LOD–43.2 μg L^{-1}, Cu 0.02–40.0 mg L^{-1}, F 0.2–4.54 mg L^{-1}, Mn 0.1–250 mg $L^{-1}$and Ni <LOD–0.16 mg L^{-1}.

The use of CPE has been reported often as a way of preconcentrating analytes in difficult matrices and has been used for the determination of *Cd in soft drinks*.[62] Under optimized

conditions, 0.13 mM pyridylazonaphthol was used to form hydrophobic Cd-chelates and these were extracted in 0.03% m/v Triton X-114–2.3% m/v NaCl. The achieved LOD using TS-FF-AAS was 0.0178 μg L^{-1} with a concentration factor of 55.5.

7.2.9 Alcoholic beverages. A review of analytical techniques to determine the concentrations of *metals in wines* was undertaken by Grindlay *et al.*[11] with special emphasis on matrix effects and their mitigation along with an update on speciation. The advantages of using HR-ICP-MS for resolving spectral interferences in the determination of trace elements in wine were assessed by Fiket *et al.*[209] who also compared the quantitative and semi-quantitative modes. Matrix-matching calibration with In as internal standard as well as a 10-fold dilution was required to achieve optimum results. Quantitative and semi-quantitative determination yielded comparable results in terms of LOD values, precision (RSD < 5%) and trueness (<20%) although the semi-quantitative mode of HR-ICP-MS offered higher precision. The measurement of toxic metals in Turkish wines sourced from local supermarkets was undertaken using ICP-AES with HG used for Cd, Hg and Pb.[210] Concentrations found in red and white wines were comparable to published values. A Pt-wire atomizer for a CH_4-air FAES was used to determine the Rb content in wine, beer and other juices.[211] The method was, unusually, devised for a sample size of 3 μL and delivered an LOQ (6σ only) of 4.3 ± 1.8 pg when analysed with 50 mg L^{-1} K and 5% acetone in the matrix. The use of V as internal standard for the determination of As in wines using ICP-AES was proposed by Mutic *et al.*[212] The RSD was improved three-fold with the internal standard and recoveries from spiked samples were within the 95–103% range. A portable TXRF spectrometer was evaluated for analysis of wines.[211] Only Fe, K, Mn and Rb were detected and quantified using Co as internal standard. The authors noted a high background scattering effect due to the organic matrix resulting in RSD values from 4 to 28% although low LODs were achieved.

7.3 Food authenticity

The *geographical provenance* of tomato products from Italy was demonstrated using ICP-MS and IRMS on juice, passata and paste derived from three regions (Piedmont, Emilia Romagna and Apulia).[213] Of the parameters determined, 17 variables (elements: Cd, Co, Cr, Cs, Eu, Gd, K, La, Mg, Mo, Ni, Rb, Tl, U; stable isotope ratios: δ13C, δ15N and δ 34*S*) were chosen by linear discriminant analysis to correctly classify 95% for all samples. Stable isotopes of O and Sr, measured by MC-ICP-MS and IRMS also provided highly useful data on the geographical origin of green coffee beans.[73] Both isotope ratio parameters are influenced by environmental factors which, in turn, have an effect on the growth of the beans. Use of PCA indicated that these parameters are discriminant of coffee provenance, especially those from South America and island regions (Hawaii, Jamaica, East Timor, Indonesia and Papua New Guinea). A similar outcome was reached by Akamine *et al.*[101] who used XRF with three-dimensional polarized optics to detect the elements Ba, Fe, Mn, Ni, Rb and Sr. Beans from six worldwide coffee-producing regions were successfully discriminated, whether green or roasted. This work underscores the commonality with other food products which are often discriminated using some of these elements.

Abbreviations

2D	two dimensional
3D	three dimensional
AB	arsenobetaine
AC	arsenocholine
AAS	atomic absorption spectrometry
AES	atomic emission spectrometry
AEC	anion exchange chromatography
AFS	atomic fluorescence spectrometry
ASU	Atomic Spectrometry Updates
CE	capillary electrophoresis
CPE	cloud point extraction
CRM	certified reference material
CSF	cerebrospinal fluid
CV	cold vapour
DMA	dimethylarsinic acid
DMDSe	dimethyldiselenide
DMSe	dimethylselenide
DRC	dynamic reaction cell
EDXRF	energy dispersive X-ray fluorescence
ELSD	Evaporative Light Scattering Detector
ESI	electrospray ionization
ETAAS	electrothermal atomization AAS
EtHg	ethylmercury
ETV	electrothermal vaporization
FAAS	flame AAS
FAES	flame AES
FDA	Food and Drug Agency
FF	flame furnace
FTIR	Fourier transforn infrared
GaM	gallium maltolate
GC	gas chromatography
GPx	glutathione peroxidase
HG	hydride generation
HPLC	high performance liquid chromatography
HR-ICP-MS	high resolution ICP-MS
iAs	inorganic As
IC	ion chromatography
ICP	inductively coupled plasma
ICP-MS	ICP mass spectrometry
ID-ICP-MS	isotope dilution ICP-MS
iHg	inorganic mercury
INAA	instrumental neutron activation analysis
IRMS	isotope ratio mass spectrometry
iSe	inorganic selenium
kDa	kiloDalton
LA	laser ablation
LC	liquid chromatography
LIBS	laser ionization breakdown spectroscopy
LOD	limit of detection
LOQ	limit of quantitation
MALDI	matrix-assisted laser desorption ionization
MC-ICP-MS	multicollector ICP-MS
MeHg	methylmercury

MMA	monomethylarsonic acid
Mr	relative molecular mass
MRI	magnetic resonance imaging
MS	mass spectrometry
NIST	National Institute of Standards and Technology
NSF	nephrogenic systemic fibrosis
PB-HC-AES	particle beam hollow cathode optical emission spectrometry
PCA	principal component analysis
PIXE	particle-induced X-ray emission
PrHg	propylmercury
PTWI	provisional tolerable weekly intake
ICP-QMS	inductively coupled plasma quadrupole MS
REE	rare earth element
RM	reference material
RP	reversed phase
RSD	relative standard deviation
SDS	sodium dodecyl sulfate
SDS-PAGE	SDS-polyacrylamide gel electrophoresis
SEC	size exclusion chromatography
SeCys	selenocysteine
$SeCys_2$	selenocystine
SeMet	selenomethioneine
SeMetCys	selenomethylcysteine
SF-ICP-MS	sector field ICP-MS
SPE	solid phase extraction
SRM	standard reference material
SR-TXRF	synchrotron radiation XRF
Tf	transferrin
TLC	thin layer chromatography
TMAH	tetramethylammonium hydroxide
TOF-MS	time-of-flight-MS
TS	thermospray
TXRF	total reflection XRF
USN	ultrasonic nebulizer
UV-VIS	ultraviolet-visible
WDXRF	wavelength dispersive XRF
XANES	X-ray absorption near-edge structure
XRF	X-ray fluorescence

References

1 A. Taylor, S. Branch, M. P. Day, M. Patriarca and M. White, *J. Anal. At. Spectrom.*, 2011, **26**(4), 653–692.
2 M. West, A. T. Ellis, P. J. Potts, C. Streli, C. Vanhoof, D. Wegrzynek and P. Wobrauschek, *J. Anal. At. Spectrom.*, 2010, **25**(10), 1503–1545.
3 S. Carter, A. S. Fisher, P. S. Goodall, M. W. Hinds, S. Lancaster and S. Shore, *J. Anal. At. Spectrom.*, 2010, **25**(12), 1808–1858.
4 O. T. Butler, W. Cairns, J. M. Cook and C. M. Davidson, *Journal of Analytical Atomic Spectrometry*, **26**(2), pp. 250–286.
5 E. H. Evans, J. A. Day, C. D. Palmer and C. M. M. Smith, *J. Anal. At. Spectrom.*, 2011, **26**(6), 1115–1141.
6 C. F. Harrington, R. Clough, L. R. Drennan-Harris, S. J. Hill and J. F. Tyson, *J. Anal. At. Spectrom.*, 2011, **26**(8), 1561–1595.
7 O. Butler, H. Evans, A. Fisher, S. Hill, C. Harrington, A. Taylor, M. West and A. Ellis, *J. Anal. At. Spectrom.*, 2010, **25**(10), 1546–1566.
8 Y. Ha, O. G. Tsay and D. G. Churchill, *Monatshefte Fur Chemie*, 2010, **142**(4), 385–398.
9 N. Lewen, *J. Pharm. Biomed. Anal.*, 2010, **55**(4), 653–661.
10 X. D. Yuan, R. L. Chapman and Z. Q. Wu, *Phytochem. Anal.*, 2010, **22**(3), 189–198.
11 G. Grindlay, J. Mora, L. Gras and M. T. C. de Loos-Vollebregt, *Analytica Chimica Acta*, 2010, **691**(1–2), 18–32.
12 M. Petkovic and T. Kamceva, *Metallomics*, 2011, **3**(6), 550–565.
13 J. P. Antignac, F. Courant, G. Pinel, E. Bichon, F. Monteau, C. Elliott and B. Le Bizec, *TrAC, Trends Anal. Chem.*, 2011, **30**(2), 292–301.
14 J. S. Becker and D. Salber, *TrAC, Trends Anal. Chem.*, 2010, **29**(9), 966–979.
15 Z. Y. Qin, J. A. Caruso, B. Lai, A. Matusch and J. S. Becker, *Metallomics*, **3**(1), pp. 28–37.
16 L. H. Cazares, D. A. Troyer, B. H. Wang, R. R. Drake and O. J. Semmes, *Anal. Bioanal. Chem.*, 2011, **401**(1), 17–27.
17 D. R. Chettle, *Pramana*, 2011, **76**(2), 249–259.
18 S. Miyashita and T. Kaise, *J. Food Hyg. Soc. Jpn.*, 2010, **51**(3), 71–91.
19 A. A. Oliveira, L. C. Trevizan and J. A. Nobrega, *Appl. Spectrosc. Rev.*, 2010, **45**(6), 447–473.
20 L. H. Reyes, J. L. G. Mar, A. Hernandez-Ramirez, J. M. Peralta-Hernandez, J. M. A. Barbosa and H. M. S. Kingston, *Microchim. Acta*, 2010, **172**(1), 3–14.
21 H. Bertelsmann, D. Behne, M. Hammadeh and A. Kyriakopoulos, *Trace Elem. Electrolytes*, 2010, **27**(4), 232–234.
22 I. L. Heras, M. Palomo and Y. Madrid, *Anal. Bioanal. Chem.*, 2010, **400**(6), 1717–1727.
23 J. Far, S. Berail, H. Preud'homme and R. Lobinski, *J. Anal. At. Spectrom.*, 2010, **25**(11), 1695–1703.
24 B. Michalke and V. Nischwitz, *Anal. Chim. Acta*, 2010, **682**(1–2), 23–36.
25 I. M. Kempson and E. Lombi, *Chem. Soc. Rev.*, 2011, **40**(7), 3915–3940.
26 M. Kosanovic and M. Jokanovic, *Environmental Monitoring and Assessment*, 2010, **174**(1–4), 635–643.
27 R. Haselberg, G. J. de Jong and G. W. Somsen, *Electrophoresis*, 2010, **32**(1), 66–82.
28 V. M. O. Carioni, R. Chelegao, J. Naozuka and C. S. Nomura, *Accredit. Qual. Assur.*, 2011, **16**(8–9), 453–458.
29 T. Oguri, J. Yoshinaga, H. Tao and T. Nakazato, *Bunseki Kagaku*, 2011, **60**(8), 653–658.
30 W. C. Davis and S. E. Long, *J. Anal. At. Spectrom.*, 2011, **26**(2), 431–435.
31 B. Bocca, D. Mattel, A. Pino and A. Alimonti, *Rapid Commun. Mass Spectrom.*, 2010, **25**(3), 453–458.
32 H. Lamadrid-Figuero, M. M. Tellez-Rojo, G. Angeles, M. Hernandez-Avila and H. Hu, *Environ. Res.*, 2010, **111**(1), 17–20.
33 P. Y. T. Hon, P. K. Chan, S. T. C. Cheung and Y. C. Wong, *Microchem. J.*, 2011, **98**(1), 44–50.
34 K. Ito, W. Goessler, H. Gurleyuk, B. Wels, C. D. Palmer, M. F. Verostek and P. J. Parsons, *J. Anal. At. Spectrom.*, 2011, **26**(9), 1740–1745.
35 M. Ikeda, F. Ohashi, Y. Fukui, S. Sakuragi and J. Moriguchi, *Int. Arch. Occup. Environ. Health*, 2010, **84**(2), 139–150.
36 B. Bocca, R. Madeddu, Y. Asara, P. Tolu, J. A. Marchal and G. Forte, *J. Trace Elem. Med. Biol.*, 2011, **25**(1), 19–26.
37 G. Forte, R. Madeddu, P. Tolu, Y. Asara, J. A. Marchal and B. Bocca, *Int. J. Hyg. Environ. Health*, 2011, **214**(2), 102–109.
38 Z. Ignasiak, T. Slawinska, R. M. Malina and B. B. Little, *Polish Journal of Environmental Studies*, 2010, **20**(2), 503–508.
39 A. Navas-Acien, K. A. Francesconi, E. K. Silbergeld and E. Guallar, *Environ. Res.*, 2010, **111**(1), 110–118.
40 J. Morton, E. Leese, R. Cotton, N. Warren and J. Cocker, *Int. Arch. Occup. Environ. Health*, 2011, **84**(6), 697–704.
41 D. C. Baxter, M. Faarinen, H. Osterlund, I. Rodushkin and M. Christensen, *Anal. Chim. Acta*, 2011, **701**(2), 134–138.
42 S. Millour, L. Noel, A. Kadar, R. Chekri, C. Vastel, V. Sirot, J. C. Leblanc and T. Guerin, *Food Chem.*, 2010, **126**(4), 1787–1799.
43 W. Becker, L. Jorhem, B. Sundstrom and K. P. Grawe, *J. Food Compos. Anal.*, 2011, **24**(2), 279–287.
44 W. Quiroz, H. Arias, M. Bravo, M. Pinto, M. G. Lobos and M. Cortes, *Microchem. J.*, 2010, **97**(1), 78–84.
45 M. Klein, H. Preud'homme, M. Bueno and F. Pannier, *J. Anal. At. Spectrom.*, 2011, **26**(3), 602–607.

46 M. Schrag, A. Dickson, A. Jiffry, D. Kirsch, H. V. Vinters and W. Kirsch, *BioMetals*, 2010, **23**(6), 1123–1127.
47 M. Costas, I. Lavilla, S. Gil, F. Pena, I. de la Calle, N. Cabaleiro and C. Bendicho, *Anal. Chim. Acta*, 2010, **679**(1–2), 49–55.
48 B. L. Batista, J. L. Rodrigues, S. S. de Souza, V. C. O. Souza and F. Barbosa, *Food Chem.*, 2010, **126**(4), 2000–2004.
49 M. D'Amato, F. Aureli, S. Ciardullo, A. Raggi and F. Cubadda, *J. Anal. At. Spectrom.*, 2011, **26**(1), 207–213.
50 V. Dufailly, M. Nicolas, J. Richoz-Payot and E. Poitevin, *Journal of Aoac International*, 2011, **94**(3), 947–958.
51 J. Moreda-Pineiro, E. Alonso-Rodriguez, A. Moreda-Pineiro, C. Moscoso-Perez, S. Muniategui-Lorenzo, P. Lopez-Mahia, D. Prada-Rodriguez and P. Bermejo-Barrera, *Anal. Chim. Acta*, 2010, **679**(1–2), 63–73.
52 M. Khajeh and M. Ghanbari, *Food Anal. Methods*, 2011, **4**(3), 431–436.
53 J. Diederich and B. Michalke, *Anal. Bioanal. Chem.*, 2010, **399**(5), 1799–1806.
54 B. Meermann, I. Moller, S. Nowak, H. Luftmann and U. Karst, *J. Anal. At. Spectrom.*, 2010, **25**(10), 1654–1658.
55 J. L. Rodrigues, C. R. Alvarez, N. R. Farinas, J. J. B. Nevado, F. Barbosa and R. C. R. Martin-Doimeadios, *J. Anal. At. Spectrom.*, 2011, **26**(2), 436–442.
56 M. F. Mesko, P. A. Mello, C. A. Bizzi, V. L. Dressler, G. Knapp and E. M. M. Flores, *Anal. Bioanal. Chem.*, 2010, **398**(2), 1125–1131.
57 A. Afkhami, M. Saber-Tehrani, H. Bagheri and T. Madrakian, *Microchim. Acta*, 2010, **172**(1), 125–136.
58 S. Baytak, F. Zereen and Z. Arslan, *Talanta*, 2011, **84**(2), 319–323.
59 H. Jin, A. Sabarudin, M. Oshima and S. Motomizu, *Bunseki Kagaku*, 2009, **58**(8), 699–706.
60 K. Choi, J. Kim and D. S. Chung, *Bioanalysis*, 2010, **3**(7), 799–815.
61 C. X. Wu, Q. H. Wu, C. Wang and Z. Wang, *Chin. Chem. Lett.*, 2011, **22**(4), 473–476.
62 H. C. Rezende, C. C. Nascentes and N. M. M. Coelho, *Microchem. J.*, 2010, **97**(2), 118–121.
63 P. R. Aranda, S. Moyano, L. D. Martinez and I. E. De Vito, *Anal. Bioanal. Chem.*, 2010, **398**(2), 1043–1048.
64 L. Husakova, I. Urbanova, L. Audrlicka-Vavrusova, J. Sramkova, T. Cernohorsky, M. Bednarikova and L. Pilarova, *Microchimica Acta*, 2010, **173**(1–2), 173–181.
65 V. L. Dressler, D. Pozebon, M. F. Mesko, A. Matusch, U. Kumtabtim, B. Wu and J. S. Becker, *Talanta*, 2010, **82**(5), 1770–1777.
66 P. Cheajesadagul, W. Wananukul, A. Siripinyanond and J. Shiowatana, *J. Anal. At. Spectrom.*, 2011, **26**(3), 493–498.
67 I. Konz, B. Fernandez, M. L. Fernandez, R. Pereiro and A. Sanz-Medel, *Anal. Chem.*, 2011, **83**(13), 5353–5360.
68 L. N. Zheng, M. Wang, H. J. Wang, J. J. Li, W. Y. Feng and Z. F. Chai, *Progress in Chemistry*, 2010, **22**(11), 2199–2206.
69 S. Letsiou, Y. Lu, T. Nomikos, S. Antonopoulou, D. Panagiotakos, C. Pitsavos, C. Stefanadis and S. A. Pergantis, *Proteomics*, 2010, **10**(19), 3447–3457.
70 S. Y. Huang and S. J. Jiang, *Anal. Methods*, 2010, **2**(9), 1310–1315.
71 M. L. Lin and S. J. Jiang, *J. Anal. At. Spectrom.*, 2011, **26**(9), 1813–1818.
72 S. Z. Chen, S. P. Zhu and D. B. Lu, *Atomic Spectroscopy*, 2011, **32**(3), 90–94.
73 C. Rodrigues, C. Maguas and T. Prohaska, *Eur. Food Res. Technol.*, 2010, **232**(2), 361–373.
74 M. Takagi, J. Yoshinaga, A. Tanaka and H. Seyama, *Anal. Sci.*, 2010, **27**(1), 29–35.
75 A. Walter, S. Nelms, C. Harrington and A. Taylor, *Ann. Clin. Biochem.*, 2011, **48**, 176–177.
76 D. G. Filatova, I. F. Seregina, L. S. Foteeva, V. V. Pukhov, A. R. Timerbaev and M. A. Bolshov, *Anal. Bioanal. Chem.*, 2010, **400**(3), 709–714.
77 J. Vrijens, P. Couck, C. Schroijen, W. Baeyens and M. Leermakers, *J. Anal. At. Spectrom.*, 2011, **26**(9), 1819–1826.
78 I. Lopez-Garcia, M. Briceno and M. Hernandez-Cordoba, *Anal. Chim. Acta*, 2011, **699**(1), 11–17.
79 M. B. B. Guerra, R. Carapelli, K. Miranda, A. R. A. Nogueira and E. R. Pereira, *Anal. Methods*, 2011, **3**(3), 599–605.
80 I. C. F. Damin, A. V. Zmozinski, A. R. Borges, M. G. R. Vale and M. M. da Silva, *Anal. Methods*, 2011, **3**(6), 1379–1385.
81 D. R. Vieira, J. T. Castro and V. A. Lemos, *Journal of Aoac International*, 2011, **94**(2), 645–649.
82 C. V. S. Ieggli, D. Bohrer, P. C. Do Nascimento and L. M. De Carvalho, *Food Additives and Contaminants Part a-Chemistry Analysis Control Exposure & Risk Assessment*, 2011, **28**(5), 640–648.
83 H. Matusiewicz and M. Slachcinski, *Anal. Methods*, 2010, **2**(10), 1592–1598.
84 A. Terol, E. Paredes, S. E. Maestre, S. Prats and J. L. Todoli, *J. Chromatogr., A*, 2010, **1217**(40), 6195–6202.
85 L. Kekedy-Nagy, A. R. Zsigmond and E. A. Cordos, *Acta Chimica Slovenica*, 2010, **57**(4), 912–915.
86 G. Jarzynska and J. Falandysz, *J. Environ. Sci. Health, Part A: Toxic/Hazard. Subst. Environ. Eng.*, 2011, **46**(6), 569–573.
87 W. Q. Lei, J. El Haddad, V. Motto-Ros, N. Gilon-Delepine, A. Stankova, Q. L. Ma, X. S. Bai, L. J. Zheng, H. P. Zeng and J. Yu, *Anal. Bioanal. Chem.*, 2011, **400**(10), 3303–3313.
88 Z. Hosseinimakarem and S. H. Tavassoli, *J. Biomed. Opt.*, 2011, **16**(5), 8.
89 E. J. dos Santos, A. B. Herrmann, A. B. dos Santos, L. M. Baika, C. S. Sato, L. Tormen, R. E. Sturgeon and A. J. Curtius, *J. Anal. At. Spectrom.*, 2010, **25**(10), 1627–1632.
90 J. G. Dorea, W. Wimer, R. C. Marques and C. Shade, *Biol. Trace Elem. Res.*, 2011, **140**(3), 262–271.
91 J. G. Dorea, V. Bezerra, V. Fajon and M. Horvat, *Clin. Chim. Acta*, 2011, **412**(17–18), 1563–1566.
92 Y. Gao, S. De Galan, A. De Brauwere, W. Baeyens and M. Leermakers, *Talanta*, 2010, **82**(5), 1919–1923.
93 P. Herbello-Hermelo, F. M. Castro and P. Bermejo-Barrera, *Atomic Spectroscopy*, 2011, **32**(3), 102–106.
94 R. S. Li, H. T. Yan, X. M. Yang, Z. X. Li and Y. A. Guo, *J. Anal. At. Spectrom.*, 2011, **26**(7), 1488–1493.
95 S. Behinaein, D. R. Chettle, J. Atanackovic, L. M. Egden, D. E. B. Fleming, L. H. Nie, N. Richard and S. Stever, *Phys. Med. Biol.*, 2010, **56**(3), 653–665.
96 L. H. Nie, S. Sanchez, K. Newton, L. Grodzins, R. O. Cleveland and M. G. Weisskopf, *Phys. Med. Biol.*, 2010, **56**(3), N39–N51.
97 S. Arzhantsev, X. A. Li and J. F. Kauffman, *Anal. Chem.*, 2010, **83**(3), 1061–1068.
98 S. Al-Omari, *X-Ray Spectrom.*, 2010, **40**(1), 31–36.
99 H. Stosnach, *Spectrochim. Acta, Part B*, 2010, **65**(9–10), 859–863.
100 Y. Sugihara, S. Hayakawa, H. Namatame and T. Hirokawa, *Bunseki Kagaku*, 2011, **60**(8), 613–618.
101 T. Akamine, A. Otaka, A. Hokura, Y. Ito and I. Nakai, *Bunseki Kagaku*, 2010, **59**(10), 863–871.
102 T. Inui, W. Abe, M. Kitano and T. Nakamura, *X-Ray Spectrom.*, 2011, **40**(4), 301–305.
103 S. Murko, J. Scancar and R. Milacic, *J. Anal. At. Spectrom.*, 2011, **26**(1), 86–93.
104 B. Y. Deng, Y. Z. Wang, P. C. Zhu, X. Ning, H. Lu and X. S. Xu, *J. Anal. At. Spectrom.*, 2010, **25**(12), 1859–1863.
105 T. Akutsu, T. Shimizu and N. Uehara, *BunsekiKagaku*, 2009, **58**(8), 693–698.
106 Y. W. Wu, J. Zhang, J. F. Liu, Z. L. Deng, M. X. Han, F. Jiang, D. Z. Wang, H. K. Wang and H. Z. Yuan, *Atomic Spectroscopy*, 2010, **32**(1), 41–47.
107 W. Y. Feng, W. Meng, G. A. Ming, H. Yuan, J. W. Shi, W. Bing, M. T. Zhu, O. Y. Hong, Y. L. Zhao and Z. F. Chai, *J. Anal. At. Spectrom.*, 2011, **26**(1), 156–164.
108 P. Belanger and P. Dumas, *Atomic Spectroscopy*, 2010, **31**(6), 175–181.
109 J. Morton and E. Leese, *Anal. Bioanal. Chem.*, 2010, **399**(5), 1781–1788.
110 Z. Rivera-Nunez, A. M. Linder, B. Chen and J. O. Nriagu, *Anal. Methods*, 2011, **3**(5), 1122–1129.
111 C. Cascio, A. Raab, R. O. Jenkins, J. Feldmann, A. A. Meharg and P. I. Haris, *J. Environ. Monit.*, 2010, **13**(2), 257–265.
112 A. L. Seyfferth, S. M. Webb, J. C. Andrews and S. Fendorf, *Environ. Sci. Technol.*, 2010, **44**(21), 8108–8113.
113 F. Moreno, T. Garcia-Barrera and J. L. Gomez-Ariza, *Analyst*, 2010, **135**(10), 2700–2705.
114 S. Ghanthimathi, N. B. Ibrahim, Z. B. Nasir, L. Lim and K. Ong, *Atomic Spectroscopy*, 2011, **32**(3), 85–89.
115 S. W. C. Chung and B. T. P. Chan, *J. Chromatogr., A*, 2010, **1218**(9), 1260–1265.

116 Y. Yamashita, H. Amlund, T. Suzuki, T. Hara, M. A. Hossain, T. Yabu, K. Touhata and M. Yamashita, *Fish. Sci.*, 2011, **77**(4), 679–686.
117 M. Klein, L. Ouerdane, M. Bueno and F. Pannier, *Metallomics*, 2010, **3**(5), 513–520.
118 Y. L. Rao, M. McCooeye, A. Windust, E. Bramanti, A. D'Ulivo and Z. Mester, *Anal. Chem.*, 2010, **82**(19), 8121–8130.
119 Y. F. Li, L. A. Hu, B. Li, X. H. Huang, E. H. Larsen, Y. X. Gao, Z. F. Chai and C. Y. Chen, *J. Anal. At. Spectrom.*, 2011, **26**(1), 224–229.
120 K. Lunoe, S. Skov, C. Gabel-Jensen, S. Sturup and B. Gammelgaard, *Anal. Bioanal. Chem.*, 2010, **398**(7–8), 3081–3086.
121 B. Wu, S. Niehren and J. S. Becker, *J. Anal. At. Spectrom.*, 2011, **26**(8), 1653–1659.
122 D. Pozebon, V. L. Dressler, M. F. Mesko, A. Matusch and J. S. Becker, *J. Anal. At. Spectrom.*, 2010, **25**(11), 1739–1744.
123 Y. K. Hsieh, P. S. Jiang, B. S. Yang, T. Y. Sun, H. H. Peng and C. F. Wang, *Anal. Bioanal. Chem.*, 2011, **401**(3), 909–915.
124 D. Hare, C. Austin, P. Doble and M. Arora, *J. Dent.*, 2011, **39**(5), 397–403.
125 G. R. Pereira, H. S. Rocha, C. Calza, M. J. Anjos, I. Lima, C. A. Perez and R. T. Lopes, *X-Ray Spectrom.*, 2011, **40**(4), 260–264.
126 I. Hozumi, T. Hasegawa, A. Honda, K. Ozawa, Y. Hayashi, K. Hashimoto, M. Yamada, A. Koumura, T. Sakurai, A. Kimura, Y. Tanaka, M. Satoh and T. Inuzuka, *J. Neurol. Sci.*, 2011, **303**(1–2), 95–99.
127 L. Gerhardsson, T. Lundh, E. Londos and L. Minthon, *J. Neural Transm.*, 2011, **118**(6), 957–962.
128 B. Michalke and A. Berthele, *J. Anal. At. Spectrom.*, 2011, **26**(1), 165–170.
129 M. Corradi, O. Acampa, M. Goldoni, E. Adami, P. Apostoli, G. de Palma, A. Pesci and A. Mutti, *J. Breath Res.*, 2009, **3**(4), 8.
130 Y. J. Kim, Y. K. Kim and H. S. Kho, *Oral Dis.*, 2010, **16**(8), 823–830.
131 D. A. Roman, I. Pizarro, L. Rivera, C. Camara, M. A. Palacios, M. M. Gomez and C. Solar, *Hum. Exp. Toxicol.*, 2011, **30**(9), 1150–1164.
132 Y. Yoshimura, Y. Endo, Y. Shimoda, K. Yamanaka and G. Endo, *J. Occup. Health*, 2011, **53**(1), 45–49.
133 V. A. Lemos and A. L. de Carvalho, *Environ. Monit. Assess.*, 2010, **171**(1–4), 255–265.
134 S. V. Adams, P. A. Newcomb, M. M. Shafer, C. Atkinson, E. J. A. Bowles, K. M. Newton and J. W. Lampe, *Sci. Total Environ.*, 2011, **409**(9), 1632–1637.
135 Y. Fukui, F. Ohashi, S. Sakuragi, J. Moriguchi and M. Ikeda, *Ind. Health*, 2011, **49**(3), 338–343.
136 J. Yang, B. Shen, Z. K. Zhou, F. X. Pei and P. D. Kang, *J. Arthroplasty*, 2011, **26**(1), 65–70.
137 C. D. Quarles, J. L. Brumaghim and R. K. Marcus, *Metallomics*, 2010, **2**(12), 792–799.
138 C. Arnold, M. K. Chaffin, N. Cohen, V. R. Fajt, R. J. Taylor and L. R. Bernstein, *Am. J. Vet. Res.*, 2010, **71**(11), 1371–1376.
139 J. K. Kim, S. J. Seo, K. H. Kim, T. J. Kim, M. H. Chung, K. R. Kim and T. K. Yang, *Nanot*, 2010, **21**(42), 10.
140 J. H. Lee, O. J. Ji, M. J. Song, H. D. Park, H. K. Kim, S. W. Kim, J. M. Chung and S. Y. Lee, *The Korean Journal of Laboratory Medicine*, 2010, **30**(4), 351–356.
141 W. N. Zhang, X. Q. Liu, X. Y. Jia, Y. Han, X. L. Liu, X. J. Xie, J. L. Lu, T. C. Duan and H. T. Chen, *Chromatographia*, 2010, **72**(9–10), 1009–1012.
142 C. Langkammer, N. Krebs, W. Goessler, E. Scheurer, F. Ebner, K. Yen, F. Fazekas and S. Ropele, *Radiology*, 2011, **257**(2), 455–462.
143 Z. Polgari, F. Meirer, S. Sasamori, D. Ingerle, G. Pepponi, C. Streli, K. Rickers, A. Reti, B. Budai, N. Szoboszlai and G. Zaray, *Spectrochim. Acta, Part B*, 2011, **66**(3–4), 274–279.
144 M. Grebe, D. Profrock, A. Kakuschke, J. A. C. Broekaert and A. Prangea, *Metallomics*, 2011, **3**(2), 176–185.
145 G. Mergen and T. Soylemezoglu, *At. Spectrosc.*, 2011, **31**(2), 61–66.
146 J. H. Amaral, V. B. Rezende, S. M. Quintana, R. F. Gerlach, F. Barbosa and J. E. Tanus-Santos, *Basic Clin. Pharmacol. Toxicol.*, 2010, **107**(6), 971–975.
147 G. R. C. de Almeida, C. D. Guerra, G. D. S. Leite, R. C. Antonio, F. Barbosa, J. E. Tanus-Santos and R. F. Gerlach, *Sci. Total Environ.*, 2011, **409**(10), 1799–1805.
148 M. L. Praamsma, J. G. Arnason and P. J. Parsons, *J. Anal. At. Spectrom.*, 2011, **26**(6), 1224–1232.
149 I. Al-Saleh and A. Al-Sedairi, *Sci. Total Environ.*, 2011, **409**(16), 3003–3015.
150 J. L. Rodrigues, J. M. Serpeloni, B. L. Batista, S. S. Souza and F. Barbosa, *Arch. Toxicol.*, 2010, **84**(11), 891–896.
151 R. Airaksinen, A. W. Turunen, P. Rantakokko, S. Mannisto, T. Vartiainen and P. K. Verkasalo, *Public Health Nutr.*, 2011, **14**(3), 480–489.
152 R. N. Easter, K. K. Kroning, J. A. Caruso and P. A. Limbach, *Analyst*, 2010, **135**(10), 2560–2565.
153 C. Moller, R. R. Sprenger, S. Sturup and P. Hojrup, *Anal. Bioanal. Chem.*, 2011, **401**(5), 1619–1629.
154 T. Falta, P. Heffeter, A. Mohamed, W. Berger, S. Hann and G. Koellensperger, *Journal of Analytical Atomic Spectrometry*, **26**(1), pp. 109–115.
155 M. L. Mena, E. Moreno-Gordaliza, I. Moraleja, B. Canas and M. M. Gomez-Gomez, *Journal of Chromatography A*, **1218**(9), pp. 1281–1290.
156 D. Cleveland, S. E. Long, L. C. Sander, W. C. Davis, K. E. Murphy, R. J. Case, C. A. Rimmer, L. Francini and A. K. Patri, *Anal. Bioanal. Chem.*, 2010, **398**(7–8), 2987–2995.
157 K. N. Christensen, C. U. Lee, M. M. Hanley, N. Leung, T. P. Moyer and M. R. Pittelkow, *J. Am. Acad. Dermatol.*, 2011, **64**(1), 91–96.
158 N. Fretellier, J. M. Idee, A. Dencausse, O. Karroum, S. Guerret, N. Poveda, G. Jestin, C. Factor, I. Raynal, P. Zamia, M. Port and C. Corot, *Investigative Radiology*, 2011, **46**(5), 292–300.
159 S. Letsiou, T. Nomikos, D. Panagiotakos, S. A. Pergantis, E. Fragopoulou, S. Antonopoulou, C. Pitsavos and C. Stefanadis, *Eur. J. Nutr.*, 2010, **49**(8), 465–472.
160 S. Eichler and O. Mestek, *Chemicke Listy*, 2011, **105**(3), 200–206.
161 L. Hu, Z. Q. Dong, X. H. Huang, Y. F. Li, B. Li, L. Y. Qu, G. P. Wang, Y. X. Gao and C. Y. Chen, *Chin. J. Anal. Chem.*, 2011, **39**(4), 466–470.
162 M. B. Stockier-Pinto, D. Mafra, N. E. Farage, G. T. Boaventura and S. M. F. Cozzolino, *Nutrition*, 2010, **26**(11–12), 1065–1069.
163 J. Chen, D. Lariviere, R. Timmins and K. Verdecchia, *Radiat. Prot. Dosim.*, 2011, **144**(1–4), 379–383.
164 S. Khan, T. G. Kazi, J. A. Baig, N. F. Kolachi, H. I. Afridi, S. K. Wadhwa, A. Q. Shah, G. A. Kandhro and F. Shah, *J. Hazard. Mater.*, 2011, **182**(1–3), 371–376.
165 L. Jayaram, S. Chunilal, S. Pickering, R. E. Ruffin and P. D. Zalewski, *Respirology*, 2011, **16**(3), 459–466.
166 T. Lech and J. K. Sadlik, *Biol. Trace Elem. Res.*, 2011, **142**(1), 11–17.
167 L. A. Portugal, G. D. Matos, D. C. Lima, G. B. Brito, A. P. Fernandes and S. L. C. Ferreira, *Microchem. J.*, 2011, **98**(1), 29–31.
168 P. F. Jin, X. J. Wu, D. Zou, Y. M. Kuang, X. Hu, W. Q. Jiang and C. H. Sun, *Spectroscopy and Spectral Analysis*, 2011, **31**(3), 816–819.
169 E. D. Liu and Y. J. Zheng, *Asian Journal of Chemistry*, 2011, **23**(3), 1091–1094.
170 P. Cuderman and V. Stibilj, *Acta Chim. Slov.*, 2011, **57**(3), 668–676.
171 J. Feldmann and E. M. Krupp, *Anal. Bioanal. Chem.*, 2010, **399**(5), 1735–1741.
172 S. Taebunpakul, C. Liu, C. Wright, K. McAdam, J. Heroult, J. Braybrook and H. Goenaga-Infante, *J. Anal. At. Spectrom.*, 2011, **26**(8), 1633–1640.
173 C. Garcia-Sartal, V. Romaris-Hortas, M. D. Barciela-Alonso, A. Moreda-Pineiro, R. Dominguez-Gonzalez and P. Bermejo-Barrera, *Microchem. J.*, 2011, **98**(1), 91–96.
174 Y. Anan, T. Mikami, Y. Tsuji and Y. Ogra, *Anal. Bioanal. Chem.*, 2010, **399**(5), 1765–1772.
175 H. W. Sun and B. Feng, *Food Anal. Methods*, 2011, **4**(2), 240–244.
176 K. Boutakhrit, M. Crisci, F. Bolle and J. Van Loco, *Food Additives and Contaminants Part a-Chemistry Analysis Control Exposure & Risk Assessment*, 2011, **28**(2), 173–179.
177 V. Romaris-Hortas, C. Garcia-Sartal, M. D. Barciela-Alonso, R. Dominguez-Gonzalez, A. Moreda-Pineiro and P. Bermejo-Barrera, *Food Chem.*, 2010, **124**(4), 1747–1752.
178 C. Cabrera-Vique, M. Mesias and P. R. Bouzas, *Sci. Total Environ.*, 2011, **409**(8), 1584–1588.
179 S. Millour, L. Noel, A. Kadar, R. Chekri, C. Vastel and T. Guerin, *J. Food Compos. Anal.*, 2011, **24**(1), 111–120.
180 S. Millour, L. Noel, A. Kadar, R. Chekri, C. Vastel, V. Sirot, J. C. Leblanc and T. Guerin, *Food Chem.*, 2011, **126**(4), 1787–1799.

181 B. L. Batista, V. C. D. Souza, F. G. Da Silva and F. Barbosa, *Food Addit. Contam., Part B*, 2010, **3**(4), 253–262.
182 J. F. Sun, C. A. Wang, X. Y. Song, Y. N. Wu, B. J. Yuan and P. Liu, *Int. J. Hyg. Environ. Health*, 2011, **214**(3), 246–250.
183 Z. A. Al Othman, *Molecules*, 2010, **15**(10), 7482–7497.
184 A. Lesniewicz, A. Wroz, A. Wojcik and W. Zyrnicki, *J. Food Compos. Anal.*, 2010, **23**(5), 424–431.
185 F. R. de Amorim, M. B. Franco, C. C. Nascentes and J. B. B. da Silva, *Food Anal. Methods*, 2011, **4**(1), 41–48.
186 N. Zand, B. Z. Chowdhry, F. B. Zotor, D. S. Wray, P. Amuna and F. S. Pullen, *Food Chem.*, 2011, **128**(1), 123–128.
187 A. Alzate, M. C. Perez-Conde, A. M. Gutierrez and C. Camara, *Int. Dairy J.*, 2010, **20**(11), 761–769.
188 N. Herwig, K. Stephan, U. Panne, W. Pritzkow and J. Vogl, *Food Chem.*, 2010, **124**(3), 1223–1230.
189 N. Bilandzic, M. Dokic, M. Sedak, B. Solomun, I. Varenina, Z. Knezevic and M. Benic, *Food Chem.*, 2011, **127**(1), 63–66.
190 D. J. Hart, S. J. Fairweather-Tait, M. R. Broadley, S. J. Dickinson, I. Foot, P. Knott, S. P. McGrath, H. Mowat, K. Norman, P. R. Scott, J. L. Stroud, M. Tucker, P. J. White, F. J. Zhao and R. Hurst, *Food Chem.*, 2010, **126**(4), 1771–1778.
191 H. Goenaga-Infante, *Metrologia*, 2010, **47**, 33.
192 S. I. Khan, A. K. M. Ahmed, M. Yunus, M. Rahman, S. K. Hore, M. Vahter and M. A. Wahed, *Journal of Health Population and Nutrition*, 2010, **28**(6), 578–584.
193 Y. Q. Zhao, J. P. Zheng, M. W. Yang, G. D. Yang, Y. N. Wu and F. F. Fu, *Talanta*, 2010, **84**(3), 983–988.
194 Y. L. Chu and S. J. Jiang, *J. Chromatogr., A*, 2011, **1218**(31), 5175–5179.
195 E. J. Llorent-Martinez, P. Ortega-Barrales, M. L. Fernandez-de Cordova, A. Dominguez-Vidal and A. Ruiz-Medina, *Food Chem.*, 2011, **127**(3), 1257–1262.
196 C. V. S. Ieggli, D. Bohrer, P. C. do Nascimento, L. M. de Carvalho and L. A. Gobo, *J. Food Compos. Anal.*, 2011, **24**(3), 465–468.
197 R. W. Dabeka, A. D. McKenzie and D. S. Forsyth, *Food Additives and Contaminants Part a-Chemistry Analysis Control Exposure & Risk Assessment*, 2011, **28**(6), 740–743.
198 C. A. Eperesi, D. E. Nelson and M. T. Stauffer, *Spectrosc. Lett.*, 2010, **43**(7–8), 597–601.
199 F. Percin, O. Sogut, C. Altinelataman and M. Soylak, *Food Chem. Toxicol.*, 2011, **49**(4), 1006–1010.
200 T. Guerin, R. Chekri, C. Vastel, V. Sirot, J. L. Volatier, J. C. Leblanc and L. Noel, *Food Chem.*, 2011, **127**(3), 934–942.
201 P. Y. Liu, M. H. Chen, Y. Y. Tsai and M. S. Kuo, *Food Chem.*, 2010, **126**(3), 1460–1464.
202 T. L. Gerke, K. G. Scheckel and J. B. Maynard, *Sci. Total Environ.*, 2010, **408**(23), 5845–5853.
203 M. Birke, U. Rauch, B. Harazim, H. Lorenz and W. Glatte, *J. Geochem. Explor.*, 2010, **107**(3), 245–271.
204 M. Birke, C. Reimann, A. Demetriades, U. Rauch, H. Lorenz, B. Harazim and W. Glatte, *J. Geochem. Explor.*, 2011, **107**(3), 217–226.
205 W. Liu, H. X. Yang, B. Li and S. Q. Xu, *Geostand. Geoanal. Res.*, 2011, **35**(1), 69–74.
206 E. Kilinc, S. Bakirdere and M. Yaman, *Food Additives and Contaminants Part a-Chemistry Analysis Control Exposure & Risk Assessment*, 2011, **28**(4), 455–460.
207 V. A. Lemos and E. M. Gama, *Environmental Monitoring and Assessment*, 2011, **171**(1–4), 163–169.
208 T. Karak and R. M. Bhagat, *Food Res. Int.*, 2010, **43**(9), 2234–2252.
209 Z. Fiket, N. Mikac and G. Kniewald, *At. Spectrosc.*, 2011, **31**(2), 44–55.
210 I. Aydin, U. Yuksel, R. Guzel, B. Ziyadanogullari and F. Aydin, *At. Spectrosc.*, 2011, **31**(2), 67–71.
211 S. Kunimura and J. Kawai, *Bunseki Kagaku*, 2009, **58**(12), 1041–1045.
212 J. Mutic, D. Manojlovic, R. Kovacevic, J. Trifunovic, N. R. Amaizah and L. Ignjatovic, *Microchem. J.*, 2011, **98**(1), 11–14.
213 L. Bontempo, F. Camin, L. Manzocco, G. Nicolini, R. Wehrens, L. Ziller and R. Larcher, *Rapid Commun. Mass Spectrom.*, 2011, **25**(7), 899–909.
214 S. M. A. Azeem, W. A. A. Arafa and M. F. El-Shahat, *J. Hazard. Mater.*, 2011, **182**(1–3), 286–294.
215 K. Na, S. A. Lee, S. H. Jung and B. C. Shin, *Colloids Surf., B*, 2011, **84**(1), 82–87.
216 T. Kosla, E. M. Skibniewska and M. Skibniewski, *Bulletin of the Veterinary Institute in Pulawy*, 2011, **55**(1), 149–153.
217 Y. P. Tong, H. B. Sun, Q. Luo, J. X. Feng, X. H. Liu, F. Liang, F. Yan, K. Yang, X. H. Yu, Y. L. Li and J. M. Chen, *Biol. Trace Elem. Res.*, 2011, **142**(3), 380–387.
218 K. Van Calsteren, R. Verbesselt, R. Devlieger, L. De Catte, D. C. Chai, R. Van Bree, L. Heyns, J. Beijnen, S. Demarsin, E. de Bruijn, J. de Hoon and F. Amant, *International Journal of Gynecological Cancer*, 2010, **20**(9), 1456–1464.
219 M. E. Froudarakis, L. Greillier, S. Monjanel-Mouterde, A. Koutsopoulos, B. Devictor-Pierre, R. Guilhaumou, G. Karpathiou, S. Botaitis and P. Astoul, *Lung Cancer*, 2011, **72**(1), 78–83.
220 M. L. Cozzella, A. Leila and R. S. Hernandez, *Radiat. Meas.*, 2011, **46**(1), 109–111.
221 N. A. Monteiro-Riviere, K. Wiench, R. Landsiedel, S. Schulte, A. O. Inman and J. E. Riviere, *Toxicol. Sci.*, 2011, **123**(1), 264–280.
222 R. Grun, M. Aubert, J. Hellstrom and M. Duval, *Quat. Int.*, 2011, **223**, 87–93.
223 B. Boulassel, N. Sadeg, O. Roussel, M. Perrin and H. Belhadj-Tahar, *Forensic Sci. Int.*, 2011, **206**(1–3), E79–E81.
224 G. S. Guandalini, L. Zhang, E. Fornero, J. A. Centeno, V. P. Mokashi, P. A. Ortiz, M. D. Stockelman, A. R. Osterburg and G. G. Chapman, *Chem. Res. Toxicol.*, 2011, **24**(4), 488–493.
225 D. Bass and D. Jones, *Atomic Spectroscopy*, 2010, **31**(5), 165–169.
226 M. Spilde, A. Lanzirotti, C. Qualls, G. Phillips, A. M. Ali, L. Agenbroad and O. Appenzeller, *PLoS One*, 2011, **6**(6), 14.
227 E. M. Wells, J. M. Jarrett, Y. H. Lin, K. L. Caldwell, J. R. Hibbeln, B. J. Apelberg, J. Herbstman, R. U. Halden, F. R. Witter and L. R. Goldman, *Environ. Res.*, 2011, **111**(3), 411–417.
228 T. Kosla, E. M. Skibniewska and M. Skibniewski, *Polish Journal of Veterinary Sciences*, 2011, **14**(1), 81–86.
229 R. B. Khouzam, R. Lobinski and P. Pohl, *Anal. Methods*, 2011, **3**(9), 2115–2120.

