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

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*This annual review covers the published literature on the analysis of clinical and biological materials, foods and beverages using atomic spectrometric techniques for the year up to the end of October, 2003. Tables 1 and 2 summarise details of these publications. Our previous Update*[1] *covered the twelve months up to October 2002. Among the innovations and trends that we have discerned we would note the application of* in vivo *XRF to clinical studies of Pb metabolism, which follows on from the fine analytical developments of the previous two to three years. The ever popular speciation work is now bearing fruit with identification of new species of As and Se in clinical and foods specimens. Analytical developments include further application of permanent modifiers in ETAAS, of cloud-point extraction to enhance the analyte concentrations prior to measurement and the beginnings of collision or reaction cell technology for ICP-MS.*

## 1 Analysis of clinical and biological materials

### 1.1 General reviews and articles

The identification, characterisation and determination of *metal-binding proteins* by liquid chromatography has been reviewed by Guntinas *et al*.[2] They discussed the advantages and disadvantages of chromatography based on size exclusion, ion exchange, reverse phase and affinity.

The development of occupational and environmental medicine of the elements, especially the heavy metals, was discussed by Apostoli.[3] He pointed out that, during the last two decades of the 20th century, the availability of *indicators of exposure or of internal dose* had substantially increased thanks to the improvement in ETAAS techniques and to the entrance of ICP-MS into the field of biological monitoring.

A group of organisers of external quality assessment schemes for occupational and environmental biological monitoring considered the degree of accuracy that was necessary for measurements of Al in serum and Pb in blood. After consideration of several approaches they developed *quality specifications* which proposed that methods should give results that are within $\pm 5$ μg $L^{-1}$ or $\pm 20\%$ of the target concentration, whichever is the greater, for Al in serum and within $\pm 30$ μg $L^{-1}$ or $\pm 10\%$ for Pb in blood.[4]

### 1.2 Sampling and sample preparation

**1.2.1 Sample digestion.** An adaptation of a high pressure asher was evaluated by Maichin *et al.*[5] for *pressurised wet digestion in open vessels*. The asher was fitted with a PTFE liner and partly filled with 5% v/v $H_2O_2$. Open digestion vessels made of quartz or PFA were dipped into this solution or were arranged on a rack on top of it. The asher was closed and pressurised with $N_2$ to 100 bar and the sample digested at 250–270 °C for 90–120 min and then allowed to cool for 30 min. Digestion of 50 mg samples could be carried out in PFA autosampler cups with 0.2 ml $HNO_3$ + 0.5 ml $H_2O$ + 0.2 ml $H_2O_2$ for subsequent analysis by ETAAS. No losses of volatile elements such as As, Hg or Se were found and there was no evidence for cross-contamination of samples.

Several applications described *digestion with bases*. Ju[6] used 2 M NaOH to dissolve hair and nails for determination of nine elements by FAAS and ETAAS. Values for Ca, Cd, Cu, Fe, Mn, Ni, Pb and Zn agreed well with reference values quoted in other work, but values for Bi did not. The concentrations of the elements in hair did not correlate with those in the corresponding nails. According to Martins *et al.*,[7] digestion with TMAH for 2 h at 60–70 °C produced a stable homogeneous slurry from milk powder, bovine liver and bovine muscle for subsequent analysis of trace elements by ETAAS. In a similar approach, da Silva *et al.*[8] mixed biological samples with a small volume of 25% TMAH. The volume was made up to 50 ml and heated at 60 °C for 1 h. Cadmium was determined by ETAAS with a Ru permanent chemical modifier. Results on biological CRMs were within the certified range.

Much faster digestion is possible in the high temperature high pressure *flow digestion system* developed by Jacob and Berndt.[9] The sample, as a suspension in 2.5 M $HNO_3$, was passed through a Pt–Ir capillary at 320 °C for 1 min to a flame AA spectrometer for direct measurement. Total time for the whole procedure was between 3 and 8 min. A variant of this approach, reported by Pereira-Filho *et al.*,[10] was to pump slurried samples in 0.3 M $HNO_3$ through a ceramic thermospray nozzle into a Ni tube heated in an air–$C_2H_2$ flame. Digestion was said to occur in the $HNO_3$ atmosphere in the Ni tube. The LODs for Cd, Cu and Pb in this system were 0.5, 4.3 and 3.5 μg $g^{-1}$, respectively. Analysis of a range of biological and environmental CRMs gave results which were in good agreement with the certified values. Degradation of the Ni-tube by the acid environment was negligible and a lifetime of at least 400 working hours was reported.

**1.2.2 Slurry sampling.** For determination of Cu, Mn and Pb in deciduous teeth, Santos *et al.*[11] developed a cryogenic grinding procedure to reduce particle size to lower than 150 μm for *slurry preparation*. The sample, in a cryogenic mill, was cooled with liquid $N_2$ for 5 min and then ground for 2 min. The powder was slurried by sonication with a solution containing 0.04% Triton X-100 and 0.2% v/v $HNO_3$. Determination was by ETAAS using a platform coated with W–Rh as a permanent modifier. Comparison of results on 12 teeth with those obtained by microwave digestion and subsequent determination with a Pd–Mg chemical modifier showed no statistical difference. For the determination of Pb in marine biological samples by ETAAS, Cid *et al.*[12] prepared slurries by magnetic shaking and by microwave heating. Results compared well with each other and with results obtained after full microwave digestion. Although precision was generally better than 6.7% RSD, on one sample, *Dicentrarchus labrax*, both slurry preparations gave poorer precision, the worst being with magnetic shaking. Amin *et al.*[13] slurried herbal medicine with 10% glycerol solution using ultrasonic agitation for the determination of Cu by ETAAS with a molybdenum-tube atomiser. Glycerol also acted as a modifier removing chemical interferences. Samples from different sections of the human brain were slurried in deionised water by Marco *et al.*[14] for determination of Mn by ETAAS with a Pd–Mg chemical modifier. Results agreed well with those obtained after microwave digestion of the samples with $HNO_3$.

**1.2.3 Solid sampling.** An application of *the dry aerosol solid sampling technique* for the determination of Cd by FAAS was described by Flores *et al.*[15] A small mass (0.5–2.0 mg) of powdered biological sample was weighed into a small polythene vial. A dry aerosol obtained by passing air through the vial was carried through to a flame-heated quartz tube with a slot in the upper part, allowing generation of Cd atoms and diffusion out of the slit into the optical path. The signal was integrated for 1 s. Calibration was made with different masses of solid CRMs. The precision was between 3.9 and 6.7% RSD and results for Cd in a range of CRMs and in-house RMs showed good accuracy.

The homogeneity of CRMs has been estimated by Stupar *et al.*[16] using solid-sampling ETAAS with a graphite cup atomiser. Samples were prepared using the "tape-sandwich" technique. Using determination of the elements Cd, Cr and Pb,

they established that the minimum sample sizes representative of the CRMs were, with one exception, 11–75 mg, which was lower than recommended by the producers. The exception was a Chinese Hair CRM, for which Cd and Pb showed the presence of nuggets, associated with severe radial and longitudinal gradients of these elements in the hair.

**1.2.4 Sample preconcentration.** An unusual use of *human hair for preconcentrating trace elements* was described by Sweileh.[17] At pH 7.0, metal sorption decreased in the order: $Pb^{II} > Cd^{II} > Cr^{VI} > Fe^{III} > Cu^{II} > Ni^{II} > Mn^{II}$. After 30 min of equilibration, recovery was quantitative for Cd and Pb, but, for the others, it was less complete and varied with pH. Desorption was carried out with 0.5 M acids or 0.1 M EDTA. The method was applied to the determination of Cd and Pb in treated waste water samples attaining a preconcentration factor of 40.

*Cloud-point extraction* featured in four recently-published methods. Borges *et al.*[18] complexed Cd, Pb and Pd with *O,O*-diethyldithiophosphate in HCl solution and extracted this into a phase rich in the surfactant Triton X-114. The phases were separated by heating at 50 °C for 20 min. This approach was used to determine these elements in blood by ETAAS with Ir or Ru as a permanent modifier. Samples were first digested with $H_2O_2$–$HNO_3$ with microwave heating. Enrichment factors were 71, 34 and 100 for Cd, Pb and Pd, respectively. Good accuracy was demonstrated by analysis of three CRMs and by recovery data. The chelating agent, 5-bromo-2-pyridylazo-5-diethylaminophenol, was used by Willoud *et al.*[19] to complex V. The non-ionic surfactant, polyethyleneglycol mono-*p*-nonylphenyl ether (PONPE 5.0), was added for cloud-point extraction. With 50 ml of sample solution, an enrichment factor of 250 was achieved. Final determination was by ICP-AES and the approach was applied to the determination of V in parenteral solutions. In their method to determine Al in parenteral solutions by ICP-AES, Sombra *et al.*[20] enriched Al by a factor of 200 using cloud-point extraction with the non-ionic surfactant, PONPE 7.5. No chelating agent was required. For Co in urine, Manzoori and Karim-Nezhad[21] used 1-(2-pyridylazo)-2-naphthol as chelating agent and Triton X-114 as the surfactant. They found that removing water from the final diluted surfactant-rich phase improved the enhancement factor by a further 4-fold, giving a value of 115 for a 10 ml sample. Using FAAS for measurement, the LOD was 0.38 μg $l^{-1}$.

An *on-line preconcentration* procedure for the determination of low concentrations of Co by ETAAS was developed by Anthemidis *et al.*[22] Cobalt was complexed with APDC and the complex retained on a column of PTFE turnings at pH 5.5–7.0. A flow of air took 35 μl of IBMK through the column to elute the complex into the transversely heated graphite atomiser (THGA). Enhancement by 87-fold was obtained giving an LOD of 4 ng $l^{-1}$. The method was successfully applied to the determination of Co in natural waters and biological samples. Zougagh *et al.*[23] used a mini-column of silica gel treated with 1,5-bis(di-2-pyridyl)methylenethiocarbohydrazide placed in the injection valve of an FI system in order to separate Mn from the matrix. Elution with dilute $HNO_3$ into an ICP-AE spectrometer allowed determination down to 1.5 μg $l^{-1}$. Good accuracy was demonstrated when biological CRMs were analysed. In the method developed by Antheraidis *et al.*,[24] Ga as a chloride complex was sorbed onto a polyether-type polyurethane foam in a mini-column. The analyte was eluted with IBMK into the nebuliser of a flame AA spectrometer. An enhancement factor of 40 allowed an LOD of 6 μg $l^{-1}$. The method was applied to determine Ga in urine.

In order to increase the sensitivity by *off-line preconcentration* in the determination of Cd in blood and urine by ETAAS, Cerny and Bhattacharyya[25] used an anion-exchange resin to bind the Cd from a 1–2 ml sample, a Bio-Spin column to remove interfering ions and 100 μl of 1 M $HNO_3$ to elute the Cd. With a 7-fold enhancement for blood and 10-fold for urine, LODs were improved to 8 ng $l^{-1}$ and 3 ng $l^{-1}$, respectively. They reported that, using this method, the values they obtained for the blood of "non-exposed" animals (51–229 ng $l^{-1}$) were about 10-fold lower than those obtained with a conventional acid-deproteinisation procedure with Zeeman background correction. Mondal *et al.*[26] showed that 6-mercaptopurinylazo resin was a highly selective solid phase extractor for Cd, Cu and Zn in digested biological samples. The method developed for FAAS determination was claimed to be simple, rapid and free from interferences.

### 1.3 Developments in and applications of multi-element techniques

**1.3.1 Atomic emission spectrometry with the inductively coupled plasma.** There is little to report this review year on *the application of plasma emission techniques*. Eliades *et al.*[27] described the application of ICP-AES to determine Cr, Fe and Ni released from orthodontic appliances into saliva. Samples from 17 patients undergoing treatment were compared with samples from seven untreated subjects. No statistically significant difference was found between the two groups for any element. Matrix interferences in the determination of B and Ti in biological samples were studied by Garavaglia *et al.*[28] Memory effects for B solutions prepared from boric acid were absent when the B was present as boronphenylalanine. Interferences for both elements became more severe at higher rf power and lower carrier gas flow rate. Yttrium was found to be a suitable internal standard provided the equivalent concentration of albumin in the nebulised solution was kept below 0.2% m/v.

**1.3.2 Inductively coupled plasma mass spectrometry and other mass spectrometric techniques.** *1.3.2.1 Multielement determination by ICP-MS.* Concentrations of Ag, Cd, Pb and Sb in *paediatric liver tissue* were reported by Lyon *et al.*[29] Liver samples from 157 subjects, aged $<1$ d to 6 y, were digested under pressure and the digest analysed by quadrupole ICP-MS. For all measured elements, there was no significant difference in liver concentration between infants who died from Sudden Infant Death Syndrome (SIDS) and those who died from an identified disease. Silver concentrations were highest at birth and decreased with age. Cadmium, however, was present in negligible concentrations at birth and increased with age.

*Matrix interferences* from elements present in biological samples on the signal intensity of As, Ge and Se in ICP-MS were studied by Park *et al.*[30] The elements C, Cl and S caused an enhancement, K and Na a depression and N and P had minimal effect.

On-line standard addition enabled Huang and Beauchemin[31] to simultaneously determine a range of *elements in human serum* by ICP-MS. In an FI system, 50 μl aliquots of sample were injected into two carriers, one containing 1% $HNO_3$ alone and a second containing a multielement standard solution in 1% $HNO_3$. The standard concentration should be greater than that in the sample. Results for Al, Co, Cu, Mn and Zn in a Seronorm serum CRM showed good accuracy. Analysis time for four replicates was 20 min.

Partial *speciation* of As and Se was made possible by a novel approach developed by Anderson and Pergantis[32] for ICP-MS. Sample introduction by pneumatic nebulisation or by HG could be made sequentially simply by rotating a four-way switching valve. The conventional nebulisation gave total element concentration while the HG mode gave only the As or Se species which formed hydrides. This was particularly useful for As as it allowed the rapid estimation of the toxic and non-toxic forms of As in a sample. A variety of samples were analysed, including water and urine CRMs. To speciate essential trace elements in porcine liver, Nischwitz *et al.*[33] used SEC and reversed phase HPLC coupled either online to

ICP-MS for metal detection or offline to ES-MS for species identification by their $M_r$. The best extraction procedure tried was with Tris buffer. Freezing for several weeks did not significantly affect the stability of the species. Copper and Zn species were found mainly in the cytosolic fraction, Fe in the microsomal fraction, whereas Mn was present in both cytosolic and mitochodrial/lysosomal fractions.

To determine *platinum, rhodium and palladium* in urine, serum and road dust, Benkhedda *et al.*[34] used ICP-TOF-MS with ultrasonic nebulisation (USN). The analytes were preconcentrated in an FI system by complexation with diethylthiourea and sorption of the complexes on the inner walls of a PTFE knotted reactor. Desorption then followed with 500 μl of $CH_3OH$ acidified with 1% $HNO_3$. This gave enrichment factors of 55, 5 and 2 for Pd, Pt and Rh, respectively; corresponding LODs were 0.36, 0.54 and 2.12 ng $l^{-1}$. The accuracy of the method was demonstrated by the analysis of serum, urine and road dust CRMs. Prior digestion of samples was found to be necessary.

*1.3.2.2 Sector field ICP-MS (SF-ICP-MS). A comparison of three different ICP-mass spectrometers* as detectors in the study of Cd speciation of rabbit liver metallothionein-1 showed that SF-ICP-MS is not always best. Ferrarello *et al.*[35] coupled reverse phase HLPC with a $H_2O$–$CH_3OH$ gradient. The SF-ICP mass spectrometer was badly affected by the $CH_3OH$ gradient and gave the worst performance. The best performer was by an ICP-TOF mass spectrometer which could resist up to 50% $CH_3OH$ with no serious changes in sensitivity or plasma stability. It gave the lowest LOD. The quadrupole mass spectrometer gave intermediate performance. Post-column isotope dilution analysis allowed correction for matrix effects and signal drift.

However, the principal advantages of SF-ICP-MS are better *resolution from interferences and superior sensitivity* which are shown in the following publications. Yang *et al.*[36] showed that spectral interference from a ClO species was completely resolved from the $^{51}V$ isotope in the *measurement of vanadium* by SF-ICP-MS at a medium resolution of 4000. Vanadium could be measured in 20-fold diluted urine or serum samples against matrix-matched standards down to 10 ng $l^{-1}$. They found V concentrations from $<10$ to 1500 ng $l^{-1}$ and $<10$ to 760 ng $l^{-1}$ in urine and serum, respectively. The high sensitivity of SF-ICP-MS with a torch with a "guard-electrode" allowed Schramel[37] to determine $^{238}U$ and $^{235}U$ isotopes in urine samples down to the physiological level of $<10$ ng $l^{-1}$ total U. Samples were first degraded by UV photolysis.

*1.3.2.3 Collision and reaction cells in ICP-MS.* Applications in the clinical and biological field describing *the use of collision and reaction cells in ICP-MS* are still rare and seem to centre on Se. Sloth *et al.*[38] used $CH_4$ in a dynamic reaction cell in the determination of total Se and $^{77}Se$ in isotopically enriched human plasma, urine and faeces. Faecal samples were first digested and all samples were diluted with a solution containing 0.5% Triton X-100, 2% $HNO_3$ and 3% $CH_3OH$. The isotopes $^{76}Se$, $^{77}Se$ and $^{80}Se$ were measured. The accuracy was controlled by analysis of the CRMs Seronorm Serum and BCR 185 Bovine Liver. Hydrogen was used by Reyes *et al.*[39,40] in an octapole reaction cell to eliminate interferences from $^{40}Ar^{38}Ar$ and $^{40}Ar^{40}Ar$ in the measurement of $^{78}Se$ and $^{80}Se$, respectively. Determination of Se in biological materials[39] was made with ID using an enriched $^{77}Se$ solution and measurement of the ratios $^{78}Se$ : $^{77}Se$ and $^{80}Se$ : $^{77}Se$. The ratios could be measured with a precision of 0.2% RSD. A correction of about 3% had to be applied to allow for the formation of $SeH^+$. This approach was also used to measure Se-containing proteins in human serum after separation by affinity chromatography.[40] Anion-exchange chromatography was also tried, but separation was unsatisfactory. Results for both healthy volunteers and patients on haemodialysis showed about 20% of Se as glutathione peroxidase, 55% as selenoprotein P and 20% bound to albumin.

*1.3.2.4 Laser ablation ICP-MS.* Laser ablation SF-ICP-MS was used by Ghazi *et al.*[41] to study *the migration of nickel from implants* into surrounding tissue. Pure Ni wires were implanted into rats for seven days. The tissues were then ablated with a Nd:YAG laser and the isotopes $^{24}Mg$ and $^{60}Ni$ measured. The $^{24}Mg$ acted as an internal standard and allowed quantification based on a uniform nominal Mg concentration of 97 μg $g^{-1}$ in the tissue. Results showed that Ni did diffuse into tissue, reaching a concentration of 60 μg $g^{-1}$ near the implants but falling off to undetectable concentrations 3–4 mm from the implant.

*1.3.2.5 Stable isotopes.* In a published plenary lecture, Becker[42] outlined *progress in precise and accurate measurement of isotope ratios* by ICP-MS and LA-ICP-MS. Stable isotope methodologies for the study of mineral metabolism in humans were becoming more widespread due to the decreased cost of isotopes and increasing acceptance of these techniques. The limitation has been the cost and availability of analytical methods that could measure isotope enrichments with sufficient precision and at acceptable cost. Becker foresaw that SF-ICP-MS would be increasingly adopted as it promised adequate precision at reasonable cost.

In the last review year, methods using quadrupole ICP-MS have been used in studies of Fe after separation,[43] Mg[44–46] and Mo.[47] Sector-field ICP-MS was adopted for studies on Ca,[48,49] Fe[50] and Zn.[51] Methods are discussed under the respective elements in section 1.8.

*1.3.2.6 Secondary ion mass spectrometry.* To localise *magnetic resonance imaging (MRI) contrast agents* based on Eu, Fe and Gd, Kahn *et al.*[52] used SIMS microscopy. The agents were injected into mice and the livers examined. Europium could also be detected by confocal microscopy. The results indicated that Eu was a suitable model to determine the fate of contrast agents based on Gd.

**1.3.3 X-ray fluorescence spectrometry.** *1.3.3.1 Elemental mapping.* Single neurons from *brain tissues* from Alzheimer's disease patients were studied by Ishihara *et al.*[53] using SRXRF. Clear images of the distribution of Ca, Fe and Zn were obtained and there appeared to be a correlation between the Ca and Zn distribution. Szczerbowska-Boruchowska *et al.*[54] studied brain and spinal cord samples from patients with Parkinson's disease and amyotrophic lateral sclerosis. Microbeam SRXRF imaging showed increased concentrations of selected elements in the perikarial parts of the neurons and significant differences between the concentrations of these elements in patient samples and control samples.

*The release of metals from fillings and prostheses* has been studied by element mapping. Using SRXRF with 100 μm spatial resolution, Carvalho *et al.*[55] examined the distribution of Bi, Cu, Hg and Zn in teeth restored with dental amalgam. The Hg concentrations increased markedly towards the amalgam region reaching 500 μg $g^{-1}$ in a few cases. In one restored tooth, the Bi concentration was extremely high, reaching over 2000 μg $g^{-1}$. Concentrations of Cu and Zn were also higher in restored teeth. Titanium released from Ti dental implants was examined with a PIXE microbeam by Passi *et al.*[56] An implant removed after 70 days showed no evidence of release of Ti but three others removed after 6, 7 and 9 years of service showed small Ti deposits in about 5% of the bone surrounding the implant. Aluminium, when present in the implant, showed significant leakage into the surrounding bone.

The concentration profiles of a range of elements in *Adelie penguin bones* from the Antarctic were measured by SRXRF in a study reported by Xie *et al.*[57] The concentration profiles differed and the relationships between the elements were complex. Toxic elements were also detected in the bones.

The high spatial resolution of SRXRF was used to good effect by Gao *et al.*[58] to quantify *the metal content of protein*

*bands after electrophoretic separation*. Proteins in human liver cytosol were speciated by gel-filtration chromatography and thin layer isoelectric focusing. The results showed two bands containing Zn and 11 containing Fe. Bands containing Cu were also detected.

*1.3.3.2 Fundamental developments in* in vivo *XRF determination of lead in bone.* Todd and Chettle[59] derived a revised method for calculating *the uncertainty in bone lead measurement* by *in vivo* XRF, in view of a published change in the mathematical treatment for calculating the calibration line intercept. A number of prominent workers in the field got together to publish a letter[60] outlining an agreed statement on calculating Pb concentration and uncertainty in this measurement.

*1.3.3.3 Applications of* in vivo *XRF determination of lead in bone.* An important study by Needleman *et al.*[61] indicated a relationship between *delinquency and lead exposure*. Using *in vivo* K-line XRF measurements, they showed that tibia Pb in 194 delinquent youths ($11.0 \pm 32.7$ μg $g^{-1}$) was significantly higher than in 146 non-delinquent youths ($1.5 \pm 32.1$ μg $g^{-1}$). Evaluation of the data adjusted for covariates and interactions indicated that the delinquents were four times more likely than controls to have bone Pb $> 25$ μg $g^{-1}$.

*The effect of the season on blood Pb and bone Pb* was examined by Oliveira *et al.*[62] as part of the Normative Aging Study. Bone Pb was measured by K-shell XRF on middle-aged and elderly men giving results of 34.3, 29.7 and 29.0 μg $g^{-1}$ for summer, spring/fall and winter, respectively. Corresponding mean blood Pb concentrations were 5.8, 6.1 and 6.6 μg $dl^{-1}$. Decreased exposure to sunlight during winter, they concluded, resulted in lower vitamin D and increased mobilisation of Pb from bone stores. Hence, blood Pb concentrations increased and bone Pb decreased.

Lead appears to have *an effect on the outcome of pregnancy*. According to a study by Hernandez-Avila *et al.*,[63] the size of a baby is related to its mother's bone Pb stores. The length and head circumference of 223 newborns were measured together with the tibia and patella Pb of the mother by *in vivo* K-shell XRF. Mean bone Pb concentrations were 9.8 and 14.4 μg $g^{-1}$ for tibia and patella, respectively. They estimated that women with a tibia Pb concentration in the upper quartile had a 79% increase in risk of having a newborn with lower birth length than women in the lower quartile. Rothenberg *et al.*[64] examined the relationship between blood pressure and bone Pb levels in women during pregnancy. Lead in the tibia and calcaneus (heel) was measured by K-shell XRF. The results showed that each 10 μg $g^{-1}$ increase in calcaneus Pb concentration was associated with a 0.70 mm Hg increase in third-term systolic blood pressure and a 0.54 mm Hg increase in diastolic blood pressure. However, tibia Pb concentrations were not correlated with increased blood pressure in the third term or *postpartum*.

*1.3.3.4 Determination of elements in tissues by XRF.* Several groups have studied *the difference in trace element concentrations between cancerous tissue and healthy tissue* but the results are not entirely in agreement. Particle-induced X-ray emission was used by Reddy *et al.*[65] to determine 13 elements in carcinoma of the kidney and stomach. In kidney carcinomas, concentrations of As, Cd, Co, Ti and Zn were higher than in normal tissues whereas Ca, Fe, K, Ni and Se were lower. In carcinomas of the stomach, the elements present at higher than normal concentrations were As, Br, Cr and Ni and those at lower concentration were Ca, Cl, Co, Cu, Fe, K, Mn, Ti and Zn. The results were said to support the designation of Cr and Ni as carcinogens and to indicate that Se and Mn deficiency promotes the growth of cancer in the kidney and stomach, respectively. Of the nineteen elements measured by Dobrowolski *et al.*[66] in renal cell carcinoma using SRXRF, the most significant change compared to normal tissue was a decrease in Cd concentration from $81 \pm 39.2$ to $16.6 \pm 22.2$ μg $g^{-1}$. Other changes were a decrease in Pb, Rb and Ti and an increase in Fe and Zr. In a further study by Kwiatek *et al.*,[67] a microbeam was used to compare the distribution of trace elements in cancerous and non-cancerous parts of the kidney. The elements Cd, Cr, Cu, Se, Ti, V and Zn were at a lower concentration in the cancerous tissue whereas Fe was higher. Low Se and Zn concentrations in the thyroid tissue of patients with thyroid cancer were reported by Kucharzewski *et al.*[68] They used TXRF to determine Cu, Se and Zn in whole blood and thyroid tissue of patients with various thyroid disorders. The patients with thyroid cancer had higher levels of these elements in blood than other thyroid disorders and controls. Moreover, Cu : Zn, Cu : Se and Zn : Se ratios were significantly higher.

Further data from the comparison study of Greenlandic Inuits and Danes has been published. Copper in autopsy liver tissue samples was measured by Milman *et al.*[69] using XRF. Whereas there was no significant difference in liver Cu concentration between Inuit men and women, there was amongst Danes, primarily because of three notably higher values amongst the 44 men. Overall, the conclusion was that the Inuit have a hepatic Cu content similar to that found in Caucasian Danes and other populations from western societies.

**1.3.4 Other multi-element techniques and studies.** *The exposure of the neonate to toxic elements* transferred from the mother has been assessed in various studies. Falcon *et al.*[70] measured Cd and Pb in human placenta from 86 mothers by AAS. The levels were related to environmental contamination from industry but smoking was a greater contributor to the Cd concentration. Cadmium exposure seems to be a factor involved in hypertension in pregnancy, according to Kosanovic *et al.*[71] They measured Cd and Se concentrations in maternal and umbilical cord blood and amniotic fluid by ETAAS and HGAAS, respectively. Smokers had higher Cd and lower Se concentrations than non-smokers. Hypertensive pregnant women had higher blood Cd concentrations than normotensive women. The Cd is eventually transferred into human milk. Honda *et al.*[72] measured Cd by ETAAS in human milk and urine samples from 68 Japanese mothers. Concentrations of Ca, Mg, Na, K and P were also measured by ICP-AES and Cu and Zn by FAAS. Cadmium concentrations in the human milk were inversely correlated to the Ca concentration, suggesting that the Cd concentration affected Ca secretion into breast milk. Lead and Hg concentrations in the breast milk of Austrian mothers were measured by Gundacker *et al.*[73] using AAS after wet digestion. Concentrations were below critical levels and the risk from exposure to these elements was considered minimal. The suitability of meconium analysis to assess the exposure of the fetus to environmental toxins was evaluated by Ostrea *et al.*[74] Stools (meconium) from 426 infants were analysed for Cd, Hg and Pb by AAS and for pesticides by GC-MS. The authors believed the results showed that meconium analysis was a sensitive tool to detect fetal exposure to toxins.

Sufficient *supply of the essential trace elements* is also important for the development of the fetus. Osada *et al.*[75] measured concentrations of six essential elements, Cu, Fe, Mg, Mn, Se and Zn and four other elements, Cd, Cs, Rb and Sr, in maternal blood, fetal blood and placental tissue by ICP-AES and ICP-MS. Compared with term babies, premature babies had higher Cu, Mg, Se and Zn concentrations in the umbilical cord arterial blood and higher Mg and Se concentrations in placental tissue. The authors concluded that reduced "consumption efficiency" of Cu, Mg, Se and Zn may be associated with retarded fetal development.

The possible influence of *trace elements in fertility* in men was studied by Seren *et al.*[76] Measurements by AAS of Cd, Cu, Pb and Zn in the seminal plasma and blood serum of 30 fertile and

30 infertile men showed that infertile men had lower Zn and higher Cu concentrations, especially in the seminal plasma. There were no marked differences in Cd or Pb concentrations. Massanyi *et al.*[77] found that there were significant differences in the concentrations of trace elements in the semen of various animals. They measured with AAS the concentrations of Cd, Cu, Fe, Ni, Pb and Zn in the semen of bulls, rams, boars, stallions and foxes. The highest Cu, Fe and Pb concentrations were found in the ram, the highest Zn in the boar and the highest Ni in the fox and ram. Cadmium concentrations were all relatively low.

*The interaction between selenium and toxic metals* continues to be of interest. Falnoga *et al.*[78] examined the relationship between exposure to Hg and both total plasma Se concentrations and the selenoprotein P fraction. The latter was isolated by affinity chromatography and the Se determined by radiochemical NAA and HGAFS. Residents of a community near to a mercury mine showed no significant difference in plasma Se or selenoprotein P concentrations when compared with those for controls. They did find that physical stress lowered the selenoprotein P fraction by 7–24%. In a study of residents living near an As contaminated area in Bangladesh, Miyazaki *et al.*[79] measured urine As and Se concentrations by HGAAS. A negative correlation was found between the two concentrations in both males and females, suggesting that the As exposure influenced the Se metabolism in this population.

Two studies provide new data on *occupational exposure*. Horng *et al.*[80] used ETAAS and HGAAS to measure urinary As, Be and Se concentrations in steel production workers and quality control personnel and compared results with those from healthy controls. Concentrations of all elements were highest in the production workers and both exposed groups had significantly higher concentrations than controls. In their study of autopsy tissue samples from 32 long-term exposed copper smelter workers, Gerhardsson *et al.*[81] measured Cd, Cu and Zn by AAS. The smelter workers showed significantly higher levels of Cd in kidneys, liver and lung, Cu in brain, lung and kidney and Zn in kidney, liver and brain. The authors noted that neither the Cu nor the Zn concentrations in hair and nails, which they measured by EDXRF, proved to be a useful measure of the trace element status of the smelter workers.

In a study of the Fe and Zn content of *human cataractous lenses* measured by AAS, Dawczynski *et al.*[82] showed that diabetic patients had increased concentrations of both Fe and Zn compared with non-diabetic subjects. They also found that the Zn concentration increased with increasing lens coloration.

In a large-scale study of Al, Cr, Mn and Pb concentrations in the whole blood and serum of 200 healthy subjects and 105 patients on *regular haemodialysis*, Torra *et al.*[83] found that the patients had significantly higher Al and Cr concentrations and lower Mn concentrations. Blood Pb concentrations were similar. Measurements were by ETAAS.

Melo *et al.*[84] reported that, in multiple sclerosis, Mn in *cerebrospinal fluid* (CSF) is significantly decreased whereas Cu concentrations are increased. They measured Cu and Mn by AAS and SF-ICP-MS with measurements of Zn by SF-ICP-MS only. There were no differences in CSF Zn between patients and controls. Data on the concentration of 20 elements in bone marrow fluid were obtained by Hasegawa *et al.*[85] using ICP-AES and ICP-MS after digestion of samples with $HNO_3$. They observed that Fe, Sb and Zn concentrations were 264-, 15- and 7-fold higher, respectively, than in blood serum.

Two *studies on cancer* reveal changes in trace elements and application of this to diagnosis. The accuracy of the serum Cu : Zn ratio as a tool in diagnosing hepatocellular carcinoma was assessed by Poo *et al.*[86] Measurements by AAS showed that the Cu : Zn ratio was significantly higher in patients with hepatocellular carcinoma ($1.52 \pm 0.64$) than in patients with benign digestive diseases ($0.95 \pm 0.39$). With a cut-off value of 1.15, the specificity for diagnosis was 86.1% and they concluded that the ratio might be useful in evaluation of suspected hepatocellular malignancy. It should be noted that, as a result of the acute phase response, Zn concentrations in serum decrease and Cu concentrations increase. This will occur in all inflammatory diseases and many cancers. Thus, calculation of the Cu : Zn ratio may only be helpful in certain areas, such as digestive disorders, as used in this work and, even then, will be complicated by other existing conditions generating an acute phase response. In a study of trace elements in cervical cancer, Han *et al.*[87] measured Ca, Cu, Fe, Mn, Se and Zn concentrations in the tissue and serum of 40 patients with cervical cancer, 30 patients with uterine myoma and 50 healthy subjects. Selenium was measured by AFS, the other elements by AAS. Here also the serum Cu : Zn ratio was significantly higher in the cancer patients. The tissue measurements showed that the cancer tissue had higher Cu and Fe concentrations than paired non-lesion tissue. The authors concluded that Se and Zn deficiency may be risk factors for the development of cervical cancer.

Some *chelating agents used in treatment cause a loss of the essential trace elements*. The agent, sodium 2,3-dimercaptopropane-1-sulfonate (DMPS), is used in the removal of Hg in severe exposure and has been used to treat supposed mercury toxicity from dental amalgam. In their study, Hol *et al.*[88] set out to establish whether this would affect the Cu, Se and Zn stores of the patient. Using AAS, they measured Cu, Se and Zn in the blood and urine of 80 individuals, divided into four groups according to the presence and absence of amalgam fillings and symptoms related to these fillings. Although the DMPS caused an increase in the excretion of Cu and Zn in urine, this constituted only 0.1–0.7% of the body content of these elements. There was no change in Se excretion. Blood concentrations of the three elements decreased after DMPS, but this seemed related to dilution of the blood from the injection.

### 1.4 Developments in single element techniques

Interest in *permanent chemical modifiers in ETAAS* continues. Zhou *et al.*[89] used a W–Rh coating on the integrated platform of a THGA in the determination of Pb in blood. The permanent modifier increased the lifetime of the tube by a factor of 2–3 compared with the use of a conventional $NH_4H_2PO_4$ modifier. Calibration was possible with simple aqueous standards, but, when an end-capped THGA tube was used, the standards had to be matrix-matched. Interestingly, Tsalev *et al.*[90] showed that phosphate could be a permanent modifier. They applied small amounts of $NH_4H_2PO_4$ (0.2 μmol) to a THGA pre-treated with Zr–Ir or W–Ir. This combined permanent modifier allowed pyrolysis temperatures of 400–600 °C for Cd in biological fluids and 750–850 °C for Pb. This treatment overcame some of the drawbacks of a conventional phosphate modifier, *i.e.* a high reagent blank and high background absorption. This modifier was successfully used in the determination of Cd and Pb in a range of blood, urine and tissue CRMs. A study by Parsons *et al.*[91] provides an insight into how Rh acts as a chemical modifier with the tungsten-filament atomiser. They directly coupled a tungsten-filament atomiser in the ET-AA spectrometer to an ICP-mass spectrometer to monitor the analyte $^{208}Pb$, the modifier $^{103}Rh$, the atomiser material ($^{180}W$, $^{183}W$) and the organic matrix ($^{40}Ar^{12}C$). This showed the effective removal of the matrix during pyrolysis without significant loss of Pb. The permanent modifier was only lost during the final cleaning stage of the programme but, if Rh was added to the diluent, it was lost in the pyrolysis stage. This showed that periodic coating of the filament surface is necessary and that addition of Rh to the diluent has no effect as a modifier. Ruthenium was used as a permanent modifier in the determination of Cr and Cu in urine by ETAAS, giving better sensitivity than a Pd–Mg modifier.[92] Samples were diluted 1 + 1 with 1% v/v $HNO_3$. The Ru

modifier gave LODs of 0.22 and 0.32 μg $l^{-1}$ for Cr and Cu, respectively.

The *transverse heated filter atomiser* was evaluated by Ngobeni *et al.*[93] for the determination of Cd and Pb in urine by simultaneous ETAAS. Compared to the THGA, this filter atomiser showed a significant reduction of background and chemical interference from the urine matrix and an increase of sensitivity by a factor 1.5–2.0. The LODs were 0.018 and 0.2 μg $l^{-1}$ for Cd and Pb, respectively. When a collector made from carbon fibre and tungsten wire was used, the recovery improved to over 92% for both elements. Analysis of Seronorm RMs showed good agreement with recommended values.

*The adsorption of proteins from blood serum on the sample capillary* in ETAAS has been studied by Bohrer *et al.*[94] The polymer used has an effect with adsorption decreasing in the order: Tygon > silicone rubber > PTFE. Dilution did not affect the adsorption and only 30 s of contact was sufficient for adsorption to occur. They further showed that metals were co-absorbed by the proteins and that total removal was only achieved with $CH_3OH$. Water, dilute $HNO_3$ and Triton X-100 solutions did not achieve complete desorption of the proteins. Use of $CH_3OH$ in the rinse solution improved the precision in the determination of Al, Cr and Mn in serum.

### 1.5 Hair and nail analysis

Several investigations have shown the relevance of hair As measurements in the investigation of arsenism. Yang *et al.*[95] showed that in one particular region of Inner Mongolia, the prevalence was 15.5% with hyperkeratosis as the symptom with the highest occurrence rate. There was a significant correlation between hair As concentration and the severity of symptoms and also between As concentrations in hair and drinking water. Measurements were made by HG-ICP-AES. Ali and Tarafdar[96] reported hair As concentrations in a group of subjects in Bangladesh whose drinking water supply was contaminated with As. The mean hair As concentration was 14.1 μg $g^{-1}$ compared with normal levels of less than 3.0 μg $g^{-1}$. Speciation of As in the hair and nails of inhabitants of West Bengal, India, was carried out by Mandal *et al.*[97] using HPLC-ICP-MS. The species were extracted with water at 90 °C. The percentage of As present as $As^{III}$ was 58.6% in nails and 60.9% in hair. In nails, 19.9% of As was found as methylated arsenicals but in hair only 5.8%. The authors proposed that $DMA^{III}$ content in fingernails or $DMA^{V}$ content in nails and hair could be suitable biomarkers for As exposure. Against this background, it may seem surprising that As is being used for treating leukaemia. Nicolis *et al.*[98] used SRXRF to study the elimination of As in hair in patients treated with a new As-based drug. Both longitudinal and transverse profiles were established with analysis of 30 μm slices.

An international interlaboratory comparison programme for Hg in human hair has been running for over 12 years. Gill *et al.*[99] reported that, of the 31 participants from four continents, 92% consistently met quality assurance performance limits. Many different digestion procedures and instrumental techniques were used, but all seemed to give equivalent results. The techniques most frequently used were CVAAS, CVAFS and ICP-MS.

The application of laser ablation to the multielement analysis of hair and nails by SF-ICP-MS was studied by Rodushkin and Axelsson.[100] Calibration was carried out with matrix-matched standards in tablet form and correction for variations in ablation efficiency was made by internal standardisation using S present in the matrix. Significant enrichment of most of the elements was found in the surface of nails. The distribution along the length of hair could be measured with a spatial resolution of 2.5 mm.

Kurogouchi *et al.*[101] developed a method for the determination of As and Se in human hair by ETV-ICP-MS. Samples were digested with $HNO_3$–$H_2O_2$ at high pressure. The digest was evaporated to dryness after addition of $KMnO_4$. Without this addition, losses of up to 50% of the analytes were found in this step. The residue was dissolved in 1 M $HNO_3$ and a 5 μl aliquot placed on a tungsten filament for vaporisation into the plasma and measurement of $^{75}As$ and $^{82}Se$ by MS. Results for a hair CRM agreed well with certified values.

### 1.6 Drugs and pharmaceuticals

Work is continuing on the use of trace element composition to help trace the source of *drugs of abuse*. Muratsu *et al.*[102] used SRXRF, which allowed pg amounts of trace elements to be determined in 10 μg of various drugs. Water-soluble drugs were spotted as solutions onto silicon wafers, whereas opium as a soft lump was smeared onto the wafer and marijuana placed directly as a leaflet. Ten elements present in illicit heroin samples from Turkey were determined by Bora *et al.*[103] using ETAAS and ICP-AES after microwave digestion with $HNO_3$. Calcium was the most abundant element, probably because of the use of lime in manufacturing or as a diluting agent. Concentrations of Al, Fe and Zn were moderately high, possibly because of a use of metal pots in processing and storage.

The origin of Al contamination in *parenteral nutrition solutions* has been investigated by Bohrer *et al.*[104] using ETAAS. Concentrations in 35 different commercial products and in the raw chemicals used for formulation were measured. The most contaminated chemicals were cystine, NaOH, vitamin C, biotin, gluconate and Cr and Fe salts. However, comparison with the final Al concentrations in the prepared products showed that this alone could not account for the high Al concentrations and that Al must also have been introduced in the manufacturing process. A method for the determination of Al in parenteral solutions by ICP-AES was described by Sombra *et al.*[20] Enrichment by a factor of 200 was made by cloud-point extraction with the non-ionic surfactant PONPE 7.5. For a sample volume of 50 ml, an LOD of 0.25 μg $l^{-1}$ was achieved. For determination of Cr in parenteral solutions using FAAS, Wuilloud *et al.*[105] preconcentrated the analyte with 4-(2-thiazoylazo)resorcinol at pH 5 and collected the complex on an Amberlite XAD-16 column in an FI system. The complex was removed from the microcolumn with $C_2H_5OH$. For 50 ml of sample, an enrichment of 50 was achieved, allowing an LOD of 20 ng $l^{-1}$. The precision at 5 μg $l^{-1}$ was 2.9% RSD.

Metal complexes are used as *active agents in some pharmaceuticals* and for them atomic spectrometry is a useful technique for quality control. Bouma *et al.*[106] described a method they developed for quality control of the antimetastatic Ru complex NAMI-A. The compound and its degradation complex were separated by HPLC on a $C_{18}$ column with a mobile phase of 0.5 mM Na dodecylsulfate in 3% $CH_3OH$ at pH 2.5. Detection was by UV at 358 nm, but experiments with NMR identified one degradation product as the monohydroxy species of NAMI-A while off-line detection of Ru by ETAAS identified the Ru-containing compounds and showed that, under most conditions, Ru was recovered quantitatively. Hydride generation AAS has been used by Flores *et al.*[107] to determine Sb in commercial drugs used in South America for treatment of leishmaniasis. Antimony(III) was reduced with 2% $NaBH_4$ in 20% m/v citric acid in an FI system to produce $SbH_3$, allowing determination down to an LOD of 0.95 ng Sb.

There appears to be growing interest in the determination of *trace element impurities in pharmaceuticals*. Approaches to the determination of trace elements in synthetic vitamin E products were explored by de Leon *et al.*[108] Comparison was made between acid microwave digestion of the oil and emulsion preparation for measurement by ICP-MS. Digestion gave slightly lower LODs. The elements Cr, Ni, Pb and Sn were found in the vitamin E product. Lasztity *et al.*[109] used ICP-MS to measure Pd, Pt and Rh impurities introduced into

pharmaceuticals from the use of catalysts in manufacture. Comparison of Rh results was made with results by ETAAS. Application of ICP-MS and TRXRF to determine other impurities in pharmaceuticals was also described.

There is also concern about the *concentrations of toxic elements in medicinal plants*. The contribution of medicinal plants (including herbal teas) to the daily intake of As, Cd, Hg and Pb in Catalonia, Spain, was assessed by Falco *et al.*[110] A total of 115 samples of 15 different species were analysed by ICP-MS. All had Hg concentrations less than the LOD of the method and the contribution of medicinal plants to the total daily intake of As, Cd and Pb were only 0.2, 1 and 5%, respectively. Dwivedi and Dey[111] were concerned about the toxic metal levels they found in medicinal herbs in India. Cadmium concentrations ranged between 0.056 and 0.419 mg $kg^{-1}$ and Pb between 2.62 and 32.8 mg $kg^{-1}$ in 28 commonly used medicinal plants. Measurements were by AAS. Concentrations were higher in leaves than in the stem bark or roots. In Malaysia, the quality and safety of traditional medicines are controlled by legislation. Ang *et al.*[112] found that, in 100 products monitored, 8% contained Pb in the range 10.6–20.7 mg $kg^{-1}$ and therefore did not comply with the quality requirement. They found that batch to batch inconsistencies meant that a single measurement for registration of a medicine was insufficient to ensure safety.

In a study of the *speciation of extracts of medicinal plants*, Weber and Konieczynski[113] used ultrafiltration and SEC to speciate Mg, Mn and Zn in birch, sage and peppermint leaves and valerian and dandelion roots. Ultrafiltration showed that 60–100% of these metals were present as low $M_r$ species ($<5000$ Da). Whereas the Mg and Mn species measured by AAS seemed related to the carbohydrate profile, for Zn many more species were detected which were related to complexation with polyphenols.

Interest in the *trace element composition of Chinese traditional medicines* remains high, particularly because of the suggestion that this could have a role in their curative properties. Liang and Sun[114] measured Cu, Fe, Ge, Mn, Se and Zn in three kinds of traditional medicine by ETAAS after acid digestion with $HNO_3$–$HClO_4$. Concentrations of Cu, Fe, Mn and Zn were high in all medicines. Selenium was especially high in *Ginko biloba* and Ge in *Gynostemma pentaphyllum*. Concentrations of Ca, Co, Cr, Cu, Mg, Mn, Mo, Fe, Ni and Zn in medicines used to treat diabetes were high, according to results obtained using AAS reported by Sun *et al.*[115] Concentrations of Cd and Pb were low. Dong and Zhu[116] showed that Taponin tablet recipe, used in treating heart and brain blood vessel disease, was rich in nutritional elements, especially Fe. For the 7 elements measured by FAAS, the order of decreasing concentration was Fe > Ca > Mg > Zn > Cu > Mn > Cd. A review by Chen *et al.*,[117] in Chinese, discussed the determination of total trace element content and speciation analysis by ICP-AES and ICP-MS. A discussion on sample preparation technique led to a conclusion that microwave digestion was ideally suited to the preparation of samples. A method for the simultaneous determination of Cd and Hg in Chinese herbal medicines was developed by Sun *et al.*[118] using vapour-generation non-dispersive AFS with an intermittent flow system. Ascorbic acid, Co and thiourea were used as masking or enhancement agents to improve the generation efficiency of the volatile Cd and Hg species. The LODs on sample solutions were 10 and 19 ng $l^{-1}$ for Cd and Hg, respectively.

### 1.7 Marine and freshwater biology

Interest in methods for the speciation of Hg in fish remains high. Ortiz *et al.*[119] evaluated different sample pre-treatment and extraction procedures. Freeze-drying and microwave drying showed losses of Hg; best results were obtained by oven drying. Quantitative extraction (97%) was only achieved with HCl leaching. Extractions with sodium dodecylsulfate, $CH_3OH$–TMAH and $CH_3OH$–KOH were incomplete. Speciation of the extracts with capillary GC with AFS detection showed that dimethylmercury was artificially produced when TMAH was used as the extractant. They applied a method of HCl leaching with determination by capillary GC-AFS to measure methylmercury in tuna fish and swordfish. Concentrations found were 0.78–1.93 μg $g^{-1}$. Enzymatic hydrolysis with protease type XIV was used by Rai *et al.*[120] for extraction of Hg and methylmercury in fish muscle tissues. Subsequent separation was by HPLC on an ODS2 80A PEEK column with a mobile phase of 5% $CH_3OH$–water containing $CH_3COONH_4$ and cysteine. Without cysteine, there were problems with adsorption, peak tailing and memory. The recovery from CRMs and fish tissue samples was 92–107%. Yang *et al.*[121,122] used species-specific ID calibration in their method. The species were extracted by digestion with $CH_3OH$–KOH, derivatized with sodium tetrapropylborate and headspace sampled with a poly(dimethylsiloxane) coated solid phase microextraction (SPME) fused silica fibre. The fibre was transferred to the head of a GC column for desorption by heating. Detection was by ICP-MS. Reverse spike ID analysis was performed to determine the accurate concentration of an in-house synthesized $^{198}$Hg-enriched monomethylmercury spike using two natural abundance methylmercury standards. The precision of determination using ID was nearly 4-fold better than using the method of standard additions. Results for methylmercury in two CRMs were in good agreement with the certified values. The automatic online system developed by Liang *et al.*[123] coupled HPLC to post-column microwave digestion with $K_2S_2O_8$ and then to detection of Hg by CVAFS. Separation was carried out on a reverse phase $C_{18}$ column with a mobile phase of 50% v/v $CH_3OH$ containing 0.1 M NaCl and 10 mM tetrabutylammonium bromide. An ice-water bath was used to cool the digestion mixture to avoid water vapour and $CH_3OH$ entering the AF detector. Results on the dogfish muscle CRM DORM-2 were in good agreement with certified values. A completely different approach based on the fact that methylmercury will selectively displace Cu from CuDDC was adopted by Yan *et al.*[124] to determine methylmercury without chromatography. Using an FI system, Cu was complexed with NaDDC and the complex sorbed on a microcolumn packed with the sorbent from a cigarette filter. The sample was then passed through the column at pH 6.8 when the methylmercury was retained, but inorganic Hg, ethylmercury and phenylmercury passed through. The methylmercury was eluted with 50 μl $C_2H_5OH$ for determination of Hg by ETAAS. For 3.4 ml of sample solution, an enhancement of 75-fold was obtained with an LOD of 6.8 ng $l^{-1}$ Hg. The method appeared to be relatively free of interference from other metals and gave a result on the CRM DORM-2 within the certified range.

Concentrations of Cu, Fe, Mn and Zn in the hard tissues of shellfish were measured by Fukui and Fujino[125] using ICP-AES. Because Ca interfered in the determination, the elements were first separated by extraction with NaDDC into hexyl acetate at pH 6. High Mn concentrations were found in certain shellfish.

### 1.8 Progress for individual elements

**1.8.1 Aluminium.** A comprehensive study of Al contamination in raw chemical materials used in the preparation of parenteral solutions was reported by Bohrer *et al.*[104] *Levels of Al contamination in 35 different commercial chemical products, including amino acids, albumin, vitamins, trace elements and glucose*, was determined using AAS. The highest Al concentrations were recorded in cysteine, vitamin C and Fe and Cr salts. The authors noted, however, that the levels of Al contamination in commercial parenteral formulations were too high to only have come from contamination in the raw constituents and concluded that steps in the manufacturing process of these

solutions may also contribute to the elevated Al levels. Sombra *et al.*[20] also examined Al contamination of parenteral solutions. The researchers extracted Al from samples of parenteral solutions using cloud-point precipitation with PONPE 7.5 non-ionic surfactant for quantitative determination using FI-ICP-AES. With optimised conditions, an extraction efficiency greater than 99.9%, a pre-concentration factor of 200 and LOD of 0.25 μg $l^{-1}$ were reported for a 50 ml sample volume. The authors considered that the method fully satisfied requirements for pharmaceutical quality control monitoring during the preparation of parenteral solutions.

Ping *et al.*[126] examined the effects of the *aluminium chelating agent deferiprone*, alone or in combination with ascorbic acid or sodium-2-mercaptoethane sulfate (mesna), on urinary excretion of Al in rabbits. New Zealand rabbits were injected with $Al_2(SO_4)_3$ (600 μmol Al $kg^{-1}$) for 5 days per week over 2 weeks. After a further 2 weeks, the chelator was administered intragastrically either alone or in combination with ascorbate or mesna. Urine samples were collected for 6 h following administration of the chelator and the Al concentration determined using AAS. The researchers observed that deferiprone significantly increased urinary Al excretion. Deferiprone administered in combination with ascorbate or mesna was equally potent in increasing Al elimination but the peak times of excretion were shifted. They concluded that deferiprone might be a suitable alternative to desferrioxamine in the treatment of Al toxicity and accumulation.

**1.8.2 Arsenic.** An *extremely sensitive method* for the determination of As and Se in hair using ETV-ICP-MS was described by Kurogouchi *et al.*[101] A 500 μg hair sample was microwave digested with $HNO_3$–$H_2O_2$ and the digest reacted with 25 μl of 1 μM $KMnO_4$ and evaporated to dryness. The residue was redissolved in 500 μl of 1 M $HNO_3$ and 5 μl aliquots injected onto a tungsten filament, which acted as the atomiser. The filament was rapidly heated to 2500 °C and the atomised sample transported to the plasma in an Ar stream for quantitative determination of $^{75}As$ and $^{82}Se$. The method was validated by analysing a hair CRM and the results obtained were in good agreement with the certified values for both elements. Park and colleagues[30] examined the interference effects of concomitant elements on the determination of As, Ge and Se in urine and serum using ICP-MS. They reported that C, Cl, and S gave a signal enhancement, whilst K and Na caused signal suppression and N and P had no significant effect.

*Many of the published papers, as in past reviews, have examined speciation of As in biological matrices*. The current status regarding speciation analysis of As in biological matrices was reviewed by Gong *et al.*,[127] Suzuki *et al.*[128] and McSheehy.[129] It was interesting to see the publication of further studies on urinary As excretion following controlled seafood consumption some 10 years after similar work was reported by the UK Health and Safety Executive Occupational Medicine and Hygiene Laboratory. The group of Heinrich-Ramm *et al.*[130] determined As species in urine following consumption of different seafoods. The As species were separated by anion-exchange chromatography and quantitatively determined using HGAAS. As in the study 10 years earlier, the researchers reported that consumption of certain seafoods led to increased urinary excretion of dimethylarsinic acid (DMA). However, this latest study clearly demonstrated that the increased DMA excreted was not caused by metabolism of inorganic As but other As species, such as arsenobetaine, present in the consumed seafood. Wrobel and colleagues[131] described a rapid, sensitive method for the quantitative determination of five primary As species in urine and fish tissues using HPLC coupled with ICP-MS. Separation of $As^V$, monomethylarsonic acid (MMA), $As^{III}$, DMA and arsenobetaine (AB) was achieved in less than four minutes using an Altima $C_{18}$ column with a citric acid–hexanesulfonic acid mobile phase at pH 4.5. The LODs for all species were reported to be suitably low for quantification at normal physiological levels. The method was validated by analysing As species in DORM-2 dogfish muscle CRM and NIST 2670 human urine SRM. The same author with a different group of co-workers[132] studied the urinary excretion of As species in a patient with acute $As_2O_3$ poisoning receiving chelation therapy with dimercaptopropanesulfonic acid (DMPS). Arsenic species were separated and quantitatively determined using ion-exchange chromatography coupled with HGAAS. The major urinary As species was $As^{III}$, which represented 37.4% of the total amount excreted. The researchers highlighted the observation that the second methylation step in As metabolism was almost completely inhibited, which they hypothesised was due to the high dosage of DMPS. This was supported by the work of Gong *et al.*[133] who also studied the urinary excretion of As complexes in urine following administration of DMPS. The authors identified a DMPS–MMA complex, which was characterised using ES-MS-MS and quantitatively determined using HPLC-AFS. The complex did not form a volatile hydride on reaction with $NaBH_4$ but was decomposed by treatment with 0.1 M NaOH. The authors concluded that formation of the complex reduced the availability of MMA for biomethylation.

The group of Chen *et al.*[134] evaluated *the stability of arsenic species in urine and aqueous standards* during different sample pre-treatment procedures prior to determination using HPLC-ICP-MS. They reported that As in freshly collected urine and in NIST 2670 urine CRM remained stable for up to 6 months when stored at −20 °C, whereas aqueous standards were stable for only 4 weeks. They also reported that a significant fraction of 'insoluble' As, which could represent up to 50% of the soluble As fraction, was lost when urine samples were centrifuged prior to analysis. They concluded that the urine matrix has an important stabilising effect on As species and that centrifugation of samples before analysis may result in significant underestimation of urinary As concentrations. Hwang *et al.*[135] used HPLC coupled with HGAAS to determine As species in urine samples from maintenance engineers, in the semiconductor industry, exposed to low levels of As. They observed that both the total urinary MMA and its percentage of the total inorganic As were significantly higher in exposed engineers compared with controls and suggested that this latter parameter was a suitable indicator of low level As exposure in this industry.

The *enormous environmental arsenic problem in north western areas of the Indian subcontinent* continues to be widely reported. Ali and Tarafdar[136] examined the relationship between As in drinking water and in scalp hair from people living in As contaminated regions of Bangladesh. Concentrations of As in drinking water and hair were quantitatively determined using EDXRF. The mean concentration of As in drinking water was 0.26 mg $l^{-1}$ and the average concentration in hair from the people drinking the water was 14 mg $kg^{-1}$ compared with a normal 'reference' value of $<3$ mg $kg^{-1}$. Mandal *et al.*[97] examined the suitability of hair and nail samples as biomarkers of As exposure in the heavily contaminated regions of West Bengal. Arsenic species were extracted from both sample types by simple treatment with $H_2O$ at 90 °C and separated by HPLC for quantitative determination using ICP-MS. The researchers reported that As in both hair and nails was strongly positively correlated with As exposure but that As species in fingernails were better correlated with symptoms of arsenism, whilst hair was affected by exogenous contamination. Chowdhury *et al.*[137] compared the patterns of urinary As excretion in children and adults living in As contaminated regions of Bangladesh. Urinary As species were separated and quantitatively determined using HPLC-ICP-MS and FI-HG-AAS. The authors noted that urine concentrations of inorganic As were lower in children than adults, whilst DMA concentrations were higher. Also, the second methylation step of MMA to DMA was more

active in children than adults. They concluded that children retained less As in their bodies than adults, which would support the observation that children drinking the same water as adults do not exhibit the same skin lesions as adults.

**1.8.3 Beryllium.** Verma *et al.*[138] investigated *whether the determination of Be levels in lung tissue could be used to differentially diagnose chronic beryllium disease (CBD) from pulmonary sarcoidosis and other related diseases*. The researchers repeatedly determined Be in autopsy lung tissue from a diagnosed case of CBD, 3 cases of sarcoidosis and 25 control subjects, using a modified method for the determination of Be in air filter samples by ETAAS. They noted that, whilst mean levels of Be were elevated in the lung tissue of the CBD case, some individual measurements from the CBD tissue were similar to levels in control tissues and concluded that a definitive diagnosis could not be made on analytical measurements alone. The occupational history record was equally important in diagnosis of this disease.

**1.8.4 Bismuth.** Magalhaes *et al.*[139] investigated *the performance of a variety of chemical modifiers, as either solutions or permanent graphite tube coatings, for the quantitative determination of Bi in urine* using ETAAS. Urine samples were simply diluted 1 + 1 v/v with 1% $HNO_3$, directly into autoanalyser cups. A permanent Ir–Rh modifier gave the best sensitivity and a characteristic mass of 29.2 pg compared with the instrument manufacturers recommended value of 30 pg for an aqueous solution of Bi. Aqueous calibration was reported to be satisfactory for accurate determination of Bi in this matrix.

Bismuth compounds are widely used as *anti-ulcer drugs*. Sun and Szeto[140] combined HPLC with ICP-MS to investigate the binding of Bi to serum proteins. The authors found that at physiological pH, over 70% of Bi was bound to transferrin even in the presence of an excess of serum albumin (albumin/transferrin ratio 13 : 1). However, Bi bound to albumin when transferrin was saturated with iron. They concluded that the binding of Bi to transferrin is much stronger than to albumin and that transferrin is the primary target protein for Bi and may play a role in the pharmacological action of Bi.

**1.8.5 Boron.** *Matrix interference effects* on the determination of B and Ti in biological specimens, using ICP-AES with CCD detection, were comprehensively investigated by Garavaglia *et al.*[28] Human serum was selected as the test matrix to investigate different operating conditions on the B response. The researchers recorded that high rf power and low carrier gas flow rates contributed to large variations in the intensity of the B signal. Improved sensitivity was observed using a crossflow nebuliser and Scott-type spray chamber. Severe memory effects were observed in test samples prepared with boric acid, but no memory effects were noted for samples spiked with boronophenylalanine (BPA). Yttrium was an effective internal standard for determination of both B and Ti in serum and plasma samples provided the albumin concentration in the diluted sample was below 0.2%.

Svantesson *et al.*[141] emphasised *the advantages of using the coupled techniques of ICP-AES and TOF-MS for the determination of B and boron containing compounds in urine and plasma samples from patients undergoing boron neutron capture therapy* with BPA. A previously unreported possible BPA metabolite was identified in both plasma and urine samples and the ratio of BPA to suspected metabolite differed from patient to patient. Most patients had a urine metabolite concentration around 10% of urine BPA some 5–11 hours after administration of the drug and this increased to 30–80% after 24 hours. Preliminary studies with ES-MS-MS showed the metabolite to have a higher mass than parent BPA.

**1.8.6 Bromine.** Frances *et al.*[142] used ICP-MS *to monitor serum Br in a case of Br intoxication from a non-prescription preparation* (Calcibronat). On hospitalisation the serum Br concentration was 1717 mg $l^{-1}$. Serum Br gradually declined over 8 months with an elimination half life of 10 days.

**1.8.7 Cadmium.** Two groups examined the use of a permanent chemical modifier for the determination of Cd in biological matrices. The recognised problems of high blank values and background absorption from the use of ammonium phosphate solutions as chemical modifiers for the determination of Cd and Pb by ETAAS were eliminated in the method described by Tsalev *et al.*[90] Small quantities of phosphate were stabilised on the integrated platform of a THGA pre-treated with W or Ir–Zr. The method was used to determine Cd and Pb in biological fluids and tissue samples solubilised with TMAH. Da Silva *et al.*[8] investigated the use of *Ru as a permanent chemical modifier for the determination of Cd in biological matrices using ETAAS*. A single treatment of the graphite tube with a Ru solution was sufficient for 300 atomisation cycles. Biological samples were digested with 25% TMAH, diluted to 50 ml with $H_2O$ and incubated at 60 °C for 1 h. The method was validated by analysing six biological CRMs and an LOD of 0.05 μg $l^{-1}$ was reported. The same group[143] also described a method for the quantitative determination of Cd and Pb in blood using cloud-point extraction and ETAAS. The elements were separated from the digested blood matrix by complexation with *O,O*-diethyldithiophosphate (DDTP) and extraction with Triton X-114. After centrifugation, $HNO_3$–$CH_3OH$ was added to the surfactant-rich phase and aliquots injected into a graphite tube pre-treated with Ru or Ir as a permanent chemical modifier. Enrichment factors of 71 and 34 were reported for Cd and Pb, respectively, giving LODs of 0.02 μg $l^{-1}$ for Cd and 0.08 μg $l^{-1}$ for Pb. The method was validated by analysing human blood CRMs. The results obtained were in good agreement with certified values for both elements.

The group of Ngobeni *et al.*[93] described the use of *a transverse heated filter atomiser* for the simultaneous determination of Cd and Pb in urine using ETAAS. The filter atomiser was constructed from a standard THGA into which was inserted a porous graphite filter with a sample collector of carbon fibre and tungsten wire, packed between the tube wall and the spool shaped filter. Urine samples were diluted five- or ten-fold with 0.2% $HNO_3$ and injected into the sample collector held at a temperature of 150 °C, which eliminated the need for a sample drying step. The filter atomiser significantly reduced spectral and chemical interferences, removing the need for a chemical modifier. Analytical sensitivity was improved two-fold compared with ETAAS using a conventional integrated platform tube, giving reported LODs of 0.018 μg $l^{-1}$ and 0.02 μg $l^{-1}$ for Cd and Pb, respectively.

Pereira *et al.*[10] determined Cd, Cu and Pb in biological samples using *thermospray flame atomic absorption spectrometry with slurry sample introduction*. Slurry samples (0.1–1% w/v) of various biological CRMs were prepared in 0.3 M $HNO_3$. Samples of the slurry were injected through a flame-heated capillary into a nickel tube placed in an oxidising air–$C_2H_2$ flame of the spectrophotometer. The samples were simultaneously digested and oxidised in the $HNO_3$ vapour environment of the tube for quantitative determination of the elements. The reported LODs were 0.5 μg $g^{-1}$, 4.3 μg $g^{-1}$ and 3.5 μg $g^{-1}$ for Cd, Cu and Pb, respectively. Flores *et al.*[15] described a method for the determination of Cd in biological matrices using AAS with solid sampling. Samples of 0.05–2 mg were finely ground and weighed into polyethylene vials. The vials were connected to a device which introduced the sample as a dry aerosol directly into a quartz cell placed in a conventional air–$C_2H_2$ flame. Vaporisation of the Cd produced a signal that was totally integrated over 1 s. The method gave a

characteristic mass for Cd of 0.29 ng and calibration was achieved by analysing different masses of a selected solid CRM.

Salpietro *et al.*[144] determined *maternal and cord blood cadmium* concentrations at the time of delivery in 45 healthy non-smoking pregnant women who had low environmental exposure to the trace element. The authors reported a highly significant positive correlation between Cd in maternal and cord blood samples and a significant inverse relationship between cord blood Cd levels and birth weight. They hypothesised that even low environmental Cd exposure may be a risk factor for impairment of development in infants.

**1.8.8 Caesium.** Centeno *et al.*[145] used ETAAS with Zeeman-effect background correction to determine *blood and tissue Cs concentrations in post mortem samples from two patients administered CsCl and aloe vera as an alternative cancer treatment*. Blood Cs levels were 1100 times higher than reported normal values. The highest tissue concentrations were determined in liver (1029 μg $g^{-1}$), kidney (815 μg $g^{-1}$) and brain (219 μg $g^{-1}$). The authors hypothesised that high liver accumulation of Cs might lead to hepatotoxicity as an early symptom in Cs poisoning cases.

**1.8.9 Calcium.** The accurate determination of Ca in biological matrices using ICP-MS with a conventional spray chamber is severely affected by numerous polyatomic and isobaric interferences. *Expensive enriched Ca isotopes are used in human metabolism studies and it is important, therefore, that precise and accurate Ca isotope ratios can be measured with limited use of these isotopes*. Field and colleagues[49] investigated methods to reduce polyatomic interferences on the determination of Ca in urine using HR-ICP-MS in medium resolution mode. Precipitation of Ca with oxalate and desolvation prior to sample introduction to the plasma reduced interferences sufficiently for $^{42}Ca$, $^{43}Ca$ and $^{44}Ca$ isotopes to be determined with ratio precisions better than 0.1%. The authors used this method in clinical studies to examine Ca metabolism in post-menopausal women.

Beck and colleagues[48] described a *dual isotope method, using stable and radioisotopes*, for the measurement of Ca absorption in human volunteers. Volunteers were given a meal containing 63 mg of Ca together with water containing $^{47}Ca$ (0.11 MBq). Following ingestion of the meal, the volunteers were administered an *i.v.* injection of 18 mg $^{44}Ca$. The absorption of Ca was estimated from the urinary excretion of $^{47}Ca$ and $^{44}Ca$ in a 24 h urine sample and by measurement of the whole body retention of $^{47}Ca$. Urine $^{44}Ca$ was determined by ICP-MS. Mean Ca absorption determined by the dual isotope method was 74% compared with a mean value of 75% determined by the whole body retention method. The authors concluded that the dual isotope method was satisfactory for measuring Ca absorption from a single meal.

**1.8.10 Chromium.** There has been renewed interest this review period in *methods for pre-concentration of elements prior to quantitative determination by flame and flameless AAS*. Wuilloud *et al.*[105] described a method employing on-line pre-concentration coupled with FI for the determination of Cr in parenteral solutions by FAAS. Chromium ions were complexed with 4-(2-thiazolylazo)resorcinol (TAR) and adsorbed onto an Amberlite XAD-16 column. The Cr–TAR complexes were eluted with $C_2H_5OH$. An enrichment factor of 50 was reported, for an initial sample volume of 50 ml, which gave an LOD of 20 ng $l^{-1}$. An alternative enrichment method was described by Divrikli *et al.*[146] for the determination of Cr, Fe and Pb in urine using chelation with calmagite and adsorption on cellulose nitrate membrane filters. The authors investigated the effect of major urine constituents, such as urea and creatinine, on the quantitative recovery of the analyte ions.

Two groups examined different chemical modifiers for the determination of Cr in biological matrices. Lelis *et al.*[92] used a permanent Ru chemical modifier to determine Cr and Cu in urine samples by ETAAS. Urine samples were simply diluted 1 + 1 v/v with 1% $HNO_3$. With the *permanent modifier*, optimum pyrolysis and atomisation temperatures were 1400 °C and 2500 °C, respectively. The authors reported that the permanent Ru modifier gave improved analytical sensitivity for both Cr and Cu compared with the more conventional Pd–$Mg(NO_3)_2$ modifier solution. The reported LODs for Cr and Cu were 0.22 μg $l^{-1}$ and 0.32 μg $l^{-1}$, respectively.

Nunes *et al.*[147] investigated both Pd–$Mg(NO_3)_2$ in solution and Ir, Ru and Zr permanent graphite tube coatings as *chemical modifiers* for the determination of Cr in human serum. Serum samples were diluted 1 + 4 v/v with 1% $HNO_3$ containing 0.02% cetyltrimethylammonium chloride. They noted that permanent chemical modifiers produced a pronounced broad plateau signal, which did not return to baseline, and that the Pd–$Mg(NO_3)_2$ solution produced erratic noisy peaks with reduced sensitivity. They concluded that optimal analytical sensitivity was obtained without any chemical modification.

Aguilar and colleagues[148] used ETAAS with deuterium background correction to determine *chromium in cerebrospinal fluid* (CSF) samples. Optimum sensitivity and reproducibility was achieved with 1 + 1 v/v sample dilution with 0.25% Triton X-100 in 4.5% $HNO_3$. Standard additions calibration was necessary for quantitative determination. The authors reported a mean value of 14.6 μg $l^{-1}$ for Cr in CSF from 43 healthy subjects.

**1.8.11 Cobalt.** *The use of cloud-point precipitation to pre-concentrate element ions for quantitative determination by AAS was described in last year's ASU review*.[1] In this review period, a number of methods employing this technique have been published. In the method described by Manzoori *et al.*[21] for the determination of Co in urine by FAAS, 1-(2-pyridylazo)-2-naphthol (PAN) and Triton X-114 were used respectively as the hydrophobic ligand and non-ionic surfactant. Residual water in the $CH_3OH$ surfactant solution was found to severely reduce the analyte signal: therefore, an additional clean-up step was introduced to remove water from the surfactant phase. An enrichment factor of 115 was reported from a starting sample volume of 10 ml and the LOD was 0.38 μg $l^{-1}$.

The method developed by Anthemidis *et al.*[22] for the determination of Co in biological samples by ETAAS used an *on-line FI system with pre-concentration on a micro-column packed with inert PTFE turnings* as a sorbent material. Samples were mixed on-line with APDC solution and the Co–APDC complexes adsorbed onto the PTFE column at pH 5.5–7.0. The Co complexes were eluted with IBMK directly into the tube of a THGA for determination by ETAAS. An enrichment factor of 87 was reported and the LOD was 4 ng $l^{-1}$. The method was validated by analysing natural water and mussel tissue CRMs.

**1.8.12 Copper.** There has been renewed interest this review period in the determination of Cu in a variety of biological matrices. Santos *et al.*[11] described a simple method for the determination of Cu, Mn and Pb in *deciduous teeth* using ETAAS. Teeth samples were ground in a cryogenic mill using liquid $N_2$ and 2% m/v slurries prepared by suspending 20 mg of the ground material in 1 ml of 0.2% $HNO_3$–0.04% Triton X-100. A W–Rh coated platform was used. The permanent modifier allowed quantitative determination of all three elements with aqueous standards. Reported LODs were 18 ng $g^{-1}$ for Cu, 7.4 ng $g^{-1}$ for Mn and 34 ng $g^{-1}$ for Pb in a 2% m/v slurry. The method was validated by analysis of IAEA H-5 animal bone CRM.

Melo *et al.*[84] determined Cu, Mn and Zn levels in CSF from healthy subjects and *patients with multiple sclerosis* using AAS and HR-ICP-MS. The researchers noted significantly decreased concentrations of Mn in CSF from patients compared with controls (1.07 μg $l^{-1}$ *versus* 1.78 μg $l^{-1}$) and

significantly increased CSF Cu levels in the patients (10.9 μg $l^{-1}$ *versus* 8.7 μg $l^{-1}$). No difference in Zn concentrations in CSF between patients and controls was observed. They hypothesised that the differences in CSF levels of Cu and Mn between multiple sclerosis patients and controls might be associated with alterations in the Mn containing enzyme glutamine synthase and the Cu containing enzyme cytochrome oxidase.

*A number of groups have used XRF to determine cellular and tissue concentrations of Cu and other trace elements*. Milman and colleagues[69] used XRF to determine Cu concentrations in liver tissue samples from Greenlandic Inuit and Caucasian Danes. The median value for liver Cu in the Inuit was 0.298 mmol $kg^{-1}$ compared with a median value of 0.377 mmol $kg^{-1}$ in Danes. However, the difference was considered to be due solely to the 3 highest liver Cu levels determined in Danish men. The authors concluded that there was no evidence to suggest that the prevalence of Cu deficiency or Cu overload differed between the two populations and that Inuit have a liver Cu content similar to that in populations from western societies. Kucharzewski *et al.*[68] used TXRF to determine concentrations of Cu, Se and Zn in whole blood and thyroid tissue samples from patients with various thyroid diseases. They reported that mean concentrations of all three elements and the Cu : Zn and Cu : Se ratios in whole blood were significantly higher in patients with thyroid cancer than patients with other thyroid disorders or controls. Tapia *et al.*[149] also used TXRF to determine the concentration of Cu, Fe and Zn in different cultured cell lines. The group also examined how extracellular exposure to 100 μmol $l^{-1}$ Cu altered the intracellular content and distribution of these elements. In HepG2 and CaCo2 cell lines exposure to extracellular Cu led to an increased intracellular Cu content and decrease in intracellular Fe and Zn.

The observation that serum Cu : Zn ratios are altered in a wide rage of disease states is not new. Both Delves and Fell and colleagues reported such changes in Cu : Zn ratios as far back as 1970. The *diagnostic value of copper : zinc ratio determinations* in hepatocellular carcinoma (HCC) was examined by Poo *et al.*[86] Serum Cu and Zn levels were determined in 3 groups of patients (patients with HCC, patients with liver cirrhosis and patients with benign digestive disease) using AAS. Serum Cu was significantly increased in HCC patients (97.4 μg $dl^{-1}$) compared with the two other groups (73.7 μg $dl^{-1}$ for cirrhosis, 77.1 μg $dl^{-1}$ for digestive disease). The serum Cu : Zn ratio was also significantly greater in patients with HCC with a sensitivity of 87.5%. The authors concluded that measurement of the Cu : Zn ratio might be useful in the diagnosis of patients with suspected hepatocellular malignancy. Olusi *et al.*[150] investigated the role of the 'obesity gene' protein product, leptin, in trace element metabolism. Serum leptin levels in 570 healthy men and women were determined using a commercial immunoassay. Serum Cu and Zn levels were measured by AAS. When the confounding factors of age, sex and body mass index were eliminated, serum leptin was still positively associated with serum Cu but there was no significant association between serum leptin and Zn. The authors suggested that Cu but not Zn has an effect on serum leptin levels. Arancibia *et al.*[151] investigated the intrauterine dissolution of Cu from a copper intrauterine contraceptive device (IUD). Uterine fluid was collected, at different times throughout a menstrual cycle, from women who had been using the IUD for periods greater than 6 months. Copper concentrations in the uterine fluid were determined using ASV and AAS. Protein concentrations were determined by HPLC. The researchers reported that the Cu released from the device was complexed with protein and the rate of release was constant for at least 6–12 months.

Finally, the lack of data on trace element *reference values in cats* was addressed by the study of Fascetti *et al.*,[152] who determined plasma and whole blood Cu levels in a pathogen-free colony of cats. Tom cats had significantly higher mean plasma Cu levels (15.4 μmol $l^{-1}$ *versus* 11.3 μmol $l^{-1}$) and whole blood Cu levels (16.16 μmol $l^{-1}$ *versus* 13.36 μmol $l^{-1}$) than female cats.

**1.8.13 Gallium.** A sensitive method was developed by Antheraidis *et al.*[24] for *the determination of Ga in natural waters and urine* using on-line FI coupled with FAAS. Samples were reacted with HCl. The GaCl complexes adsorbed onto a polyether type polyurethane foam mini-column and eluted with IBMK directly into the pneumatic nebuliser of the AA spectrometer. An enrichment factor of 40 was achieved for a 90 s pre-concentration cycle, which gave a reported LOD of 6 μg $l^{-1}$ and an RSD of 6.6% at a concentration of 1 mg $l^{-1}$.

**1.8.14 Gold.** *An association between gold dental restoration and gold allergy has been postulated in recent studies*. Ahnlide *et al.*[153] examined the relationship between blood Au levels and gold alloy restorations in patients with and without contact allergy to Au. Blood samples were taken from patients referred for patch tests and the concentration of Au determined using ICP-MS. An LOD of 0.04 μg $l^{-1}$ was reported for the method. Patients with gold restorations had statistically significantly higher blood Au concentrations ($<$0.04–0.07 μg $l^{-1}$) than patients with no restorations ($<$0.04–0.15 μg $l^{-1}$) and a positive correlation between blood Au and number of gold surfaces was observed. However, there was no significant difference in blood Au levels between patients with and without contact allergy to Au.

**1.8.15 Iron.** Sternberg and colleagues[43] evaluated *different procedures for the separation of Fe from human whole blood matrix for the determination of Fe isotope ratios* using multi-collector ICP-MS. The whole blood matrix was decomposed by microwave digestion and ashing, and the Fe ions separated from the residue either by anion exchange or precipitation procedures. Mass discrimination correction with Ni isotopes was used for quantitative measurement of $^{54}Fe$, $^{56}Fe$ and $^{57}Fe$ isotopes. The authors considered precipitation with $NH_3$ to be the most rapid and cost effective for high Fe recovery and accurate determination of Fe ratios. Crews *et al.*[50] used HR-ICP-MS to determine total Fe levels and Fe isotope ratios in acid digests of faecal samples from a human nutritional study designed to examine Fe absorption from different diets. A resolution setting of 4000 was required to separate the analyte signal from overlapping Ar interferences. The method was validated by repeated analysis of NIST 1577b bovine liver SRM. The reported mean Fe concentration of 182 μg $g^{-1}$ was in excellent agreement with the reference value of 184 μg $g^{-1}$. Isotope ratios determined by ICP-MS were not significantly different from those determined using TIMS for the same faecal samples.

Serfass *et al.*[154] studied the *solubilisation of extrinsic iron* by human breast milk protein fractions using SEC and ICP-MS. Low $M_r$ whey fractions were found to be very effective in solubilising extrinsic Fe. Dawczynski *et al.*[155] determined levels of Fe and Zn in human cataractous lenses using AAS. A significant increase in lens Zn was noted with increasing lens colouration (0.33 μmol $l^{-1}$ in light brown lenses compared with 0.52 μmol $l^{-1}$ in dark brown lenses). Cataractous lenses from diabetics had significantly increased Fe and Zn concentrations compared with lenses from non-diabetics. The authors suggested a possible influence of Fe and Zn lens content on the development of lens opaqueness.

**1.8.16 Lead.** Cid *et al.*[12] investigated *different preparation conditions for the determination of Pb in marine biological materials using slurry sampling ETAAS*. Slurries were prepared either by magnetic stirring or microwave heating. Results from analyses of CRM samples prepared by both methods were comparable with those obtained from acid digested samples and in good agreement with certified values.

Zhou *et al.*[89] developed a method for the determination of Pb in whole blood using ETAAS, in which a Rh–W coated integrated platform atomiser acted as a permanent modifier. Blood samples were diluted 1 + 9 v/v with 0.2% $HNO_3$–0.5% Triton X-100 and the reported LOD was 1.5 μg $dl^{-1}$. The use of the *permanent chemical modifier* allowed aqueous standards to be used for calibration and improved atomiser lifetime by a factor of 2–3 compared with a conventional $NH_4H_2PO_4$ chemical modifier. The method was validated by analysis of a range of whole blood CRMs and proficiency testing samples. In an interesting approach, researchers from the same group[91] studied the pyrolysis and atomisation behaviour of Pb in whole blood using a Rh-coated tungsten wire filament atomiser. The atomiser was coupled to an ICP-mass spectrometer, which allowed the filament to be operated both as an electrothermal atomiser and electrothermal vaporiser for pseudo-simultaneous ETAAS and ETV-ICP-MS. With this arrangement, the researchers could monitor the analyte ($^{208}$Pb), the matrix ($^{40}$Ar$^{12}$C), the $^{103}$Rh permanent modifier and the metal atomiser ($^{180}$W, $^{183}$W) throughout the thermal cycle whilst also determining the Pb concentration by AAS. They reported that most of the organic matrix was removed during pyrolysis without loss of analyte. Part of the permanent Rh coating modifier was only lost during the final cleaning step of the cycle. However, when Rh was added to the diluent it was lost during pyrolysis and so was ineffective as a chemical modifier. Bonnefoy *et al.*[156] validated a method for the determination of Pb in whole blood using ICP-MS. Samples were simply diluted 1 + 44 v/v with $NH_4OH$–EDTA–Triton X-100–n-butanol. The use of $^{187}$Re as an internal standard improved both the reproducibility and uncertainty of the measurements.

The merits and disadvantages of *filter paper sampling* for blood Pb analysis were reported and discussed in an earlier ASU review. In this review period, Shen and colleagues[157] compared venous blood and capillary filter paper sampling methods for the determination of blood Pb levels in a large geographically dispersed population of Chinese children. Good agreement ($r^2$ = 0.87) was reported between the two sample types. The authors concluded that the filter paper method had sufficient sensitivity and specificity for routine screening and provided an attractive method for sampling large widely dispersed populations for analysis at centralised laboratories.

The relationship between exposure to *lead and blood pressure* was investigated by several groups. Rothenberg *et al.*[64] reported the findings of a large-scale study of the association between current and past Pb exposure and risk of hypertension and raised blood pressure in the later stages of pregnancy. Tibia and calcaneus bone Pb was determined using K shell-XRF and blood Pb levels using AAS. Geometric mean pre-natal and post-natal blood Pb levels were 1.9 μg $dl^{-1}$ and 2.3 μg $dl^{-1}$, respectively. The authors reported that calcaneus bone Pb was related to third trimester hypertension but not *post partum* hypertension, whilst tibia Pb was not related to hypertension either in the third trimester or *post partum*. Glenn and colleagues[158] reported the findings of a longitudinal study on the relationship between occupational Pb exposure and blood pressure. Blood Pb levels, tibia bone Pb levels and blood pressure were repeatedly determined between 1994 and 1998 in 496 workers exposed to inorganic and organic Pb. The authors noted that changes in systolic blood pressure during the study period were associated with Pb dose, which indicated an aetiological role for Pb in the elevation of systolic blood pressure.

The relationship between *maternal blood lead and pregnancy outcome* was investigated by Sowers *et al.*[159] The mean Pb level in maternal blood samples taken four times during pregnancy was 1.2 μg $dl^{-1}$ and maternal blood Pb showed a significant correlation with hypertension and toxaemia during pregnancy, after adjusting for age and Ca intake. However, no association between maternal Pb and birth weight or gestational age was observed. The same researchers[160] studied the influence of maternal bone Pb turnover and blood Pb levels on breast milk Pb concentrations. Concentrations of Pb in blood were determined using ETAAS and in breast milk using ICP-MS. They concluded that bone turnover was correlated with breast milk Pb but there was no evidence that maternal Pb and breast milk Pb levels were a public health issue. Hernandez-Avila *et al.*[63] investigated the relationship between maternal bone Pb and birth length and head circumference of newborns. Cortical and trabecular bone Pb concentrations were determined using K shell-XRF in 223 women one month after giving birth. The birth length of infants decreased as maternal cortical bone Pb increased. Trabecular bone Pb was correlated with an increased risk of low head circumference in a newborn. The same group[161] conducted a randomised placebo-controlled study to examine whether dietary Ca supplements during pregnancy reduced blood Pb levels. Blood Pb levels were determined, using ETAAS, in lactating women receiving either Ca supplement or placebo. Trabecular bone Pb was determined using K shell-XRF. The authors reported that women with high bone Pb levels showed a 16.4% reduction in mean blood Pb if they were receiving the Ca supplement. Gulson and colleagues[162] presented a comprehensive review of their long-term research on mobilisation of Pb from bone during pregnancy and lactation. In these studies, ICP-MS was used to determine very small changes in blood Pb isotopic composition in migrants to Australia, who had a different skeletal Pb isotopic composition compared to multi-generational Australians.

Latorre *et al.*[163] investigated the relationship between bone Pb, blood Pb and menopause in 232 pre- and post-menopausal women from Mexico City. Blood Pb levels ranged from 2.1 μg $dl^{-1}$ to 32 μg $dl^{-1}$. After adjusting for age and bone Pb, the mean blood Pb level was 1.95 μg $dl^{-1}$ higher in *post-menopausal women* than in pre-menopausal women. The researchers hypothesised that mobilisation of Pb from bone increased during menopause and constituted a potential health risk in menopause. Oliveira *et al.*[62] studied the seasonal variations in relationship between bone and blood Pb levels. Using multivariate regression models, they found a strong relationship between the season and the influence of bone Pb on blood Pb levels. They hypothesised that the elevated blood Pb, observed in winter months, was associated with increased mobilisation of bone Pb, possibly from the reduced levels of light leading to lower levels of activated vitamin D and enhanced bone resorption. Finally, Lee and colleagues[164] reported trends in blood Pb levels in children from urban and suburban areas of Ulsan, Korea. Over the period 1997 to 2001 the authors reported an increase in mean blood Pb levels from 5.1 μg $dl^{-1}$ to 5.4 μg $dl^{-1}$ for children in industrial areas, and from 3.8 μg $dl^{-1}$ to 4.9 μg $dl^{-1}$ for children in the suburbs, indicating that environmental exposure to Pb is increasing year on year in this region.

**1.8.17 Magnesium.** *The metabolism of Mg was investigated by Sabatier and colleagues*[46] *using a double Mg isotope labelling method.* An oral dose of $^{24}$Mg and *i.v.* dose of $^{25}$Mg was administered to healthy male volunteers. Blood, urine and faeces samples were collected over a 12 day period and Mg isotope ratios determined in the collected samples using ICP-MS. The authors developed a two compartment model, which described the rapid exchange of plasma Mg with two extra-plasma pools and gave estimations for fractional Mg absorption and faecal endogenous excretion.

Feillet-Choudray *et al.*[44] described a novel *in-vitro* blood *load test as a biomarker of magnesium status*. Wistar rats were fed either Mg replete or Mg deficient diets for 1 month. Blood samples were taken and incubated with an enriched $^{25}$Mg solution (10 mg $l^{-1}$). Erythrocytes, lymphocytes and platelets were separated from the incubated blood samples and concentrations of $^{25}$Mg in the respective fractions determined using ICP-MS. The method was subsequently tested on human whole blood samples. Compared with the rat model, Mg enrichment

was low in human erythrocytes but high in lymphocytes and platelets. The authors considered that these latter cellular fractions were most appropriate for examining Mg status in humans.

**1.8.18 Manganese.** A *simple slurry sampling method* was described by Marco *et al.*[165] for the quantitative determination of Mn in brain tissue samples using ETAAS. Slurries of 2% w/v were prepared in de-ionised distilled water from different sections of brain material and were stable for 30 min. A mixed Pd–$Mg(NO_3)_2$ chemical modifier was used to stabilise Mn in the atomiser to achieve a pyrolysis temperature of 1300 °C. Aqueous standards were satisfactory for calibration and an LOD of 0.3 μg $l^{-1}$ was reported. The method was validated by analysing NIST 1577a bovine liver CRM and good agreement was obtained with results from a method using microwave assisted $HNO_3$ digestion of brain tissue samples.

An on-line FI-ICP-AES method was described by Zongagh *et al.*[23] for the determination of *Mn in biological samples*. The analyte was pre-concentrated by adsorption onto a silica column treated with 1,5-bis(di-2-pyridyl)methylene thiocarbohydrazide and subsequently eluted with $HNO_3$ directly into the nebuliser of the ICP-AE spectrometer. The effects of sample flow rate, eluent flow rate, pH, buffer and eluent concentration on analytical performance were investigated. With optimised conditions, an enrichment factor of 26 was achieved, giving a reported LOD of 1.5 μg $l^{-1}$ and RSD of 0.5%. Results from analysis of a range of biological CRMs showed good agreement with certified values.

**1.8.19 Mercury.** Ongoing concerns over the health risks from Hg in dental amalgam continues to stimulate work on this element. Pizzichini and colleagues[166] investigated *the impact of amalgam fillings on concentrations of Hg and total anti-oxidant activity in plasma of healthy individuals*. Plasma Hg concentrations were determined using AAS. The group reported that plasma Hg was positively correlated with the number of amalgam fillings and that anti-oxidant activity was negatively correlated with plasma Hg, which suggested a pro-oxidant role for Hg released from fillings. Vamnes *et al.*[167] investigated the effects of *i.v.* injections of dimercaptopropane sulfonate (DMPS) on blood Hg levels in groups of subjects with or without amalgam fillings. Four groups (healthy subjects with amalgam fillings, subjects with self reported symptoms from existing fillings, subjects who had all fillings removed and a control group with no history of fillings) were administered a single injection of DMPS. Blood samples were taken before injection and at defined times following injection and Hg concentrations determined using CV-AAS. In all groups a 24–30% fall in blood Hg was observed 2 h after injection but no significant differences were observed between the 3 groups with dental amalgam experiences. The effect of resin cement linings on the pulpal uptake of Hg from amalgam restorations was investigated by Akyuz and Calgar.[168] Cavities were created in the incisor teeth of guinea pigs and lined with either conventional liners or resin modified glass cements prior to restoration with Hg amalgam. Restored teeth were extracted after 1, 7 or 30 days and the Hg concentration in dental pulp determined using AAS. The researchers reported that the resin modified cement significantly reduced the uptake of Hg into dental pulp. Okabe *et al.*[169] studied the *in vitro* dissolution of Hg amalgams, with high and low copper content, in aqueous solutions using a dynamic flow cell system. Amalgam samples were suspended in the flow cell and de-ionised water or acidified solutions pumped through the cell for up to 6 days. The solution was sampled throughout the experiments and Hg concentrations determined using CVAAS. The dissolution of Hg was found to be enhanced in an acidic solution, particularly from amalgam formulations with a high copper content.

Speciation studies of Hg in biological matrices continue to be reported by many groups. Ortiz and colleagues[119] comprehensively evaluated sample pre-treatment and extraction conditions for the quantitative determination of Hg species in fish using FI-CV-AFS. They examined three different drying methods and noted that freeze drying or microwave drying led to losses of Hg, whereas no losses were observed with oven drying. Of the four extraction methods examined only HCl leaching achieved quantitative extraction of Hg (>97%). *Investigation of species integrity* was also performed using capillary GC-AFS. The authors reported that a dimethyl Hg species was artificially produced when TMAH was used to extract Hg from fish tissues. Yan *et al.*[124] described a simple and novel non-chromatographic method for the selective speciation of methylmercury from biological matrices and determination using ETAAS. Methylmercury was separated from ethylmercury, phenylmercury and $Hg^{II}$ through a displacement reaction of methylmercury with $Cu^{II}$–DDC, which was pre-sorbed onto a micro-column packed with cigarette filter sorbent. The bound methylmercury was subsequently eluted with 50 μl of $C_2H_5OH$ directly into the graphite furnace for determination by ETAAS. No interferences from competing metal ions were observed. With a sample volume of 3.4 ml, an enhancement factor of 75 and corresponding LOD of 3.4 ng $g^{-1}$ were reported. The method was validated by determining methyl Hg in DORM-2 CRM. The method described by Montiero *et al.*[170] employed the selective reduction of $Hg^{II}$ and methyl Hg with $NaBH_4$, using two gas–liquid separators in series, for the quantitative determination of these species in biological materials using CVAAS. Inorganic $Hg^{II}$ was reduced with 0.01% w/v $NaBH_4$ in the first separator and methyl Hg reduced with 0.3% w/v $NaBH_4$ and $FeCl_3$ in the second separator. The results from analysis of dogfish muscle and liver CRMs were in good agreement with certified values.

The group of Yang *et al.*[121,122] described a method for the determination of *methylmercury in fish tissue* using SPME and ID-GC-ICP-MS. Samples were digested with methanolic KOH, derivatised with sodium tetrapropyl bromate and adsorbed onto a polydimethylsiloxane coated capillary fibre for determination by GC-ICP-MS. Isotope dilution measurements with a laboratory synthesised methylmercury enriched with $^{198}Hg$ gave a three- to four-fold improvement in precision compared with standard additions calibration. An LOD of 37 ng $g^{-1}$ was reported and results from analysis of DOLT-2 and DORM-2 CRMs were in good agreement with certified values. Qvarnstrom *et al.*[171] also synthesised isotopically enriched organo-Hg species to study the metabolism of ethylmercury in mice treated with thimerosal (sodium ethylmercurithiosalicylate). Tissue samples were spiked with aqueous solutions of methylmercury containing $^{200}Hg$, ethylmercury containing $^{199}Hg$ and $^{201}Hg^{II}$ and were digested with 20% TMAH. Mercury species were extracted with DDC–toluene and derivatised with butylmagnesium chloride for quantitative determination using GC-ICP-MS. The authors reported that ethylmercury from thimerosal was rapidly taken up in kidney, liver and lymph node tissue. Tissue levels of both ethylmercury and inorganic Hg increased over 14 days of treatment, which indicated that ethylmercury was metabolised to $Hg^{II}$ in these tissues. Methylmercury determined in the tissues was found to be due to impurities in the thimerosal. The same author and Frech[172] used a $C_{18}$ column with an aqueous $CH_3COONH_4$–cysteine eluent to study the abiotic transformation of organomercury species during sample digestion with TMAH for their determination using HPLC-ICP-MS. They reported that abiotic methylation of inorganic Hg occurred during pH adjustment of the digested sample, but this was significantly reduced by prolonged treatment of tissue samples with TMAH over 24 h. Rai and colleagues[120] determined $Hg^{II}$ and methylmercury in fish tissues using HPLC-ICP-MS. Following enzymatic treatment with protease, extracts were applied to an ODS-PEEK column and Hg species eluted with 5% $CH_3OH$–$H_2O$ containing 0.06 M $CH_3COONH_4$–cysteine for quantitative determination

by ICP-MS. The addition of cysteine to the mobile phase eliminated peak tailing and memory problems. Analysis of DORM-2 dogfish and RM 50 albacore tuna CRMs gave results in good agreement with certified values.

Perhaps the 'bravest' piece of analytical chemistry undertaken in this review period was that reported by Rumbold and colleagues,[173] who determined levels of Hg in liver and tail muscle tissue *samples taken from 28 American alligators* captured in the Florida Everglades. Levels of Hg in the tissue samples were determined using CVAAS and all tissues had detectable levels of Hg ranging from 0.1 to 17 mg $kg^{-1}$.

**1.8.20 Molybdenum.** Keyes *et al.*[47] developed *an isotope dilution method for the quantitative determination of total Mo and Mo isotopes in human plasma* using ICP-MS. Plasma sample volumes of 0.5 ml were microwave digested with 1.4 ml $HNO_3$ in a PTFE beaker placed inside a PFA liner, to which was added a further 8 ml of $HNO_3$. This digestion procedure reduced blank values from 6.6 ng to 0.03 ng Mo. The method was validated by analysis of human serum CRM, giving a mean value of 1.02 μg $l^{-1}$ compared with a reference value of 1.07 μg $l^{-1}$.

**1.8.21 Nickel.** The highly sensitive technique of LA-HR-ICP-MS was used by Ghazi *et al.*[41] for quantitative profiling of Ni in *tissues surrounding nickel wire implants*. Pure nickel wire was implanted subcutaneously into rats for periods of 7 days. Tissue samples were analysed for Ni and Mg content using ablation with a Nd:YAG laser and quantitative determination of $^{24}Mg$ and $^{60}Ni$ isotopes by HR-ICP-MS. The authors recorded significant penetration of Ni into the tissues surrounding the implant. Concentrations as high as 60 μg $g^{-1}$ were determined at the implantation site and levels fell exponentially to undetectable levels 3–4 mm from the implant site.

*The potential confounding factor of cigarette smoking in biological monitoring of nickel workers has been recognised for many years*. The group of Torjussen *et al.*[174] reported the findings of a study to examine whether endogenous Ni in tobacco or Ni contamination on hand-rolled cigarettes provided a supplementary source of Ni exposure in smoking Ni process workers. Commercial cigarettes and cigarettes made by Ni workers were 'smoked' in a smoking machine and the mainstream smoke collected on electrostatic filters. The Ni content of the filters and the residual ash was determined by AAS. Levels of blood and urine Ni in smoking and non-smoking process workers were also determined by AAS. Less than 1.1% of the tobacco Ni was recovered in the mainstream smoke. The majority was recovered in the residual ash. No difference was observed in the levels of Ni in blood and urine between smokers and non-smokers. The authors concluded that inhaled Ni from the working atmosphere was the main source of Ni exposure for these workers.

**1.8.22 Platinum and noble metals.** Benkhedda *et al.*[34] simultaneously determined Pd, Pt and Rh in biological fluids (serum and urine) using FI-ICP-TOF-MS with USN sample introduction. All three analytes were selectively extracted from the biological matrix by complexation with diethylthiourea on a PTFE knotted reactor and subsequently eluted with 500 μl of $C_2H_5OH$ acidified with 1% $HNO_3$. Enrichment factors of 55, 5 and 2 were reported for Pd, Pt and Rh, respectively, giving LODs of 0.36 ng $l^{-1}$ for Pd, 0.54 ng $l^{-1}$ for Pt and 2.12 ng $l^{-1}$ for Rh. The researchers examined the effect of a number of potential interfering elements also present in the sample matrices on the extraction and determination of the Pt group elements. Hann and colleagues[175] *comprehensively assessed different sample preparation procedures and sample introduction systems for the determination of Pt in biological fluids and lung tissue* using SF-ICP-MS. Sample treatments included microwave digestion, open vessel digestion and simple dilution. Microconcentric nebulisation and USN, with and without membrane desolvation, were examined as sample introduction systems. With appropriate conditions selected reported LODs were 0.35 pg $g^{-1}$ for urine, 420 pg $g^{-1}$ for serum, 400 pg $g^{-1}$ for lung tissue and 13 pg $g^{-1}$ for microdialysates. Standard additions calibration was used for quantitative determination of Pt in urine, whilst ID-MS was used for quantification of Pt in other matrices.

As was the case last year, *the majority of papers published, during the review period, on the determination of Pt were associated with pharmacokinetic studies of anticancer drugs*. Several groups have published studies on cisplatin. Zamboni *et al.*[176] examined inter- and intra-tumour deposition of Pt following administration of cisplatin to mice with B16 melanoma tumours or H23 human xenografts. Serial extracellular fluid samples were collected using an implanted microdialysis probe and tumour tissue samples taken from around the probe site. Unbound Pt in extracellular fluid or plasma, and total Pt in tumour tissue, was quantitatively determined using ETAAS. The authors observed variable penetration of Pt from plasma into tumour extracellular fluid and suggested that this might be associated with the variable responses of tumours to cisplatin treatment. Kern *et al.*[177] also used ETAAS to determine concentrations of ultrafilterable Pt in patients with advanced gastric cancer who were undergoing intra-operative hyperthermic peritoneal lavage with cisplatin. Maximum plasma levels of Pt were significantly higher in lavage patients (2392 μg $ml^{-1}$) compared with patients administered *i.v.* cisplatin (1349 μg $ml^{-1}$) and the authors concluded that a significant proportion of intra-peritoneally administered cisplatin was available systemically. Two groups presented studies on the interaction of cisplatin with proteins. Hagrman *et al.*[178] studied the *in vitro* binding of cisplatin to metallothionein using HPLC, UV spectroscopy and AAS to monitor the reaction. Reaction conditions were selected to mimic clinical concentrations of cisplatin in tissue cytosol. The researchers calculated that the reaction kinetics of cisplatin with intracellular metallothionein was pseudo-first order and they concluded that cellular metallothionein could trap significant amounts of cisplatin. Mandal *et al.*[179] studied the interaction of cisplatin with haemoglobin (Hb) using a combination of HPLC-ICP-MS and nanoES-MS). The researchers identified Hb-bound Pt complexes in which cisplatin was bound to the α-chain, haem-α,β-chain and haem-β sub-units of the protein. The formation of Hb–cisplatin complexes was observed at clinical concentrations of cisplatin in the μM and sub-μM range. Pharmacokinetic studies of the anti-cancer drug oxaliplatin were published. Delord *et al.*[180] used ETAAS to determine Pt in blood, ultrafilterable plasma and urine samples from 40 patients receiving oxaliplatin treatment for advanced colorectal cancer. The analytical data was analysed using the NONMEM pharmacokinetic computer programme. Changes in the blood Pt concentration with time were best described by a three-compartment model, with first-order elimination from the central compartment. Elias *et al.*[181] conducted a clinical study of intra-peritoneal chemo-hyperthermia with oxaliplatin in hypotonic solution. Concentrations of Pt in plasma and peritoneal tissue were determined using AAS. The researchers reported that, in contrast with experimental studies, results from this clinical study showed no significant increase in tumour or systemic penetration of oxaliplatin with hypotonic solutions. They did, however, note an unexplained increase in peritoneal bleeding and thrombocytopaenia with this administration regime.

Smith and colleagues[182] compared HPLC-MS-MS with HPLC-ICP-MS for the quantitative determination of the Pt *anticancer drug ZD0473* and its related biologically active metabolites in plasma samples from dogs administered the drug. The authors considered that HPLC coupled with ICP-MS detection had an advantage over the MS-MS system due to its better linear dynamic range and greater analytical

sensitivity. An LOQ of 0.1 ng $ml^{-1}$ was reported for the drug using HPLC-ICP-MS. Bouma and colleagues[183] used ETAAS to determine free Pt and release of small Pt species in formulations of a novel polymer conjugated Pt drug, AP5280. Total Pt concentrations in the co-polymer were determined using FAAS. The analytes formed part of an array of quality control tests developed to monitor the molecular integrity of the drug during manufacture. The stability of carboplatin solutions stored at room temperature for up to 78 months was investigated by Schnurr *et al.*[184] Decomposition of the drug was monitored using HPLC coupled with AAS. The researchers reported losses of carboplatin between 3% and 7.3% and noted that degradation was only dependent on time of storage. In solutions containing CBDCA additive, the breakdown of carboplatin was not suppressed but the pattern of degradation products was altered to include both hydrophilic aqua complexes, hydroxy Pt and hydrophobic products.

Finally, two groups presented findings *of environmental and biological monitoring studies of hospital personnel* exposed to Pt drugs. Leboucher *et al.*[185] used a surface sampling approach to monitor contamination in a hospital pharmacy drug preparation area. Concentrations of Pt in the surface samples were determined using AAS. The group observed that, whilst the inside of the biological safety cabinet used for drug preparation was contaminated, the area immediately outside of the cabinet showed little or no contamination. Gloves worn by the staff preparing drugs were often contaminated. The authors recommended that gloves be changed frequently and that the safety cabinet and surrounding area be thoroughly cleaned every day. Turci *et al.*[186] monitored the exposure of hospital workers to different anticancer drugs. Urine samples were collected from 9 staff at the beginning, the end and during a work shift on two consecutive days. Concentrations of Pt in the urine were determined using ICP-MS, whilst urine levels of ifosfamide, cyclophosphamide and methotrexate were determined using HPLC-MS-MS. Three workers had elevated urinary Pt levels (920–1300 ng $l^{-1}$). The researchers considered the methods to be suitably simple and reliable to identify exposure of hospital staff to hazardous anti-neoplastic drugs.

**1.8.23 Selenium.** *Interest in the metabolism of Se and its role in health and disease continues to stimulate much research on this element*. Many groups have described methods for the quantitative determination of total Se and Se species in biological matrices. Hernandez-Caraballo *et al.*[187] described a simple method for the determination of total Se in serum using ETAAS. Serum samples were diluted 1 + 4 v/v with 1% $NH_4OH$–0.5% Triton X-100 and injected with a Pd–$Mg(NO_3)_2$ chemical modifier. Standard additions calibration was used for quantitative determination of Se and an LOD of 6 μg $l^{-1}$ was reported. Milde and colleagues[188] reported the results of a comprehensive study of analytical conditions for the determination of Se in serum using AAS. The researchers examined various chemical modifiers for determination by ETAAS and the effect of interfering substances in acid digested samples on quantitative determination by HGAAS. A rapid simple method for the determination of Se in serum using ICP-MS was described by Labat *et al.*[189] Serum samples were diluted with $HNO_3$–Triton X-100–n-butanol and an LOD of 0.5 μg $l^{-1}$ was reported. Good agreement ($r^2 = 0.96$) was reported for serum Se values determined by this method and by a method using ETAAS.

Determination of Se by ICP-MS is affected by interferences from $^{38}Ar^{40}Ar$ and $^{40}Ar^{40}Ar$ species on $^{78}Se$ and $^{80}Se$ masses. *These interferences were almost completely eliminated* in the method described by Reyes and colleagues,[39] which used ICP-MS with an octapole reaction system and $H_2$ as the reaction gas. Detection limits for $^{78}Se$ were improved five-fold compared with conventional quadrupole ICP-MS and enabled $^{80}Se$ to be quantitatively determined. The method was used to determine $^{78}Se$ : $^{77}Se$ and $^{80}Se$ : $^{77}Se$ isotope ratios in biological samples spiked with an enriched $^{77}Se$ solution. Selenium concentrations in serum, urine and tissue CRMs were determined using this isotope dilution method and results were in good agreement with certified values. The same group[40] used affinity chromatography coupled with the same reaction cell ICP-MS system to determine Se containing proteins in human serum. Quantitative measurements were made by ID analysis in which a $^{77}Se$ enriched spike solution was added to the chromatography column eluent and the $^{78}Se$ : $^{77}Se$ and $^{80}Se$ : $^{77}Se$ ratios determined. The measured distribution of Se among serum proteins was glutathione peroxidase (20%), selenoprotein P (55%) and albumin (20%). Sloth *et al.*[38] also used ICP-MS with a dynamic reaction cell to determine total Se and $^{77}Se$ in human plasma, urine and faeces samples collected from subjects who had been given a single dose of intrinsically $^{77}Se$ labelled yeast. Liquid samples and acid digested faecal samples were diluted with 2% $HNO_3$–3% $CH_3OH$–0.5% Triton X-100 and the $^{76}Se$, $^{77}Se$ and $^{80}Se$ masses were measured. Reported LODs were 0.1 μg $l^{-1}$, 0.2 μg $l^{-1}$ and 6 μg $kg^{-1}$ for plasma, urine and faeces, respectively.

Several groups have used *chromatography coupled with various spectroscopic detection systems* for the quantitative determination of Se species in biological matrices. Sanz-Medel and Blanco-Gonzalez[190] presented an important review on the application of chiral speciation methods for seleno-amino acids in biological samples. Zheng *et al.*[191] used reversed-phase HPLC coupled with ICP-MS to examine the stability of five major Se species: selenate ($Se^{VI}$), selenourea, trimethylselenonium (TmSe), selenomethionine (SeMet) and selenoethionine (SeEt) in a pooled human urine sample. The urine was stored in the dark at various temperatures without addition of any stabilising agents. The researchers reported that all five species remained stable for short periods of up to one month when stored at −20 °C, but stability decreased as the storage temperature was increased. Chatterjee *et al.*[192] used gel permeation HPLC and cation-exchange chromatography to separate selenite, selenate, SeEt and SeMet and TMSe in aqueous and urine samples for quantitative determination using ICP-MS. Two additional unknown Se species were detected in NIES 18 urine CRM by both chromatographic systems. Gammelgaard and colleagues[193] used multi-dimensional HPLC coupled with ICP-MS together with atmospheric pressure chemical ionisation MS (APCI-MS) to identify a major Se metabolite in human urine collected from volunteers given Se nutritional supplements. The metabolite was quantitatively determined in urine samples, from six male volunteers, using ion-pair chromatography and ICP-MS. Urine samples containing the metabolite were pooled and the Se metabolite further purified and concentrated using reverse-phase chromatography followed by SEC. The *m/z* of the Se metabolite was determined to be 300 using APCI-MS and was identified by the authors as being the selenosugar methyl-n-acetylselenohexosamine. Ogra *et al.*[194] identified monomethylseleninic acid in a partially purified rat urine sample using HPLC coupled with ICP-MS. They established that the Se species was a metabolite artefact caused by oxidation of selenosugar, which emphasised the need for care in handling and storing of samples before analysis to prevent formation of these artificial seleno compounds. Suzuki and Ogra[195] investigated the metabolism of $Se^{III}$ and $Se^{VI}$ in rats given *i.v.* doses of $^{82}Se$ enriched $Se^{VI}$ and $Se^{III}$. The authors used gel filtration HPLC coupled with ICP-MS to quantitatively determine Se species in body fluids and tissues. They reported that selenite was rapidly taken up by erythrocytes, reduced to selenide and then transported to the plasma where it was bound to albumin and transferred to the liver. Selenate was either directly taken up by the liver or excreted in the urine.

The *relationship between selenium status and cancer risk* continues to be investigated. Prevo and colleagues[196] reported

the results of a cross sectional study of serum Se levels and markers of neoplastic progression in patients with Barrett's oesophagus. Serum Se concentrations were determined using ETAAS, and DNA content of oesophageal tissue determined by flow cytometry. The authors noted that patients with serum Se levels in the upper three quartiles ($>1.5$ μM) were less likely to have high-grade dysplasia or aneuploidy than those with Se levels in the lower quartile. They hypothesised that higher serum Se levels may be associated with a reduced risk of oesophageal cancer for patients with Barrett's oesophagus. Last *et al.*[197] examined the relationship between serum Se status and both first treatment response and overall survival in patients with aggressive non-Hodgkins lymphoma. Serum samples were taken from patients at presentation and were frozen for retrospective determination of Se using ICP-MS. Serum Se concentrations ranged from 0.33 μM to 1.51 μM. The researchers used multivariate analysis to show a positive correlation between serum Se level and response to first treatment with chemotherapy and radiotherapy and also achievement of long-term remission. They concluded that serum Se concentration at presentation was a prognostic factor for treatment response and long term survival, and that Se supplementation may offer a therapeutic strategy for non-Hodgkin's lymphoma.

**1.8.24 Sodium.** To support the accurate determination of Na in serum, an analysis routinely carried out in clinical laboratories, the National Institute of Standards and Technology (NIST) produces serum CRMs (series 909 and 956). *Long and Vetter*[198] *developed a method for the accurate determination of Na in serum CRM using ICP-MS, as an alternative to the time consuming gravimetric method presently employed to assign certified values to the RMs*. The method was described as a cross between ID and internal standardisation. Diluted serum was spiked with an enriched $^{26}Mg$ isotope and the $^{23}Na : {}^{26}Mg$ isotope ratio measured in analog detection mode. Measured ratios were standardised against a Na primary standard spiked with $^{26}Mg$.

**1.8.25 Strontium.** *In a study to investigate the relationship between bone Sr levels and bone histomorphometric parameters, Gerstenfeld et al.*[199] *used ICP-MS to determine Ca : Sr ratios in bone biopsy specimens taken from haemodialysis patients*. Bone samples were classified into different groups based on histological criteria. The authors noted that patients giving biopsy samples with Sr levels higher than 1.4 μg Sr per mg Ca showed higher levels of bone formation histomorphometric parameters and higher levels of serum alkaline phosphatase. They reported, however, that although biopsy samples with higher bone Sr had higher levels of osteoid tissue, the hypothesis of Sr induced osteomalacia could not be proven.

**1.8.26 Titanium.** Frisken *et al.*[92] used ETAAS *to determine Ti in organ tissues of sheep, following implantation into the mandible of Ti screw implants*. Levels of Ti in tissue samples taken from the regional lymph nodes, lung, liver and spleen of sheep with successful implants were not statistically different from control animals. In contrast, sheep whose implants failed to integrate had higher levels of Ti in lung (2–4 times higher) and lymph node (7–9.4 times higher). The authors concluded that debris from failed implants was unlikely to pose an additional health risk and that the sheep was an excellent model for monitoring biological changes associated with successful and failed Ti implants.

**1.8.27 Uranium.** *There has been further interest during this review period in the quantitative determination of U in biological matrices*. Bouvier-Capely *et al.*[200] described a rapid method for the determination of U in urine using ICP-MS. The method was used to determine U concentrations in occupationally exposed workers and the results obtained were in good agreement with results obtained using conventional fluorimetric and α-spectrometric methods. The authors noted, however, that the described ICP-MS method was insufficiently sensitive for accurate measurement of the $^{234}U$ isotope and considered that a chemical purification step was necessary.

Durakovic and colleagues[201] determined *U isotopes in urine* samples from 27 Gulf War veterans, using TIMS with a secondary electron multiplier detector and ion counting system. The researchers reported the presence of depleted uranium, with a $^{238}U : {}^{235}U$ ratio greater than 207.15, in nearly half of the individuals tested. Kryslek and Ritsema[202] used HR-ICP-MS to determine total U and U isotope ratios in human urine samples from non-occupationally exposed subjects. The researchers examined the effects of sample storage conditions on the stability of U in the urine matrix. Uranium concentrations remained stable in acidified refrigerated samples, but decreased in non-acidified samples stored at room temperature. Schramel also determined $^{235}U : {}^{238}U$ isotope ratios in human urine using HR-ICP-MS. Sample preparation involved UV photolysis of the urine matrix. The method was sufficiently sensitive to quantitatively determine urinary U concentrations of less than 10 ng $l^{-1}$.

An estimation of *dietary intake of U in Italy* was made by Galletti *et al.*[203] The authors determined U in food, water and other beverages using ICP-MS and estimated a daily U intake of 2.9–4.8 μg. Both tap water and bottled mineral water were major contributors to the daily intake. The authors also determined U in urine samples from 38 unexposed subjects from the Rome district. A mean urine U concentration of $10 \pm 7$ ng $l^{-1}$ was reported. Zamora *et al.*[204] also used ICP-MS to investigate dietary U uptake and excretion in Canadian subjects, in order to establish an appropriate value for gastrointestinal absorption of U in setting a guideline for drinking water.

**1.8.28 Vanadium.** In addition to the method described for the determination of Cr in *parenteral solutions*, Wuilloud and colleagues[19] developed a method for the determination of V in the same matrix using cloud-point precipitation and FI-ICP-AES. Vanadium was extracted, as a complex with 2-(5-bromo-2-pyridylazo)-5-diethylaminophenol (PADAP) at pH 3.7, in micelles of PONPE 5.0, a non-ionic surfactant. A 100 μl aliquot of the surfactant rich extract was mixed with an equal volume of $C_2H_5OH$ and injected into the nebuliser of the ICP–AE spectrometer for quantitative determination of V. An enrichment factor of 250 from a starting volume of 50 ml was reported, giving an LOD of 16 ng $l^{-1}$. Yang *et al.*[36] described a rapid sensitive method for the determination of V in biological fluids using HR-ICP-MS. Samples were simply diluted 1 + 19 v/v in 0.3% $HNO_3$. Using a resolution setting of 4000, the $^{51}V$ signal was completely separated from the spectral interference by $^{35}Cl^{16}O$ which is present in both serum and urine matrices. Quantitative determination of V was achieved using standard additions calibration with a pooled urine or serum sample. An LOD of 10 ng $l^{-1}$ and precision better than 4% RSD was reported for both matrices. The method was assessed by analysing SLRS-4 river water CRM. The mean value determined for repeated daily analyses (0.337 ng $ml^{-1}$) was in good agreement with the certified value (0.32 ng $ml^{-1}$).

*Vanadium concentrations in autopsy lung tissue from residents of Mexico city* were determined by Fortoul *et al.*[205] using AAS. The researchers reported that lung samples from the 1990s had significantly higher concentrations of V than samples from the 1960s and the increase was not correlated with smoking status, occupation or cause of death. They concluded that ambient air concentrations of V were increasing in the city and represented a potential health hazard for city residents.

Oral administration of V is currently being investigated as a drug treatment for *non-insulin-dependent diabetes*. Heinemann

*et al.*[206] investigated the pharmacokinetics of V in humans following administration of a single 90 ml *i.v.* dose of a 20% albumin infusion containing 47.6 μg of V. Serum and urine concentrations of V were determined using ETAAS. The elimination of V from serum was described by a three-compartment model with half-lives of 1.2 h, 26 h and 10 d, respectively. A steady state volume of distribution of 54 l was calculated and around 52% of the administered dose of V was recovered in the urine after 12 days.

**1.8.29 Zinc.** Ingle and colleagues[51] determined total Zn and Zn *isotope ratios in human faecal samples*, using HR-ICP-MS with a multi-collector detector, in a study investigating the absorption of Cu, Fe and Zn from different diet types. Volunteers were administered a solution containing $^{70}$Zn and absorption was monitored by measuring the change to the natural Zn isotope ratio in the collected faecal samples. The $^{70}$Zn isotope was determined using an instrument resolution of 2350 and detection with an electron multiplier in the multi-collector array. The $^{67}$Zn, $^{68}$Zn, $^{69}$Ga and $^{71}$Ga isotopes were simultaneously determined using a low-resolution setting (400) and Faraday collectors. The authors noted that use of internal standardisation to correct for instrument drift was limited because of the use of different detector types. The method was validated by analysing NIST 1577b CRM over a 7 month period. Total Zn measurements and Zn isotope ratio measurements made with this HR method showed good agreement with total Zn determined using conventional ICP-MS and isotope ratios determined using TIMS.

*Kelishandi et al.*[207] *examined the relationship between dietary Cu and Zn intake and premature risk of cardiovascular disease in children*. Four-day dietary Cu and Zn intake was monitored in 100 children whose parents had premature myocardial infarction, and in 100 age and gender matched controls. Serum Cu and Zn concentrations were determined using FAAS. The researchers reported that daily Zn intake was significantly lower in the study group (6.89 mg *versus* 8.3 mg) but the mean serum Zn was not significantly different between study cases and controls (82.2 μg dl$^{-1}$ *versus* 92.3 μg dl$^{-1}$). They did note, however, that Zn deficiency was more prevalent among boys in the study group compared with controls (58% *versus* 18%). There was no significant difference in dietary intake of Cu or serum Cu levels between study subjects and controls. The authors concluded that emphasis be placed on the consumption of Zn rich food by children, particularly those with a family risk of premature cardiovascular disease. Schlegel-Zawadka *et al.*[208] investigated the dietary habits and Zn status of healthy adolescents. Levels of Zn in serum, erythrocytes and hair samples from 157 eleven-year-olds were determined using AAS. The parents of the children completed a food frequency questionnaire to assess the types of food eaten by the children and the frequency of consumption. Mean levels of Zn determined in erythrocytes and serum were 8.6 mg l$^{-1}$ and 0.79 mg l$^{-1}$, respectively. The authors reported significant correlation between serum, erythrocyte and hair Zn levels and the frequency of intake of specific food products. For example, hair Zn was correlated with meat and fish intake, erythrocyte Zn with fruit and cheese and serum Zn with fruit, bread and milk.

Sampson and colleagues[209] reported a *new disorder of zinc metabolism* characterised by repeated infections, inflammation and hyperzincaemia. Plasma Zn was determined using AAS and plasma concentrations of the Zn-binding protein calprotectin using an ELISA assay. The researchers assessed 5 patients with the disease, two of whom were related. All patients showed extreme hyperzincaemia (77–200 μmol l$^{-1}$, reference 11–18 μmol l$^{-1}$) and had elevated plasma calprotectin levels (1.4–6.5 g l$^{-1}$, reference level $<1$ mg l$^{-1}$).

Weisstaub *et al.*[210] investigated the *effect of low dietary calcium during pregnancy on zinc levels in maternal blood and bone* of rats. Zinc levels in erythrocytes and ashed femur samples were determined using AAS. Both erythrocyte Zn concentrations and femur Zn levels showed an increase in rats fed a low Ca diet throughout pregnancy and lactation, which led the authors to hypothesize that dietary Ca deficiency, during pregnancy, causes an increase in Zn utilisation. Cho and colleagues[211] studied changes in serum and prostate tissue Zn levels following intra-prostate injections of Zn in rats. Rats were injected with 2 ml of 0.04 M $ZnSO_4$, either as a solution or in liposomes. Serum and prostate tissue Zn concentrations were quantitatively determined using ICP-AES. The researchers reported that serum Zn levels did not change significantly following injection of Zn. Prostate Zn levels rose to a peak level after 2 days and remained elevated over the 4-week study period. The authors concluded that intra-prostate injections of Zn increase and maintain prostate Zn levels without any local or systemic toxicity and may have clinical relevance to the treatment of chronic prostatitis.

## 2 Analysis of foods and beverages

The comprehensive ASU for 2003 *reviewed recent developments* in atomic spectroscopy applied to the analysis of foods and beverages.[1] Careri *et al.*[212] discussed the use of several MS-based techniques for determining naturally occurring compounds and contaminants in food. They included speciation procedures with MS for analyte detection. Specific issues relating to measurement of As and its species found in seafood were reviewed by McSheehy *et al.*[129] Topics included the validation of methods, separation techniques and preparation of a candidate oyster RM.

### 2.1 Sampling and sample preparation

**2.1.1 Extraction.** *To achieve a meaningful speciation analysis it is imperative that there are no structural changes to analyte compoundslions during the course of extraction and separation procedures*. In a monumental investigation to determine Se in broccoli, 27 variables covering pH values from 1 to 9 and different liquid and solid phase extractions were explored.[213] Whatever system was used, it appeared that some volatile compounds were lost (up to 30% of the total) and the authors concluded that extraction conditions should match those within the matrix. In addressing the same problem proteolytic enzymes were employed by a number of workers to disrupt samples while preserving the natural speciation. Measurements of As, Hg and Se in a range of sample types including oyster, fish and yeast were reported.[120,214,215] However, conclusive evidence that no changes had taken place was often lacking. Extraction with cold $HClO_4$ was also claimed to maintain the original Se species in yeast.[216] Use of TMAH is not new nor uncommon but it is now being recognised that problems may be introduced by this agent. When the extraction of Hg from fish was investigated it was found that leaching with HCl gave excellent results while $CH_3OH$–TMAH, $CH_3OH$–KOH, or sodium dodecylsulfate were less satisfactory and the use of TMAH led to formation of dimethylmercury.[119] In another comparative extraction experiment, to determine Fe in rice, use of TMAH gave poor precision and contamination.[217] Extraction into a slurry with 1.4 M $HNO_3$ and ultrasonic agitation proved to be effective and gave accurate results for a CRM. Yebra and Moreno-Cid[218] described a simple method for the determination of Mn in solid seafood samples by FAAS, using a continuous ultrasound extraction system to extract Mn from the biological matrix. An LOD of 0.4 μg g$^{-1}$ was reported for a 30 mg dry sample and the method was validated by analysing TORT-1 CRM. To determine $BrO_3^-$ Akiyama *et al.*[219] developed an unusually prolonged procedure that included extraction with water, a 0.2 μm filter and thenx removal of fat, halide anions and protein with a $C_{18}$ cartridge, a silver cartridge and centrifugal ultracentrifugation,

**Table 1** Analysis of clinical and biological materials

| Element | Matrix | Technique; atomization; presentation[a] | Sample treatment/comments | Ref. |
|---|---|---|---|---|
| Ag | Nasal mucosa | MS;ICP;LA | A case was reported of Ag tattooing of the nasal mucosa in a silver polisher. The diagnosis was confirmed by LA-ICP-MS, which eliminated concerns that there may have been melanoma | 335 |
| Al | Parenteral nutrition solutions | AA;-;- | Al content was determined in 35 commercial products and in substances used as raw material for their preparation. Contamination during the manufacturing process was identified | 104 |
| Al | Parenteral solutions | AE;ICP;FI | A method based on combined cloud point preconcentration with PONPE 7.5 and FI-ICP-AES was developed to measure Al in parenteral solutions. For an initial sample of 50 ml of parenteral solution LOD was 0.25 $\mu g\ l^{-1}$ | 20 |
| Al | Serum | AA;ETA;L | Retention of serum proteins in the autosampler capillary, depending on the tubing material (Tygon > silicone rubber > PTFE), was observed. Rinsing with water, diluted $HNO_3$ or diluted Triton X-100 did not promote complete desorption of the proteins. Total elution and improved RSD% (<10%, $n = 10$) was achieved with $CH_3OH$ | 94 |
| Al | Tissue | PIXE;-;- | Micro-beam PIXE was applied to study the distribution of elements in tissue surrounding dental Ti implants, after up to 9 y from insertion. The elemental maps indicated small Ti deposits, while Al leaked diffusely into the surrounding bone and V was not found in the tissues | 56 |
| Al | Urine (rabbit) | AA;-;L | A significant increase of Al urinary excretion was observed in rabbits treated with deferiprone, a chelating agent, alone or in combination with ascorbic acid or sodium-2-mercaptoethane sulfate (mesna) | 126 |
| As | Blood, bile, urine, liver and kidneys | AF;Hy;HPLC | The effect of $Se^{IV}$ administration (10 $\mu mol\ kg^{-1}$, *i.v.*) on the appearance of As metabolites in blood, bile and urine and their distribution in the liver and kidneys was evaluated in rats injected *i.v.* with 50 $\mu mol\ kg^{-1}$ $As^{III}$ or $As^{V}$ | 336 |
| As | Blood, hair, urine and nails | MS;ICP;- | The difficulties of As determination in clinical samples by ICP-MS were overcome using a simple correction equation and adding an organic solvent. Samples were digested in concentrated $HNO_3$ (blood and hair) or by means of a microwave oven (urine and nails) | 337 |
| As | Chinese medicines | AF;Hy;FI | Samples were digested with $HNO_3$–$HClO_4$. Thiourea was added to reduce $As^{V}$ to $As^{III}$, and minimize interferences from $Cu^{II}$, $Fe^{III}$, $Hg^{II}$ and $Se^{IV}$ on the determination of total As. The mechanisms of interference were discussed. LOD was 0.114 ng $ml^{-1}$. Analytical recovery of 4 ng $ml^{-1}$ As from Chinese medicines ranged from 95 to 105%. RSD ($n = 11$) was 0.68% at 5 ng $ml^{-1}$ | 244 |
| As | Environmental and biological samples | MS;ICP;HPLC AA;Hy;- MS;ES;- | The progress over the last decade of analytical methodologies for As speciation in environmental and biological matrices was reviewed | 127 |
| As | Hair | MS;ICP;ETV | As and Se were determined in human hair by ETV-ICP-MS. Sample (0.5 mg) pretreatment required digestion with $HNO_3$–$H_2O_2$ in a PTFE high-pressure decomposition vessel, followed by addition of 25 µl of 1 µM $KMnO_4$ and evaporation to dryness. $KMnO_4$ was essential to prevent analyte losses (30–50%), as shown by the results of analyses of a CRM | 101 |
| As | Hair | XRF;-;- | SRXRF was applied to follow the As content in hair of patients receiving $As_2O_3$ as a new treatment against leukaemia. The transverse distribution of As was obtained in hair cut in 30 µm slices | 98 |
| As | Hair, drinking water | AE;ICP;Hy | Patients (311) with arsenism, due to long term exposure from As in drinking water, from the rural district Bayinmaodao, Inner Mongolia, China, were examined. As levels in hair were higher with increasing severity of the disease, and were positively correlated with As in water from local wells | 95 |
| As | Nail, hair | MS;ICP;HPLC | To investigate the speciation of As in human nail and hair, samples were collected from the As-affected area of West Bengal, India, and their water extracts were analysed by HPLC-ICP-MS. $As^{III}$, $As^{V}$, $MMA^{V}$ and $DMA^{V}$ were identified in nail and hair, but $DMA^{III}$ was only present in nail. The determination of DMA in nail and hair was suggested as a possible biomarker of As exposure | 97 |
| As | Plasma, bile, urine | MS;ICP;HPLC | Free and glutathione-conjugated As metabolites in the bile and urine were speciated simultaneously on ion exchange columns by HPLC-ICP-MS | 128 |
| As | Plasma, whole blood | AA;-;L | The bioavailability of As from oral or *i.v.* intravenous $As_2O_3$ dosage was compared by measuring As concentrations in timed collections of blood from patients treated for haematological malignancies | 338 |
| As | Reaction mixtures with metallothionein | MS;ICP;SEC MS;ES;- | The interactions of As and its trivalent metabolites with metallothionein were investigated by SEC-ICP-MS, and ES quadrupole TOF-MS/MS | 339 |
| As | Urine | AA;ETA;L AA;Hy;L | As, Be and Se concentrations in urine of workers in the steel industry and controls were determined after microwave oven digestion. Steel workers showed significantly higher levels than controls | 80 |
| As | Urine | AA;ETA;L | The trueness, precision, recovery, LOD and LOQ of a method for the determination of As in urine by ETAAS after toluene extraction were determined. The method was applied to the measurement of urine samples from workers of a large coal-fired Slovak power plant | 340 |
| As | Urine | MS;ES;L AF;Hy;HPLC | The mechanism of action of DMPS in the treatment of acute As poisoning was investigated. A DMPS complex with $MMA^{III}$ was identified in human urine after administration of DMPS, and characterized using HPLC-HG-AF and ES-MS | 133 |

**Table 1** Analysis of clinical and biological materials (*Continued*)

| Element | Matrix | Technique; atomization; presentation[a] | Sample treatment/comments | Ref. |
|---|---|---|---|---|
| As | Urine | AA;Hy;HPLC | The influence of controlled consumption of marine fish on the urinary excretion of As metabolites ($AsO_3^-$, $AsO_4^-$, DMA, MMA) was investigated | 130 |
| As | Urine | MS;ICP;HPLC | As species ($As^{III}$, $As^{V}$, $MMA^{V}$, $MMA^{III}$, $DMA^{V}$ and AB) in human urine were stable for up to 6 months when stored at −20 °C. Losses of As occurred during urine filtration (<5%) and centrifugation (from 1/2 to 1/17 of soluble As) | 134 |
| As | Urine | AA;Hy;- AA;Hy;HPLC | Total As and As metabolites ($As^{III}$, $As^{V}$, MMA and DMA) were monitored in urine of samples collected for 7 consecutive days from 30 maintenance engineers and controls from six wafer fabrication facilities to assess exposure | 135 |
| As | Urine | AA;Hy;FI | The speciation of $As^{III}$, $As^{V}$, MMA and DMA in human urine was achieved by means of a low cost technique, based on ion-exchange chromatography and FI-HG-AAS. LODs for individual species ranged from 1.0 to 2.0 μg $l^{-1}$. In urine samples from patients in Hajiganj, Bangladesh, $As^{III}$ was the major As species | 341 |
| As | Urine | MS;ICP;HPLC AA;Hy;FI | Total As in urine was determined by FI-HG-AAS and $As^{III}$, $As^{V}$, $MMA^{V}$ and $DMA^{V}$ were separated and quantified using HPLC-ICP-MS. The results of a study in children and adults from an As contaminated area in Bangladesh were discussed | 137 |
| As | Urine | AA;Hy;HPLC | The urinary excretion of $As^{III}$, $As^{V}$, $MMA^{V}$ and $DMA^{V}$ was determined in a case of attempted suicide by ingestion of $As_2O_3$ (*ca.* 0.6 g) receiving immediate therapy with DMPS | 132 |
| As | Urine | AA;Hy;L | As and Se concentrations were measured by HGAAS in spot urine samples from the inhabitants of two rural communities of north east Bangladesh. A negative correlation between As and Se levels was found in both males and females. The possible toxicological significance of the interaction was discussed | 79 |
| As | Urine (sheep) | MS;ICP;HPLC MS;ES;HPLC | A new As metabolite, found in sheep's urine after arsenosugar ingestion, was identified by the parallel use of HPLC-ICP-MS and HPLC-ES-MS as dimethylarsinoylacetate | 342 |
| As | Urine, serum | MS;ICP;L | The effect of 1% concomitant elements, such as C, Cl, K, N, Na, P and S, on the signal of 100 μg $l^{-1}$ Ge, As or Se in human urine and serum was investigated | 30 |
| As | Water, hair | EDXRF;-;- | As content was measured by EDXRF in samples of drinking water and scalp hair from the As affected areas of Bangladesh. About 61% of the water samples had As levels >0.05 mg $l^{-1}$ with a maximum level of 0.83 mg $l^{-1}$, thus contributing significantly to the As intake. The average concentration of As in hair samples from subjects drinking contaminated water was 14.1 mg $kg^{-1}$, as compared with reference levels of <3.0 mg $kg^{-1}$ | 96 |
| Au | Blood | MS;ICP;L | Au levels in blood samples from 80 patients referred for patch testing because of eczematous disease were higher in those with dental gold restorations (range <0.04–1.07 μg $l^{-1}$) than in those without (range <0.04–0.15 μg $l^{-1}$), but no statistically significant difference was observed for blood Au levels between persons with and without contact allergy to gold | 153 |
| B | Human albumin, blood and plasma | AE;ICP;L | Matrix effects in the analysis of B and Ti in blood and plasma samples by axial view ICP-AES were investigated, using human albumin as a model, several elements (Y, Pd and Pt) and analytical wavelengths for internal standardization and different instrumental settings | 28 |
| B | Urine, blood plasma | AE;ICP;- MS;ICP;L | A possible metabolite of *p*-boronophenylalanine–fructose, a compound administered for boron neutron capture therapy, was detected for the first time in urine and blood plasma of patients, using separation on a porous graphitic carbon column coupled on-line to ICP-AES and TOF-ICP-MS. The preliminary investigations carried out on this compound were reported | 141 |
| Be | Lung tissue | AA;-;- | To investigate its usefulness to differentiate between chronic beryllium disease (CBD) and sarcoidosis, Be was determined in the autopsied lung tissues of 29 subjects, including one case of CBD, three confirmed cases of sarcoidosis and 25 controls. However, the CBD case had Be levels within the range of reference values reported in the literature | 138 |
| Be | Urine | AA;ETA;L AA;Hy;L | See As, ref. 80 | 80 |
| Bi | Serum | MS;ICP;FPLC | The competitive binding of Bi to serum proteins (albumin and transferrin) was investigated. Over 70% of Bi was bound to transferrin even in the presence of a large excess of albumin (albumin : transferrin = 13 : 1) unless iron-saturated transferrin was used | 140 |
| Bi | Urine | AA;ETA;L | The performance of chemical modifiers (none, Pd + Mg, Ir in solution, Ru, Ir or Zr independently as permanent modifier and Ir + Rh as permanent modifier) was investigated for the direct determination of Bi in urine by ETAAS. Samples were diluted 1 + 1 with 1% v/v $HNO_3$. The best performance was obtained with Ir + Rh, which gave a $m_0$ of 29.2 pg *v* a technical specification of 30 pg and an LOD of 50 pg | 139 |
| Ca | Brain cells | XRF;-;- | SRXRF was applied to the mapping and quantification of Ca, Fe and Zn in neurons from brain tissues of patients with Alzheimer's disease. Clear images of single neurons were obtained | 53 |

**Table 1** Analysis of clinical and biological materials (*Continued*)

| Element | Matrix | Technique; atomization; presentation[a] | Sample treatment/comments | Ref. |
|---|---|---|---|---|
| Ca | Food, faeces, urine | AA;F;- | Ca intake from food and Ca output in faeces and urine was measured to determine Ca balance from vegan and lactovegetarian diets, investigated experimentally in human volunteers. Neither Ca balance nor urinary deoxypyridinoline, a marker of bone resorption, were significantly affected | 343 |
| Ca | Urine | MS;ICP;- | A novel dual radio- and stable-isotope method for measuring Ca absorption from a single meal in humans was compared with the whole-body radioisotope retention method. There was a high degree of agreement between the methods | 48 |
| Ca | Urine | MS;ICP;L | ICP-MS operating at medium resolution (4300) was used to investigate methods to reduce polyatomic interferences on Ca isotope ratios in urine. Oxalate precipitation of urinary Ca and desolvation sample introduction were proved useful in reducing interferences and allowed the determination of the $^{42}Ca$, $^{43}Ca$, $^{44}Ca$, $^{46}Ca$ and $^{48}Ca$ isotopes at low resolution | 49 |
| Cd | Biological samples | AA;F;S | A direct solid sampling FAAS procedure was developed for the determination of Cd in biological samples. Analysis of RMs gave results typically within the 95% confidence interval of the certified and/or reference values, and precision, as RSD, was between 3.9 and 6.7% | 15 |
| Cd | Biological samples | AA;ETA;L | Samples were mixed with 25% m/v TMAH, made up to 50 ml and heated at 60 °C for 1 h. A Ru permanent modifier was employed (one addition lasted for 300 atomization cycles). The LOD was 0.05 μg $l^{-1}$ | 8 |
| Cd | Blood | AA;ETA;L | After complexation with *O,O*-diethyldithiophosphate in HCl, Cd, Pb and Pd in digested blood were quantitatively extracted to the phase rich in the nonionic surfactant Triton X-114 (cloud-point extraction). 0.1 mol $l^{-1}$ $HNO_3$ in $CH_3OH$ was added to the surfactant-rich phase prior to analysis by ETAAS using Ir or Ru as permanent modifiers. LODs were 0.02 μg $l^{-1}$, 0.08 μg $l^{-1}$ and 0.014 μg $l^{-1}$ and the enrichment factors were 71, 34 and 100 for Cd, Pb and Pd, respectively. The method was validated by analysis of two blood CRMs and recovery tests | 18 |
| Cd | Blood, cord blood and amniotic fluid | AA;ETA;L AA;Hy;L | Cd and Se concentrations in maternal and umbilical cord blood and amniotic fluid from 60 women during the last trimester of pregnancy were investigated in relation to smoking habit. In smokers, Cd in blood was higher and Se in both maternal and cord blood was lower, suggesting that Cd may be an independent factor involved in hypertension | 71 |
| Cd | Blood, tissues | AA;-;- | The effects of Fe status and exposure to Cd on the tissue distribution of Zn were investigated. Fetal viability was also studied | 344 |
| Cd | Blood, urine | AA;ETA;L | Samples (1–2 ml) of whole blood and urine were preconcentrated on 15 mg anion-exchange resin, interfering ions were removed in a 2 ml Bio-Spin column, and Cd was extracted into 100 μl of 1 M $HNO_3$ prior to measurement by $D_2$ corrected ETAAS. LODs were 0.008 ng $ml^{-1}$ for blood and 0.003 ng $ml^{-1}$ for urine. Mean intra- and inter-assay CV% at 0.1 ng $ml^{-1}$ Cd were 11–12%. Recovery for 0.1–0.6 ng of added Cd was 107 ± 4% for blood and 94 ± 4% for urine (mean ± standard error, $n = 3$) | 25 |
| Cd | Blood, urine, hair and tissues (liver, muscle) | AA;ETA;L | A method to improve the performance of phosphate-based modifiers for the ETAAS determination of Cd and Pb in biological fluids (urine, blood) and tissues (hair, liver and muscle solubilized with TMAH) was presented. It consisted of the application of *ca.* 2 μmol of $NH_4H_2PO_4$ or $(NH_4)_2HPO_4$ on the integrated platform of a THGA pre-treated with 2.7 μmol of Zr or W and 0.1 μmol of Ir (20 μg) | 90 |
| Cd | Chinese herbal medicines | AF;-;- | A method for the simultaneous determination of Cd and Hg by vapour generation non-dispersive AFS using an intermittent flow system was proposed and satisfactorily applied to Chinese herbal medicines. Parameters such as acid concentration of the reaction medium, flow rate of the carrier gas and shield gas, the observation height and the atomizer temperature, were optimized. LODs were 0.010 μg $l^{-1}$ for Cd and 0.019 μg $l^{-1}$ for Hg, respectively. RSD% for Cd and Hg at 1.00 μg $l^{-1}$ were 2.6% and 0.97% ($n = 11$), respectively | 118 |
| Cd | Chinese herbs | AA;F;- | A method was developed for the determination of Cd by FAAS with the atom trapping technique. Experimental conditions were optimised. For 2 min collection time, LOD was 0.42 ng $ml^{-1}$, *i.e.*, 5 times better than that of conventional FAAS. RSD was 1.8% and recovery ranged from 89.5% to 104% | 345 |
| Cd | CRMs | AA;-;- | The performance characteristics of the 6-mercaptopurinylazo resin for the preconcentration of Cd, Cu and Zn, from certified biological samples after microwave-aided digestion, were assessed and its high selectivity for these metals was confirmed | 26 |
| Cd | Daily foods, blood and urine | AA;ETA;- | A study was performed to determine dietary intake, blood and urinary concentrations of Pb and Cd among children and their mothers in Korea | 271 |
| Cd | Intestine, kidney, liver, lungs | AA;F;- AA;ETA;- | The relationship between Cd and Zn levels in the renal cortex, liver, lungs and three fragments of the small intestine (duodenum, jejunum, ileum) was investigated in 29 subjects deceased at the age of 42 ± 13 years | 346 |

**Table 1** Analysis of clinical and biological materials (*Continued*)

| Element | Matrix | Technique; atomization; presentation[a] | Sample treatment/comments | Ref. |
|---|---|---|---|---|
| Cd | Liver | MS;ICP;HPLC | TOF, DF and quadrupole ICP-MS were compared for the determination of Cd in sub-isoforms of rabbit liver metallothionein-1, after separation by reverse phase HPLC and post-column ID. TOF-ICP-MS showed the best tolerance to the organic solvent gradient (up to 50% $CH_3OH$) and the lowest LODs | 35 |
| Cd | Liver, lung, kidney, brain, hair and nails | AA;-;- XRF;-;- | The exposure to heavy metals of workers at a Cu and Pb smelter in northern Sweden was assessed by measuring the concentrations of Cd, Cu and Zn in liver, lung, kidney and brain tissues in 32 deceased long-term exposed male workers, and compared with those of 10 male controls. Cu and Zn levels were determined in hair and nails as well. The results of this investigation were discussed | 81 |
| Cd | Maternal and cord blood | AA;-;- | A highly significant direct correlation was found between Cd concentrations in maternal and cord blood of 45 healthy non-smoking pregnant women exposed to a low Cd challenge. The newborn birth weight was inversely correlated with Cd concentrations | 144 |
| Cd | Medicinal herbs | AA;-;- | Cd and Pb concentrations were measured in 28 commonly used medicinal plants in India. Analyses of leaves, stem bark, root, or seeds were carried out depending on the medicinal value of the plant portion. Mean concentrations ranged from 3 to 33 ppm for Pb and between 0.06 and 0.42 ppm for Cd | 111 |
| Cd | Placenta | AA;-;- | Cd and Pb concentrations were measured in 86 human placentas. Higher Cd and Pb levels were observed according to urban–industrial areas of residence, but, whereas Pb concentrations reflected environmental exposures, smoking during gestation explained a large proportion of placental Cd | 70 |
| Cd | Urine | AA;ETA;L | A transverse heated filter atomizer, mounted on a PerkinElmer SIMAA 6000 AA spectrometer, was applied to the direct determination of Cd and Pb in urine. Compared with the THGA, it provided a significant reduction of spectral background and matrix interferences, increased sensitivity and, therefore, lower LODs (0.018 and 0.2 μg $l^{-1}$ for Cd and Pb, respectively) | 93 |
| Cd | Urine | AA;ETA;L | A fast acid digestion method was used. Calibration was made against matrix matched solutions and the LOD was 0.08 μg $l^{-1}$. No differences were observed among the concentrations in populations from metropolitan and rural areas but higher values were seen in women and in individuals aged over 46 y | 347 |
| Co | Urine | AA;F;L | An improved procedure for the cloud-point extraction of Co was described, based on water removal from the surfactant rich phase, which increased the enhancement factor by 4-fold. 1-(2-Pyridylazo)-2-naphthol (PAN) and Triton X-114 were used as a hydrophobic ligand and a nonionic surfactant, respectively. LOD was 0.38 μg $l^{-1}$ | 21 |
| Co | Water, mussel tissue | AA;ETA;FI | A novel FI on-line column preconcentration system was developed for the determination of Co by ETAAS, after treatment with APDC and on-line column (PTFE) pre-concentration of the Co-PDC complex at a pH range of 5.5–7.0. LOD was 4 ng $l^{-1}$ and RSD 4.5% at 0.1 μg $l^{-1}$. Satisfactory agreement with CRMs was reported | 22 |
| Cr | CSF | AA;ETA;L | Cr was determined in CSF by $D_2$ corrected ETAAS with and 1 + 1 sample dilution with 0.25% m/v Triton X-100–4.5% v/v $HNO_3$. Repeatability was 3.2% and intermediate precision ($n$ = 20) 4.7%. The mean Cr level observed in samples from 43 healthy volunteers, collected in such a way to avoid contamination, was 14.6 ± 6.3 ng $ml^{-1}$ | 148 |
| Cr | Parenteral solutions | AA;F;FI | An on-line system for Cr preconcentration and determination by FI-FAAS was studied. The retention media were 4-(2-thiazolylazo)resorcinol and Amberlite XAD-16, at pH 5.0. For 50 ml of sample, the enrichment factor was 50 and LOD 20 ng $l^{-1}$. The RSD ($n$ = 10) at 5 μg $l^{-1}$ Cr was 2.9% and linearity up to at least 100 μg $l^{-1}$ | 105 |
| Cr | Saliva | AE;ICP;L | Salivary samples obtained from 17 orthodontic patients and 7 controls, before and after rinsing with double distilled water, were analysed by ICP-AES. No statistically significant difference was detected between control and patient groups | 27 |
| Cr | Serum | AA;ETA;L | The effect of various permanent chemical modifiers (Ir, Ru, Zr and Ir–Rh) on the determination of Cr in serum was studied and compared to the use of Pd + Mg or no modifier. Samples were diluted 1 + 4 with 1% v/v $HNO_3$–0.02% v/v cetyltrimethylammonium choride. The best results were obtained without a modifier, with pyrolysis and atomization temperatures of 1000 and 2200 °C, respectively. LOD was 0.04 μg $l^{-1}$ | 147 |
| Cr | Serum | AA;ETA;L | See Al, ref. 94 | 94 |
| Cr | Urine | AA;-;L | Cr, Fe and Pb were determined in urine by AA after separation and preconcentration of the calmagite chelates of the analytes on a cellulose nitrate membrane filter. The effects of major components of urine, such as urea and creatinine, on the quantitative recoveries of Cr, Fe and Pb were discussed. Recovery was >95% and RSD <10% | 146 |
| Cr | Urine | AA;ETA;L | Ru was used as a permanent modifier for the determination of Cu and Cr in urine samples, diluted 1:1 with 1% v/v $HNO_3$. Higher sensitivities than with a Pd+ Mg modifier were obtained ($m_o$ = 7.3 pg Cr and 17.7 pg Cu). LODs were 0.22 and 0.32 μg $l^{-1}$, for Cr and Cu, respectively | 92 |

**Table 1** Analysis of clinical and biological materials (*Continued*)

| Element | Matrix | Technique; atomization; presentation[a] | Sample treatment/comments | Ref. |
|---|---|---|---|---|
| Cs | Blood, tissues | AA;ETA;L | Cs was measured in samples from two subjects to whom CsCl had been given in the treatment of cancer. Blood concentrations were >1000 times higher than normal | 145 |
| Cu | Blood | AA;-;- | See Pb, ref. 348 | 348 |
| Cu | Blood (cat) | AA;-;- | Serum Cu concentrations and cuproenzyme (caeruloplasmin, extracellular superoxide dismutase, diamine oxidase and erythrocyte superoxide dismutase) activities were determined in a pathogen-free colony of cats, to evaluate age and sex related differences | 152 |
| Cu | Blood and thyroid tissue | XRF;-;- | The concentrations of Cu, Se and Zn in whole blood and thyroid tissue of people with various thyroid diseases were investigated in relation with the type of disease | 68 |
| Cu | Blood, urine | AA;-;L | Cu, Se and Zn were measured in blood and urine of 80 individuals, with or without dental amalgam fillings, after administration of a single *i.v.* dose of DMPS. Results indicated that body stores of Cu, Zn and Se were not affected by this treatment | 88 |
| Cu | Chinese herbs | AA;F;- | Cu was measured in Chinese herbs by derivative FAAS combined with modified atom trapping equipment. LOD was 0.52 μg $l^{-1}$ | 349 |
| Cu | CRMs | AA;-;- | See Cd, ref. 26 | 26 |
| Cu | CSF | AA;-;L MS;ICP;L | The concentrations of Cu, Mn and Zn in CSF from patients with multiple sclerosis and patients with no known neurological disease (control group) were measured by HR-ICP-MS and repeated by AAS (Cu and Mn only). Mn levels were significantly decreased and Cu levels significantly increased in patients with multiple sclerosis | 84 |
| Cu | Herbal medicines | AA;ETA;Sl | A low cost method, based on ETAAS with a molybdenum tube atomiser and ultrasonic slurry sampling, gave results in good agreement with those obtained for acid-digested samples. The 10% glycerol solution used as the slurry medium also acted as chemical modifier, eliminating matrix interferences. LOD was 72 fg | 13 |
| Cu | Liver | AA;-;- | Methods for sample pretreatment (dry ashing in a muffle furnace or in a low pressure oxygen plasma; high pressure acid digestion, solubilisation with TMAH and slurry sampling) were compared for the determination of Cu in liver tissue by AAS | 350 |
| Cu | Liver | XRF;-;- | Cu was measured in autopsy liver tissue samples from Greenlandic Inuit (50) and Danes (74) by XRF. There was no evidence to suggest that the prevalence of Cu deficiency or overload differ in Inuit and Dane adults | 69 |
| Cu | Liver cytosol | XRF;-;- | SRXRF was applied to the detection of metal ions in protein bands obtained from human liver cytosol after separation with gel filtration chromatography and thin layer isoelectric focusing | 58 |
| Cu | Liver, kidney, lung, spleen, brain, and serum (rat) | AA;ETA;- AA;F;- | The distribution of Ni administered as $NiCl_2 \cdot 6H_2O$ in drinking water was studied using male Wistar rats. In addition, the effect of Ni administration on the concentration of Zn and Cu in selected organs and serum was determined | 351 |
| Cu | Liver, lung, kidney, brain, hair and nails | AA;-;- XRF;-;- | See Cd, ref. 81 | 81 |
| Cu | Mammalian cultured cells | XRF;-;- | The alterations of the content and distribution of Cu, Fe and Zn induced in mammalian cultured cells by exposure to 100 μM Cu-Histidine were studied | 149 |
| Cu | Plasma, hair | AA;-;- | In three experimental rat models of epilepsy, Cu, Mg and Zn levels were determined in plasma and hair of rats, to elucidate their role in the mechanisms of CNS excitability | 352 |
| Cu | Serum | AA;-;L | The Cu:Zn ratio in serum from patients with hepatocellular carcinoma, evaluated in a case control study, was significantly higher, with a diagnostic sensitivity of 87.5% | 86 |
| Cu | Serum | AA;F;L | The results of a study of Cu and Zn status in 100 randomly selected children (2–18-year-old) whose parents had premature myocardial infarction and 100 matched controls were reported. A four-day food record questionnaire was used to assess Cu and Zn intakes and serum Cu and Zn levels were measured by FAAS | 207 |
| Cu | Serum | AA;-;L | In 570 healthy men and women aged 15 years and older, serum leptin, the obesity gene protein product, was positively associated with serum Cu ($r = 0.197$, $p = 0.02$) and the serum Zn:Cu ratio ($r = -0.182$, $p = 0.03$) | 150 |
| Cu | Serum | AA;-;L | The effects of inflammation and anti-inflammatory treatment on serum Cu and Zn were investigated in guinea pigs | 353 |
| Cu | Teeth | AA;ETA;Sl | Samples were ground in a mill in two steps: pre-cooling (5 min) and cryogenic grinding (2 min) in liquid $N_2$. Powder, 5–20 mg, was weighed directly in autosampler cups followed by addition of 1 ml of a solution of 0.04% Triton X-100–0.2% v/v $HNO_3$. The slurry was added onto a W–Rh coated platform and measured against aqueous calibration. LODs for 2% m/v slurries were 18.0 ng $g^{-1}$ Cu, 7.4 ng $g^{-1}$ Mn and 34.0 ng $g^{-1}$ Pb | 11 |
| Cu | Tissues (rat) | AA;-;- | Changes of Cu, Fe and Zn levels in rat tissues (temporal lobe, brain stem, spleen, and liver) under acute and chronic immobilization stress were investigated | 354 |

**Table 1** Analysis of clinical and biological materials (*Continued*)

| Element | Matrix | Technique; atomization; presentation[a] | Sample treatment/comments | Ref. |
|---|---|---|---|---|
| Cu | Urine | AA;ETA;L | See Cr, ref. 92 | 92 |
| Cu | Uterine fluids | AA;-;L | To investigate the release of Cu from contraceptive intrauterine devices (IUD) and its effect on protein concentration, samples of uterine fluids were collected at three different times of the cycle from 27 women who used IUDs for 0.5, 1 and 3 years. Cu concentrations were between 3.9 and 19.1 μg $ml^{-1}$, with a Cu release from IUDs approximately constant for at least 6–12 months. $Cu^{I}$ was not detected. Cu induced a change in the total protein concentration, which was much higher than in controls | 151 |
| Eu | Liver (mouse) | SIMS;-;- | Methods (confocal microscopy and SIMS) for the detection of magnetic resonance imaging contrast agents (fluorescent Eu, nonfluorescent, paramagnetic Gd and a product combining nanoparticles of Fe and Texas Red) were compared | 52 |
| Fe | Blood | MS;ICP;- | Anion-exchange and precipitation procedures for Fe separation from unspiked human whole blood after microwave digestion and ashing decomposition were evaluated for subsequent Fe isotope ratio measurements by multi-collector ICP-MS. Precipitation with $NH_3$ was the most rapid and cost-effective method | 43 |
| Fe | Blood, tissues | AA;-;- | See Cd, ref. 344 | 344 |
| Fe | Brain cells | XRF;-;- | See Ca, ref. 53 | 53 |
| Fe | Breast milk | MS;ICP;HPLC | Scintillation counting of radio-Fe and SEC-ICP-MS were applied to assess the solubilization of extrinsic Fe by breast milk fractions in a study of the bioavailability of extrinsic Fe from breast milk, investigated using Caco-2 cells | 154 |
| Fe | Faeces | MS;ICP;L | A method was developed, based on HR-ICP-MS, for the measurement of Fe and Fe isotope ratios in acid digests of faecal samples from a human nutrition study and compared successfully with TIMS | 50 |
| Fe | Human lenses | AA;-;- | The Fe and Zn content of human lenses in different types of cataract were examined in relation to diabetes. Both Fe and Zn were increased in mature compared to corticonuclear cataracts and in diabetic compared to non diabetic subjects. Lens Zn content also increased with increasing lens coloration | 82 |
| Fe | Liver (mouse) | SIMS;-;- | See Eu, ref. 52 | 52 |
| Fe | Liver cytosol | XRF;-;- | See Cu, ref. 58 | 58 |
| Fe | Liver, kidney, spleen, lung, heart, and brain (rat) | AA;ETA;- | The release of Fe and Si from an injectable cement with oncotherapeutic potential was evaluated in organs from implanted and control rats. No evidence of release was found in most analysed organs | 355 |
| Fe | Mammalian cultured cells | XRF;-;- | See Cu, ref. 149 | 149 |
| Fe | Saliva | AE;ICP;L | See Cr, ref. 27 | 27 |
| Fe | Tissues (rat) | AA;-;- | See Cu, ref. 354 | 354 |
| Fe | Urine | AA;-;L | See Cr, ref. 146 | 146 |
| Ga | Urine | AA;F;L | Using an FI arrangement, Ga was trapped on a polyurethane foam mini-column and then eluted with IBMK. From a 90 s sampling time, an enhancement factor of 40 with an LOD of 6 μg $l^{-1}$ and an RSD of 3.3% was achieved. Chemical and flow variables and possible interferences were studied | 24 |
| Gd | Liver (mouse) | SIMS;-;- | See Eu, ref. 52 | 52 |
| Ge | Urine, serum | MS;ICP;L | See As, ref. 30 | 30 |
| Hg | Biological and environmental samples | AA;CV;FI | An optimised FI mercury system permitted the separate determination of inorganic Hg and total Hg using different concentrations of $NaBH_4$ as reducing agent. LODs were 24 and 3.9 ng $l^{-1}$ for total Hg and inorganic Hg, respectively. RSD% was less than 1.5% at 10 ng $ml^{-1}$ Hg. In biological and sediment samples LODs were in the range of 1.2–19 and 6.6–18 ng $g^{-1}$ for inorganic and total Hg, respectively | 356 |
| Hg | Biological tissues | MS;ICP;HPLC | The abiotic formation of methylmercury from $Hg^{2+}$, as well as demethylation to $Hg^{2+}$ in biological tissues during treatment with TMAH followed by pH adjustment, was studied by HPLC-ICP-MS with species-specific isotope tracers and ID calibration | 172 |
| Hg | Blood | AA;CV;L | Blood Hg was higher in infertile subjects (couples, males with abnormal semen and females with unexplained infertility) than in controls (Hong-Kong). Blood Hg concentrations were positively correlated with seafood consumption | 357 |
| Hg | Blood | AA;CV;L | The effect on blood Hg following DMPS administration was evaluated in: subjects without amalgam experience; subjects with amalgam fillings; patients with self-reported symptoms from existing dental amalgams; and patients who had removed amalgam fillings. There was no evidence of differences among the groups with amalgam experience | 167 |
| Hg | Chinese herbal medicines | AF;-;- | See Cd, ref. 118 | 118 |
| Hg | Hair | AA;CV;- AF;CV;- MS;ICP;- | The results of an interlaboratory comparison programme for Hg in human hair were reported. A variety of analytical methods using different digestion and instrumental techniques gave similar results. 92% of the participants consistently met the performance limits | 99 |

**Table 1** Analysis of clinical and biological materials (*Continued*)

| Element | Matrix | Technique; atomization; presentation[a] | Sample treatment/comments | Ref. |
|---|---|---|---|---|
| Hg | Liver, tail muscle (alligator) | AA;CV;- | Hg was measured in liver and tail muscle from alligators from the Florida Everglades. Hg concentrations ranged from 0.6 to 17 mg $kg^{-1}$ in liver and from 0.1 to 1.8 mg $kg^{-1}$ in tail muscle. Animals from different locations had significantly different concentrations of Hg in tissue, with those from Everglades National Park having Hg concentrations 2-fold higher than basin-wide averages | 173 |
| Hg | Plasma | AA;-;L | Plasma Hg concentrations in 26 non-occupational exposed subjects were positively correlated with the number of amalgam fillings and negatively with plasma total antioxidant activity | 166 |
| Hg | Pulp tissue | AA;-;- | In guinea pigs, cavity lining with resin-modified glass ionomer cements significantly diminished the transport of Hg into the pulp between 7 and 30 days after amalgam insertion | 168 |
| Hg | Rat brain | AF;CV;- | Small portions (100 mg) of brain tissue were digested for 6–8 h at high temperature in $HNO_3$–$H_2SO_4$, then oxidized with $KbrO_3^-/Br^-$ at room temperature and treated with a continuous flow of $SnCl_2$ to generate Hg vapour. LOQ was 1.5 ng $g^{-1}$ Hg brain tissue. The recovery of spiked amounts at this level was 89.8% $\pm$ 6.9% ($n = 4$). The ruggedness of the method was studied by repeated analyses ($n = 36$) of the CRM DOLT-2 over a four year period | 358 |
| Hg | Soil, plants and Chinese medicines | AA;-;FI | A method was developed for the determination of Hg in soil, plants and traditional Chinese medicines by FI-AA with a quartz tube. Samples were decomposed with $V_2O_5$–$HNO_3$–$H_2SO_4$. LOD was 0.028 μg $l^{-1}$, $m_o$ 59 pg, RSD $< 3.9\%$ and analytical recovery between 94% and 102% | 223 |
| Hg | Tissues | MS;ICP;GC | Mice were treated with thimerosal to study its uptake and biotransformation. Tissue samples were spiked with isotopically enriched methyl- ($^{200}$Hg) and ethyl mercury ($^{199}$Hg), and solubilised in 20% TMAH. Hg species were extracted at pH 9 with DDTC–toluene, reacted with butylmagnesium chloride to form butyl derivatives then measured by ID-GC-ICP-MS | 171 |
| Hg | Urine | AA;CV;L | The prevalence of elevated urinary Hg in an urban pediatric population (aged 1–18 years) was determined. Assays were conducted simultaneously in two laboratories ($r = 0.8$). 5% of subjects had unsuspected elevated urinary Hg levels | 359 |
| Hg | Urine | AA;-;L | Severe Hg intoxication developed after a short period of application of an ointment containing 10% $HgNH_2Cl$ for eczema, as diagnosed and monitored, after chelating treatment, by urinary Hg determination | 360 |
| Mg | Blood | MS;ICP;L | A new *in vitro* test for the assessment of Mg status was proposed, based on a stable tracer and the assumption of increased cellular Mg uptake in Mg deficiency. Blood was incubated with $^{25}$Mg (10 mg $l^{-1}$) for 2 h at 37 °C. Erythrocytes, lymphocytes and platelets were isolated and $^{25}$Mg concentrations were determined by ICP-MS. $^{25}$Mg enrichments in blood cells from Mg-deficient rats were greater than those from controls. In humans, $^{25}$Mg enrichments were low (3%) in erythrocytes, but high in lymphocytes and platelets, which may be the most appropriate cells for this test in humans | 44 |
| Mg | Blood, urine, faeces | MS;ICP;L | $^{26}$Mg and $^{25}$Mg were administered orally and *i.v.*, respectively, and samples were collected for 12 d. Data were used to build a compartmental model of Mg kinetics | 46 |
| Mg | Faeces, urine, plasma | MS;ICP;- | Two methods (double-labeling and faecal monitoring) for the determination of Mg absorption in humans by means of stable-isotope tracers were compared. The two methods compared well and double labeling was suggested as a less cumbersome alternative, with appropriate choice of sampling time intervals | 45 |
| Mg | Medicinal plants | AA;-;SEC | Aqueous extracts of birch leaves, peppermint leaves, sage leaves, valerian roots and dandelion roots were analysed for the speciation of Mg, Mn and Zn by SEC with AA, diode array UV-VIS and electrochemical detection | 113 |
| Mg | Plasma, hair | AA;-;- | See Cu, ref. 352 | 352 |
| Mn | Biological samples | AE;ICP;FI | Sample preparation involved preconcentration on a pre-packed column and elution with $HNO_3$. Sample flow rate, eluent flow rate, eluent concentration, pH, and buffer concentration were optimised. The performance details of the method were: LOD, 1.5 ng $ml^{-1}$, precision (RSD) 0.5% for 100 ng $ml^{-1}$, enrichment factor, 26 with a 60 s preconcentration time, and satisfactory results for the analysis of biological CRMs | 23 |
| Mn | Brain | AA;ETA;Sl | A procedure for the determination of Mn in human brain samples was developed, with Pd + Mg as chemical modifiers and aqueous standards for calibration. Both slurry sampling (2% w/v) and microwave-assisted acid digestion with $HNO_3$ were evaluated for sample preparation. LODs were 0.3 and 0.4 ng $ml^{-1}$ for the slurry and the digested samples, respectively | 165 |
| Mn | CSF | AA;-;L MS;ICP;L | See Cu, ref. 84 | 84 |
| Mn | Medicinal plants | AA;-;SEC | See Mg, ref. 113 | 113 |
| Mn | Serum | AA;ETA;L | See Al, ref. 94 | 94 |
| Mn | Teeth | AA;ETA;Sl | See Cu, ref. 11 | 11 |

**Table 1** Analysis of clinical and biological materials (*Continued*)

| Element | Matrix | Technique; atomization; presentation[a] | Sample treatment/comments | Ref. |
|---|---|---|---|---|
| Mo | Blood plasma | MS;ICP;- | A method for the determination of total Mo and Mo stable isotope concentrations in 0.5 mL of blood plasma by ICP-MS was developed and applied to the study of total Mo and $^{97}$Mo in plasma from a subject given *i.v.* adminstration of $^{97}$Mo | 47 |
| Na | Serum | MS;ICP;- | A method has been developed for the accurate determination of Na in serum CRMs, as an alternative to time-consuming gravimetric procedures | 361 |
| Ni | Cigarette, blood and urine | AA;-;- | The contribution of cigarette smoking, especially if hand-made, to Ni exposure of workers in nickel processing plants was investigated. Ni was measured in cigarettes and samples of blood and urine from 318 randomly selected employees from the Falconbridge Nickel Refinery in Kristiansand, Norway. The results did not indicate differences between Ni concentrations in body fluids from smokers or non-smokers | 174 |
| Ni | Liver, kidney, lung, spleen, brain, and serum (rat) | AA;ETA;- AA;F;- | See Cu, ref. 351 | 351 |
| Ni | Saliva | AE;ICP;L | See Cr, ref. 27 | 27 |
| Ni | Tissue | MS;ICP;LA | The Ni content and degree of tissue inflammation was assessed, using $^{60}$Ni and $^{24}$Mg isotopes, after pure Ni wires were implanted subcutaneously into rats for 7 days | 41 |
| Pb | Blood | MS;ICP;L | The validation of a method for the determination of Pb in blood samples, after diluting 1:45 v/v with 0.1 mg $l^{-1}$ $NH_4OH$–0.1 g $l^{-1}$ EDTA–5 mg $l^{-1}$ n-butanol–0.1% Triton X-100, was reported, including assessment of residual interferences, LOD (0.01 μg $l^{-1}$), LOQ (0.1 μg $l^{-1}$) and comparison with ETAAS | 156 |
| Pb | Blood | AA;ETA;L | Blood Pb levels were measured twice a year, between 1997 and 2001, in children from an industrial complex or a suburban area (Ulsan, Korea). Over the years, the Pb levels increased and the difference between the two groups decreased. In 2001 the geometric means were 5.41 μg $dl^{-1}$ and 4.93 μg $dl^{-1}$, respectively | 164 |
| Pb | Blood | XRF;-;- | The ASU 2003 review on XRF covered the developments of this technique and a survey of applications, including archaeological, forensic, biological and clinical studies, among which was the application of EDXRF to the study of blood Pb concentrations of gunshot victims | 362 |
| Pb | Blood | AA;ETA;L | The use of a W–Rh permanent modifier (250 μg W + 200 μg Rh) for the determination of Pb in blood by ETAAS with a THGA was investigated. Blood samples were diluted 1 + 9 with 0.2% v/v $HNO_3$–0.5% v/v Triton X-100. The results indicated improved performance in comparison with a conventional $NH_4H_2PO_4$ modifier | 89 |
| Pb | Blood | AA;ETA;L MS;ICP;L | As part of ongoing investigations, the processes occurring ETAAS with a rhodium-coated tungsten-filament during the pyrolysis and atomization of Pb from diluted blood were studied by coupling with ICP-MS | 91 |
| Pb | Blood | AA;ETA;L | Blood Pb was significantly higher in prostate cancer and benign prostate hyperplasia cases than in controls ($P < 0.05$), whereas Cu and Zn in blood were significantly lower ($P < 0.05$). In both cases and controls, blood Pb was correlated with thiobarbituric acid reactive substances (positively) and glutathione (negatively) | 348 |
| Pb | Blood | AA;-;L | New, lower, age-related reference values for Pb in blood were established for a paediatric population | 363 |
| Pb | Blood | AA;ETA;L | The results of a randomized trial conducted among women in Mexico City to assess if dietary Ca supplements were effective in lowering maternal blood Pb levels during lactation were presented. Among lactating women with relatively high Pb burden, Ca supplementation was associated with a modest reduction in blood Pb levels | 161 |
| Pb | Blood | AA;ETA;- | Pb measurements in samples of capillary blood collected on filter paper were compared with those performed in paired venous blood samples from 159 Chinese children aged 0–6 y ($r = 0.87$) | 157 |
| Pb | Blood | AA;-;L | The study investigated the relation between blood Pb and pregnancy outcomes in 705 women, aged 12–34 y. Mean blood Pb concentration was 1.2 μg $dl^{-1}$ (standard error = ±0.03) and a significant relation to hypertension in pregnancy/toxemia was observed | 159 |
| Pb | Blood | AA;-;L | In a sample of 14 952 whites and blacks aged 18 y or older, examined as part of the Third National Health and Nutrition Examination Survey, mean blood Pb was significantly higher for blacks and associated with higher systolic blood pressure | 364 |
| Pb | Blood | AA;ETA;L | See Cd, ref. 18 | 18 |
| Pb | Blood | XRF;-;- AA;-;- | A retrospective review of study findings on 5 patients who sustained gunshot injuries to the maxillofacial region was presented, as part of a larger study on the effects of retained lead bullets on blood Pb | 365 |
| Pb | Blood | AA;ETA;L | Pb levels were measured by ETAAS in blood samples from 350 adults aged 15 to 70 y, from a mining area in Brazil. Higher blood Pb levels were significantly associated with: residential area close to the lead refinery, former dwelling at the refinery village, male gender, smoking habits, and consumption of fruits from home backyard | 366 |

**Table 1** Analysis of clinical and biological materials (*Continued*)

| Element | Matrix | Technique; atomization; presentation[a] | Sample treatment/comments | Ref. |
|---|---|---|---|---|
| Pb | Blood and bone | AA;-;- | Among middle-age women (Mexico City), the mean blood Pb concentration, adjusted for age and bone Pb levels, was 1.98 μg $dl^{-1}$ higher in postmenopausal women than in premenopausal women ($p = 0.024$) | 163 |
| Pb | Blood, bone | -;-;- | In children aged 10–12 y, half heavily exposed to Pb from the prenatal period onward, and half relatively unexposed, both blood and bone Pb levels were associated with intelligence decrements, small relative to the contribution of social factors | 367 |
| Pb | Blood, bone (tibia) | -;-;- | The relation of Pb, measured in blood and tibia, to changes in blood pressure between 1994 and 1998 was examined in 496 current and former employees of a company in the USA who had previous occupational exposure to inorganic and organic Pb | 368 |
| Pb | Blood, breast milk | AA;ETA;L MS;ICP;L | Pb concentrations were measured in blood and breast milk samples collected at set times after delivery from 15 lactating and 30 bottle-feeding women. The results were compared to osteocalcin levels and bone mineral density change to investigate whether Pb in breast milk and blood was correlated with bone loss, or bone turnover, during reproduction | 160 |
| Pb | Blood, urine, hair and tissues (liver, muscle) | AA;ETA;L | See Cd, ref. 90 | 90 |
| Pb | Bone | XRF;-;- | Pb exposure, as reflected in bone Pb levels, was associated with elevated risk for adjudicated delinquency in a case control study | 61 |
| Pb | Bone | XRF;-;S | In a study of 223 mother–infant pairs, maternal bone Pb (on average, 9.8 and 14.4 μg $g^{-1}$ bone mineral for the tibia and patella, respectively) was inversely associated with length of newborns and positively and significantly related to the risk of a low head circumference score | 63 |
| Pb | Bone | XRF;-;S | A revised mathematical treatment of the calibration line intercept for *in vivo* bone lead measurements using $^{109}$Cd-based K-shell XRF. Changes to the method for calculating the measurement uncertainty were proposed | 59 |
| Pb | Bone, blood | XRF;-;- AA;-;- | The effects of blood and bone Pb on hypertension and elevated blood pressure in the third trimester and postpartum were investigated in a group of 1006 women. Past Pb exposure appeared to influence hypertension and elevated blood pressure during pregnancy | 64 |
| Pb | Bone, blood | XRF;-;- | Bone and blood Pb were measured in middle-aged and elderly men from the Normative Aging Study in summer, spring/fall and winter. In multivariate regression models, bone Pb had an almost 2-fold greater influence on blood Pb levels during the winter months than the summer months. It was suggested that higher blood Pb levels in winter may be related to increased mobilization of endogenous bone Pb stores, potentially from decreased exposure to sunlight, lower levels of activated vitamin D, and enhanced bone resorption | 62 |
| Pb | Bone, blood, urine, breast milk | -;-;- | The results of a longitudinal investigation into the mobilization of Pb from the human maternal skeleton during pregnancy and lactation were summarised | 162 |
| Pb | Ca supplements | AA;ETA;L | Pb was measured in 55 brands of dietary Ca supplements available in Korea after microwave-aided digestion in concentrated $HNO_3$. $NH_4H_2PO_4$ and $Mg(NO_3)_2$ were used as chemical modifiers. The mean daily intake of Pb from the supplement was estimated as 5 μg, which is about 2% of the Provisional Tolerable Daily Intake set by FAO/WHO | 272 |
| Pb | Daily foods, blood and urine | AA;ETA;- | See Cd, ref. 271 | 271 |
| Pb | Fish, marine algae | AA;ETA;Sl | No significant difference was observed between slurry sampling and microwave-assisted acid digestion for the determination of Pb by ETAAS in several biological samples (fish and marine algae). Methods of slurry preparation (by magnetic shaking or by microwave-heating) were also compared | 12 |
| Pb | Herbal preparations | AA;-;L | From a sample of 100 herbal preparation products sold in Malaysia, 8% were found at 10.64–20.72 ppm Pb and failed the quality requirement for traditional medicines. The products that did comply cannot be assumed free from Pb contamination because of batch-to-batch inconsistency | 112 |
| Pb | Placenta | AA;-;- | See Cd, ref. 70 | 70 |
| Pb | Teeth | AA;ETA;Sl | See Cu, ref. 11 | 11 |
| Pb | Urine | AA;-;L | See Cr, ref. 146 | 146 |
| Pb | Urine | AA;ETA;L | See Cd, ref. 93 | 93 |
| Pd | Blood | AA;ETA;L | See Cd, ref. 18 | 18 |
| Pd | Pharmaceuticals | MS;ICP;- AA;ETA;- | Methods were developed for the determination of trace element (Pd, Pt and Rh) impurities in pharmaceuticals | 109 |
| Pd | Urine, serum | MS;ICP;L | Simultaneous and selective preconcentration of Pd, Pt and Rh was performed by sorption of their complexes formed on-line with diethylthiourea on the inner walls of a PTFE knotted reactor, in a range of sample acidity (0.1–0.5 M $HNO_3$ for Pd and Rh and 0.05–0.2 M $HNO_3$ for Pt). Quantitative elution was achieved using 500 μl $CH_3OH$–1% $HNO_3$ and the metals determined by ICP-TOF-MS. The LODs were 0.36, 0.54 and 2.12 ng $l^{-1}$ for Pd, Pt, and Rh, respectively. Using a preconcentration time of 120 s and a sample flow rate of 5 ml $min^{-1}$, enrichment factors of 55, 5 and 2 for Pd, Pt and Rh, respectively, were obtained | 34 |

**Table 1** Analysis of clinical and biological materials (*Continued*)

| Element | Matrix | Technique; atomization; presentation[a] | Sample treatment/comments | Ref. |
|---|---|---|---|---|
| Pt | Anticancer drug | AA;ETA;- AA;F;- | AP 5280 is a novel polymer-conjugated Pt anticancer agent, currently in Phase I clinical trials. Among the array of tests applied to warrant the product integrity, total Pt, free Pt and the release profile of small Pt species were determined | 183 |
| Pt | Anticancer drugs, plasma ultrafiltrate (dog) | MS;ICP;HPLC | A method based on HPLC-ICP-MS was developed for the quantitation of the anticancer drug ZD0473 and its performances compared with those of an HPLC-MS/MS method. The HPLC-ICP-MS method had advantages of extended linear range and lower LOQ (0.1 ng $ml^{-1}$ *v* 5 ng $ml^{-1}$). Additional information on the *aqua* compounds was obtained using a single combined HPLC-ICP-MS/MS/MS system | 182 |
| Pt | Haemoglobin | MS;ICP;SEC MS;ES;- | The interactions of cisplatin with haemoglobin were studied using both nanoscale ES-MS and SEC-ICP-MS. The presence of haemoglobin-Pt complexes was demonstrated by simultaneous monitoring of $^{195}Pt$ and $^{57}Fe$ | 179 |
| Pt | Infusion solutions | AA;-;- | The content of carboplatin and the profile of decomposition products were investigated in 11 infusion solutions with a nominal carboplatin concentration of *ca.* 10 mg $ml^{-1}$, stored for 5–78 months at room temperature. Carboplatin losses were between 3.1% and 7.3% | 184 |
| Pt | Metallothionein | AA;-;- | Measurements of Pt by AAS were used together with measurements by other techniques (HPLC, UV) to investigate the binding of cisplatin to metallothionein in conditions mimicking the passage of clinical concentrations of cisplatin through the cytosol | 178 |
| Pt | Pharmaceuticals | MS;ICP;- AA;ETA;- | See Pd, ref. 109 | 109 |
| Pt | Plasma and tissue | AA;-;- | Sixteen patients with peritoneal carcinomatosis underwent complete cytoreductive surgery followed by intraoperative i.p. administration of a heated oxaliplatin solution (chemohyperthermia) in increasingly hypotonic solutions. The pharmacokinetics of oxaliplatin were evaluated by means of Pt determinations in plasma and tissues. The results did not confirm the usefulness of this administration procedure | 181 |
| Pt | Plasma ultrafiltrates | AA;ETA;L | The pharmacokinetics and nephrotoxicity of cisplatin administered to patients as intraoperative hyperthermic peritoneal lavage was assessed, by measuring the concentrations of ultrafiltrable Pt by ETAAS and urinary marker-proteins by nephelometry | 177 |
| Pt | Plasma ultrafiltrates, blood, and urine | AA;ETA;L | A programme to study population pharmacokinetics (NONMEM) was applied to data from 40 patients receiving oxaliplatin for the treatment of advanced colorectal cancer, including body surface area, age, sex, serum creatinine and measurements of Pt in body fluids | 180 |
| Pt | Plasma, plasma ultrafiltrate, erythrocytes and urine | MS;ICP;L | The pharmacokinetic interaction of oxaliplatin with paclitaxel were investigated in the rat, by measuring Pt levels in plasma and plasma ultrafiltrate, Pt binding to proteins, red blood cell uptake and urinary elimination of Pt | 369 |
| Pt | Plasma, ultrafiltrate | AA;ETA;L | Total and ultrafilterable Pt were measured in samples from patients treated with oral Satraplatin (JM216). Phamakokinetic data were presented | 370 |
| Pt | Serum, tissue | AE;ICP;- | A method was proposed for the determination of Pt in serum and tissues by ICP-AES, which can be applied in pharmacokinetics and biodistribution studies | 371 |
| Pt | Tissue homogenates, extracellular fluid and plasma | AA;ETA;- | The inter- and intratumoral disposition of unbound Pt after cisplatin administration to mice was evaluated after microdialysis, by ETAAS measurements of total Pt in tumour homogenates and of unbound Pt in tumour extracellular fluid and plasma | 176 |
| Pt | Urine | MS;ICP;L | Urinary Pt was measured as part of a programme for the biological monitoring of hospital personnel occupationally exposed to antineoplastic agents. The LOD was 1 ng $l^{-1}$. Pt was detected in urine samples from three out of nine subjects | 186 |
| Pt | Urine, serum | MS;ICP;L | See Pd, ref. 34 | 34 |
| Pt | Urine, serum, microdialysate, lung tissue | MS;ICP;- | Methods for the determination of Pt in human tissues and fluids by SF-ICP-MS with microconcentric nebulisation and USN with and without membrane desolvation were investigated. Sample preparation involved microwave digestion and open vessel treatment or simple dilution (microdialysates). LODs were 0.35 pg $g^{-1}$ for urine, 420 pg $g^{-1}$ for serum, 400 pg $g^{-1}$ for lung tissue and 13 pg $g^{-1}$ for microdialysates | 175 |
| Rh | Pharmaceuticals | MS;ICP;- AA;ETA;- | See Pd, ref. 109 | 109 |
| Rh | Urine, serum | MS;ICP;L | See Pd, ref. 34 | 34 |
| Ru | Antimetastatic drug | AA;F;- | A range of analytical techniques (HPLC, NMR, FAAS) were applied to the pharmaceutical quality control of NAMI-A, a novel Ru complex with antimetastatic properties, currently in Phase I clinical trials | 106 |
| Sb | Drugs | AA;Hy;FI | The selective determination of $Sb^{III}$ in commercial drugs for the treatment of leishmaniasis, based on $Sb^{V}$, was reported. The optimal conditions for $Sb^{III}$ determination in the presence of $Sb^{V}$ were: 20% (m/v) citric acid, 2.0% (m/v) $NaBH_4$, 125 μl injection volume, 180 cm for reactor length and allowed for 60 determinations $h^{-1}$. LOD was 0.95 ng and $m_o$ 55 pg. RSD was 3.8% and analytical recovery ranged from 97.1–100.8% | 107 |
| Se | Biological samples | MS;ICP;HPLC MS;ICP;GC | Methods for the chiral speciation of seleno-amino acids in biological samples were compared and applications in biological samples reviewed, to highlight the importance of chiral speciation | 190 |

**Table 1** Analysis of clinical and biological materials (*Continued*)

| Element | Matrix | Technique; atomization; presentation[a] | Sample treatment/comments | Ref. |
|---|---|---|---|---|
| Se | Blood and thyroid tissue | XRF;-;- | See Cu, ref. 68 | 68 |
| Se | Blood plasma, urine and faeces | MS;ICP;- | Total Se and $^{77}$Se were determined simultaneously in isotopically enriched human plasma, urine and faeces by dynamic reaction cell ICP-MS, in a study of human metabolism. Plasma, urine and the digested faecal samples were diluted with 0.5% Triton X-100–2% $HNO_3$–3% $CH_3OH$. LODs for Se with natural abundance were 0.1 μg $l^{-1}$, 0.2 μg $l^{-1}$ and 6 μg $kg^{-1}$, respectively | 38 |
| Se | Blood, cord blood and amniotic fluid | AA;ETA;L AA;Hy;L | See Cd, ref. 71 | 71 |
| Se | Blood, plasma and protein fractions | AF;Hy;L | Se was determined by HGAFS in whole blood, plasma and the plasma protein fractions, selenoprotein-P and glutathione peroxidases + albumin, obtained by affinity chromatography. Prior to analysis, whole blood and plasma were digested using $H_2SO_4$, $H_2O_2$ and $V_2O_5$ in $H_2SO_4$, whereas for the decomposition of plasma protein fractions, $HNO_3$ and $H_2O_2$ were sufficient. The main advantages of the described procedures are a low LOD (0.2 ng Se $g^{-1}$ of solution) and the high throughput | 372 |
| Se | Blood, urine | AA;-;L | See, Cu ref. 88 | 88 |
| Se | Diet, blood and urine | AA;Hy;-INAA;-;- | Se balance was determined in healthy American and Hungarian children (8–17 years) living in Budapest, by measurements of Se content in duplicate diet collection, whole blood and serum samples and 24 h urine collections | 288 |
| Se | Erythrocytes, prostatic tissue | MS;ICP;L | Samples were collected from men with benign prostatic hyperplasia, who had received Se supplements for 1 month. There was poor correlation between erythrocyte and tissue concentrations | 373 |
| Se | Hair | MS;ICP;ETV | See As, ref. 101 | 101 |
| Se | Organs and body fluids | MS;ICP;HPLC | The metabolic pathways of Se, as $SeO_3^{2-}$ or $SeO_4^{2-}$, were studied in rats using enriched $^{82}$Se as tracer. The concentrations of $^{82}$Se in organs and body fluids and the distributions of Se species, according to time elapsed and the administered dose, were determined by gel filtration HPLC-ICP-MS | 195 |
| Se | Plasma | NAA;-;- AF;Hy;L | No significant difference in plasma Se concentrations was observed between subjects living next to a mercury mine, subjects exposed to excessive physical stress, two retired miners treated with the chelating agent DIMAVAL and controls. A significant change of selenoprotein-P concentration was noted only in the group exposed to physical stress | 78 |
| Se | Plasma | AA;ETA;L | Reference values for Se in plasma were determined for groups of healthy and diseased subjects in Barcelona. Significantly lower values were observed in subjects with malignancies or chronic renal failure compared to controls. Children of mothers infected with HIV-1 had significantly lower Se values than healthy children | 374 |
| Se | Renal cortex, liver, and hair | AA;Hy;- | Se concentrations were determined in the renal cortex, liver and hair of 64 residents from northern Poland (Gdansk region) aged 17–81 years, who died suddenly. There was no correlation of Se concentrations with age, nor between Se levels in hair, renal cortex and liver | 375 |
| Se | Serum | AA;ETA;- AA;Hy;- | The performances (LODs, LOQs, repeatability and results of the analysis of Seronorm Trace Element Serum) for methods for the determination of Se in serum were compared | 188 |
| Se | Serum | AA;ETA;- | A solution of 1% v/v $NH_4OH$–0.05% w/v Triton X-100 was proposed for the dilution (1:5) of serum samples, prior to introduction into a THGA, with 10 μg Pd–3 μg $Mg(NO_3)_2$ as chemical modifier. Under optimized conditions, $m_o$ was 49 pg and LOD 30 μg $l^{-1}$ Se | 187 |
| Se | Serum | AE;ICP;L | An "interference-free" method was proposed for the determination of Se in serum, after acid digestion. Analytical recovery was 91.6% and RSD ($n$ = 10) 2.1%. Addition of KOH to the digested samples greatly reduced interferences | 376 |
| Se | Serum | AA;Hy;L | Changes in serum Se levels of patients with head and neck cancer were followed for 1 year after radiotherapy. In all patients, serum Se levels were significantly lower than controls. After radiotherapy, Se levels increased in 10 patients who were cured but remained low in those who were not | 377 |
| Se | Serum | MS;ICP;L | Blood serum was diluted in 1 M $HNO_3$–0.1% TritonX-100–0.8% 1-butanol. LOD was 0.5 μg $ml^{-1}$. Repeatability and intermediate precision were (RSD%) 2.0% and 3.2%, respectively. The analysis of RMs was satisfactory. The correlation between ICP-MS and AAS results was $r^2$ = 0.96 | 189 |
| Se | Serum | MS;ICP;L | Serum Se was determined in a retrospective study in 100 patients with aggressive B-cell non-Hodgkin's lymphoma subjects. The results suggested that serum Se concentration at presentation predicted positively for dose delivery, treatment response and long-term survival, and, unlike other existing prognostic factors, Se supplementation might offer a novel therapeutic strategy | 197 |

**Table 1** Analysis of clinical and biological materials (*Continued*)

| Element | Matrix | Technique; atomization; presentation[a] | Sample treatment/comments | Ref. |
|---|---|---|---|---|
| Se | Serum | AF;Hy;L | The measurement uncertainty of the result of a determination of Se in serum was estimated according to the 'ISO guide to the expression of uncertainty in measurement'. The method included a digestion procedure using $H_2SO_4$, $V_2O_5$ in $H_2SO_4$ and $H_2O_2$ and detection by HG-AFS. The major sources of uncertainty were found to be due to recovery of the procedure, measurement of peak heights and the purity of $Na_2SeO_3$ | 378 |
| Se | Serum | AA;ETA;L | Serum Se levels were measured by ETAAS in samples from 399 members of a cohort study of Barrett's oesophagus patients undergoing endoscopic surveillance and compared with markers of neoplastic progression. The preliminary results suggested that higher serum Se levels may be associated with a reduced risk of oesophageal adenocarcinoma among persons with Barrett's oesophagus | 196 |
| Se | Serum | MS;ICP;HPLC | Se-containing proteins were separated by anion exchange (Mono Q HR 5/5) and affinity chromatography (Hi-Trap Heparin- and Hi-Trap Blue-Sepharose columns) with post-column ID analysis coupled to an octapole reaction system for ICP-MS. The Ar dimers on $^{78}Se$ and $^{80}Se$ were suppressed by pressurizing the octapole chamber with $H_2$. The three main Se fractions were selenoprotein P, albumin and glutathione peroxidase | 40 |
| Se | Serum, CRMs (serum, urine and tissues) | MS;ICP;- | A method was developed for the determination of Se in biological materials by ICP-MS with an octapole reaction system, using $H_2$ as reaction gas and ID. The measured isotope ratios were $^{78}Se$:$^{77}Se$ and $^{80}Se$:$^{77}Se$. RSD was 0.2% ($n = 5$) for both isotope ratios | 39 |
| Se | Tissues | AA;ETA;fluorimetry | Se concentrations in *post-mortem* tissues from a case of fatal poisoning with sodium tetraoxoselenate were evaluated and compared with four other fatal cases | 379 |
| Se | Urine | AA;ETA;- AA;Hy;L | See As, ref. 80 | 80 |
| Se | Urine | MS;ICP;HPLC | The stability of $Se^{VI}$, selenourea, TmSe, SeMet and SeEt in urine, at concentrations from 30 to 60 μg $l^{-1}$, stored in the dark at −20 °C, 4 °C or *ca.* 25 °C, was evaluated. Se species were determined by mixed ion-pair reverse phase LC-ICP-MS. The results indicated that urine samples for Se speciation can be safely stored at −20 °C for a up to a month | 191 |
| Se | Urine | MS;ICP;HPLC MS;APCI;- | The major Se metabolite from human urine was separated, purified and identified as a selenosugar, possibly Se-methyl-*N*-acetylselenohexosamine, by preparation techniques and multi-dimensional HPLC-ICP-MS and APCI-MS | 193 |
| Se | Urine | MS;ICP;HPLC | A method for the determination of Se species ($SeO_3^{2-}$, $SeO_4^{2-}$, SeMet, SeEt and TmSe) by gel-permeation chromatography and ICP-MS was developed. The eluent was 25 mM TMAH and 25 mM malonic acid at pH 7.9. Method performance were assessed by the analysis of CRMs and spiked samples and by comparison with separation by cation-exchange chromatography. Two unknown Se compounds were detected in human urine | 192 |
| Se | Urine | AA;Hy;L | See As, ref. 79 | 79 |
| Se | Urine | MS;ICP;HPLC | Several minor selenometabolites were detected in rat urine, one of which, monomethylseleninic acid, was artefactually generated *in vitro* from selenosugar under aerobic conditions and also transformed through oxidation by $H_2O_2$ | 194 |
| Se | Urine | MS;ICP;HPLC | Samples were prepared by solid phase extraction and eluted with $CH_3OH$. Se species were separated by ion-pairing HPLC-ICP-MS with a mobile phase of 2 mmol $l^{-1}$ hexanesulfonic acid, 0.4% acetic acid, 0.2% triethanolamine (pH 2.5), and 5% $CH_3OH$. To identify possible metabolites, compounds not commercially available were synthesized and characterized by ES-MS. Selenoadenosylmethionine was detected for the first time | 380 |
| Se | Urine, serum | MS;ICP;L | See As, ref. 30 | 30 |
| Se | Water and urine, kelp powder, tobacco | ICP;MS;Hy | See As, ref. 32 | 32 |
| Si | Liver, kidney, spleen, lung, heart, and brain (rat) | AA;ETA;- | See Fe, ref. 355 | 355 |
| Sr | Bone | MS;ICP;- | The relationship between Sr and histomorphometric parameters in iliac crest bone biopsies was assessed in 74 patients with chronic renal failure undergoing haemodialysis. No correlation was found between the various histomorphometric parameters and the Sr:Ca ratio, but statistically significant differences were observed among the Sr:Ca ratio for the different histological forms. Biopsies with higher bone Sr had higher levels of osteoid tissue | 199 |
| Ti | Human albumin, blood and plasma | AE;ICP;L | See B, ref. 28 | 28 |

**Table 1** Analysis of clinical and biological materials (*Continued*)

| Element | Matrix | Technique; atomization; presentation[a] | Sample treatment/comments | Ref. |
|---|---|---|---|---|
| Ti | Regional lymph nodes, lungs, spleens and livers (sheep) | AA;ETA;- | Ti release into body organs from single threaded screw implants into the mandibles of sheep was investigated. The analysis of Ti content in regional lymph nodes, lungs, spleens and livers showed no statistically significant difference for successful implants, but higher Ti levels in the lungs and regional lymph nodes, compared to controls, for implants that failed to integrate | 381 |
| Ti | Tissue | PIXE;-;- | See Al, ref. 56 | 56 |
| U | Brain perfusate | MS;ICP;L | An *in situ* brain perfusion technique showed some uptake of U across the blood-brain barrier | 382 |
| U | Urine | MS;ICP;L | A method for the determination of U in urine by HR-ICP-MS was optimised to achieve the best precision for both the isotope ratios and the total U concentration and applied to study the stability of U in urine under pre-set storage conditions | 202 |
| U | Urine | MS;ICP;L | SF-ICP-MS was applied to the determination of $^{235}U$, $^{238}U$ and their isotope ratio in human urine, after UV photolysis | 37 |
| U | Urine | TIMS;-;- | The concentration and ratio of U isotopes in 24 h urine samples from 27 allied forces Gulf War veterans were determined. Results confirmed the presence of depleted U in 14 samples | 201 |
| U | Urine | MS;ICP;L | The results of an ICP-MS method for the determination of U in urine, over a wide range of concentration and isotopic composition, were consistent with those obtained by two currently used techniques, fluorimetry and alpha spectrometry after a purification procedure. The ICP-MS method has limited sensitivity for the determination of the minor isotope $^{234}U$ | 200 |
| U | Urine | MS;ICP;L | Normal U concentrations in subjects living in rural and urban areas were determined to be 0.001–0.06 μg $l^{-1}$ | 204 |
| V | Food and Chinese medicine | AA;ETA;- | Experimental conditions for the determination of V by ETAAS were investigated. The combination of a pyrolytic coated graphite tube and fast increasing temperature gave enhanced sensitivity and removed memory effects | 257 |
| V | Lung tissue | AA;-;- | V concentrations in lung tissue taken at autopsy from residents of Mexico City in the 1990s were significantly higher (mean ± SD: 1.36 ± 0.08) than those from people deceased in the 1960s (1.04 ± 0.05).V concentrations were not correlated with gender, smoking habit, age, cause of death, or occupation | 205 |
| V | Parenteral solutions | AE;ICP;FI | Cloud point extraction of V, as the V–2-(5-bromo-2-pyridylazo)-5-diethylaminophenol complex, was employed for its preconcentration prior to determination by FI-ICP-AES. The enrichment factor was 250, LOD was 16 ng $l^{-1}$ and precision (RSD) 2.3% at 2.0 μg $l^{-1}$ | 19 |
| V | Serum, urine | MS;ICP;L | V was measured in urine and serum by HR-ICP-MS after 20-fold dilution with 0.3% $HNO_3$, using matrix-matched standards. LOD was 10 pg $ml^{-1}$, repeatability was <2.0% at 200 pg $ml^{-1}$ and day-to-day precision <4.0%. Recoveries of spiked amounts were 99 ± 2 and 98 ± 3% ($n = 3$) from urine and serum, respectively. V concentrations ranged from 10 to 1500 pg $ml^{-1}$ in urine and from <10 to 760 pg $ml^{-1}$ in serum | 36 |
| V | Serum, urine | AA;ETA;L | The pharmacokinetics of V were assessed in 5 human volunteers who received *i.v.* 90 ml of a commercial 20% albumin infusion solution containing 47.6 μg V as an impurity, by monitoring the concentrations of V in serum and urine | 206 |
| V | Tissue | PIXE;-;- | See Al, ref. 56 | 56 |
| W | Plasma | MS;ICP;L | A method for the determination of W in blood plasma within the range 10–500 ng $ml^{-1}$ was validated and applied to the study of W binding to plasma proteins by ultrafiltration | 383 |
| Zn | Blood | AA;-;L | See Pb, ref. 348 | 348 |
| Zn | Blood and bone | AA;-;- | The effect of low dietary Ca on maternal Zn nutritional status was studied in rats. The results suggested that a low Ca intake during pregnancy and lactation would produce an increase of Zn utilisation, reflected in increased Zn content in maternal blood and bone | 210 |
| Zn | Blood and thyroid tissue | XRF;-;- | See Cu, ref. 68 | 68 |
| Zn | Blood, tissues | AA;-;- | See Cd, ref. 344 | 344 |
| Zn | Blood, urine | AA;-;L | See Cu, ref. 88 | 88 |
| Zn | Brain cells | XRF;-;- | See Ca, ref. 53 | 53 |
| Zn | CRMs | AA;-;- | See Cd, ref. 26 | 26 |
| Zn | CSF | AA;-;L MS;ICP;L | See Cu, ref. 84 | 84 |
| Zn | Faeces | MS;ICP;L | Zn concentrations and Zn isotope ratios were determined in acid digested faecal samples from a human nutrition study using an ICP with a novel combination of high-resolution and multi-collector mass spectrometric detectors. Good agreement with TIMS was found for isotope ratios | 51 |
| Zn | Human lenses | AA;-;- | See Fe, ref. 82 | 82 |
| Zn | Intestine, kidney, liver, lungs | AA;F;- AA;ETA;- | See Cd, ref. 346 | 346 |
| Zn | Liver cytosol | XRF;-;- | See Cu, ref. 58 | 58 |

**Table 1** Analysis of clinical and biological materials (*Continued*)

| Element | Matrix | Technique; atomization; presentation[a] | Sample treatment/comments | Ref. |
|---|---|---|---|---|
| Zn | Liver, kidney, lung, spleen, brain, and serum (rat) | AA;ETA;- AA;F;- | See Cu, ref. 351 | 351 |
| Zn | Liver, lung, kidney, brain, hair and nails | AA;-;- XRF;-;- | See Cd, ref. 81 | 81 |
| Zn | Mammalian cultured cells | XRF;-;- | See Cu, ref. 149 | 149 |
| Zn | Medicinal plants | AA;-;SEC | See Mg, ref. 113 | 113 |
| Zn | Plasma and protein fractions | AA;-;L | A range of analytical techniques (ELISA, SEC, electrophoresis and MALDI-TOF-MS) were used to define the biochemical alterations of a new disorder of Zn metabolism, characterized by recurrent infections, inflammation, hyperzincaemia and high plasma concentrations of calprotectin, the the major Ca and Zn-binding protein in phagocytes | 209 |
| Zn | Plasma, hair | AA;-;- | See Cu, ref. 352 | 352 |
| Zn | Prostatic tissue, serum (rat) | AE;ICP;- | Experimental studies were carried out in rats treated with intraprostatic injections of Zn to compare two forms of Zn delivery, as a solution or as liposome. Changes in serum and prostatic Zn concentrations were assessed. The findings were discussed | 211 |
| Zn | Serum | AA;-;L | See Cu, ref. 86 | 86 |
| Zn | Serum | AA;F;L | See Cu, ref. 207 | 207 |
| Zn | Serum | AA;-;L | See Cu, ref. 150 | 150 |
| Zn | Serum | AA;-;- | See Cu, ref. 353 | 353 |
| Zn | Tissues (rat) | AA;-;- | See Cu, ref. 354 | 354 |
| Various | Biological specimens | XRF;-;- | The combination of SRXRF microprobe with other micro-analytical techniques based on accelerated particle beams, such as Rutherford backscattering spectrometry and PIXE, for the imaging and quantification of trace metals in thin biological specimens was discussed | 384 |
| Various | Blood, urine, faeces | MS;ICP;- | Methods for the study of mineral metabolism in humans by means of stable isotopes were reviewed. HR-ICP-MS provided adequate precision at acceptable cost | 42 |
| Various | Bone (penguin) | XRF;-;S | The distribution of chemical elements in Adelie penguin bone was determined by XRF. As, Br, Co, Cr, Cu, Fe, Hg, Mn, Ni, Rb, Sr, Ti and Zr were among the detected trace elements | 57 |
| Various | Carcinoma kidney and stomach | PIXE;-;- | The results of simultaneous trace elemental analysis carried out in samples of carcinoma kidney and stomach using PIXE were reported and discussed in relation to the role played by the trace elements in initiating, promoting or inhibiting cancer in various organs | 65 |
| Various | Chinese medicines | AE;ICP;- MS;ICP;- | Sample digestion techniques and applications of ICP-AES and ICP-MS to the determination and speciation of trace elements in traditional Chinese medicines were reviewed | 117 |
| Various | Clinical and biological materials, foods and beverages | -;-;- | The 2003 ASU highlighted recent trends, in particular the growth in the employment of permanent chemical modifiers for electrothermal atomisers and the important contribution to most of the reported innovations made by China-based scientists | 1 |
| Various | Cytosol of human organs | MS;ICP;L | The binding of metals to biomolecules present in tissue cytosols of human organs was investigated by SEC-ICP-MS. Identification of metalloproteins was carried out by specific protein assays, *i.e.*, enzymatic assays or immunochemical reactions, in collected fractions of the chromatographic separations. The results of this study and their biological significance were discussed | 385 |
| Various | Drugs of abuse | XRF;-;- | SRTXRF was applied to determine the trace element profile in small samples (10 μg) of drugs of abuse, to help with the identification of their origin. Such a test would not be possible with standard TXRF or other techniques for elemental analysis | 102 |
| Various | Environmental and biological samples | AA;F;L AA;ETA;L | The performances of hydraulic high pressure nebulization techniques for sample introduction in AA were assessed. Analytical methodologies were developed for Ag, Al, Ba, Be, Bi, Cd, Co, Cr, Cu, Fe, Mn, Mo, Ni, Pb, V, Sr and Tl in a variety of environmental and biological samples and human samples of clinical interest | 386 |
| Various | Hair | XRF;-;S | Hair samples from two Egyptian mummies were analysed using a conjunction of structural and elemental synchrotron methods. Elemental mapping showed a heterogeneous distribution which was related to mummification and cosmetic treatments | 387 |
| Various | Hair | XRF;-;S | Concentrations of certain elements in hair were shown to vary as a function of the position on the head | 388 |
| Various | Human and food samples | XRF;-;- | SRXRF analysis has been investigated for the simultaneous determination of the multielement composition of human, animal and vegetable samples. Concentrations of the following elements were determined: K, Ca, Ti, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, Ga, Ge, As, Se, Br, Rb, Sr, Y, Zr, Nb, Mo, Hg, Pb, Bi, Th, U. SRXRF was shown to be fairly informative for estimating the specific features of the multielement composition of biosubstrates | 389 |

**Table 1** Analysis of clinical and biological materials (*Continued*)

| Element | Matrix | Technique; atomization; presentation[a] | Sample treatment/comments | Ref. |
|---|---|---|---|---|
| Various | Human biological matrices | AA;-;- MS;ICP;- | A review of trace element analysis in relation to occupational and environmental medicine was presented | 3 |
| Various | Human CNS tissue | XRF;-;S | The role of metals in the pathogenesis of two neurodegenerative diseases, *i.e.*, Parkinson's Disease (PD) and amyotrophic lateral sclerosis (ALS), was investigated by quantitative and topographic elemental analysis, performed using synchrotron microbeam-XRF, on samples of selected parts of human brain and spinal cord, taken at autopsy from subjects with PD, ALS and controls. The results and the differences between patients and controls were discussed | 54 |
| Various | Kidney | XRE;-;- | The distribution of selected elements in cancerous and non-cancerous kidney tissues was determined by SR induced XRE. The differences between perfused and non-perfused tissues were described | 67 |
| Various | Proteins | -;-;- | The advantages and drawbacks of different chromatographic techniques (size exclusion, ion exchange, reversed phase and affinity) for the separation and determination of metal-binding proteins were discussed | 2 |
| Various | Tissues | PIXE;-;CZE MS;ICP;CZE | Methods for the separation and identification of mammalian metallothioneins using CZE coupled with PIXE or ICP-MS were reviewed | 390 |
| Various | Urine | XRF;-;- | The determination of electrolytes and heavy metals in urine of children with a congenital cyanotic heart defect and after heart transplantation suggested they may have an increased loss of electrolytes. In the urine of children from polluted areas, higher concentrations of heavy metals were observed | 391 |
| Various (10) | Blood, placenta | MS;ICP;- AE;ICP;- | The concentration of Cd, Cs, Cu, Fe, Mg, Mn, Rb, Se, Sr and Zn was determined in maternal and umbilical cord blood and in placental tissue from subjects with intrauterine growth restriction and controls. The results were discussed in relation to fetal growth | 75 |
| Various (10) | Heroin | AA;ETA;- AE;ICP;- | Trace and major elements were determined in 44 samples of illicit heroin from Southeast Anatolia, Turkey, after microwave oven digestion with $HNO_3$, by ETAAS (Cd and Pb) and ICP-AES (Al, Ba, Ca, Cu, Fe, Mg, Mn, and Zn) | 103 |
| Various (11) | Breast milk | MS;ICP;L | The concentrations of As, Ca, Cu, Fe, K, Na, Mg, Mn, Pb, Se and Zn, were measured in 32 breast milk samples from healthy women living in the Dongting Lake area (China) | 392 |
| Various (12) | Chinese traditional medicines | AA;-;- | Ca, Cd, Co, Cr, Cu, Fe, Mg, Mn, Mo, Ni, Pb and Zn were determined in nine (Xiaokewan, Yuquanwan, Kelening, Jiangtangshu, Jiangtang I–V) Chinese traditional medicines, used to cure diabetes, after digestion with 4:1 $HNO_3$–$HClO_4$. Analytical recovery ranged from 97% to 105% and RSD was lower than 5% | 115 |
| Various (12) | Chinese traditional medicines | AA;F;L | Concentrations of twelve elements (Ca, Cd, Cr, Cu, Fe, K, Mg, Mn, Na, Ni, Pb, and Zn) and the Cu:Zn and Ca:Mg ratios, were determined in 'Maitong' | 393 |
| Various (19) | Kidney | XRF;-;- | The distribution of 19 trace elements, including Ca, Cd, Fe, Pb, Rb, S, Se, Ti, Zn and Zr, in renal cell carcinoma was investigated in relation to stage of disease in a case control study. Changes in element concentration was related to progress of the disease | 66 |
| Various (20) | Bone-marrow fluid | AE;ICP;- MS;ICP;- | The bone-marrow fluid sample was centrifuged and then digested with $HNO_3$. Twenty elements were determined over the concentration range from 1610 μg $g^{-1}$ for Na to 0.00043 μg $g^{-1}$ for W. The elements Cs, Fe, K, Rb, Sb and Zn were enriched in bone-marrow fluid, compared with human blood serum | 85 |
| Various (20) | Human placenta, fetal membranes | TXRF;-;S | TXRF was applied to determine the trace element contents in human full-term placenta and fetal membranes in a comparative study of the effect on environmental pollution. The problems of the 'truncation' of the measured concentration distribution by the LOD were discussed | 394 |
| Various (4) | Blood | XRF;-;L | XRF was used to determine Cu, Fe, Pb and Zn in blood samples from children living in the Gharb region (Morocco), after sample microwave aided digestion with $HNO_3$ and $H_2O_2$. Pb levels in blood were $<50$ μg $l^{-1}$ | 395 |
| Various (4) | Blood, serum | AA;ETA;L | Al, Cr, Mn and Pb concentrations were determined in blood samples from 105 patients with chronic renal failure who had undergone regular dialysis treatment and 200 controls (Barcelona, Spain). Chronic haemodialysed patients had higher levels of Al and Cr, but lower Mn, whereas Pb levels were similar in both groups | 83 |
| Various (4) | Blood, urine | AA;ETA;L | As, Cd, Pb and Se concentrations were determined in blood and urine of children from areas with high or low levels of pollution in Saint Petersburg | 396 |
| Various (4) | Faeces | AA;-;- | The concentrations of As, Cd, Hg, Pb and organochlorine and organophosphate pesticides were measured by AAS and GC in stools from 426 infants (Manila, Philippines). Stool analysis was suggested as a method to assess fetal exposure to environmental pollutants | 74 |
| Various (4) | Hair | AA;F;- | Cu, Mg, Pb and Zn levels were determined in scalp hair from 173 children and young people (1–18 years) with osteomuscular pains of unknown origin ("growing pains") and 108 controls. The observed differences were discussed | 397 |

**Table 1** Analysis of clinical and biological materials (*Continued*)

| Element | Matrix | Technique; atomization; presentation[a] | Sample treatment/comments | Ref. |
|---|---|---|---|---|
| Various (4) | Hard tissues (shellfish) | AE;ICP;- | The determination of Cu, Fe, Mn and Zn in hard tissues of shellfish by ICP-AES was reported. Solvent (hexyl acetate) extraction of the DDC chelates was used to separate the analytes from interfering Ca ions | 125 |
| Various (4) | Liver | MS;ICP;- | Ag, Cd, Sb and Pb were determined in human liver tissue collected at autopsy from 157 paediatric subjects. No significant difference was observed for the four elements between Sudden Infant Death Syndrome cases and those who had died of an identified disease. Age dependence of the element concentrations was investigated | 29 |
| Various (4) | Medicinal herbs | AA;-;- | The contents of As, Cd, Cr and Pb was determined in 13 herbs after either incineration, wet or microwave-aided digestion. Microwave-aided digestion had the best recovery and precision. LODs were 0.64, 0.03, 0.20 and 0.45 ppb for As, Cd, Pb and Cr, respectively | 220 |
| Various (4) | Medicinal plants | MS;ICP;- | The As, Cd, Hg and Pb content was determined by ICP-MS in 115 samples of the most consumed species (15) of medicinal plants in Catalonia, Spain. Hg was not detected in any of the samples. Median daily intakes of As, Cd and Pb, from 2 herbal teas of 2 g per day, contributed to about 0.2%, 1% and 5%, respectively, of the total dietary intake for the population of Catalonia | 110 |
| Various (4) | Serum, seminal plasma | AA;-;L | Concentration of Cd, Cu, Pb and Zn were measured in seminal plasma and blood serum collected from fertile and infertile men in Turkey. All levels were within the normal values | 76 |
| Various (5) | Cerebral cortex and hippocampus | XRF;-;- | Changes of the relative contents and distributions of Br, Cl, Cu, Fe and Zn in the cerebral cortex and hippocampus brain regions were observed in neonatal, iodine-deficient model rats | 398 |
| Various (5) | Medicinal herbs | AA;F;- | Cd, Pb, Mo, Ni and Zn were determined by FAAS and differential pulse polarography (anodic and stripping voltammetry) in 27 samples of medicinal herbs taken from various places in Bielsko Biala and the neighbouring area, after wet digestion in a microwave oven. A CRM (Oriental tobacco, CTA-ATL-1) was analysed for calibration and validation of analytical procedures | 399 |
| Various (55) | Nails, hair | MS;ICP;LA | The capabilities of LA-DF-SF-ICP-MS for the determination of 55 elements in nails and hair were studied. Quantification was performed by external calibration using in-house matrix-matched standards in tablet form and correction for variations in ablation efficiency by internal standardisation | 100 |
| Various (6) | Chinese herbal medicines | AA;ETA;- | Methods for the determination of Cu, Fe, Ge, Mn, Se and Zn in three Chinese traditional and herbal drugs were studied. Samples (0.5 g) were digested with $HNO_3$–$HClO_4$ (4:1). High levels of Cu, Fe, Mn and Zn were reported and their therapeutical significance discussed | 114 |
| Various (6) | Chinese traditional medicines | AA;-;- | Trace elements (Co, Cu, Fe, Mn, Ni and Zn), were determined in seven Chinese traditional medicines (Dang-gui, Jixueteng, Dihuang, Honghua, Tusizi, Yinyanghuo, and Shechuangzi), after digestion with 4:1 $HNO_3$–$HClO_4$. Analytical recovery ranged from 96.4% to 102.1%. The invigorating drugs contained more Cu, Fe, Mn, Zn than other elements | 400 |
| Various (6) | Semen (animal) | AA;-;- | The concentrations of Cd, Cu, Fe, Ni, Pb and Zn were determined in semen samples from bulls, rams, boars, stallions and foxes | 77 |
| Various (6) | Serum | MS;ICP;L | 50 μl sample was injected into 1% $HNO_3$ in a simple FI system, with on-line standard addition. No other sample preparation was required. Results in good agreement with certified values were obtained for Al, Mn, Fe, Co, Cu and Zn in a serum RM | 31 |
| Various (7) | Chinese traditional medicines | AA;F;- | The content of 7 elements was measured in a Chinese traditional remedy (Taponin tablet recipe I) and found to be in the order Fe > Ca > Mg > Zn > Cu > Mn > Cd. Fe was significantly higher than the others | 116 |
| Various (7) | Human breast milk, urine | AE;ICP;L AA;F;L AA;ETA;L | Seven elements, Ca, Cd, Cu, K, Mg, Na, P and Zn, were determined in human breast milk and urine of Japanese mothers and their interrelations were discussed | 72 |
| Various (7) | Teeth | XRF;-;- | The elemental distribution in human teeth treated with dental amalgam was measured by XRF from the root to the enamel, especially around the amalgam, after its total removal | 55 |
| Various (8) | Hair | AE;ICP;- | Temperature, digestion time and $HNO_3$:$H_2O_2$ ratio for the dissolution of hair samples prior to ICP-AES analysis were optimised. The method was applied to the analysis of Cd, Co, Cu, Fe, Mn, Ni, Pb and Zn in CRMs and hair samples from residents of India | 401 |
| Various (9) | Hair, nails | AA;F;- AA;ETA;- | Bi, Ca, Cd, Cu, Fe, Mn, Ni, Pb and Zn were determined by FAAS or ETAAS in hair or nails after digestion with 2 M NaOH. Percent recoveries were 90.0–110.8% | 6 |

[a] Hy indicates hydride and S, L, G and Sl signify solid, liquid, gas or slurry introduction, respectively.

respectively, followed by cation exchange to take out the Ag. Despite these multiple steps the recovery of $BrO_3^-$ was reported as 90% with a precision of 2% RSD when measured by ICP-MS.

**2.1.2 Digestion.** It is surprising and of some concern that after so many years experience with different digestion procedures there is so much variation in results obtained, dependent on the technique adopted. *Reports from projects*

*where comparisons of, for example, dry ashing, acid digestion and microwave acid digestion were made, consistently indicate differences in recovery and repeatability*. Fuh *et al.*[220] obtained average recoveries of 80, 86 and 95%, respectively, with these three methods for measurements of As, Cd, Cr and Pb in herbs. In a similar study by Juranovi *et al.*[221] trace elements were measured by ICP-AES in seeds and seed oils after open vessel, closed vessel and microwave heated closed vessel digestions. Closed vessel digestion was found to give best recovery and precision. These variations were evident despite the routine observations from primary validation of methods, where good recoveries, consistency with certified values of RMs and excellent repeatability were reported.[222–224] A combination of focused microwave digestion and ultrasonic leaching speeded up sample preparation of meat and provided for accurate, precise results.[225] Claims that a single procedure is applicable to a variety of food matrices[222] might, therefore, be best viewed with caution. Use of aggressive reagents, such as $V_2O_5$, tends to afford the better results.[223,224] Optimised digestion procedures for specific applications seen include those for measuring Se in yeast[226] and Hg in various foods.[227] A rapid automated digestion apparatus was developed by Jacob and Berndt[9] with direct coupling for FAAS. Powdered samples suspended in 2.5 M $HNO_3$ passed through a Pt–Ir capillary heated electrically to 320 °C and the analysis was completed within 3 min. Addition of HF permitted the digestion of samples with high silicate content. In a novel approach, pressurised acid digestion was accomplished in open vessels.[5] Samples, with $HNO_3$ or $HNO_3$–$H_2O_2$, were placed inside the chamber of a high pressure asher. Nitrogen was introduced to a pressure of 100 bars and heating achieved with microwave energy. Results for volatile elements such as As, Hg and Se in CRMs were within the 95% confidence intervals.

**2.1.3 Preconcentration.** A research group in Argentina explored *several different devices for analyte enhancement* and applied these to a number of investigations. On-line preconcentration of Pb in drinking water was achieved using 2-(5-bromo-2-pyridylazo)-5-diethylaminophenol (5-Br-PADAP) and Amberlite XAD-16.[228] Together with ultrasonic nebulisation an enhancement factor of 150 was found compared with a conventional ICP-AES system and the LOD from a 10 ml sample was 0.2 ng $ml^{-1}$. To measure Cd in drinking water, again by ICP-AES, a complex with 8-hydroxyquinoline was collected onto activated carbon.[229] Sample volumes of 50 ml were used and the LOD was 18 ng $l^{-1}$. These workers also analysed honey, measuring Cd by FAAS after forming the Cd-5-Br-PADAP complex[230] and Pb by ICP-MS as the 8-hydroxyquinoline complex.[231] Finally, this group measured Al and Cr in solutions used for parenteral nutrition[20,105] using ICP-AES and FAAS, respectively. The Al was concentrated with a micelle-mediated phase separation with PONPE, while Cr was retained from the sample by 4-(2-thiazolylazo) resorcinol (TAR) and Amberlite XAD-16. With 50 ml samples the LODs were 0.25 μg $l^{-1}$ and 20 ng $l^{-1}$, respectively, for Al and Cr. Other descriptions of on-line FI systems, such as functionalised resins, for analysis of different foods and beverages were similar in principle to those reported in previous Updates. Somewhat more novel were the measurements of Hg in food CRMs and Sn in canned foods, by ETAAS.[124,232,233] An on-line arrangement using copper pyrrolidinedithiocarbamate (Cu-PDC) was employed for concentrating either total Hg[232] or methylmercury,[124] with the achievement of around 6 ng $l^{-1}$ LOD. Manora *et al.*[234] preconcentrated Hg in drinking water onto an electrode of glassy carbon particles coated with gold for measurement by FAAS. For the measurement of Sn, the element was collected onto a tungsten probe by an electrodeposition process and ETAAS detection. The LOD was 0.08 μg $l^{-1}$ and the authors also discussed the atomisation mechanism of Sn from the tungsten probe.[233] Unfortunately for many readers the full text of this paper is in Chinese. In an ingenious procedure, As in a liquid sample was reduced to $AsH_3$ in a closed headspace vial. A 4 μl drop of 1 : 3 pyridine–benzyl alcohol, with AgDDC, suspended at the tip of a microsyringe and within the vial reacted with the $AsH_3$ during 7 min at 35 °C. After equilibration had taken place the microdrop was retracted and immediately injected for measurement by ETAAS. From a 2 ml sample the LOD was 45 pg $ml^{-1}$.[235]

### 2.2 Speciation

Published work relating to *element speciation* divided equally among As, Hg and Se. A small minority of reports reflect on binding of a variety of elements to proteins or other larger molecules within foods–milk whey,[236] liver,[33] and medicinal plants.[113] In these studies a variety of detection systems were used following chromatographic separation to characterise the species associated with the elements, which were also quantified.

Investigations of just a single element within a sample type were directed at features such as extraction and subsequent stability (see 2.1.1 above), the separation itself, and techniques for identification and analysis of specific food types. Apart from the now well-established HPLC separation methods, developments seen in the last year included comparisons of different elutions. For example, it was observed that better separation of As species in drinking water is obtained using Tris rather than phosphate buffer.[237] Innovative refinements involved two-step separations to demonstrate even more of the many Se species in foods. Chassaigne *et al.*[238] used HPLC and gel electrophoresis, while SEC and then graphitic carbon HPLC were employed by Lindemann and Hintelmann.[239] *With the greater number of species now being observed the challenge is to confirm their identity*. For this purpose there is increasing use of ES-MS techniques. Yoshida *et al.*[215] found that while most Se in yeast is present as selenomethionine, a number of other species, some of which were unidentified, are also present. The presence in yeast of selenodiglutathione and the selenotrisulfide of glutathione and cysteinylglycine were reported for the first time.[239] Worryingly high concentrations of toxic As species were reported to be present in fish from the North Sea.[240] Vinas *et al.*[241] found that As is present in baby foods and that this derives from raw fish ingredients, especially plaice. However, the only species that was detected was the non-toxic arsenobetaine. Setting aside chromatographic methods, $As^{III}$ and $As^{V}$ in milk were determined by HGAFS.[242] Measurements before and after reduction with KI gave values for the two oxidation states. The procedure was also used to measure $Sb^{III}$ and $Sb^{V}$.

### 2.3 Applications using hydride generation

*Several routine applications involving hydride generation procedures were reported* for many different food types. Measurements of Cd in Chinese herbal medicines[118] and Te in milk[243] by HGAFS were among the slightly unusual pieces of work. Yin *et al.*[244] employed thiourea to reduce $As^{V}$ to $As^{III}$ and to minimise interference from transition metals. Many workers used microwave heating to digest organometallic specimens. Renard and Tompkins,[226] deliberately avoiding the use of $HClO_4$, heated yeast with $HNO_3$–$H_2O_2$ and compared the results then obtained using FAAS, ICP-MS, HGAAS, fluorimetry and NAA. Most were comparable but HGAAS values were higher by about 10%, with high SDs. Marrero *et al.*[245] studied the effects of acetic, citric, nitric and tartaric acids on the continuous formation of lead hydride. Optimum acid concentrations were determined and many potential interferences were studied. Tartaric acid was preferred and the LOD was 4.4 μg $l^{-1}$.

### 2.4 Applications using flame atomic absorption spectrometry

Although there is little that is new to report, a couple of items are of interest. Jacob and Berndt[9] took a Pt–Ir capillary, electrically heated to 320 °C, to act as a digestion column. This was included in a high pressure (>300 MPa) FI arrangement to effect on-line sample digestion. Dried powdered samples were suspended in 2.5 M $HNO_3$ for the measurement of Cd, Cu, Mn, Pb and Zn. The entire analysis was completed within 8 min while the digestion took less than 1 min. In an analogous device, Yebra and Moreno-Cid[218] analysed solid seafood samples following an on-line continuous ultrasound extraction step. With a 30 mg sample the LOD was 0.4 mg $g^{-1}$ and the analysis rate was 60 $h^{-1}$. However, *the majority of work reported where FAAS was used involved preconcentration developments* as reported in section 2.1.3 above, and is not fundamentally different to anything reported in previous Updates.

### 2.5 Applications using electrothermal atomic absorption spectrometry

In an imaginative piece of work, the *distribution of metals across the surface of a platform and the performance of different modifiers were examined* using scanning electron microscopy, multivariate analysis and micro-SXRF. A Zr permanent modifier was found suitable for determining Al in milk.[246] Two papers from the same research group explored the measurement of Hg in foods using automated sample preparation coupled to determination by ETAAS. Total Hg was collected by a displacement sorption pre-concentration procedure involving Cu-DDC. The Hg-DDC complex thus formed was sufficiently thermostable that no modifier was necessary and the LOD was 6.2 ng $l^{-1}$.[232] In a development of this work using a novel adsorption medium the team showed that selective trapping of methylmercury could be accomplished[124] (see 2.8.4 below). A molybdenum tube atomiser was used to measure Cu in herbal medicines prepared as slurries in 10% glycerol.[13] The glycerol also eliminated matrix interferences.

The probe, as an alternative to the L'vov platform, has never been widely exploited. As described in section 2.1.3, above, Wang *et al.*[233] used this device in a method that involved electrolytic separation and concentration of Sn from the sample matrix. With the *tungsten probe* the LOD, from a 200 s deposition time, was 0.08 μg $l^{-1}$. The authors also discussed the mechanism of atomisation. Other reports describe fairly unexciting developments with chemical modifiers and the results from analyses of unusual sample/determinand combinations (see Table 2).

### 2.6 Applications using inductively coupled plasma mass spectrometry

Interesting work featuring ICP-MS for the analysis of foods and beverages was hard to find. *Most publications simply reported useful data from measurements of different sample types*. One report of the use of a dynamic reaction cell was seen, for measurement of Ca and P in foods.[247] Two reaction gases were introduced in succession, $CH_4$ to reduce the $^{40}Ar^+$ signal and $O_2$ to convert $^{31}P^+$ to $^{31}P^{16}O$ for measurement at *m/z* 47, where there was less interference. A high accuracy procedure involving solid phase microextraction, GC separation and ID-ICP-MS was developed for the certification of a fish RM for methylmercury.[121] The RM had been prepared using methylmercury spiked with $^{198}Hg$. The method had an LOD of 2.1 ng $g^{-1}$ and, at a concentration of 1.54 μg $g^{-1}$, the SD was 0.025 μg $g^{-1}$. A sensitive method to measure Hg in water involved the addition of a $^{203}Hg$ enriched spike to the sample for ID-CV-ICP-MS.[248] The LOD was 0.05 ng $l^{-1}$, blanks were low and the method was accurate. Isotope ratio measurements did not feature prominently in this review period except for one study in which Sr was determined in rice.[249] Samples were digested with an aggressive mixture of $HNO_3$–$HClO_4$– HF and then the Rb was removed using Dowex 50W X8. The $^{87}Sr$ : $^{86}Sr$ ratios, measured with a precision of <0.01% CV, permitted discrimination of rice from Australia, California, Japan and China/Vietnam. Work involving multi-technique approaches to increasing the information generated is of note. Nischwitz *et al.*[33] used SEC and HPLC to separate Cu, Fe, Mn and Zn species extracted from porcine liver. The species were identified by ES-MS, while quantitative measurements were produced by ICP-MS. The concentrations of As and other elements in rice were determined by ICP-AES, quadrupole ICP-MS and by magnetic sector ICP-MS.[250] An unusual application that also used magnetic sector ICP-MS was the determination of Pu in foods, in preparation for a "nuclear incident".[251] The LOD, at 0.02 pg $g^{-1}$, is testimony to the exquisite sensitivity that can be achieved by the technique for certain elements. Elements such as Am and Np were also measured. It is hoped that the investigations will not be necessary.

### 2.7 Applications using other analytical techniques

A method for *certification of methylmercury in a fish tissue* RM, using ID-GC-MS, was developed.[121,122] The propylated (Pr) species ($MeHgPr^+$)–$^{202}Hg$ and ($MeHgPr^+$)–$^{198}Hg$ were used to determine the methylmercury concentration of samples with counting at *m/z* 260 and 256, respectively. Several examples of multielement analysis using ICP-AES have been reported (see Table 2). Among the more unusual applications were the analysis of pumpkin seeds and seed oils.[221] For those elements that can be determined in the ICP with higher sensitivity, reports of single element analyses are also of note. Thus, B was measured in varieties of teas and coffees.[252] These workers investigated possible matrix interferences and used an In internal standard. Concentrations of B were in the range from 3 to 28 mg $kg^{-1}$. Methods that exploit EDXRF continue to be reported regularly with multielement analysis of grapes and wine,[253] milk products[254] and measurement of As in drinking water.[96,255]

*Is it appropriate to challenge the use of words?* When elements in SRMs are reported to be at 92–119% and recoveries from composite diet samples as 75–129% with SDs of 0–11.3%, can the method be claimed to give "precise and accurate measurements"?[256] Such statements are not restricted to ICP-MS work but this is a particularly glaring example.

### 2.8 Progress for individual elements

*Elements that are of regular and common interest are discussed in the following sections but it is appropriate to remark here on some others that rarely receive special attention.* Reference has already been made to the analysis of foods for Am, Np and Pu by SF-ICP-MS.[251] It is also unusual to find reports concerning Te but measurement of this element in milk sold in Spain, at concentrations of 1.04–9.7 ng $ml^{-1}$, using HG-AFS, was presented.[243] Zon *et al.*[257] developed an ETAAS procedure to determine V in foods and traditional Chinese medicines. They reported that with very fast heating, pyrolytic coated graphite and measurement of the signal when the temperature was stable, the signal shapes were improved, sensitivity enhanced and memory effects eliminated. In an interesting project reported by Dejneka and Lukasiak[258] both total and 'potentially bioavailable' concentrations of Si in different foods were investigated using ETAAS. The reported concentrations were 1.5–48.38 mg $kg^{-1}$ and 3 μg $kg^{-1}$ to 4.13 mg $kg^{-1}$ dry weight, respectively, with no correlation between the observations. The lists within Table 2 give a flavour of the many other elements that have been occasionally determined in foods and beverages and reported on during the last year.

These are in addition to those unusual elements that feature in reports where results are simply offered by the multi-element measurement technique.

**2.8.1 Aluminium.** The *total daily intake* of Al by adults in Mumbai (Bombay), India, was determined by Tripathi *et al.*[259] At 6.4 mg, this is very similar to intakes reported from other countries. In seeking to focus attention on which food types have the more important contribution to daily intakes of Al, Lopez *et al.*[260] looked particularly at convenience and fast foods. Fresh weight concentrations were from 0.85 to 38.10 μg $g^{-1}$. Pork and chicken based foods had the highest mean concentrations at 8.45 and 13.94 μg $g^{-1}$, respectively. Also of note were foods with spices and aromatic herbs, pasta, certain vegetables and additives. Foods packaged in aluminium containers were also highlighted. These workers also estimated "absorbable Al" using an *in vitro* technique, which gave results of 0.85–2.15% of the total. Given that *in vivo* investigations suggest gastrointestinal absorption of Al is $<1\%$ the relevance of these results may be open to further debate. In a more restricted investigation, Al was determined in 18 different types of sausage.[261] Concentrations were from 0.28 mg $kg^{-1}$ in Zungenwurst (tongue sausage) to 11.39 mg $kg^{-1}$ in Blutwurst (blood sausage). Interestingly, it was the vegetable ingredients and spices that made the greater contribution, rather than materials of animal origin. The authors note that intakes are unlikely to exceed the WHO provisional tolerable weekly intake (PTWI). In other studies designed primarily to demonstrate that methods could be used to provide accurate reliable results, Al was determined in milk powders and in parenteral nutrition solutions.[20,246]

**2.8.2 Arsenic.** Contamination of drinking water in parts of Bangladesh and West Bengal has been known for several years.[96] As a consequence, locally grown vegetables accumulate As. *A survey of As in foods was carried out in a contaminated area of West Bengal* and concentrations of several hundreds of μg $kg^{-1}$ were found.[262] Concentrations were higher in the leafy parts than the fleshy parts of vegetables. Daily dietary intakes in two population groups were 171.2 and 189 μg for adults and 92 and 102 μg for children. The WHO tolerable intake is 2.1 μg $kg^{-1}$ $d^{-1}$. In a later publication the same workers reported similar results together with data for Cu, Mn, Ni, Se and Zn.[263] From a similar survey carried out in Bangladesh, the total As content of vegetables were found to be 0.30–0.49 μg $g^{-1}$. High levels of Pb were also reported.[264] Reports of total As concentrations in other food types included: liquorice confectionery products, 0.55 μg $g^{-1}$;[265] rice, 81–283 ng $g^{-1}$;[250] cow's milk, 3.4–11.6 ng $g^{-1}$;[266] trout raised in fish farms where high concentrations were found and shown to derive from the feeds used;[267] various fish caught in the North Sea;[240] traditional Chinese medicines.[244] A review of As speciation, which discussed the forms found in foods, methods for separation and determination, and certification of RMs, was prepared by McSheehy *et al.*[129] Various As species were detected in sunflower oils,[268] rice,[269] baby foods[241] and milk.[242]

**2.8.3 Lead.** Barton *et al.*[270] analysed drinking water samples collected early in the morning and again in the evening from households in urban, peripheral and rural parts of southern Poland. Morning samples had significantly higher concentrations of Pb and there were also differences associated with location which were attributed to the incidence of leaded plumbing. Geometric mean morning concentrations were 1.42, 2.16 and 2.97 μg $l^{-1}$, while in the evening they were 0.68, 1.24 and 2.28 μg $l^{-1}$ for urban, peripheral and rural samples, respectively. Two studies from Korea showed potential contributions from foodstuffs to daily intakes of Pb. Duplicate diets from 38 households were found to provide a mean intake of 0.337 μg $kg^{-1}$ $d^{-1}$, with no difference between mothers and their children.[271] In a more specialised investigation Pb was measured in 55 brands of dietary calcium supplements.[272] Concentrations were from none-detected to 6.7 μg $g^{-1}$, with highest values in those prepared from bone. The mean intake, on the basis of recommended doses, was calculated to be about 5 μg $d^{-1}$. Lead in wine is a favourite topic for investigation. Stockley *et al.*[273] measured Pb at different stages of the winemaking process in Australia. Features that were associated with higher concentrations of Pb were: use of open top vessels, storage in concrete or waxed wood containers, fining with bentonite or filtering with diatomaceous earth. However, the final concentrations were generally $<30$ μg $l^{-1}$. In a similar project, Pb was measured in Portuguese table and fortified wines.[274] Concentrations increased from 4.7 to 17.2 μg $l^{-1}$ during the vinification process and were attributed to contact with metallic fittings in the equipment. In 83 Italian wines Pb was present at 10–149 μg $l^{-1}$, with higher concentrations in those from the northwest of the country. Isotope ratios were also determined.[275]

**2.8.4 Mercury.** Studying *the consequences of uncontrolled use of mercury to extract gold* in South America has been attractive for a number of years. Santos *et al.*, however, have chosen to look at uncontaminated areas to establish "baseline" data.[276] They examined carnivorous and non-carnivorous fish species and reported Hg concentrations of 0.006–2.529 and 0.008–0.871 μg $g^{-1}$, respectively. Most studies indicate that the major proportion of the Hg is in the methylated form, a trend that is consistent with the results of Rai *et al.*[120] who found 88–100% methylmercury in fish (herring, catfish, barramundi, anchovy) from Australia. Wild mushrooms are not usually considered as a major source of Hg and specimens collected from an area of Poland not subjected to contamination were shown to have trivial amounts, 50–3700 ng $g^{-1}$ dry weight.[277] In another Polish study Hg was determined in plant foods.[278] In a range of vegetables, cereals and beverages, concentrations of $<0.1$ to 14 μg $kg^{-1}$ were obtained and the authors calculated that the weekly ingestion of Hg from these sources would be 8 μg or 3% of the WHO tolerable intake. Sweet and dry wines from the Canary Islands had concentrations of 2.6–4.9 and 1.5–2.6 μg $l^{-1}$, respectively.[279] Using an exquisitely sensitive ID-CV-ICP-MS procedure, Hg in bottled drinking waters from seven countries was measured.[248] The LOD was 0.05 ng $l^{-1}$. In basic method development projects, total and speciated Hg were determined in different food types by CVAAS, CVAFS, ETAAS and ICP-MS (Table 2). In a particularly innovative piece of work, methylmercury in fish was preconcentrated in an FI procedure.[124] The technique involved formation of a Cu–DDC complex which was adsorbed onto a column packed with filter material from a cigarette. Methylmercury was selectively retained at pH 6.8 as it displaced the Cu–DDC. Retained methylmercury was eluted with $C_2H_5OH$ with on-line determination by ETAAS. Recoveries were 97–108%. The intricate methodology developed to determine methylmercury in a candidate CRM was mentioned earlier.[122]

**2.8.5 Selenium.** A method for measuring Se in a range of food types with Se concentrations of 0.05–1 mg $kg^{-1}$ was developed by Das *et al.*[280] This involved digestion and formation of a complex with diethyldithiophosphate which was trapped on a minicolumn of 30 mg $SiO_2$–$C_{18}$. The complex was eluted with a small volume of $C_2H_5OH$ for measurement of Se by ETAAS. *So-called 'new methods' for Se speciation* were described by Chassaigne *et al.*[281] (see 2.2 above). These workers remarked on a number of unidentified species in addition to selenomethionine, selenocystine, $Se^{IV}$ and $Se^{VI}$ in yeast. Yeast is clearly a popular material for analysts eager to face the speciation challenge! Thus, Yoshida *et al.*[215] reported at least three unknown compounds while selenoadenosylmethionine and selenohomocysteine were identified by Wrobel and

Caruso;[216] Lindemann and Hintelmann[239] showed the presence of selenodiglutathione and the mixed selenotrisulfide of glutathione and cysteinylglycine. Enciner *et al.*[282] disclosed a family of Se-proteins derived from replacement of methionine residues by selenomethionine, in the salt-stress-induced protein (SIP18) and heat shock protein (HSP12). Turning away from yeast, Vonderheide *et al.*[283] found selenomethionine, selenoethionine, selenocystine and a number of other species in extracts from Brazil nuts. The same group also reported volatile Se species present in roasted coffee beans.[284] It will be interesting to see if these unusual compounds can be detected in other species where the total Se concentrations are lower than in yeast and nuts. An important feature of the analytical process was examined by Moreno *et al.*,[214] who determined that Se species extracted from lyophilised oyster were stable for up to 10 days when stored at 4 °C in Pyrex containers. Total Se concentrations were reported for cereal-based infant formulae (0.43–17.17 μg per 100 g), seafood (0.63–2.01 μg $g^{-1}$) and dietary supplements (15.9–81.1 μg per tablet).[285–287] The later study revealed that the information given on labels is often inaccurate. Analysis of duplicate diets was carried out to compare total daily Se intakes in American and Hungarian children aged 8–17 years.[288] Results for the Hungarian subjects were about 35% less than their American peers.

### 2.9 Single and multi-element analysis of foods and beverages

In recent years, we have seen reports where the elemental composition of samples has been used to *demonstrate their geographic origins*. Such data have typically been derived from analysis of wines and one particular group, from the Canary Islands, are responsible for much of the work. Continuing their studies Perez-Trujillo and co-workers[289,290] have reported on the concentrations of even more elements in different wines and have refined the way in which the data are treated, setting results into three groups, *i.e.*, rare earths, lead isotopes and other metals. The contribution of each group to the overall procedure and the capacity to discriminate between 'denomination of origin' has been established in a series of publications.[289,291,292] Similar work is now beginning to be reported by others. Taylor *et al.*[293] were also interested in wines. They measured 34 elements in Canadian samples and used multivariate analysis to select a set of ten that permitted 100% discrimination between the two main wine-producing regions. A huge number of measurements from Portuguese wines were reported by Almeida and Vascocelos[294] who suggested that fingerprinting could be applied. From their Cu, Fe and Zn data derived from analyses of 'Cocuy de Penca Firewater' (an illegal Venezuelan spirit drink), Hernandez-Carabello *et al.*[295] developed models with discriminant analysis and artificial neural networks which, they claimed, would identify the location of manufacture. However, Larcher *et al.*[275] were less convinced. In their work they measured Pb and its isotope ratios in wine from 42 provinces of Italy. They concluded that the data were not sufficient to give an effective authentication of sample origin. Other sample types are now the subjects of similar investigations. Identification of origins for hazelnuts,[296] carrots,[297] rice,[249] wheat,[298,299] coffee[300] and tea[301] were reported.

A couple of *unusual sample types* which attracted attention were edible seaweeds[302,303] and mustard plants.[304] Apart from developments in analytical methods for measuring Sn in canned foods,[233,305] little work involving food packaging was seen in the last year.

**2.9.1 Dietary intake studies.** *Total intakes from whole daily duplicate diets* or from individual food items were given earlier for Al, As, Hg and Pb (sections 2.8.1 to 2.8.5). Reports of other elements include further work from a Belgian group (see previous Updates) with emphasis this year on the intakes of Ca, Cu, Fe, Mg and Zn by 2–3 year-old children.[306,307] Concern was expressed about the low levels of Fe (4.8 ± 0.2 mg $d^{-1}$) compared with other countries. A duplicate diet investigation reported from Nigeria[308] showed that weaning foods are poor sources of Ca (16–250 mg $d^{-1}$) and Zn (1.42–3.56 mg $d^{-1}$) when compared against the US recommended dietary allowances (400 and 5 mg $d^{-1}$, respectively). In a study from France, the daily intakes of 21 elements in meals purchased from catering establishments were determined and no undue results were apparent.[309] Skibniewska[310] chose to analyse diets provided to hospital patients in Poland. Intakes of Fe, Mn and Zn were satisfactory but attention was drawn to the inadequate provision of Cu. A Spanish study[308] focused on the non-essential elements As, Cd, Hg and Pb in diets consumed by children, adolescents and adults. Greatest amounts were observed among adult males with the major contribution from seafood. However, intakes were lower than reported in previous studies and were well below the PTWIs. Analysis of 243 foods, 69 beverages and 11 water samples was undertaken to assess Ca and Mg in foods available in south eastern Spain.[311] The daily intakes were calculated to be 1266.6 and 366.1 mg, respectively, which are comparable to the recommended dietary allowances.

**2.9.2 Human milk and infant formulas.** In an interesting piece of work, Serfass and Reddy[154] determined *the rate at which iron(III) is transported across cells*. In this *in vitro* study, the Fe was added to human milk that had been subjected to ultrafiltration to give fractions of differing $M_r$ ranges. The whey fraction of 1–10 kDa $M_r$ very effectively solubilised the added Fe and further analysis demonstrated an Fe-containing protein at 4.2 kDa. This protein was resistant to digestive enzymes and may be responsible for the good bioavailability and absorption of Fe from human milk. In experiments that complement this work, Martino *et al.*[236] separated samples of human, cow and formula milks into four fractions, each of which was analysed to give concentrations of Br, Ca, Cu, Fe, I, Mg, Mn and Sr. Elemental distributions among the four fractions were different in human milk compared with other sample types indicating the presence of specific ligands required for appropriate bioavailability.

*Concentrations of lead and mercury in human milk were found to be associated with area of residence, prematurity, fish and cereal intakes, vitamin supplements and smoking*, but not with dental fillings.[73] In this Austrian study, no samples contained elevated concentrations and the respective concentrations of Hg and Pb were 1.59 ± 1.21 μg $l^{-1}$ and 1.63 ± 1.66 μg $l^{-1}$. Exposure to Cd is higher in Japan than in many other countries. In some work to determine the possible influence of Cd on essential elements, Honda *et al.*[72] analysed samples from 68 lactating mothers at 5–8 d *post partum*. The Cd concentrations were not high, 0.28 μg $l^{-1}$, and the only significant interaction was an inverse correlation with the Ca concentration ($r = -0.248$, $p < 0.05$), suggesting that there may be an effect on Ca secretion in human milk.

When the Se concentrations in 11 *cereal-based infant formulas* were compared, a wide range of results were obtained, 0.43 to 17.17 μg 100 $g^{-1}$.[285] The expected daily intakes were calculated and only four were deemed to contain adequate Se for children up to 12 months of age.

**2.9.3 Milk and dairy products.** Various studies reported the normal concentrations of As, Bi, Sb, Se and Te in cows milk.[243,266,312] Nwosu *et al.*[313] determined *concentrations of seven elements in yoghurt and human milk in Ethiopia*. According to Cava-Montesinos *et al.*[242] $As^V$ and $Sb^V$ make up 62% and 73%, respectively, of these elements in milk while the trivalent species form the remainder. The total concentrations of As and Sb were also reported. The I concentrations in Norwegian milks, whey cheeses and casein cheeses were

reported by Dahl *et al.*[314] Concentrations in milk were lower in summer than in winter, but sampling location was not a significant factor. The concentrations of Cd, Cu, Fe, Pb and Zn in ten brands of Kasar cheese sold in Turkey were measured by Yuzbasi *et al.*[315] Ranges reported were very wide, *e.g.*, 10–421 μg $kg^{-1}$ for Pb. It was also found that there were differences in concentrations of Cd, Fe and Pb, depending on the time of year.

**2.9.4 Wheat, flour and rice.** Analysis of rice in the context of geographical variations, stability of extracted As species and method developments have been described earlier. Al-Dayel *et al.*[316] stated that irrigation of rice with solutions of REE influences yields and resistance to disease. However, in their work, in which they analysed rice grains which was on sale in local markets but were of different origins, there is no discussion of results in the light of this assertion. The project appears to be an attempt to show how many numbers can be generated by ICP-MS, as they report on more than 60 elements, rather than investigating a specific question. Moriyama *et al.*[317] monitored concentrations of Cd as rice was taken through the milling process and found that there was very little change. In a more ambitious piece of work Cubadda *et al.* studied the effects of milling, processing and cooking on As, Cd, Ni and Pb in durum wheat.[318] Reduction in content caused by milling was most evident for Ni with other changes in the order As > Cd > Pb. Cooking the pasta caused decreases of 50–60%.

**2.9.5 Vegetables, nuts and fruit.** *Species of selenium* in broccoli were determined by Roberge *et al.*[213] and in Brazil nuts by Vonderheide *et al.*[283] Vegetables grown in areas of Bangladesh where groundwater is contaminated with As were analysed by Alam *et al.* for As, Cd, Cu, Pb and Zn. In addition to As, accumulation of Pb to levels that constitute a hazard to health were recorded.[264] Cabrera *et al.*[224] developed a panoramic undertaking and determined mineral elements in no less than 40 different types of legumes and 56 varieties of nuts. Concentrations of Al, Cd, Cr, Cu, Fe, Ni, Pb and Zn were reported in these foods, which are widely available in Spain. Mushrooms growing wild in Poland were analysed for Hg.[277] Concentrations in stalks, caps and whole fruiting bodies of 13 species were reported; no alarming results were obtained. Hazelnuts from Turkey were taken for the determination of B. Concentrations in 16 specimens were 13.8 to 22.2 mg $kg^{-1}$.[319] Lychee fruit was found to be rich in Ca, Fe, Mg and Zn.[320]

**2.9.6 Yeast and food supplements, medicinal plants.** As a rich source of highly bioavailable Se, *yeast is a material that is important to those interested in methodological developments* and in human nutrition, where it may be used as a dietary supplement. This is in addition to its role in brewing and baking. Analytical work was discussed in sections 2.1.4 and 2.7.5, above. Valiente *et al.*[287] reported on Se concentrations of 15.9 ± 0.7 to 81.1 ± 3.3 μg in tablets of yeast and other nutritional supplements. Most other work involving food supplements has been to determine the amounts of non-essential elements that might be consumed at the same time with the vitamins or minerals listed on the labels. Concentrations of Cr, Ni, Pb and Sn in a Vitamin E preparation were given by de Leon *et al.*,[108] while Kim *et al.*[321] noted the content of Pb in 55 brands of Ca supplements. Two separate reports of As, Cd, Hg and Pb in supplements were produced.[322,323] Both observed that while low concentrations were found in many preparations there were some that contained toxic elements far in excess of the WHO PTWI and that this market needed to be monitored carefully.

Attention was drawn in our last Update to the *increasing amount of work involving medicinal herbs and plants*. This is a trend that has continued in the last twelve months (see Tables 1 and 2) and the majority of publications refer to traditional Chinese medicines. Topics generally divide between measurement of essential elements, particularly Cu, Fe, Mn and Zn, where associations are drawn between high concentrations and efficacy, and elements such as Cd and Pb, where the possibility of excessive intakes is considered. Two reports are particularly alarming if the data given are correct. Dwivedi *et al.*[111] analysed 28 medicinal plants commonly used in India and obtained Pb concentrations of 2.6 to 32.8 ppm. Medicinal plants available in Spain were analysed for As, Cd, Hg and Pb by Falco *et al.*,[285] who calculated that the daily intakes of Pb would be in the range 0.12–39.44 μg. Given that the typical daily intake of Pb is well below 50 μg, it would require only one gram of these preparations to at least double the daily intake. While most reports suggest that concentrations of Pb are usually within the ppb range, Ang *et al.*[112] obtained results of 10.64–20.72 ppm in eight of the 100 products that they tested, sold in Malaysia. Virtually all the work with medicinal plants relates to total concentrations, but one study described techniques for the speciation of Mg, Mn and Zn in aqueous extracts.[113] Complexes with carbohydrates predominated for Mn and Mg, while Zn tended to be associated with polyphenol compounds.

**2.9.7 Fish and seafood.** As was observed for yeast, most of the recent publications seen refer to analytical developments, with the more innovative featuring speciation of Hg. Among those that report on the analysis of samples, a detailed study of common edible fish and shellfish from the Adriatic Sea was given by Juresa and Blanusa.[324] Hake, mackerel and shellfish were analysed for As, Cd, Hg and Pb. The concentrations of As and Hg measured were highest in hake (23.3 ± 3.6 and 0.373 ± 0.075 μg $g^{-1}$, respectively). Cadmium and Pb concentrations were about 10 times higher in shellfish than in fish. Mussels had concentrations of 0.142 ± 0.017 μg $g^{-1}$ Cd and 0.150 ± 0.009 μg $g^{-1}$ Pb. The estimated daily intake of these elements from seafood by the general population did not exceed advised limits. *Surveys of total and toxic arsenic* in 25 species of fish and 4 types of shellfish caught in the North Sea[240] and in 30 examples of Chinese seafood[325] provided useful data. A comparison of farmed rainbow trout and native brown trout indicated that, as a consequence of using contaminated feed materials, As was much increased in the farmed variety.[267] Interest in the accumulation of Hg in fish from contaminated Amazonian waters is ongoing but Santos *et al.*[276] found that, even in uncontaminated regions, the Hg concentrations can exceed limits set by the WHO. Taking advantage of the new analytical methodologies, Ortiz *et al.*[119] reported that methylmercury was present at 0.78–1.93 mg $kg^{-1}$ in tuna and swordfish. It has been recognised for many years that oily fish are an especially good source of organoselenium compounds. Therefore, it is surprising that there are few reports of this element in fish. Chien *et al.*[286] analysed specimens caught in 'contaminated' Taiwanese waters and found Se at concentrations from 0.63 to 2.01 μg $g^{-1}$ wet weight, approximately in the order molluscs < crustaceans < fish. They calculated that a seafood diet easily provides at least the recommended daily intakes of Se. Pilchard taken from the Adriatic Sea contained somewhat lower concentrations of Se at 473–713 ng $g^{-1}$.[326]

**2.9.8 Drinking water.** The enormous problems associated with As in drinking waters of Bangladesh and West Bengal are now so well recognised that little new work from this area is reported. *The possibility of another example of widespread water contamination was reported from Ethiopia.*[327] Samples of drinking water from deep and shallow wells, hot springs, springs and rivers were analysed for 63 elements. Of the well water specimens, 86% failed to meet European and WHO quality standards. Raised F concentrations in 33% of the samples represented the greatest problem and the area is well known for the incidence of fluorosis. Many samples also had U

at concentrations above the WHO maximum acceptable concentration but relatively few were contaminated with As. Samples collected from drinking water fountains around the campus of a Brazilian university were analysed for Al, Cd, Cr, Cu, Pb and Zn.[328] Compared with the WHO limits unacceptable results for Cd, Pb and Zn were recorded in 20%, 40% and 13% of the samples, respectively. Intakes of Pb by children in Poland were referred to above (2.8.3). Rosberg *et al.*[329] investigated the influence of pH on the inorganic constituents of well waters in Sweden. Samples collected from 'acid regions' (pH $<6.5$) were compared with alkaline waters, with the measurement of 30 elements. Essential elements, Ca, Cr, K and Se, were significantly lower in the acid waters, while Cd and Pb were higher. High concentrations of Cu and F were found in waters at pH 6.0. The authors speculated on the health risks associated with consumption of acid waters. Resorting to bottled water may not be the solution, as revealed by a survey of 199 samples of water sold in Canada.[330] Breaches of the quality standards were seen for B in more than 10% of the samples: also, Al, As and Se concentrations were high in several specimens. Perhaps the most anomalous finding was a sample with Li at the therapeutic dose level and which could lead to intoxication if consumed by persons already on medication. At least it appears that bottled waters are quite safe as far as Hg is concerned. Analysis of 17 specimens, using a highly sensitive procedure, found results that were approximately 1000 times lower than the limits set by WHO and the US FDA.[248]

**2.9.9 Alcoholic beverages.** In two further reports from the prolific group on the Canary Islands, the normal concentrations of As, Cd, Hg, Pb and Se in locally produced wines were reported.[279,331] Use of these and previous data to develop models for identifying the origins of wines, was described above in section 2.9. Nine elements were measured in soil, grapes and wine from the Adriatic island of Krk.[253] Concentrations in soils and grapes were similar, but it was observed that higher concentrations were found in red, compared with white, grapes. Within the wines there was also a difference in the concentrations of these elements between red and white products. *Kristl et al.*[332] *determined six elements at eight stages of the wine making process from fresh grape to finished wine*. Concentrations were greatest at the mid-phase of the procedure, following pressing of the grapes. The mean and range of concentrations of Cd, Cr, Cu, Mn, Pb and Zn in ten wine samples were reported. In a similar study in Portuguese vineyards,[274] the concentrations of Pb increased during the production of wine. Even so, Pb in the finished wine was lower than was found by Krystl *et al.*,[332] indicating probable differences between the raw materials and the processes used at various vineyards. These same Portuguese workers later carried out a multielement (47) analysis of wines, also of soil and grape juice. They observed that the concentrations of most elements remained similar or were reduced during the wine making process but that contamination with Cd, Cr, Cu, Fe, Ni, Pb, V and Zn could take place.[294]

### 2.10 Reference materials and collaborative trials

Dybczynski[333] reported on the defined processes used for the *preparation and certification of CRMs* by the Institute of Nuclear Chemistry and Technology in Poland. An issue of note is homogeneity/particle size and microanalytical techniques. Reference to typical food product CRMs was made. New RMs in stages of preparation reflect current analytical interest in speciation with a Se-enriched yeast candidate RM[281] and a $^{198}$Hg-enriched monomethylmercury spike candidate CRM.[121,122] McSheehy *et al.*[129] reviewed As speciation in biological samples, methodologies and quality assurance, with the use of CRMs. Certification of an oyster candidate CRM was discussed. An artificial food digest is undergoing evaluation by metrological organisations around the world. Work undertaken by the EU Institute for Reference Materials and Methods, Geel, Belgium on the certification of Cd and Cu in this RM was described by Vassileva *et al.*[334]

## 3 Conclusions

In previous Updates, we have reported the development of *in vivo* XRF for measurement of Pb in bone. This work has resulted in *a resurgence of interest in clinical studies involving Pb*. In this review year, the results of some extensive studies have been reported which seem to indicate that the toxic effects of exposure to Pb could still be having an important effect on human health. Delinquent youths had markedly higher bone Pb than non-delinquent youths,[61] suggesting perhaps that Pb exposure could have a role in behaviour. Alternatively, is it the deprived background of delinquent youths that gives an environment in which Pb exposure is more likely? Lead also appeared to have an effect on the outcome of pregnancy[63] as the length and head circumference of the baby showed an inverse relationship with bone Pb concentrations of the mother. Increased bone Pb stores also resulted in increased blood pressure in pregnancy[64] and after occupational exposure.[158] On a positive note, taking Ca supplements in pregnancy resulted in a reduction of Pb in blood,[161] probably as a result of decreased mobilisation of Pb from bone. Mobilisation of Pb from bone is also subject to seasonal variation.[62] Decreased exposure to sunlight during winter resulted in lower vitamin D and increased release of Pb from bone stores. Hence, blood Pb concentrations increased and bone Pb decreased. Lastly, increased blood Pb concentrations were found in post-menopausal women, again as a result of increased mobilisation of Pb from bone.[163]

There is much work involving *speciation*. We have noted previously the increasing complexity of As speciation as more and more As compounds were discovered. The same is now happening with Se, with many new Se compounds identified in human and rat urine,[191–195] yeast[215] and other sample types.

Many of the investigations where *multi-element analyses* are carried out were aimed at identifying the origin of food samples. In the past, similar objectives for clinical studies have used Pb isotope measurements, but for foods and beverages combinations of several elements and isotopes have proved more successful. Applications involving reaction or collision cell technology for ICP-MS has yet to be widely reported.

Following on from observations in the last Update we note the further *use of permanent chemical modifiers in ETAAS*. Most new methods developed were going straight for permanent modifiers and not bothering with the more traditional Pd-based modifiers. Combinations used included Ru,[92] W–Rh,[89] Zr–Ir and W–Ir[90] with graphite atomisers and Rh alone with a tungsten-filament atomiser.[91] Interestingly, it has been shown that with a THGA pre-treated with Zr–Ir or W–Ir, added phosphate could act as a permanent modifier for the determination of Cd and Pb in blood, urine and tissue digests.[90]

There is *increased interest in cloud-point extraction*, because of the high enrichment factors that can be achieved.[18–21] Over the years, we have reported many methods developed using solvent extraction, often in cases where it would be quite possible to determine the same analytes directly without extraction. It will be interesting to follow developments with cloud-point extraction to see whether it progresses from being a study in itself to become a technique that practical analysts will adopt. In some of the methods, the high enrichment has enabled FAAS to be used for determinations where ETAAS or ICP-MS would normally be required.

There were interesting developments in the introduction of solid samples in FAAS. The high temperature high pressure flow digestion system allowed rapid throughput of powdered

**Table 2** Analysis of foods and beverages

| Element | Matrix | Technique; atomization; presentation[a] | Sample treatment/comments | Ref. |
|---|---|---|---|---|
| Al | Wine | AA;ETA;L | The LOD and LOQ were 1 μg $l^{-1}$ and 2 μg $l^{-1}$, respectively, for a simple method applicable to a range of wine types | 402 |
| Al | Milk powder | AA;ETA;Sl XRF;-;S | A scanning electron microscope was used in conjunction with the named techniques to investigate platform morphology, surface metals distribution and the performance of conventional and permanent modifiers after slurry analyses. Using PCA, Zr was identified as the preferred permanent modifier | 246 |
| Al | Infant formulae | AA;ETA;L | Levels of Al in 82 Spanish samples, from 9 different manufacturers, were measured. Soya formula contributed the highest intake, 15% of PTWI | 403 |
| Al | Parenteral solution | AE;ICP;FI | Al was preconcentrated using cloud point extraction with the non-ionic surfactant PONPE. A 50 ml sample had an LOD of 0.25 μg $l^{-1}$ | 20 |
| Al | Parenteral solution | AE;ICP;FI | A detailed study concluded that the manufacturing of raw materials used in parenteral solutions was leading to product contamination with Al | 104 |
| Al | Foods | AA;ETA;L | A survey of adult intakes in Mumbai, India | 259 |
| Al | Convenience and fast foods | AA;ETA;L | Samples were digested using $HNO_3$–$HClO_4$–$V_2O_5$, yielding an LOD of 4 μg $l^{-1}$. The contribution of ingredients and packaging to intakes was discussed | 260 |
| Al | Meat | AA;ETA;L | 18 intermediate and finished products were analysed. Herbs and spices were the main source of Al in the products, which themselves had Al in the range 0.28–11.39 mg $kg^{-1}$ (in German) | 261 |
| As | Water, urine and kelp RMs | MS;ICP;Hy | An interface that allowed switching between conventional pneumatic nebulisation and introduction of the hydrides of As and Se was developed to speciate these elements into toxic and non-toxic forms | 32 |
| As | Tap water | AA;ETA;Hy | Arsines were formed in a closed headspace vial. Over a 7 min period, at 35 °C, they were reacted with AgDDC dissolved in a 4 μl microdrop mixture of 1 + 3 pyridine–benzyl alcohol suspended in the tip of a microsyringe. After equilibration the microdrop was transferred to the cuvette of a ETAA spectrometer. The LOD was 45 pg $ml^{-1}$ | 235 |
| As | Drinking water | MS;ICP;LC | $As^{III}$, $As^{V}$, MMA and DMA were speciated using IEC–ICP-MS. A TRIS buffer was found to offer superior performance to a phosphate buffered mobile phase | 237 |
| As | Water, scalp hair | EDXRF;-;S,L | As in drinking water and human scalp hair from the As contaminated region of Bangladesh were analysed to assess contribution to the whole body burden | 96 |
| As | Cow's milk | AF;Hy;FI | Samples, 2 ml, were digested on-line using a microwave oven. The LODs for As and Sb were 0.006 and 0.003 ng $ml^{-1}$, respectively | 266 |
| As | Milk | AF;Hy;L | $As^{III}$, $As^{V}$, $Sb^{III}$ and $Sb^{V}$ were determined by sonication with *aqua regia* followed by direct determination of the corresponding hydrides both before and after reduction with KI. The LODs were 8.1, 10.3, 5.4 and 7.7 ng $l^{-1}$, respectively | 242 |
| As | Foods | -;-;- | A survey of As in foods was conducted as part of the ongoing interest in the West Bengal As contamination incident | 262 |
| As | Edible oils | AA;ETA;L | Oils were dissolved in n-heptane and As determined using a Zeeman-effect ETAA spectrometer. The LOD was 10 ppb | 404 |
| As | Vegetables | AE;ICP;L MS;ICP;L | A survey of village produce from a Bangladeshi region associated with contaminated well water found little evidence of bioaccumulation of As. Unfortunately, levels of Pb were found to pose a "serious health hazard" | 264 |
| As | Rice | AE;ICP;L MS;ICP;L | As was determined in 8 varieties of rice from Northern Italy following grinding and microwave-assisted digestion | 250 |
| As | Rice | MS;ICP;HPLC | As species were extracted using $H_2O$:$CH_3OH$, 1:1. Grinding the rice resulted in a loss of stability of some species, possibly due to microbial activity | 269 |
| As | Baby foods, fish | AA;Hy;HPLC AA;ETA;L | $As^{III}$, $As^{V}$, DMA and MMA were determined by HPLC–HGAAS and AB following on-line oxidation using peroxydisulfate | 241 |
| As | Fish | AA;Hy;L | Intensively reared rainbow trout contained elevated levels of As due to the high levels of As in feed—2.5–3.1 mg $kg^{-1}$ | 267 |
| As | Sugar beet | AA;Hy;L | Methods were developed for determining As and Hg by HGAAS and CVAAS, respectively | 405 |
| As | Liquorice confectionery | AA;Hy;L | In 7 out of 9 throat pearl samples the As levels exceeded Spanish regulations | 265 |
| As | Sunflower oil | AA;ETA;L | Simultaneous quantitative extraction of $As^{III}$, $As^{V}$, MMA and DMA as well as $Hg^{II}$, monomethylmercury chloride, dimethylmercury, diethylmercury and diphenylmercury was achieved by using an extraction mixture comprising of 0.1 M $NH_3$–0.01 M EDTA. The LODs for As and Hg were 2 ng $g^{-1}$ and 3 ng $g^{-1}$, respectively | 268 |
| As | Food composites | MS;ICP;IE | Lyophilisation of food followed by prewashing with acetone and extraction by sonication with 1 + 1 $CH_3OH$–$H_2O$ was the optimum method for As species extraction | 406 |
| As | Fish, shellfish | MS;ICP;L AF;Hy;L | Toxic and non-toxic concentrations in muscle and liver were determined | 240 |
| As | Fish, shellfish | MS;ICP;HPLC | $As^{III}$, $As^{V}$, MMA, DMA and AB were separated in under 4 min using a mobile phase containing citric acid and hexanesulfonic acid. The LODs were 94, 44, 56, 64 and 66 ng $l^{-1}$, respectively | 131 |
| As | Seafood | MS;ICP;HPLC | 30 types of Chinese seafood were analysed. Arsenosugars were found in all algae and fish samples. Levels of inorganic As were negligible | 325 |

**Table 2** Analysis of foods and beverages (*Continued*)

| Element | Matrix | Technique; atomization; presentation[a] | Sample treatment/comments | Ref. |
|---|---|---|---|---|
| As | Edible seaweed, urine | MS;ICP;HPLC MS;-;ES | Samples collected from the south China Sea contained As in the range 2.1 to 21.6 mg $kg^{-1}$. All of the samples contained arsenosugars, some of which were metabolised to DMA | 303 |
| B | Coffee, tea | AE;ICP;L | B was extracted either by microwave digestion or hot water extraction | 252 |
| B | Hazelnuts | AE;ICP;L | Turkish hazelnuts were found to be a good natural source of B, containing up to 22 mg $kg^{-1}$ | 319 |
| Bi | Milk | AF;Hy;L | Samples were prepared by microwave-assisted sample digestion using $HNO_3$–$H_2O_2$. The LOD was 0.01 ng $ml^{-1}$ | 312 |
| Br | Milk | AE;ICP;L | Following microwave digestion, $Br^-$, $Cl^-$ and $I^-$ were precipitated as the silver halide, redissolved in $NH_3$ and analysed by ICP-AES at LODs of 40, 30 and 280 μg $g^{-1}$ | 407 |
| Br | Bread | MS;ICP;IC | $BrO_3^-$ was extracted using $H_2O$, the extract defatted using a $C_{18}$ column, halides removed using an Ag cartridge, protein removed using centrifugal ultrafiltration and Ag ions removed by cation exchange. With IC-ICP-MS the LOD and LOQ were 2 ng $g^{-1}$ and 5 ng $g^{-1}$, respectively | 219 |
| Ca | Meat products | AA;-;- | The acceptability of a meat product formulated with mechanically deboned poultry meat (40%), bovine plasma (40%) and bovine red cells (3%) was evaluated by feeding the product to children. Some might find the science of this study less interesting than the ethics (in Spanish) | 408 |
| Ca | Foods, water, urine, faeces | MS;ICP;L | A dual-isotope method combining radioisotopes and stable isotopes was compared with a whole-body radioisotope retention method, for measuring Ca absorption from a single meal, and found to be adequate | 48 |
| Ca | Vegan and lactovegan foods, faeces, urine | AA;F;L | The results of a short term study showed, somewhat surprisingly, that both a vegan and lactovegan diet maintained Ca status | 343 |
| Ca | Foodstuffs | MS;ICP;L | ICP-MS with a dynamic reaction cell was used to determine Ca and P. $CH_4$ and $O_2$ were used to reduce interferences. The limits of detection for Ca and P were 0.2 ng $ml^{-1}$ and 0.3 ng $ml^{-1}$, respectively | 247 |
| Cd | Drinking water | AE;ICP;FI | Cd was retained as the Cd–8-hydroxyquinoline complex, at pH 10.0, on a conical minicolumn packed with activated carbon. The LOD for a 50 ml sample was 18 ng $l^{-1}$ | 229 |
| Cd | Rice | AA;F;FI | On-line merging with $NH_3$ solution precipitated Cd. The precipitates were collected using a knotted reactor, dissolved using 1 M $HNO_3$ and Cd measured using FAAS | 409 |
| Cd | Honey | AA;F;FI | Cd was retained as Cd-2-(5-bromo-2-pyridylazo)-5-diethylaminophenol complex in a knotted reactor, then eluted using $C_2H_5OH$. Enhancements of 140× were achieved | 230 |
| Cd | Mushrooms | AA;F;L | A Cd-binding protein was isolated from the popular edible mushroom *Boletus edulis*. The results suggested a role for the protein in Cd transport and storage | 410 |
| Cd | Artificial food digests | MS;ICP;ID | This paper reported results of an interlaboratory comparison between worldwide metrological organizations for the determination of Cd and Cu in artificial food digests. "Excellent" results were obtained | 334 |
| Cd | Rice | MS;ICP;L | Milling was found to only slightly decrease Cd content | 317 |
| Cd | Cocoa | MS;ICP;L | Bioavailability of Cd and Pb was assessed using an *in vitro* gastrointestinal enzymolysis procedure. Cd recovery was further enhanced using cellulase and phytase | 411 |
| Cd | Food packaging | MS;ICP;L | Cd, Cr and Pb were determined in paper and paper board using ICP-MS with a TOF analyser. The samples were digested using $HNO_3$ in a high pressure microwave | 412 |
| Cl | Milk | AE;ICP;L | See Br, ref. 407 | 407 |
| Cr | Breakfast cereals | AA;ETA;L | Samples were digested using $HNO_3$–$H_2SO_4$–$HClO_4$. The samples were found to be a rich source of Cr | 413 |
| Cr | Food packaging | MS;ICP;L | See Cd, ref. 412 | 412 |
| Cr | Food CRMs | MS;ICP;L AA;ETA;L | Quadrupole ICP-MS was compared with ETAAS. Using a USN and $^{53}Cr$ as analytical mass good accuracy was obtained and superior LODs than ETAAS | 414 |
| Cu | Water, tea | AA;F;L | An LOD of 0.34 μg $l^{-1}$ was achieved following chelation with 1-nitroso-2-naphthol-3,6-disulfonic acid, absorption onto Ambersorb 572 and elution using 0.1 M KCN | 415 |
| Cu | Alcoholic beverage | AA;F;L | Cu, Fe and Zn were determined in the dangerous sounding Venezuelan beverage "Cocuy de Penca Firewater". The results were used in an artificial neural network to identify illegal manufacture | 295 |
| Cu | Foods | AA;F;L | A study of the dietary intake of Cu, Fe, and Zn by healthy toddlers from the Antwerp region found the toddlers to be "critically low" in Fe. Methods of intake calculation were also assessed | 306 |
| Cu | Carrots | AA;ETA;L | There was a significant difference in the mean values of Cu in carrots by Japanese province, but not by soil type | 297 |
| Cu | Artificial food digests | MS;ICP;ID | See Cd, ref. 334 | 334 |
| Fe | Beer | AA;F;FI | 3 FI systems for determining trace levels of Fe were compared. The results obtained by FI-FAAS and FI-bead injection spectrometry agreed with those of an AOAC spectrometric method | 416 |

**Table 2** Analysis of foods and beverages (*Continued*)

| Element | Matrix | Technique; atomization; presentation[a] | Sample treatment/comments | Ref. |
|---|---|---|---|---|
| Fe | Alcoholic beverage | AA;F;L | See Cu, ref. 295 | 295 |
| Fe | Foods | AA;F;L | See Cu, ref. 306 | 306 |
| Fe | Meat products | AA;-;- | See Ca, ref. 408 | 408 |
| Fe | Meat | AA;F;FI | Fe was extracted using a continuous ultrasound assisted system connected directly to an FI manifold. The LOD was 0.6 μg $g^{-1}$ dry weight | 417 |
| Fe | Rice | AA;ETA;Sl | 4 micro-procedures for determining Fe in leaves and roots of rice plants were evaluated. A procedure based on an $HNO_3$ slurry was adopted | 217 |
| Hg | Water | MS;ICP;CV | Highly enriched $^{201}Hg$ was added to approximately 20 mL $H_2O$ and mixed. The $Hg^{2+}$ in the sample was reduced on line with $SnCl_2$ and the Hg separated in a ''liquid-matrix'' separator and introduced directly into a quadrupole ICP-MS where $^{201}Hg$:$^{202}Hg$ ratios were measured. The LOD was 0.05 ng $l^{-1}$ | 248 |
| Hg | Human milk | AA;-;L | An Austrian survey of Hg and Pb in breast milk concluded that levels for this population were so low that there were not even theoretical risks | 73 |
| Hg | Wine | AA;-;L | Hg and Se were determined in sweet and dry wines from the Canary Isles | 279 |
| Hg | Fish, hair | AA;-;- | A study was conducted to establish reference values for fish and hair Hg. The high fish consumption gave mean intakes above WHO norms | 276 |
| Hg | Sugar beet | AA;-;CV | See As, ref. 405 | 405 |
| Hg | Foods | AA;-;CV | Samples were weighed into a polypropylene centrifuge tube, dried at 55 °C, digested at 58 °C using $HNO_3$–HCl–$H_2O_2$, chemically modified with successive treatments of $Mg(NO_3)_2$, 0.1% Triton X-100 and $Cu^{II}$ solution and analysed using a dedicated Hg analyser. For a 2 g sample the LOD was 0.3 ng $g^{-1}$ | 227 |
| Hg | Foods | AA;-;CV | 573 samples of Polish crops were analysed; the results indicated that consumers would not exceed the PTWI | 278 |
| Hg | Mushrooms | AA;CV;L | A pair of papers reporting levels found in 2 different regions of Poland | 418, 419 |
| Hg | Fish | AF;CV;FI AF;-;GC | An investigation of the most suitable drying and extraction procedures for Hg speciation in fish. Microwave and freeze-drying resulted in losses of analyte | 119 |
| Hg | Seafood | AF;CV;FI | Inorganic, methyl-, ethyl- and phenylmercury were separated on a $C_{18}$ column, passed through a microwave for conversion of the organic species to inorganic Hg and measured using AFS | 123 |
| Hg | Sunflower oil | AA;ETA;L | See As, ref. 268 | 268 |
| Hg | Foods | AA;ETA;FI | Copper pyrrolidine dithiocarbamate (Cu-PDC) was formed on-line, presorbed onto the walls of a knotted reactor (KR) and $Hg^{II}$ selectively retained through an online displacement reaction between $Hg^{II}$ and the presorbed Cu-PDC. 50 μl of $C_2H_5OH$ was used to elute the sample into an on-line ETAA spectrometer. The absolute LOD was 15.5 pg | 232 |
| Hg | Fish | MS;ICP;L | $Hg^{II}$ and methylmercury were measured using HPLC-ICP-MS following protease extraction. The addition of cysteine during incubation with protease and HPLC-ICP-MS separation was essential to eliminate adsorption, peak tailing and memory problems | 120 |
| Hg | Fish | MS;ICP;GC | 2 similar papers described how monomethylmercury was determined by species specific ID calibration using SPME and GC-ICP-MS. The LOD was 2.1 ng $g^{-1}$ | 121, 122 |
| I | Milk | AE;ICP;L | See Br, ref. 407 | 407 |
| I | Milk, diary products | MS;ICP;L | I was determined in 85 samples of milk and dairy products from Norway. Marked seasonal effects were observed | 314 |
| Mn | Seafood | AA;F;FI | Mn was extracted using continuous ultrasound-assisted extraction and passed *via* an FI manifold to an FAA spectrometer for measurement. The LOD was 0.4 μg $g^{-1}$ for a 30 mg sample | 218 |
| P | Foodstuffs | MS;ICP;L | See Ca, ref. 247 | 247 |
| Pb | Drinking water | AA;ETA;L | Significant contamination from lead piping was found in a study of drinking water in the Krakow region of Poland | 270 |
| Pb | Drinking water | AE;ICP;FI | Using a USN and preconcentration on Amberlite XAD-16 resin an LOD of 0.2 ng $l^{-1}$ was achieved | 228 |
| Pb | Human milk | AA;-;L | See Hg, ref. 73 | 73 |
| Pb | Wine | AA;F;FI | Free $Pb^{II}$ and total Pb were determined, using the absorption of $Pb^{II}$ on a column packed with polyurethane foam which had been modified by treatment with 2-(2-benzothiazolylazo)-*p*- cresol to separate the two species | 420 |
| Pb | Wine | AA;ETA;L | $NH_4H_2PO_4$, $PdCl_2$, $Ni(NO_3)_2$ and $Mg(NO_3)_2$ were evaluated as chemical modifiers. $NH_4H_2PO_4$ was the preferred choice (in Chinese) | 421 |
| Pb | Wine | AA;ETA;L IR;-;- | Sources of Pb in Australian wine were inferred from systematic assay of grapes must and wine, during the vinification of Riesling and Shiraz | 273 |
| Pb | Wine | MS;ICP;L | Isotope ratios were found to be ineffective in classifying Italian wine | 275 |
| Pb | Honey | AE;ICP;L | $Pb^{2+}$ complexed with 8-hydroxyquinoline at pH 10 and was retained on-line in a conical minicolumn packed with activated C. 20% $HNO_3$ was used as eluent and the LOD was 0.04 μg $l^{-1}$ | 231 |
| Pb | Vegetables | AE;ICP;L MS;ICP;L | See As, ref. 264 | 264 |
| Pb | Cocoa | MS;ICP;L | See Cd, ref. 411 | 411 |
| Pb | Canned tuna | AA;F;L | The official AOAC method for determining Pb in tuna is based on dry ashing and FAAS. Validation of this method showed that, unsurprisingly, the procedure could not meet the Codex/EU method detection limit of 0.5 mg $kg^{-1}$ | 422 |

**Table 2** Analysis of foods and beverages (*Continued*)

| Element | Matrix | Technique; atomization; presentation[a] | Sample treatment/comments | Ref. |
|---|---|---|---|---|
| Pb | Food packaging | MS;ICP;L | See Cd, ref. 412 | 412 |
| Pu | Foods | MS;ICP;L | Samples were digested using $HNO_3$ in a microwave, evaporated to dryness and diluted into a mobile phase of 1.5 M $HNO_3$ and 0.1 mM 2,6-pyridinedicarboxylic acid. Following on-line ion chromatography separation of Pu from U, the Pu was oxidised to $Pu^{4+}$ using $H_2O_2$ and determined using an HR-ICP-mass spectrometer fitted with a USN. The LOD was 0.02 pg $g^{-1}$ | 251 |
| Sb | Cows' milk | AF;Hy;FI | See As, ref. 266 | 266 |
| Sb | Milk | AF;Hy;L | See As, ref. 242 | 242 |
| Se | Water, urine and kelp RMs | MS;ICP;Hy | See As, ref. 32 | 32 |
| Se | Wine | AA;-;L | See Hg, ref. 279 | 279 |
| Se | Milk | AF;Hy;L | Following microwave digestion Se and Te were determined by HGAFS, yielding LODs of 0.005 and 0.015 ng $ml^{-1}$, respectively | 243 |
| Se | Infant formula | AA;ETA;L AA;Hy;L | 7 out of 11 samples satisfied less than 63% of the daily adequate intake | 285 |
| Se | Dairy products, fruits, vegetables | AA;Hy;FI | Samples were digested in a microwave oven and then Se determined by FI-HGAAS. The LOD was 0.06 μg $kg^{-1}$ | 423 |
| Se | Soybean, okra | AF;Hy;L | Se content of soybean, soybean protein and okra was increased by supplementation of soil, and more effectively, by foliar application. Soybean cultivars exhibited different accumulation of Se | 424 |
| Se | Dietary supplements | AA;ETA;L AA;Hy;L | A comparative study of the named methods was performed. ETAAS was the preferred technique as HGAAS was compromised by low recoveries resulting from Cu, Mn, and Zn interference on the Se signal | 287 |
| Se | Foods | AA;ETA;L | Following a closed vessel $HNO_3$ digestion, an aliquot was diluted with 0.2% v/v $HNO_3$, diethyldithiophosphate added and the complex loaded onto a minicolumn containing 30 mg of $SiO_2$–$C_{18}$, using a peristaltic pump. The complex, eluted with $C_2H_5OH$, was collected into a cuvette for the determination of Se | 280 |
| Se | Seafood | AE;ICP;L | The concentration of Se in the blood of Taiwanese was predicted using a one-compartment steady-state pharmacokinetic model, using data on the levels of Se in local seafood | 286 |
| Se | Yeast | AA;F;L, AA;Hy;L, MS;ICP;L, INAA | A comprehensive study of measurement and digestion procedures for Se determination was reported. Avoiding the use of $HClO_4$ affected the recovery in some cases | 226 |
| Se | Yeast | MS;ICP;HPLC | Trypsin digestion indicated that Se was mainly present as selenomethionine non-specifically incorporated into peptide chains | 215 |
| Se | Yeast | MS;ICP;LC MS;-;ES | Selenocystine, selenoadenosyl methionine and selenoadenosyl homocysteine were identified in yeast | 216 |
| Se | Yeast | MS;ICP;LC MS;-;Nanospray | Selenodiglutathione and the mixed selenotrisulfide of glutathione and cysteinyl glycine were characterised | 239 |
| Se | Yeast | MS;ICP;HPLC | The $H_2O$-soluble protein fraction isolated by SEC was analysed by HPLC-ICP-MS. The selenopeptides were then analysed by MALDI-TOF-MS to select target ions for collision-induced dissociation MS. Using this approach a new family of selenoproteins were identified for the first time | 282 |
| Se | Yeast | MS;ICP;ETV MS;ICP;HPLC | Se-proteins were separated by HPLC or gel electrophoresis, following sequential extraction of water or non-water soluble Se fractions | 281 |
| Se | Brazil nuts | MS;ICP;LC MS;-;ES | Se was speciated in Brazil nuts | 283 |
| Se | Oysters | MS;ICP;HPLC | The effect of sample treatment and storage on the stability of selected Se species was assessed | 214 |
| Se | Broccoli | MS;ICP;HPLC | 27 extraction systems and 9 different buffers were evaluated for Se speciation. Changes in speciation were analyte-, pH-, and buffer-dependent, but generally, higher pH resulted in more highly oxidized Se compounds | 213 |
| Se | Coffee, coffee beans | MS;ICP;GC | SPME-GC-ICP-MS identified several Se-containing species present at trace levels | 284 |
| Si | Milk, infant formula | AA;ETA;L | Using Pd as modifier the LODs for cows' milk, human milk and infant formula were 16.2, 2.7 and 7.2 μg $l^{-1}$ | 425 |
| Si | Foods | AA;-;- | Bioavailable Si was in the range 3–4.13 μg $kg^{-1}$ and total Si in the range 1.5–48. 38 mg $kg^{-1}$ | 258 |
| Sn | Canned foods | AE;ICP;L | Two methods were developed based on high pressure ashing or microwave-assisted dissolution. Both yielded LOQs of approximately 0.8 mg $kg^{-1}$ at the 189.927 line | 305 |
| Sn | Canned foods | AA;ETA;L | Sn was determined by ETAAS after electrodeposition on a tungsten probe. 200 s deposition gave an LOD of 0.08 μg $l^{-1}$ (in Chinese) | 233 |
| Sr | Brown rice | MS;ICP;L | Samples, 5 g, were digested using $HNO_3$–$HClO_4$–HF and Rb removed by ion exchange. Measurement of $^{87}Sr$:$^{86}Sr$ was performed using multicollector-ICP-MS. The results were used to estimate the provenance of Japanese samples | 249 |
| Te | Milk | AF;Hy;L | See Se, ref. 243 | 243 |
| U | Foods, water | MS;ICP;L | The daily intake of U in Italy was determined | 203 |
| V | Foods, Chinese herbal remedies | AA;ETA;L | Optimum experimental conditions for V determination were identified | 257 |
| Zn | Alcoholic beverage | AA;F;L | See Cu, ref. 295 | 295 |
| Zn | Foods | AA;F;L | See Cu, ref. 306 | 306 |

**Table 2** Analysis of foods and beverages (*Continued*)

| Element | Matrix | Technique; atomization; presentation[a] | Sample treatment/comments | Ref. |
|---|---|---|---|---|
| Zn | Foods | AA;-;- | The relationship between food frequency, intake, food habits and Zn status in healthy children from southern Poland was investigated | 208 |
| Various (7) | Milk and milk-based products | EDXRF;-;S | A rapid method for the determination of Ca, Cl, Fe, K, P, S and Zn, based on forming pellets under 2 t of pressure, was described | 254 |
| Various (4) | Drinking water | XRF;-;S | Metals were preconcentrated on a chelating solid-phase extraction disk, allowing preconcentration factors of 1600× (Cd, Cu, Ni, Pb) | 255 |
| Various (30) | Well water | AE;ICP;L | Acid precipitation led to reduced levels of essential elements and increased levels of toxic elements | 329 |
| Various (63) | Well water | AE;ICP;L MS;ICP;L | A comprehensive study of drinking water quality in the Ethiopian Rift Valley found 86% of samples failed to meet the WHO standards. F was the most problematic element | 327 |
| Various (11) | Powdered coffee, powdered milk | AE;ICP;L | Samples were solubilised at 80 °C using TMAH. The LODs for Ca, Cu, Fe, K, Mg, Mn, Na, P, Se, Sr and Zn were 2.1, 0.065, 0.11, 103, 0.08, 8, 0.011, 1.5, 2.1, 1.1, 0.66 and 0.11 μg $g^{-1}$, respectively | 426 |
| Various (26) | Bottled drinking waters | MS;ICP;L, AA;F;L | A wide range of elements and $Br^-$, bromate and chlorate were determined in 199 Canadian retail samples. A number of samples exceeded WHO or Canadian regulations and 1 sample was at a Li therapeutic dose and could have posed an overdose risk to individuals on Li medication | 330 |
| Various (11) | Wine | AA;F;L AE;F;L | Chemometric methods, particularly artificial neural networks, were used to classify wines by Canarian Island of origin and maturity of grape | 289 |
| Various | Wine | -;-;- | Chemometric methods, including cluster analysis and SIMCA, were used to model 8 types of denomination of origin for wine bottled in the Canary Islands | 291 |
| Various (39) | Wine | MS;ICP;L | REEs were among the elements used to classify Canarian wine. In fact REEs were of limited use, better classification being achieved with the other analytes | 292 |
| Various (34) | Wine | MS;ICP;L | Of 34 elements measured, Sr was found to be particularly useful in classifying wines from Canada's 2 main producing regions. 100% accuracy could be achieved using just 10 elements | 293 |
| Various (47) | Wine | MS;ICP;L | The influence of the soil and vinification process on wine multielement composition was investigated | 294 |
| Various (6) | Grape juice, soft drinks | AE;ICP;L | PCA and hierarchical cluster analysis were used to discriminate between sample types (Ca, Cu, K, Mg, Na, P, S) | 427 |
| Various (9) | Orange juice | AE;ICP;FI | On-line focused microwave digestion, using 80% $HNO_3$, allowed 12 samples $h^{-1}$ to be analysed (Ca, Cu, Fe, K, Mg, Mn, Na, P and Zn) | 428 |
| Various (26) | Wine | MS;ICP;L | Comparison of methods in 2 wine analysis laboratories showed generally good agreement between the 2 | 429 |
| Various (17) | Tea | AE;ICP;L MS;ICP;L | Chemometric methods were used to classify 85 samples from Asia and Africa | 301 |
| Various (11) | Olive oil | MS;ICP;L | An automated method based on on-line emulsion formation was developed | 430 |
| Various | Food CRMs | -;-;- | Adaptations to a high pressure asher, to allow open vessel digestion of elements such as As, Hg and Se were described | 5 |
| Various (8) | Meat | AA;-;L | Focused microwave-assisted digestion and ultrasound leaching have been applied for the extraction of Ca, Cd, Cr, Cu, Fe, Mg, Pb and Zn from raw meat. Ultrasound leaching failed to give quantitative recovery of all elements | 225 |
| Various (4) | Yoghurt | AA;-;L | Ca, Mg, P and Zn distribution between soluble and micellar fractions was determined | 431 |
| Various (6) | Food, vegetables | AA;F;L | Levels of Cd, Co, Co, Mn, Ni, Pb and Zn were so high in volcanic soil, fruit and vegetables that it was hypothesised that they could be linked to the high prevalence of upper gastrointestinal cancers in the Van region of Turkey | 432 |
| Various (9) | Milk whey | MS;ICP;HPLC | Human, raw cow, UHT cow and formula milk whey were analysed using SEC–ICP-MS. Elemental binding patterns in human milk were different from those observed in cow and formula milks | 236 |
| Various (15) | Pumpkin seed oils | AE;ICP;L | 3 digestion types were applied—open vessel and closed vessel in a steel bomb and microwave digestion in a closed system. Closed vessel approaches gave the best results | 221 |
| Various (5) | Food SRMs | AA;F;FI | An electrically heated Pt–Ir capillary was used for on-line digestion at temperatures up to 320 °C. HF could be used as no glass was present in the construction (Cd, Cu, Mn, Pb, Zn) | 9 |
| Various (5) | Bread | AA;-;- | Cd, Cu, Fe, Pb and Zn were determined in bread from 20 Turkish bakeries | 433 |
| Various (8) | Legumes, nuts | AA;ETA;L | Samples, all from Spain, were mineralised using $HNO_3$–$V_2O_5$ (Al, Cd, Cr, Cu, Fe, Ni, Pb, Zn) | 224 |
| Various (18) | Honey | AE;ICP;L | Chemometric methods identified relationships between geographic origin and elemental profile. Heavy metal and xenobiotic contaminants were found in some samples | 434 |
| Various (13) | Lychee | AE;ICP;L | Al, Ba, Ca, Cr, Cu, Fe, Mg, Mn, Mo, Pb, Se, Sr and Zn were determined; the levels of Ca, Fe, Mg and Zn were high enough to suggest that the fruit was a good source of these elements (in Chinese) | 320 |
| Various (4) | Durum wheat, semolina and pasta | MS;ICP;L | Low levels of As, Cd, Ni and Pb were found in commercial samples. Cooking decreased concentrations by 50–60% | 318 |

**Table 2** Analysis of foods and beverages (*Continued*)

| Element | Matrix | Technique; atomization; presentation[a] | Sample treatment/comments | Ref. |
|---|---|---|---|---|
| Various (4) | Dietary supplements | -;-;- | A survey of supplements on the Croatian market found levels up to 35 times WHO recommendations (As, Cd, Hg, Pb) | 323 |
| Various (4) | Dietary supplements | MS;ICP;L | HR-ICP-MS was used to determine As, Cd, Hg and Pb. Some very high concentrations were found | 322 |
| Various (9) | Composite diet samples | MS;ICP;L | The measurement of Al, Cd, Cr, Cu, Mn, Ni, Pb, V and Zn by low resolution ICP-MS yielded accurate measurements | 256 |
| Various (21) | Foods | MS;ICP;L | The exposure of French consumers to a range of elements was determined | 309 |
| Various (4) | Foods | MS;ICP;L AA;F;L | A survey of 11 foods groups purchased in Catalonia, Spain, showed dietary intakes of As, Cd, Hg and Pd were well within PTWI limits | 435 |
| Various (23) | Foods, CRMs | MS;ICP;L | A single microwave programme for a wide range of foods was enabled by using an analytical portion mass based on the food's energy content calculated from macronutrient data (fat, protein and carbohydrate) | 222 |
| Various (60) | Rice | MS;ICP;L | Treatment of rice with REEs was claimed to improve yield and disease resistance | 316 |
| Various (6) | Wheat | MS;ICP;L | Elemental isotope analysis of Cd, Pb, Se and Sr plus stable isotope gas analysis of $^{13}C$ and $^{15}N$ with multivariate statistics was used to identify the geographic origin of *Triticum aestivum* | 298 |
| Various (4) | Porcine tissues | MS;ICP;HPLC MS;ES;HPLC AE;ICP;L | A detailed study of optimum extraction conditions for the determination of Cu, Fe, Mn and Zn species was reported. Tris buffer produced the best results and freezing was found not to affect species stability | 33 |
| Various | Biological and clinical samples, foods and beverages | -;-;- | A comprehensive review of applications of atomic spectrometry | 1 |
| Various (16) | Housewares | XRF;-;S | A hand held radioisotopic XRF spectrometer, based on $^{241}Am$ excitation, was used to measure surface contamination by toxic elements | 436 |
| Various (27) | Berries, honey | SRXRF;-;S | Simultaneous multielement determination of a range of biological matrices, including foods, was performed | 389 |

[a] Hy indicates hydride and S, L, G and Sl signify solid, liquid, gas or slurry introduction, respectively.

samples for direct measurement by FAAS,[9] but perhaps of greater interest, because of its greater simplicity, is the thermospray introduction system from the same research group.[10] In this, samples slurried in 0.3 M $HNO_3$ were pumped by a low-cost diaphragm pump through a ceramic thermospray nozzle into a nickel tube, both of which were heated by the air–$C_2H_2$ flame of an AA spectrometer. The greater sensitivity obtained by use of the flame-heated tube and direct injection allowed the determination of Cd, Cu and Pb in a range of biological matrices. An even simpler system was the production of a dry aerosol from powdered material by blowing an air current over a small amount in a polythene vial.[15] This was passed to a flame-heated quartz tube, but surprisingly the light path was arranged to pass above a slit in the top of the tube.

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