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Quantitative Determination of Multiple Elements in Botanicals and Dietary Supplements Using ICP-MS

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A method was developed and validated for the analysis of 21 elements in various botanicals and dietary supplements using ICP-MS. Closed-vessel microwave digestion of botanicals and dietary products was assisted by various different procedures. The samples digested with concentrated nitric and hydrochloric acid (8:2) revealed the best recoveries (91−106%) using the reference certified materials (SRM 3280, SRM 1566b). The method was validated for linearity, precision, accuracy, LOD, and LOQ. The LOD was found to be in the range from 0.005 to 1.09 ng/mL with the exception of potassium. Eleven botanicals and 21 dietary supplements were analyzed. Among the analyzed elements, K was the most abundant followed by Na, Mg, Al, Ca, Mn, and Fe, whereas V, Cr, Co, Ni, Se, Cd, Hg, and Pb were present in low concentrations in most of the samples. The results showed that the ICP-MS method is a simple, fast, and reliable for the multielement determination in dietary supplements and botanicals.

KEYWORDS: ICP-MS; botanicals; dietary supplements; method validation; digestion procedures

INTRODUCTION

Traditional medicines based on herbal products and extracts play an ever-increasing role around the world (*1*, *2*), and there is a rapidly growing trend in the consumption of herbal remedies in industrialized and developing countries. The botanicals used in the dietary supplements utilize different parts of the plant, including whole plants, roots, rhizomes, fruits, seeds, flowers, leaves, bark, and stem (*1*, *2*), and contain a wide range of inorganic elements. Among them, heavy metals and metalloids, especially As, Cd, Hg, and Pb, are of primary concern due to their bioavailability and toxicity. These elements may be introduced in various ways, including contamination during cultivation, processing, and storage. Their distribution in botanicals varies greatly within different plant parts and dietary supplements. Previous studies have indicated that relatively high concentrations of these elements may occur in dietary supplements (*3*−*11*). Other elements such as Mg, Mn, Ni, Cu, Zn, and Se are also present and found to have nutritional (*1*, *2*) as well as toxic effects for human health (*12*).

Sample digestion efficiency is the critical step affecting analytical results for multielement determinations by ICP techniques (*13*). Microwave-assisted digestion has been widely used as a novel way to digest samples for the analysis of botanicals. The use of microwave energy as the heat source in acid decomposition was first proposed by Abu-Samra et al. (*14*), who reported its application to wet digestion of biological samples. Abu-Samra's microwave energy technique is now widely used in elemental analysis and involves the total or partial decomposition of the sample, destroying most of the organic matter (*15*). In comparison with conventional methods (hot plate, dry ashing, Soxhlet, and solvent extraction) of sample digestion, these systems reduce contamination, increase the efficiency of the decomposition process, and reduce the time required for digestion (*16*). This method employs a closed vessel system under high temperature and pressure allowing for total metal recovery for volatile elements and reduces the risk of contamination from the environment or other samples (*17*). Low blank values are usually obtained due to the small amounts of the reagents used for digestion. Another important parameter in the efficiency of sample decomposition and in the final analysis is the material particle size. Grinding the samples prior to digestion allows for faster decomposition and better homogenization, leading to more precise results. The microwave digestion equipped with temperature and pressure control assisted by common mineral acids, such as nitric, perchloric, and hydrochloric acids, is frequently used for sample digestion (*13*). Various techniques were employed for elemental analysis, namely, flame atomic absorption spectrometry (FAAS) (*18*−*20*), graphite furnace atomic absorption spectrometry (GFAAS) (*21*−*23*), cold vapor atomic absorption spectrometry (CVAAS) (*24*, *25*), X-ray emission (PIXE) (*26*, *27*), X-ray fluorescence (XRFS) (*28*, *29*), inductively coupled plasma atomic emission spectrometry (ICP-AES) (*30*−*33*), and inductively coupled plasma optical emission spectrometry (ICP-OES) (*34*, *35*). Besides those mentioned previously, many other techniques such as differential pulse cathode stripping voltamperometry (DPCSV) (*36*, *37*) have also been shown to be excellent tools for trace and ultratrace analysis. The advent of collision reaction cells improved the detection

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Table 1. Operating Conditions for the ICP-MS Equipped with an Octopole Reaction System

plasma power (W)	1500		
reflected power (W)	1−2		
carrier gas (L/min)	0.9		
makeup gas (L/min)	0.15		
aux gas (L/min)	0.9		
plasma gas (L/min)	15		
sample uptake	400 μL/min		
nebulizer	glass concentric, micromist		
sample tube (mm, i.d.)	1.02		
internal standard tube (mm, i.d.)	0.19		
waste tube (mm, i.d.)	1.52		
spray chamber	quartz cooled to 2 °C		
interface cones	Ni		
octopole reaction system	standard mode (no gas), H_2 and He modes		
cell gas	no gas	He	H_2
cell gas flow rate (mL/min)	0	3.9	5.0
cell entrance (V)	−30	−30	−30
QP focus (V)	3	−10	−8
cell exit (V)	−30	−40	−40
OctP bias (V)	−6	−18	−18
QP bias (V)	−3	−14	−16
extract 1 (V)	0	0	0
extract 2 (V)	−110	−110	−110
omega bias (V)	−28	−26	−26
oct P RC (V)	150	150	150
points/peak	3		
repetitions	3		
integration time/mass (s)	0.3		
acquisition mode	multitune and scanning		
total analysis time (multitune)	6 min		
rinse time	2 min		

capabilities of quadrupole (CRC ICP-MS) (*38*, *39*) by removing spectral interferences on analytes such as V, Cr, Fe, As, and Se. Analytical instruments described above differ widely in their usage, speed, sensitivity, precision, accuracy, simplicity, cost of analysis and sample preparation techniques. Compared to other sources, CRC ICP-MS shows advantages of a multielemental determination, speed of analysis, low detection limits, large linear dynamic range, and isotopic capabilities. The selectivity of CRC ICP-MS in analytical spectrometry makes it suitable for elemental analysis in a variety of different matrices for simultaneous or sequential elemental determinations (*40*−*42*).

In this study, various digestion procedures were investigated to examine their recovery efficiency for various elements. The CRC ICP-MS was applied for the determination of 21 elements (Na, Mg, Al, K, Ca, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, As, Se, Rb, Sr, Cd, Ba, Hg, and Pb) in 11 botanicals and 21 dietary supplements, which include *Hoodia gordonii* (Masson) Sweet ex Decne., *Sutherlandia frutescens* (L.) R. Br. (SF), *Cissus quadrangularis* L., *Turnera diffusa* Willd. ex Schult., *Centella asiatica* (L.), *Centella erecta* (L. f.), *Pueraria lobata* var. *lobata* (Willd.) Ohwi, *Curcuma longa* L., *Caulophyllum thalictroides* (L.) Michx, and *Euterpe oleracea* Mart.

MATERIALS AND METHODS

Instrumentation. An Agilent 7500ce octopole reaction system ICP-MS (model G3272A, Agilent Technologies, Palo Alto, CA) was used in this study. The internal standard (Ge) was introduced via a micromist nebulizer to the spray chamber using the peristaltic pump of the ICP-MS. The pulse to analogue factor (P/A) was determined on each day of analysis, and the tuning of the instrument was carried out using Agilent ICP-MS tuning solution (10 μg/L Li, Co, Y, Ce, and Tl solution). The system was aspirated with 3% nitric acid for 30 min before tuning the instrument. The instrument operating conditions are illustrated in **Table 1**. The total analysis time was 6 min in multitune mode followed by a 2 min rinse in 2% nitric acid. The instrument was operated in hydrogen (H_2) mode for Ca, Fe, and Se and in no gas mode for Cd, Hg, and Pb, whereas the rest of the elements were analyzed in helium (He) mode (**Table 2**). The Integrated Sample Introduction System (ISIS) was used with a pump speed set at 0.1 rps during the analysis and washout to minimize the amount of matrix accumulation onto the interface and optimize sample throughput.

Standards and Chemicals. Multielement (10 μg/mL), internal standard mix (10 μg/mL), mercury (10 μg/mL) standard stock solutions, tuning mix, and PA tuning solutions were purchased from Agilent Technologies. Concentrated Optima grade nitric and hydrochloric acid were purchased from Fisher Scientific (Fair Lawn, NJ). Water was purified with a Milli-Q system (Millipore, Bedford, MA).

Calibration Standards. The concentrations of the standards ranged from 0.1 to 100 ng/mL for Hg, from 0.1 to 5 μg/mL for K, and from 1 to 5000 ng/mL for Na, Mg, Al, Ca, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, As, Se, Rb, Sr, Cd, Ba, and Pb to ensure that unknown samples were within the range of the standards. Seven-point external calibrations with standards were used to quantify the elements in the digests. Germanium (Ge) was used as an internal standard, added online (50 ng/mL).

Plant Samples. *Voucher Samples*. Aerial parts of *Hoodia gordonii* (Masson) Sweet ex Decne. (code 2925HOGOA) (HG) and leaves−stems of *Sutherlandia frutescens* (L.) R. Br. (code 3222SUFR) (SF) were obtained from Eastern Cape, South Africa. *Euterpe oleracea* Mart. (AC) was obtained from Ninole Orchard, Ninole, HI.

Plants of *Centella erecta* (L. f.) Fernald (code 3557CEERA) (CE, aerial parts) and rhizomes of *Curcuma longa* L. (MPG-AI04-CULOZ) (CL) were obtained from the cultivated living collection of the NCNPR Medicinal Plant Garden at the University of Mississippi. The leaves (code 3884PULOL) (PLL) and roots (code 3831PULOLOL) (PLR) of *Pueraria lobata* var. *lobata* (Willd.) Ohwi were obtained from wild populations. All species were identified by Dr. Aruna Weerasooriya of Medicinal Plant Garden, Coy Waller Complex, University of Mississippi.

Commercial Samples. Aerial parts of *Cissus quadrangularis* L. (code 3287CIQUV) (CQ), roots of *Caulophyllum thalictroides* (L.) Michx (code 2972CATHB) (CT), leaves of *Turnera diffusa* Willd. ex Schult. (code 2436TUDIT) (TD), and aerial parts of *Centella asiatica* (L.) Urb (code 3577CEASA) (CA) were obtained commercially.

Dietary supplements [P-1−P-21 are products claiming to contain either *Hoodia gordonii* (P1), *Sutherlandia frutescens* (P2), *Cissus quadrangularis* (P-3−P-5), *Curcuma longa* (P-6−P-8), *Centella asiatica* (P-9, P-10), *Caulophyllum thalictroides* (P-11), *Turnera diffusa* (P-12−P-15), fucoxanthin (Brown seaweed) (P-16−P-20), or *Euterpe oleracea* (P-21)] were purchased online.

Vouchers and commercial samples are deposited at the National Center for Natural Products Research (NCNPR) repository, University of Mississippi, MS.

Reference Materials. In this study two standard reference materials from the National Institute of Standards and Technology (NIST; Gaithersburg, MD), namely, multivitamin/multielement tablets (SRM 3280) and oyster tissue (SRM 1566b), were used.

Microwave Digestion. The samples were digested with a microwave system (CEM Mars 5, Matthews, NC) equipped with temperature and pressure regulation through a sensor vessel. The sample carousel was capable of holding 16 TMF PTFE digestion vessels (XP-1500 Plus) with a capacity of 100 mL and capable of withstanding pressure of 600 psi and temperatures up to 260 °C. The microwave digestion system was capable of delivering 1600 W of maximum power with controlled temperature ramping. A calibration blank consisting of 3.2% nitric acid and 0.8% hydrochloric acid in deionized water was used.

The percentage recoveries of the three digestion procedures [digestion A, assisted by concentrated nitric acid (10 mL); digestion B, assisted by concentrated nitric and hydrochloric acids (8:2) (10 mL); digestion C, assisted by concentrated nitric acid and 6 M hydrochloric acid (8:2) (10 mL)] were tested by using SRMs (3280 and 1566b). For the above-mentioned procedures, approximately 0.1−0.5 g of samples was weighed directly into the PTFE vessels, to which 10.0 mL of solvent was added and the vessels were capped immediately. The digestion program consisted of a ramp time of 5 min to reach 180 °C and digestion was performed for 15 min. The power was set at 1600 W. The vessels were cooled and then opened. Digestion was judged to be complete when the temperature reached 180 °C and light yellow clear solutions were produced. The cooled digested samples

Table 2. Calibration Data Including Correlation Coefficient (r^2)], Detection Limits (DL), Background Equivalent Concentration (BEC), and Percent Recovery (CE, CL) for 21 Elements

element	mass	mode	r^2	DL (μg/L)	BEC (ng/mL)	CE (% recovery)	CL (% recovery)
Na	23	He	1.0000	0.78	15.56	106.6	111.0
Mg	24	He	0.9999	0.33	1.856	113.2	125.3
Al	27	He	1.0000	0.53	12.78	124.5	122.8
K	39	He	1.0000	30.23	68.65	122.9	107.9
Ca	40	H_2	1.0000	1.09	14.22	112.2	118.4
V	51	He	1.0000	0.0104	0.067	104.2	106.1
Cr	52	He	1.0000	0.007	0.08	105.4	94.6
Mn	55	He	1.0000	0.08	0.138	117.5	110.4
Fe	56	H_2	0.9998	0.34	3.13	110.5	107.4
Co	59	He	1.0000	0.006	0.025	103.8	109.0
Ni	60	He	1.0000	0.034	0.26	107.5	107.2
Cu	63	He	0.9999	0.028	2.93	106.0	104.0
Zn	66	He	1.0000	0.30	3.43	102.5	111.8
As	75	He	1.0000	0.079	0.047	116.5	103.4
Se	78	H_2	0.9997	0.02	0.046	107.8	115.5
Rb	85	He	1.0000	0.013	0.018	117.7	101.5
Sr	88	He	1.0000	0.026	0.057	110.3	107.8
Cd	111	no gas	1.0000	0.005	0.004	114.6	103.2
Ba	137	He	1.0000	0.038	0.087	108.2	115.0
Hg	201	no gas	1.0000	0.011	0.027	97.4	96.3
Pb	208	no gas	1.0000	0.015	0.078	92.9	95.6

were filtered, and 1.0 mL of filtrate was then diluted to 10 mL with deionized water. Blanks (10 mL of solvents), spiked blanks, and spiked samples (CE, CL) were digested in the same manner.

Sample Preparation. For tablets, 10 tablets were weighed and then pulverized with a mortar and pestle. For capsules, 10 capsules were weighed; the contents were emptied, then mixed, and triturated in a mortar and pestle. All ground samples were passed through a sieve no. 40.

Dry ground plant samples (0.1−0.5 g) or an adequate amount of powdered tablet/or capsule contents were weighed (average weight of sample) into microwave digestion vessels. The samples were digested in the same manner.

Final solutions for the determination of Na, Mg, Al, K, Ca, and Fe were further diluted 2−10-fold. To check for contamination of the digestion procedure and sample manipulation, a blank solution containing no samples was prepared and analyzed together with the samples.

Validation Procedure. The developed ICP-MS method was validated in terms of precision, accuracy, and linearity according to ICH guidelines (*43*). For each solvent investigated, a series of standards were prepared to demonstrate linearity. The limit of detection (LOD) and limit of quantification (LOQ) were determined by injecting a series of dilute solutions with known concentrations. Intra- and interday precisions of the method were determined by analyzing spiked blank solutions and three individual sets of samples HG, CE, and P-15 on three consecutive days. The samples were digested and assayed under optimized conditions. Standard solutions were also analyzed after every seven samples to ensure instrument performance.

RESULTS AND DISCUSSION

Accuracy, Precision, and Linearity. Seven-point calibration curves for all 21 elements showed a linear correlation. Calibration data (**Table 2**) indicated linearity ($r^2 > 0.999$) for all standard elements (0.1−100 ng/mL for Hg, 100−5000 ng/mL for K, and 0.001−5 μg/mL for Be, V, Cr, Mn, Fe, Co, Ni, Cu, Zn, As, Se, Rb, Sr, Cd, Ba, Tl, Pb, Na, Mg, Al, and Ca). The LODs were found to be 0.005−1.09 ng/mL for all analyzed elements, except K. For K it was found to be 30.2 ng/mL (**Table 2**). All standards and samples were injected in triplicate. Multiple injections showed that the results are highly reproducible and showed low standard error. Intra- and interday variation of the assay was determined on three consecutive days with three repetitions each. The intra- and interday precision and accuracy values were determined by analyzing three plant samples (HG, CE, and P-15) and blank samples spiked with Hg standard solution at two different concentrations (10 and 50 ng/mL) and at 100 and 500 ng/mL for multielement standards. The intraday RSD for the blank spiked samples ($n = 6$) ranged from 0.12 to 4.09% for all elements tested, whereas that for samples HG, CE, and P-15 ($n = 9$) ranged from 0.001 to 2.87%. The day-to-day RSD ($n = 6$) was from 0.4 to 4.89%, whereas that for samples HG, CE, and P-15 ($n = 9$) ranged from 0.04 to 5.87%. Two spiked samples (CE and CL) with multielement standards of final concentration 10 ng/mL showed percent

Table 3. Recommended Dietary Allowances/Minimum Risk Levels/No Observed Adverse Effect Levels of the Elements/Day[a]

element	RDA/MRL/NOAEL/UL/AI	ref
Na	**AI** = 1.5 g for adults	*57*
Mg	**RDA** = 420 mg for men and 320 mg for women	*58*
Al	**DI** = 0.10−0.12 mg of Al/kg/day for adults	*59*
	NOAEL = 26 mg of Al/kg/day	
K	**AI** = 4.7 g for adults	*57*
Ca	**AI** = 1000 mg for adults	*58*, *60*
V	**MRL** = 210 μg	*61*, *62*
Cr	**RDA** = 35 μg for males and 25 μg for females	*60*, *61*
Mn	**RDA** = 2.3 mg for men and 1.8 mg for women	*60*, *61*
	UL = 11 mg	
Fe	**RDA** = 8 mg for men and 18 mg for women	*57*, *58*
Co	**daily dietary intake** = 0.005−1.8 mg	*61*
Ni	**UL** = 1 mg	*61*
Cu	**RDA** = 900 μg for adults	*60*, *61*
	NOAEL = 10 mg	
Zn	**AI** = 11 mg for men and 8 mg for women	*60*, *61*
As	**MRL** = 21 μg; 10 μg for adults (ANSI 173)	*45*, *60*
Se	**RDA** = 55 μg for adults	*63*
	UL = 400 μg for adults	
Rb	1−5 mg	*64*
Sr	**MRL** = 2.0 mg/kg/day	*65*
	total estimated daily exposure = 3.3 mg (0.046 mg/kg/day)	
Cd	**MRL** = 14 μg	*66*
Ba	**daily dietary intake** = 0.6−1.7 mg	*67*
Hg	50 μg for adults; 20 μg for adults (ANSI 173)	*3*
Pb	75 μg for adults, 6 μg for children; 20 μg for adults (ANSI 173)	*47*

[a] Abbreviations: AI, adequate intakes; DI, daily intakes; UL, tolerable upper intake levels; RDA, recommended dietary allowance; MRL, minimum risk levels; NOAEL, no observed adverse effect levels.

recovery between 93 and 125% for CE and between 95 and 120% for CL.

Table 4. Measured and Certified Values for Two Certified Reference Materials[a]

	NIST SRM 3280		NIST SRM 1566b	
element	certified value (mg/g)	measured value (mg/g)	certified value (mg/g)	measured value (mg/g)
Na	0.33 ± 0.020	0.341 ± 0.012		
Mg	67.8 ± 4.0	65.59 ± 2.40		
Al			197.2 ± 6.0	178.8 ± 4.12
K	53.1 ± 7.0	52.51 ± 2.49		
Ca	110.7 ± 5.3	105.13 ± 3.26		
V	0.008 ± 0.002	8.5 ± 0.46[b]		
Cr	0.094 ± 0.0027	0.095 ± 0.004		
Mn	1.44 ± 0.11	1.402 ± 0.041		
Fe	12.35 ± 0.91	12.06 ± 0.55		
Co	0.00081 ± 0.01	0.81 ± 0.04[b]		
Ni	0.0084 ± 0.0008	8.1 ± 0.41[b]		
Cu	1.4 ± 0.17	1.34 ± 0.08		
Zn	10.15 ± 0.81	9.60 ± 0.22		
As			7.65 ± 0.65	7.99 ± 0.15
Se	0.0176 ± 0.0008	0.0167 ± 0.001		
Rb			3.26 ± 0.145	3.41 ± 0.09
Sr	0.0298 ± 0.2	31.3 ± 0.63[b]	6.8 ± 0.2	7.18 ± 0.08
Cd			2.48 ± 0.08	2.47 ± 0.076
Ba			8.6 ± 0.3	8.9 ± 0.31
Hg			0.037 ± 0.0013	0.039 ± 0.001
Pb			0.308 ± 0.009	0.312 ± 0.01

[a] All certified elements are reported for each reference material, not all materials are certified for all elements. Mean values ± SD. [b] μg/g.

Interferences and Memory Effects. The ICP-MS was equipped with a highly efficient octopole reaction system, which allows careful control of ion energy, most polyatomic, and a few argon-based interferences of 39K16O on ^{55}Mn, 40Ar16O on ^{56}Fe, 44Ca16O on ^{60}Ni, and 40Ar23Na on ^{63}Cu are removed using He and H_2 in reaction mode (*42*,*43*). The elements, especially Mg, Al, K, V, Cr, Mn, Co, Ni, Cu, Zn, As, Rb, Sr, and Ba, would normally suffer polyatomic ion interferences from the chlorine matrix or undigested organocarbon matrices. He collision mode was applied in the Agilent 7500ce CRC-ICP-MS to remove these interferences. The octopole reaction system removes interferences by either reacting a gas with the interference or by preventing the interfering species from entering the analyzer stage using the process called energy discrimination. All data in this work were acquired under trimode (H_2, He, and no gas) conditions, and all analytes were measured at their elemental mass.

One problem that does occur is the long memory effect between samples caused by the contact of mercury with the materials that comprise the sample introduction system. This was usually overcome by extended washing periods at least three times between samples, using dilute solutions of Hg (0.1−100 ng/mL) for calibration curve and the use of hydrochloric acid and nitric acid in the matrix.

Analysis of Plant Samples. The samples digested with the concentrated nitric and hydrochloric acid (8:2) revealed the best recovery (>95%) except for Al (>91%) compared to the other two procedures. The results of replicate analysis of reference materials were used to assess the accuracy and precision, which are in agreement with the certified values (**Table 4**). Concentrations of elements in the dietary products are shown in **Tables 5**

Table 5. Contents (Micrograms per Gram) of Elements in Various Plant Samples and Dietary Supplements (n = 3)

sample	Na	Mg	Al	K	Ca	V	Cr	Mn	Fe	Co
HG	5.15×10^3	4.30×10^3	202	1.46×10^4	1.30×10^4	0.78	0.83	77.5	348	0.31
SF	111	3.27×10^3	629	2.54×10^4	1.36×10^4	0.94	0.78	95.4	385	0.19
CQ	154	6.26×10^3	109	1.12×10^4	4.41×10^4	0.15	3.11	91.1	157	0.30
PLL	28.9	2.81×10^3	51.8	2.84×10^4	9.67×10^3	nd[a]	1.18	101	171	0.13
PLR	95.6	2.46×10^3	858	5.02×10^3	4.62×10^3	1.32	14.2	43.0	583	0.36
CL	114	2.94×10^3	419	4.22×10^4	1.70×10^3	0.99	6.03	214	324	0.35
CA	9.22×10^3	5.72×10^3	188	2.70×10^4	1.15×10^4	0.06	1.69	423	131	0.16
CE	7.78×10^3	5.71×10^3	123	2.22×10^4	1.40×10^4	0.26	3.40	386	120	0.28
CT	93.8	2.03×10^3	1.99×10^3	1.17×10^4	2.89×10^3	2.17	7.66	183	956	1.08
TD	115	3.41×10^3	827	1.56×10^4	1.48×10^4	2.33	6.99	46.5	431	0.26
AC	118	1.03×10^3	33.2	6.95×10^3	1.28×10^3	0.006	15.7	6.93	124	0.005
P-1	1.35×10^4	5.09×10^3	1.97×10^3	1.44×10^4	2.22×10^4	2.60	4.47	127	1.51×10^3	0.52
P-2	1.61×10^3	6.62×10^3	315	3.91×10^4	1.45×10^4	0.61	2.05	92.8	324	0.42
P-3	1.77×10^3	5.93×10^3	27.9	3.55×10^4	3.96×10^3	0.07	0.30	20.6	67.8	0.60
P-4	1.06×10^3	2.60×10^3	366	5.00×10^3	3.50×10^3	0.13	94.4	25.4	82.2	1.69
P-5	6.23×10^3	5.90×10^3	43.7	2.87×10^4	3.38×10^3	0.25	2.70	23	194	0.33
P-6	551	3.30×10^3	333	1.80×10^4	1.17×10^3	0.77	1.45	49.4	380	0.19
P-7	293	2.99×10^3	396	2.37×10^4	1.48×10^3	1.15	1.15	43.8	460	0.21
P-8	150	2.46×10^3	174	1.13×10^4	870	0.42	0.72	59.7	261	0.22
P-9	421	5.88×10^3	3.59×10^3	2.54×10^4	7.82×10^3	4.41	5.11	857	2.38×10^3	1.84
P-10	265	4.12×10^3	2.47×10^3	1.66×10^4	7.80×10^3	2.44	2.16	468	1.34×10^3	0.92
P-11	164	1.83×10^3	2.63×10^3	9.85×10^3	2.96×10^3	5.05	5.83	197	4.04×10^3	1.70
P-12	76.9	2.57×10^3	572	1.36×10^4	2.19×10^4	1.73	0.77	47.7	371	0.32
P-13	87.4	2.51×10^3	566	1.38×10^4	1.84×10^4	1.67	0.84	49.8	355	0.28
P-14	126	3.57×10^3	527	1.10×10^4	1.47×10^4	1.71	1.35	43.1	452	0.20
P-15	63.6	3.42×10^3	536	1.34×10^4	1.30×10^4	1.73	0.65	46.9	359	0.24
P-16	4.26×10^4	1.12×10^4	563	3.25×10^4	1.29×10^4	2.84	1.67	39.4	666	0.99
P-17	3.91×10^4	9.91×10^3	338	2.94×10^4	1.40×10^4	2.51	1.34	37.5	593	1.03
P-18	2.98×10^4	9.0×10^3	151	2.40×10^4	9.43×10^3	1.73	0.84	29.4	192	0.75
P-19	2.32×10^4	6.92×10^3	1.39×10^3	2.19×10^4	2.27×10^4	4.04	460	112	1.59×10^3	1.02
P-20	8.77×10^3	6.76×10^3	551	2.90×10^4	2.53×10^3	0.30	7.25	404	103	0.41
P-21	2.05×10^3	2.67×10^3	15.7	7.88×10^3	4.95×10^3	0.04	0.39	79.1	11.4	nd

[a] nd = not detected.

Table 6. Contents (Micrograms per Gram) of Elements in Various Plant Samples and Dietary Supplements (n = 3)

sample	Ni	Cu	Zn	As	Se	Rb	Sr	Cd	Ba	Hg	Pb
HG	1.26	2.56	13.5	0.39	0.23	1.90	36.4	0.13	18.1	0.05	nd[a]
SF	0.68	7.77	13.4	DUL	nd	nd	nd	nd	14.8	nd	nd
CQ	2.32	4.61	13.1	0.08	0.10	7.93	169	0.05	284	0.02	0.52
PLL	3.87	17.1	92.8	0.04	0.08	13.2	34	nd	19.2	nd	0.52
PLR	4.38	5.31	12.2	0.29	0.01	3.70	99.8	0.12	162	nd	1.53
CL	2.45	7.44	39.6	0.32	0.15	26.0	14.1	0.57	38.4	0.02	0.54
CA	1.59	8.01	113	0.25	0.13	16.5	104	0.43	75.3	nd	0.14
CE	2.30	9.23	125	0.33	0.22	14.0	90.9	0.51	69	0.002	0.01
CT	6.82	28.5	80.1	0.28	0.07	12.2	37.3	0.35	128	nd	2.27
TD	4.79	8.89	54.3	0.33	0.47	6.49	79.4	0.35	17.1	0.01	0.36
AC	1.55	24.1	16.1	nd	0.07	6.29	5.85	0.08	0.18	0.002	nd
P-1	2.22	4.24	21.6	0.62	nd	nd	nd	0.09	63.5	nd	4.21
P-2	2.90	8.77	35.4	0.22	0.37	14.4	109	0.11	18.2	nd	2.01
P-3	1.58	1.79	11.4	0.06	0.19	25.6	26.3	nd	15.8	nd	0.09
P-4	1.20	1.58	5.10	0.01	39.3	3.59	27.2	nd	34.2	nd	0.07
P-5	15.4	1.92	15.2	0.08	0.08	7.23	42.8	nd	9.30	0.003	0.19
P-6	0.98	4.37	14.7	0.06	0.07	6.19	11	nd	7.99	nd	0.35
P-7	0.85	4.99	31.3	0.07	0.05	8.66	14.6	nd	12.4	nd	1.33
P-8	0.52	3.69	25.5	0.09	0.13	5.46	8.5	0.02	8.92	nd	0.62
P-9	6.23	12.5	113	0.85	0.16	28.8	44.0	3.43	123	nd	2.93
P-10	3.56	7.48	62.0	0.58	0.08	20.6	82.3	1.95	191	nd	2.03
P-11	4.83	22.5	55.6	0.82	0.26	11.2	35.5	0.22	126	nd	2.65
P-12	1.36	7.85	39.7	0.32	0.39	6.53	75.1	0.30	14	0.01	0.40
P-13	1.87	7.01	41.8	0.35	0.59	6.79	83.1	0.36	12	0.02	0.40
P-14	1.55	6.45	29.4	0.47	0.29	5.64	86.5	0.25	13.9	0.01	0.33
P-15	1.42	8.28	36.8	0.35	0.42	6.04	79.6	0.29	12.7	0.21	0.41
P-16	2.77	1.46	34.4	26.1	0.15	11.9	741	0.30	12	0.01	0.52
P-17	2.45	1.28	31.5	31.3	0.10	9.55	795	0.35	11	0.01	0.59
P-18	0.97	3.14	29.6	25.5	0.05	7.27	553	0.30	6.58	nd	0.28
P-19	6.95	2.63	28.1	36.3	0.19	16.8	556	0.39	11.2	0.01	1.07
P-20	6.50	6.33	19.5	12.9	nd	85.4	12.2	0.19	6.8	0.03	0.36
P-21	0.33	2.19	4.89	nd	nd	12.8	3.50	nd	2.18	nd	nd

[a] nd = not detected.

and **6** and represent the mean of triplicate analyses. Analysis of our present investigation documents a wide range of variation in the elemental constitution of botanicals and dietary supplements. The concentrations of elements present in the botanicals and supplements studied were compared with the minimum risk levels (MRL), the no observed adverse effect levels (NOAEL), tolerable upper intake levels (UL), or the recommended dietary allowance (RDA) for each element (*1*). The MRLs, ULs, RDAs, and NOAELs of the metals analyzed in the supplements are shown in **Table 3**.

The contents (μg/g) of all 21 elements quantified in various plant samples and dietary supplements by using CRC ICP-MS are listed in Tables **5** and **6** and represent the mean of replicate analysis. Most element concentrations were well above the LOQ.

All analyzed samples contain Na, Mg, Al, K, Ca, Cr, Mn, Fe, Ni, Cu, Zn, and Ba, whereas some elements such as Co, Se, Rb, Sr, Cd, and Hg were not detected in some of the samples. The concentrations of all 21 elements varied widely on the basis of the plant sample and dietary supplements. The contents of trace and essential elements detected in various samples were in the range from 28.9 to 4.26×10^4 μg/g for Na, from 1.03×10^3 to 1.12×10^4 μg/g for Mg, from 5.00×10^3 to 4.22×10^4 μg/g for K, from 870 to 4.41×10^4 μg/g for Ca, from 0.006 to 5.05 μg/g for V, from 0.30 to 460 μg/g for Cr, from 6.93 to 857 μg/g for Mn, from 11.4 to 4.04×10^3 μg/g for Fe, from 0.33 to 15.4 μg/g for Ni, from 1.28 to 28.5 μg/g for Cu, from 4.89 to 125 μg/g for Zn, and from 0.01 to 39.3 μg/g for Se. On the other hand, elements such as Co were detected in very low amounts. Se was detected in 28 samples, and a high amount was found in sample P-4 (120 μg/day). The high amounts of Se may be due to its claim in P-4 product (label claim, 60 μg/serving size). The level of Cr in one sample, P-19, 479 μg/day, would result in an exposure that could exceed the recommended dietary allowance (**Table 5**).

Samples 4 and 5 (PLL, PLR) are of different parts (leaves and roots) of kudzu, and observed data showed a wide range of variation in the elemental composition. Concentrations of Na, Al, and Fe were more prevalent in the roots, whereas Mg, K, Ca, and Zn were higher in the leaves of kudzu. These data are similar to the observations of Corley et al. (*44*), who documented the nutritive value of kudzu as a feed for ruminants. Other elements such as Cr, As, Sr, Ba, Pb, and Cr were also higher in the roots and Mn and Cu were higher in the leaves of kudzu (**Tables 5** and **6**). From the analysis of our present data it was noted in all samples that the concentration of copper was much higher than that of Co or Ni, and our samples were also found to contain remarkable concentrations of Fe. Concentrations of Co were observed to be in the range of 0.005−1.84 μg/g in the different samples (**Table 5**).

Concentrations of As, Cd, Hg, and Pb in the dietary supplement products are shown in **Table 6**. The highest concentrations found were 85.7 μg/day for As in sample P-16, 8.89 μg/day for Cd in sample P-9, 0.039 μg/day for Hg in sample P-20, and 7.59 μg/day for Pb in sample P-9. A number of factors preclude a thorough examination of the results to determine the product's component that may be the source of an element or variability between brands. These factors include the amount of ingredient in a product, its geographic source, and various other ingredients in a product.

Assessment of Maximum Exposures. Estimated exposures/intakes of As, Cd, Hg, and Pb were assessed with respect to safe/tolerable exposure levels described by various national and public

health organizations. Maximum daily intakes for each element from each product were calculated by multiplying maximum recommended daily intake on the product label by the mean product unit mass and by the mean element concentration determined in this study. The Cd exposures are well below the minimum risk levels of 14 μg/day (**Table 3**). Levels of As found in five of the products (sample P-16, 85.7 μg/day; sample P-17, 73.9 μg/day; sample P-18, 27.8 μg/day; sample P-19, 37.8 μg/day; sample P-20, 19.2 μg/day) could result in exposures that exceed the tolerable intake (*45*). With respect to Pb and Hg, none of the products or botanicals would result in maximum exposures that exceed a tolerable level of exposure of 10 μg/day that is deemed to be unsafe (**Table 3**) (*46*−*48*). Assessment of Hg is predicated on the assumption that the mercury measured as total Hg (THg) is present as methylmercury (MeHg). If part of the Hg exists as an inorganic form, then any potential concern would be reduced. The degree of this reduced concern is dependent in turn on the proportion of Hg present in inorganic form (*3*, *49*). There are various opinions on what the maximum safe daily limits for lead, mercury, and arsenic in dietary supplements should be (*50*, *51*). For example, the California Safe Drinking Water and Toxic Enforcement Act (California Proposition 65) states that a maximum level of Pb, as a reproductive toxin, is 0.5 μg/day (*51*, *52*). The American National Standards Institute (ANSI)/National Sanitation Foundation (NSF) International Dietary Supplement Standard 173 (*51*, *53*) suggests that dietary supplements should not contain undeclared metal that would cause intake greater than 20 μg/day of Pb, 20 μg/day of Hg, or 10 μg/day of As. The U. S. Environmental Protection Agency (U.S. EPA) recommends maximum levels of 21 μg/day for inorganic Hg and 21 μg/day for inorganic As for a 70 kg adult (*51*,*54*). The Food and Agricultural Organization/World Health Organization Joint Expert Committee on Food Additives (FAO/WHO JECFA) indicates that provisional tolerable weekly intakes correspond to 250 μg/day of Pb, 50 μg/day of Hg, and 150 μg/day of As for a 70 kg person (*51*, *55*).

Nevertheless, the total element concentration determination does not provide adequate information to understand the effects observed in the environment and biological systems. The toxicity, bioavailability, and metabolic processes are greatly dependent on the specific chemical form of the element. In our future studies the elemental speciation of these samples is to be developed for biochemical, clinical, and environmental investigations. The simultaneous determination of As speciation including As(III), As(V), monomethylarsonic acid (MMA), dimethylarsinic acid (DMA), and arsenobetaine (AsB) is being carried out for samples P-16−P-20 by coupling a HPLC column to a collision/reaction cell inductively coupled plasma mass spectrometer (CRC ICP-MS) (*56*).

In conclusion, microwave digestion followed by analysis by CRC ICP-MS has been shown to be a simple, fast, and reliable method for the multielement determination in botanicals and dietary supplements. Various microwave digestion procedures were tested, and the samples digested with concentrated nitric and hydrochloric acid (8:2) revealed the best recovery. A total of 11 botanicals and 21 dietary supplements were analyzed by using the CRC ICP-MS system for the determination of 21 elements. Determinations of trace elements at low and even sub-parts per billion levels in all samples were possible. Among the determinations, the elements Na, Mg, Al, Ca, Mn, and Fe were found to be abundant in all of the botanicals and dietary supplements analyzed. Five samples for As and one sample for Cr were found to contain elevated concentrations above the recommended 10 and 35 μg/day limits, respectively. This technique is reliable for routine analysis of multielement determination in a wide range of botanicals and dietary supplements.

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