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Contributions to Automated Trace Analysis

Part V. Determination of Cadmium in Whole Blood and Urine by Electrothermal Atomic-Absorption Spectrophotometry* **

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Beiträge zur automatisierten Spurenanalyse

V. Bestimmung von Cadmium in Vollblut und Harn mit elektrothermaler Atomabsorptionsspektrophotometrie

Zusammenfassung. Einfache, rasche Methoden für die Bestimmung von Cadmium in Vollblut und Harn mit elektrothermaler Atomabsorptionsspektrometrie werden beschrieben. 50–200 µl Aliquots von Vollblut werden mit 1 M HNO_3 zur Deproteinierung und Matrixmodifikation behandelt. Nach Zentrifugieren wird die überstehende Lösung zur automatisierten elektrothermalen Atomabsorptionsspektrophotometrie (ETAAS) verwendet. Die Reproduzierbarkeit, ausgedrückt als Tag-zu-Tag-Reproduzierbarkeit variert von 30% bei 0,4 µg Cd/l bis zu 3,8% bei 9,3 µg Cd/l Vollblut. Bei 25 µl-Eingabe eines 1 + 3 verdünnten Bluts wird eine Nachweisgrenze von ≤0,2 µg Cd/l erreicht.

Direkte automatisierte Cd-Bestimmungen im Harn sind nach Verdünnung ab 0,2 µg Cd/l durchführbar. Flüssigextraktion mit NaDDC/MIBK erlaubt Cd-Bestimmungen bis ≤0,1 µg Cd/l. Die Tag-zu-Tag-Reproduzierbarkeit variiert von 26% bei etwa 0,6 µg Cd/l bis 7,1% bei etwa 27 µg Cd/l Harn.

Die Richtigkeit dieser Methoden wurde durch Differential - Pulse - Anodic - Stripping - Voltammetrie (DPASV) und unabhängige AAS-Verfahren überprüft und als akzeptabel mit einem mittleren Gesamtfehler von ≤30% gefunden.

Im Routinebetrieb sind bis zu 200 Cd-Messungen in Blut und bis zu 160 Direkt-Messungen von Cd in Harn pro Arbeitstag (10 h) möglich.

Summary. Simple, rapid methods are described for the determination of Cadmium in whole blood and urine by means of electrothermal atomic absorption spectrophotometry. 50–200 µl aliquots of whole blood were treated with 1 M HNO_3 for deproteinization and matrix modification. After centrifuging the supernatant is taken for automated electrothermal atomic-absorption spectrophotometry (ETAAS). Precision, expressed as day-to-day precision varied from 30% at 0.4 µg Cd/l to 3.8% at 9.3 µg Cd/l whole blood. If 25 µl of an 1 + 3 diluted blood are injected a detection limit of ≤0.2 µg Cd/l is achieved.

Direct automated Cd-determinations in urine are feasible after dilution from about 0.2 µg Cd/l. Solvent extraction using NaDDC/MIBK is possible to ≤0.1 µg Cd/l. The day-to-day reproducibility varies from 26% at about 0.6 µg to 7.1% at about 27 µg Cd/l urine.

The accuracy of these methods was checked by differential-pulse-anodic-stripping voltammetry (DPASV) and independent AAS procedures and found to be quite acceptable with an average total error of ≤30%.

In routine up to 200 Cd measurements are possible in whole blood and up to 160 direct Cd measurements in urine per day (10 h).

Key words: Best. von Cadmium in Blut, Harn; Spektralphotometrie, Atomabsorption; elektrothermal, Deproteinierung/Matrixmodifikation für Vollblut, Flüssigextraktion bzw. Direktmessung für Harn

1. Introduction

Blood and urine are important biopsy materials in analytical Cd toxicology. Cd in whole blood mainly reflects recent exposure, Cd in urine predominantly the

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kidney store [4]. Thus, both materials are indispensable for occupational and environmental screening and control purposes.

Round-robin exercises on the determination of e.g. Pb and Cd in body fluids carried out in the last decade indicated that numerous laboratories had problems with achieving the requested high level of reliability [8, 9, 26]. As a contribution to the improvement of this situation we participated in programs on automation of analytical methods for toxic trace metals sponsored by the German Federal Ministry of Research and Technology. Our particular investigations on analytical methods included studies on automated sample injection in electrothermal atomic absorption spectrophotometry (ETAAS) [23, 24], and on automated cold vapour AAS [13]. Within the same program an automated ETAAS procedure for blood lead using nitric acid deproteinization/matrix modification [22] and a device for automated simultaneous voltammetric on-line determination of toxic trace metals in drinking water [28] were developed and currently applied [15, 19, 21, 28]. The ETAAS procedure for blood lead was found to be in principle useful as well for the determination of Cd in whole blood and therefore subsequently evaluated and applied to extended base line, clinical, and occupational exposure studies with Cd [12, 16, 19, 20, 21, 25]. The performance of this method together with analytical approaches for direct and solvent extraction ETAAS determination of Cd in urine are given below.

2. Experimental

Apparatus

The atomic-absorption devices used were Perkin-Elmer 400, 410 and – more recently – 4000 instruments, equipped with Cd electrodeless discharge lamps, HGA-74, 400 and 500 furnace units, the Perkin-Elmer Autosampler AS-1, printers and/or recorders. These instruments were usually on-line coupled with a PDP 11/10 system for rapid data evaluation. Centrifuging was done in Hereaus Labofuge 6000 centrifuges. The Cd laboratories were equipped with class 100 clean benches for proper storage and manipulations.

Reagents and Contamination Precautions

Argon of 99.999% purity was used throughout as purging gas for the HGA furnaces. Other chemicals were of the highest available purity (e.g. Merck Suprapur). The used labware of glass, quartz and plastics was several times cleaned by rinsing with warm dilute HCl or HNO_3 and randomly checked for Cd contamination prior to use. Dilutions etc. were only performed by colourless disposable Eppendorf pipette tips (yellow tips contain considerable Cd amounts and have thus to be strictly avoided) and in the dust-free area of the clean benches.

Procedures

a) Whole Blood. Samples were taken by means of venipuncture with sterile syringes, equipped with stainless-steel tips, to be used once only usually containing ethylene diamine-tetraacetic acid as anticoagulant (e.g. Sarstedt 10 cc EDTA K Monovette No. 02.267 with luer fitting). The Cd contents of the syringes have to be repeatedly checked and subtracted from the analytical value if concentrations ≥ 0.1 ng/ml were found; however, occasionally Cd contamination was found to be around 0.2 ng/ml.

Immediately after sampling the blood had to be thoroughly mixed, sometimes also by the aid of ultrasonification to avoid clotting during storage. The samples were then, if not subsequently analyzed, placed in refrigerators at about 4°C for short term storage. Long term storage also of quality control samples is performed at −80°C or in liquid nitrogen. Control materials usually lyophilized and also Cd spiked based on bovine blood are now under careful study (see also Table 5).

Into carefully precleaned and subsequently protected or under a clean bench stored polystyrene tubes (outer diameter: 14 mm, length: 100 mm) were pipetted 150 – 600 µl of 1 M HNO_3 (also checked for Cd content) and 50 – 200 µl of fresh or stored (i.e. thawed) whole blood. The tubes were then vigorously shaken with an electrical mixer for 30 s. After centrifuging the supernatant is transferred to a precleaned 1 ml AS-1 polyolefine or polystyrene sample cup and 10 – 25 µl portions injected into the HGA. The resulting solution is about 0.75 M in nitrate.

Matrix matched calibration graphs are obtained by addition of appropriate volumes of Cd standard solutions (100 – 1,000 ppb) to the 1 M HNO_3 (see Fig. 3).

Due to the occasional appearing of severe contamination of plastic materials despite the rigid cleaning procedures this step has always to be performed in duplicate in order to avoid erroneously high values due to contamination.

b) Urine, Direct Determination. Urine specimens were taken from random voidings (occupational exposure) as well as from 24 h collections (base line and clinical studies). For storage these samples were acidified by adding 1 ml HNO_3 or HCl to 100 ml urine [1].

500 µl fresh or slightly acidified (pH ≤ 2) stored urine is diluted for determination with 1,000 – 2,000 µl ultrapure water and usually 10 µl portions injected into the HGA. Standard addition is performed by addition of appropriate amounts of 100 – 1,000 ppb standard solutions to the ultrapure water.

From storage experiments with ^{109}Cd radiotracer also performed in the course of our analytical studies during the application of the methods described here no statistically significant adsorption on the walls of the storage containers and the urine precipitates could be observed if the samples were initially acidified to pH ≤ 2. Even in a series of samples with significant protein precipitates due to proteinuria [16] and a later acidification to pH 2 losses of Cd due to adsorption on these precipitates were rather low and did not exceed 5% [6].

c) Urine, Solvent Extraction. 1,000 µl fresh or slightly acidified urine is mixed with 100 µl of a pH 5 buffer solution (Merck buffer titrisol), and 200 µl of an aqueous 2% NaDDC (Sodium diethyl dithiocarbamate) solution. Subsequently 1,000 µl MIBK are added, vigorously mixed for 120 s and centrifuged. The supernatant MIBK layer can be directly used for ETAAS measurements of 10 – 50 µl portions.

Measurement, Temperature Program and Background Minimization

The operating conditions for the used instruments as well as the temperature programs of the HGA furnace units are given in Table 1. The effect of matrix modification on the non-specific background is demonstrated for whole blood in Fig. 1 and shows the superiority of the described method in comparison with e.g. Triton-

Table 1. Spectrophotometer operating conditions and HGA-programs

Instrument	*Conditions*
Perkin-Elmer 400/410	PE Cd EDL, 228.3 nm, 5 W, deuterium compensation, slit 7, absorbance, peak height mode
Perkin-Elmer 4000	PE Cd EDL, 228.3 nm, 5 W, background compensation, slit 7, absorbance, peak height mode

HGA programs	Time/s	Step	Approximate temperature °C	Remarks
Whole blood:				
HGA 74	20–30	drying	120	drying time depends on injected (10–25 µl) volume
	30–40	charring	350–500[a]	
	4	atomization	1,600	gas stop
	3	cleaning	2,650	
HGA 400/500	20–30	drying	120	drying time depends on injected volume
	20, 20	charring	350–500[a]	20 s ramp, 20 s hold
	1, 4	atomization	1,600	1 s ramp, 4 s hold, gas stop
	3	cleaning	2,100	ramp mode
Urine direct:				
HGA 74	20–30	drying	120	drying time depends on injected volume
	60	charring	350	ramp mode
	4	atomization	1,200	gas stop
	4	cleaning	2,650	
Urine NaDDC/MIBK extraction:				
HGA 74	20–30	drying	120	drying time depends on injected volume
	30–40	charring	350	
	4	atomization	1,900	gas stop
	3	cleaning	2,650	

[a] The charring temperature highly depends on the properties of each individual tube and thus has to be adjusted for each tube separately at its highest possible value and so, that no Cd losses appear

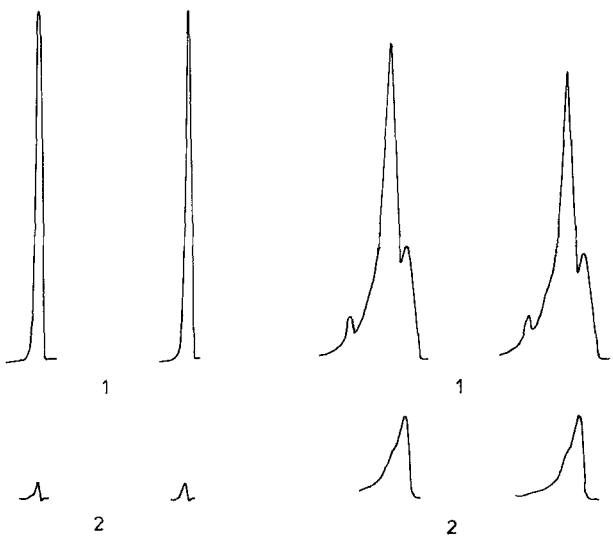

Fig. 1a and b. Comparison between direct determination of Cd in whole blood. **a** 1:10 diluted whole blood with 0.1% Triton X-100, injected volume 10 µl. **b** This method 1:4 diluted, injected 25 µl. *1* total absorption; *2* total absorption-nonspecific absorption

X-100 treatment with respect to the attainable detection limit and reliability for Cd in whole blood. The effect of the particular temperature program in the case of direct Cd measurements in urine is demonstrated in Fig. 2.

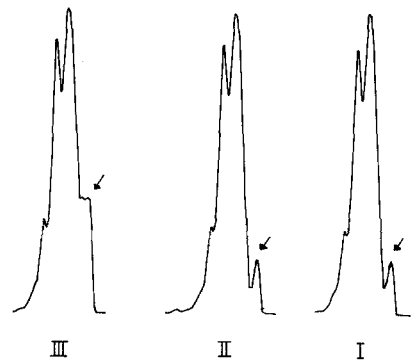

Fig. 2. Typical total absorption curves for Cd in urine. *I* und *II* urine without Cd spike; *III* 2 ppb Cd added to urine. Cd-peaks are indicated with arrows

Calibration and Evaluation

As also observed recently for Pb in whole blood [22] there was no statistically significant difference between the evaluation by individual standard addition or by matrix-matched calibration graphs from Cd-spiked blood samples with relatively low Cd contents. Thus, for series of samples the simple and fast matrix-matched calibration graph was chosen. Typical examples of such calibration graphs are shown in Fig. 3.

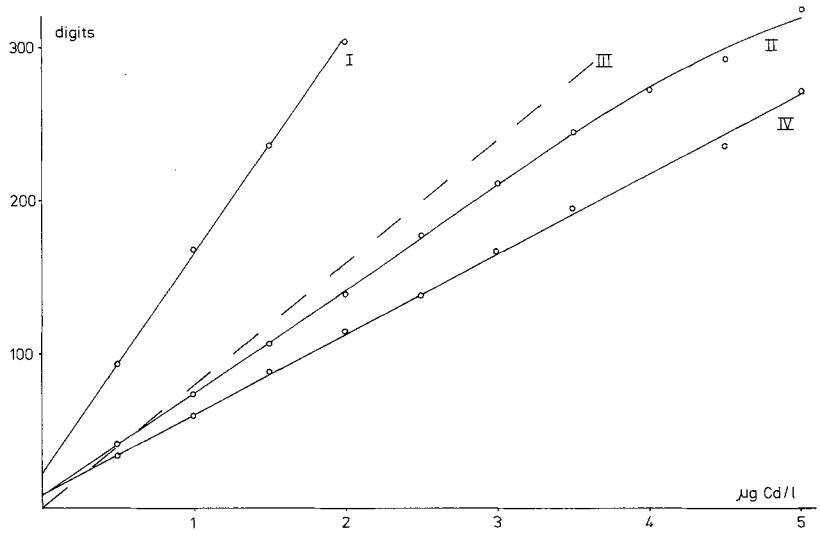

Fig. 3
Typical calibration graphs for Cd in whole blood, urine and MIBK extracts. *I* Whole blood, matrix matched, injected volume 25 µl, PE 4000/HGA 400. *II* Whole blood, matrix matched, injected volume 10 µl, PE 4000/HGA 400. *III* Cd-DDC in MIBK, injected volume 10 µl. *IV* Urine, direct measurements, matrix matched, injected volume 10 µl, (dilution 1:5) PE 410/HGA 74

Because of the varying composition of urines, direct determinations are more reliable, if individual standard addition is applied (see also Fig. 3). In the case of solvent extraction however, the evaluation against a calibration graph obtained by extraction of aqueous standard solutions is sufficient.

Due to aging of the graphite tubes, significant alteration of tube properties occurs and can sometimes lead to signal drift effects [24], as recently also confirmed by others [18]. Therefore at least two calibration graphs per measuring cycle of a graphit tube are necessary. In contrary to former observations [24] recently produced graphite tubes show frequently useful life-times on average rarely exceeding 300 firings under the conditions described here. Thus, numerous checking measurements of spiked and standard solutions with known concentrations are required. As a consequence every fifth sample cup should contain a control sample with known Cd concentration. If no extreme signal drift occurs during a working cycle, it is possible to evaluate the data with the respective matrix-matched calibration graph for a distinct set of samples. Data evaluation is carried out routinely with the PDP 11/10 system, which also includes auto zero adjustments. The instrumental arrangement and the computer coupling using CAMAC modules was recently shown in principle [22]. A detailed description of the applied systems and the software is now in preparation [13].

3. Results and Discussion

Accuracy

The accuracy of the described methods was currently checked by the application of differential pulse anodic stripping voltammetry (DPASV) as a reference method and of different atomic absorption spectrophotometric methods, the latter also as interlaboratory comparisons. If certified standard reference materials are not available which is still the case for whole blood and urine, this is the most efficient way to check the accuracy of an analytical procedure [27].

Cd in Whole Blood

Sixty five blood samples, ranging from about 0.4 to about 24 µg Cd/l from 1977–1979 comparatively analyzed by DPASV and ETAAS are shown in Fig. 4. The DPASV method very close to a definite method, also developed in this institute [29] starts with low temperature ashing or wet ashing [14]. The results are in quite acceptable agreement and demonstrate that within random variations mainly of the AAS approach no severe systematic deviations above a distinct but rather low uncertainty seem to occur.

In order to check possible Cd losses due to the described pretreatment/centrifugation step also current intercomparison measurements were performed between this method and other methods. A comparison with nitric acid pressure digestion/ETAAS is shown in Table 2 and demonstrates excellent agreement. Similar agreement could be achieved in a series comparing deproteinization/matrix modification and ETAAS after nitric acid pressure digestion NaDDC-APDC/MIBK extraction and also by comparison of this method with an in-furnace-oxidation using $HClO_4$/acetone [17]. The latter method was initially applied for Cd in whole blood, but showed unsatisfactory precision due to a strong attack of the tube walls by $HClO_4$. Thus, it was abandoned for the more precise, sensitive and elegant deproteinization technique.

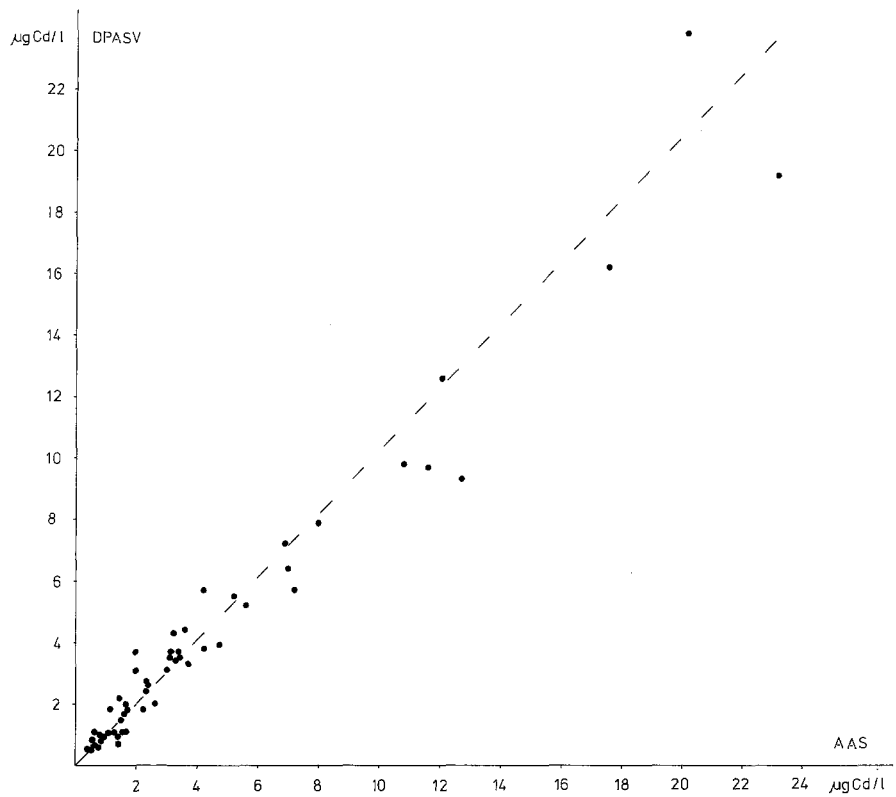

Fig. 4
Comparison of the determination of Cd in whole blood by the nitric acid method and by voltammetry (DPASV/HMDE). Number of samples = 66, equation; $y = 1.03\,x - 0.03$, correlation coefficient 0.9883, mean concentration ± std. dev. (µg/l) by DPASV: 3.658 ± 4.459 by AAS: 3.717 ± 4.677

Table 2. Cd in whole blood. Comparative measurements, values in ng/ml

This method	Pressure digestion/ETAAS
2.5	2.3
5.45	5.2
1.0	0.95
3.2	3.0
6.2	5.85
11.7	11.6
11.0	12.75
9.5	9.4
15.2	15.25
16.3	16.2
21.0	22.0
33.0	34.45
7.65	6.7
0.95	1.25
22.7	23.5
7.95	7.5
$\bar{x}$ 10.96 ± 8.86	11.12 ± 9.33

Corr. coefficient $r = 0.9991$, $y = 1.05\,x - 0.39$

Also intercomparisons were carried out with other laboratories having a long lasting experience in trace and ultratrace Cd analysis. Table 3 summarizes the results of recent intercomparisons (19 samples) with the Karolinska Institute, Stockholm, Sweden, which uses a slightly modified Delves Cup technique and quality control by neutron activation analysis [2, 10].

Cadmium in Urine

The accuracy of the described NaDDC solvent extraction of Cd has been recently checked by a new rapid DPASV procedure with simultaneous voltammetric determination of toxic trace metals in urine and found acceptable with a correlation coefficient of 0.96 and an α of 41°41′ [6]. Equally satisfactory was the interlaboratory comparison of 15 urine samples with concentrations from 0.7–52 µg/l applying direct and NaDDC/MIBK-solvent extraction-ETAAS techniques already presented very recently [27].

Also interlaboratory comparisons were carried out, but showed in contrary to whole blood only fairly good agreement with an obvious tendency to higher values after shipping. As also supposed by others [5] that is probably due to contamination from e.g. the used plastic tubes since (frequently acidified shipped) urine can leach out Cd from polyolefine vessels. Strong evidence for that are the elevated Cd values found by us in polypropylene vessels even, if they were repeatedly and carefully rinsed with dilute acids prior to the final checking measurements. For whole blood however,

Table 3. Interlaboratory comparison using different AAS procedures

	Delves cup	HNO_3
	3.7	4.8
	6.1	7.6
	14.6	12.4
	11.0	10.8
	2.7	3.0
	2.7	3.0
	0.5	0.6
	14.6	16.0
	10.6	9.4
	4.7	5.7
	22.0	20.0
	35.9	38.2
	22.3	16.4
	0.5	0.6
	0.7	0.5
	5.8	5.5
	0.4	0.5
	21.0	21.6
	5.8	5.15
$\bar{x}$	9.768	9.566
s. dev.	9.758	9.604

$n = 19$

Corr. coefficient $r = 0.9916$; $y = 0.97x + 0.11$

Table 5. Repeated determination of cadmium in 9 single samples of whole blood within at least five days, $n = 20$ aliquots, with 1 firing from each aliquot

Mean conc. µg/l	Standard deviation	Relative stand. dev. %	Remarks
0.4	0.12	30	fresh bovine blood
0.58	0.06	11	loyphilized bovine blood[a]
0.7	0.12	16	
1.23	0.18	14.6	within 3 months
1.35	0.15	11.3	
2.3	0.14	6.1	
5.2	0.26	5.0	
9.27	0.35	3.8	spiked lyophilized bovine blood[a]
20.9	1.0	5.0	

[a] These are new control materials now under detailed study designed to become later certified standard reference materials

Table 4. Determination of cadmium in pairs of samples of whole blood using nitric acid and automated electrothermal atomic-absorption spectrophotometry (day to day precision). Calculation of standard deviations, relative standard deviations and confidence intervals from pairs of subsamples arranged in five groups in order of increasing Cd concentration

Number of pairs	Mean conc.[a] µg/l	Conc. range µg/l	Standard deviation[b] µg/l	Relative confidence intervals			Remarks
				stand. dev. %	$P = 0.1$	$P = 0.05$	
60	0.79	0.2– 1.4	0.14	18	30.1	36.0	Mainly non-smokers
50	2.17	1.0– 3.0	0.18	8.3	13.9	16.6	Smokers and non-smokers
60	3.76	2.0– 6.0	0.21	5.6	9.3	11.2	Mainly heavy smokers
50	8.7	5.0– 15.0	0.40	4.6	7.7	9.2	Moderate occup. exposure
38	41.6	15 –170	1.7	4.1	6.9	8.2	Significant occup. exposure

[a] Mean values from at least two firings from each subsample, evaluated against a matrix matched calibration graph

[b] Computed for each group, from the difference in the values obtained in two parallel determinations at different days, according to the following equation:

$$\text{standard deviation} = \sqrt{\frac{\Sigma\,(\Delta x)^2}{2n}}$$

where Δx is the difference between the two single values and n is the number of chosen pairs as given above

these effects are for storage and shipping from our experience of minor importance because of the less aggressive properties of that material.

Precision and Error Estimations

The mean within-run reproducibility, computed from 12 randomly selected series of *whole blood* samples (Cd concentrations 0.5 – 170 µg/l) analyzed from May 1977 to January 1980 and based on 600 duplicate firings from the same solution was 2.2 digits (i.e. approx. 0.0022 Absorbance), range 1.4 – 3.3 digits. If a level of about 10 µg Cd/l whole blood is considered as a possible critical threshold as is now under discussion [3], at this concentration the average within-run reproducibility is about 1.3% (see Fig. 3). Nevertheless, as was also observed in the determination of lead in whole blood [22] random influences of the particular instrumental

Table 6. Determination of cadmium in pairs of urine samples using direct and solvent extraction and automated electrothermal atomic-absorption spectrophotometry (day to day precision). Calculation of standard deviations, relative standard deviation and confidence intervals from pairs of subsamples arranged in five groups in order of increasing Cd concentration

Number of pairs	Mean conc. µg/l	Conc. range µg/l	Stand. dev. µg/l	Relative confidence intervals			Remarks
				stand. dev. %	$P = 0.1$	$P = 0.05$	
27	0.58	0.2– 1.0	0.15	26	44.7	54.6	Control samples, extraction
47	2.69	1.0– 5.0	0.34	12.6	21.1	25.2	Moderate occup. exposure, extraction
15	3.31	1.0– 6.0	0.27	8.2	14.3	17.3	Moderate occup. direct measurements
15	7.24	5.1–10	0.90	12.4	21.7	26.1	Moderate occup. exposure, extraction
11	26.8	10	1.9	7.1	12.6	15.7	Remarkable occup. exposure, extraction

For explanation of statistical calculations see Table 4

arrangement, the graphite tubes, i.e. the aforementioned drift effects together with matrix effects produce marked fluctuations in signal heights with time. Additionally, the sample pretreatment and not completely controlled contamination from plastic materials introduce additional errors. That decreases the average day-to-day precision of the whole procedure as is shown from numerous determinations at different levels in Tables 4 and 5.

The same applies in principle to *urine samples* with a within-run reproducibility of 4.3 digits for the liquid extraction procedure as an average from 105 and of 2.6 digits for direct urine analysis as an average from 150 duplicate firings. Typical day-to-day precision data for Cd in urine, mainly computed from liquid extraction are given in Table 6.

The data from Tables 3–5 thus provide a realistic picture of the performance of these methods. The estimate of the *probable total error* of Cd determinations in whole blood and urine must be based on these data as well as on intercomparison measurements. From Fig. 4 it is obvious that sometimes significant differences appear between results obtained by means of ETAAS and DPASV in whole blood.

That in principle also applies to the comparative analysis of Cd in urine [6], demonstrating the possibility of hitherto unrecognized systematic deviations. Hence we propose the addition of an uncertainty value of 10% to the confidence intervals computed from the precision data. I.e. for $P = 0.05$ and for Cd concentrations in whole blood of about 2.2 µg/l (average for occupationally unexposed persons) and ≤ 10 µg/l (possible threshold level) as well as for Cd concentrations in urine of about 3 µg/l (direct determination) the total error is estimated to be ≤ 30%, ≤ 20% and ≤ 30%, respectively.

Owing to the non-linearity of calibration graphs and a necessary further dilution in instances of Cd concentrations above about 12–15 µg/l (whole blood and urine) the best attainable over-all precision seems to be at present ≤ 4% in ETAAS for Cd. Hence the uncertainties discussed above give an optimal total error of ≤ 20% at the 95% confidence level.

If the given precision is too low for the desired purpose, repeated determinations at different times can improve the data substantially. For example, from five independent determinations with a standard deviation of 0.1, the standard deviation of the mean decreases to 0.045.

Detection Limits

Since the detection limit in spectrophotometric measurements is due to an IUPAC recommendation defined as three times the standard deviation of the respective blank or noise level [7] for the first approach, the above given average precision data for the within-run-reproducibilities can be used for an estimation of detection limits. For *whole blood* that accounts to about 7 digits. From the calibration graph for 25 µl injections (Fig. 3) this is equal to ≤ 0.2 µg Cd/l whole blood. 50 µl injections are applicable in principle for a further improvement but produced erroneous readings because of problems during injection of larger volumes of deproteinized blood solution.

Due to the different slopes of calibration graphs for direct urine measurements (from the slopes, computed for $n = 20$ different urines the mean value was $\alpha = 53.4$ with a standard deviation of 7.4) and the higher inaccuracy for solvent extraction the estimation of determination limits in urine is more difficult. Under optimal conditions and with a 3 s-value of about

8 digits a detection limit of about 0.2 µg Cd/l is achievable for direct analysis if a dilution of 1 + 2 (urine + water) is made.

Despite distinct problems observed with solvent extraction for Cd from urine, as is reflected in significant signal fluctuations (3 s = 13 digits) due to occasionally appearing too high readings a simple 1 : 2 enrichment and scrupulous cleaning of all labware used leads to a detection limit < 0.1 µg/l. That is sufficiently low for base line and screening programs. Nevertheless for routine screening, particularly in occupational exposure, the direct ETAAS measurement of Cd in urine appears to be the method of choice, particularly if evaluation against matrix matched calibration graphs is performed.

Performance

Environmental screening programs as well as the surveillance of exposed workers require high measuring capacities in respect of speed and costs. Thus, the number of samples that could be analyzed for Cd in whole blood and urine per working day (i.e. 10 h automated operation) was estimated.

From the facts, discussed previously in this paper it is evident that due to the still existing contamination risks only a single aliquot and a single firing for each sample as proposed for the first approach in Pb screening programs [22] is not applicable to Cd. Therefore, the preparation of two aliquots, not to be measured in the same run of samples is mandatory. But, as also shown for Pb, a single firing for each aliquot is sufficient for Cd, too, if only statistical averages are required. As already discussed for Pb, all values around the critical threshold (e.g. 10 ± 2 µg Cd/l whole blood or urine) together with outliers from parallel determinations have to be re-analyzed and occasionally checked by independent methods (e.g. DPASV, [29]) if base-line and/or threshold values have to be established.

The mean total time required for *whole blood* analysis, including a fixed cooling time of about 25 s is ≤ 120 s. This permits a rate of 30 firings per hour, i.e. 300 per working day (10 h). If about 100 firings are estimated as calibration, control and repeat measurements, the daily workload reaches about 100 blood samples divided into two subsamples from each specimen. For round-the-clock operation, including tube replacements, an average of about 690 firings on about 230 specimens are possible per 24 h. If precision analysis is required, of course, the number of analyses per day decreases significantly to about 40 specimens per day.

The same applies in principle to *urine* if solvent extraction is applied. In screening programs, direct measurements are, despite the average time of about 150 s of the HGA program, much simpler than solvent extraction. In principle also a matrix matched calibration graph can be used and allows an average of 24 firings per hour, i.e. 240 per working day. From that a daily workload of 80 urine specimens can be estimated for rapid screening and of about 30 – 40 specimens, if precision analysis with at least one individual standard addition per specimen is required.

Thus, with computer control and evaluation a relatively small staff is able to perform a considerable number of analyses per day. This also demonstrates, that in the course of extended screening programs even a sophisticated and therefore rather expensive instrumentation is able to attain a satisfactory cost/benefit ratio.

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