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Metal concentrations of Chinese herbal medicine products in the United States

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SUMMARY

We determined arsenic, lead, mercury and cadmium concentrations in Chinese herbal medicines sold in the United States by medical use parts. 54 kinds of herbal products including 9 medical use parts (radix, rhizoma, cortex, pericarpium, fructus, lignum, semen, folium, and herba) were analyzed using inductively coupled plasma-mass spectrometry for arsenic, lead and cadmium, and using mercury analyzer for mercury. Arsenic (median concentration, 0.25 mg/g), mercury (0.20 mg/g), lead (3.78 mg/g) and cadmium (0.39 mg/g) were detected in 71%, 54%, 35%, and 18% of 143 herbal medicine samples, respectively. A total of 27% and 12% of 143 products analyzed contained mercury and cadmium above the regulatory standards. Herba and folium (leaves of herbal plants) were the most contaminated parts from metals, whereas pericarpium, lignum and semen (outer layers and seeds) were less contaminated. This study suggests that metal contamination is different by medical use parts. Our findings provide further evidence that efforts to protect people using traditional remedies from metal intoxication should be made to enforce the regulatory standards.

Key words: Chinese herbal medicine; Metals; Toxicity

INTRODUCTION

The popularity of traditional Chinese medicine has increased over the past decade as complementary and alternative therapies in the United States (Eisenberg *et al.*, 1998). Chinese herbal medicine products as one of these therapies are widely used in the United States (Ernst, 2005). Most of those products are imported from China or other Asian countries. The Chinese pharmacopeia lists over 6,000 different medicinal substances. Currently, more than 500 herbal products are commonly used in the United States (Boullata and Nace, 2000). However, recent studies have reported high

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concentrations of metals in Ayurvedic and Chinese herbal medicine products (Hasegawa *et al*., 1997; Cheng *et al.,* 1998; Emst and Thompson, 2001; Caldas and Machado, 2004). A very recent study conducted in Boston area showed that metals, such as lead, mercury and arsenic were detected in a total of 14 of 70 (20%) Ayurvedic herbal medicine produced in South Asia and available in Boston South Asian stores (Saper *et al.,* 2004). Ernst and colleagues have reviewed systematically epidemiologic and analytical studies of metals in traditional Chinese medicines and found that a considerable proportion of traditional Chinese medicines contained metals (Ernst and Thompson, 2001). The California Department of Health reported that 10 to 14 percent of 251 Asian patent medicines collected from California retail herbal stores contained lead, mercury, or arsenic in a quantity of at least 10 parts per million (Ko, 1998). Some of Chinese herbal medicine products were identified to have lead and arsenic 1,000 to 10,000 times higher than the regulatory standards (Ernst and Thompson, 2001).

Metal toxicity has been associated with use of Chinese herbal remedies. A woman in the United States hospitalized with a history of increasing abdominal pain, constipation and weight loss was identified to have consumed three types of Asian herbal pills which contained lead, mercury and cadmium (McElvaine *et al*., 1990). Bayly et al found in a series of five cases of lead poisoning due to Asian traditional remedies in the United Kingdom that the remedies contained 6% to 60% lead by weight and some traces of mercury and arsenic (Bayly *et al.,* 1995). In addition, intoxication by mercury (Kew *et al.,* 1993; Kang and Oransky, 1992), arsenic (Kew *et al.,* 1993), cadmium (Wu *et al.,* 1996), and thallium (Schaumburg *et al.,* 1992) have been reported.

Although "natural" herbal products used as folk remedies are perceived as safe, a body of evidence suggests that herbal medicines may be sources of metal toxicity. However, few studies have been reported on metal content in Chinese herbal medicines consumed in the United States. This study determined arsenic, lead, mercury and cadmium concentrations which are prioritized by the Environmental Protection Agency and the Agency for Toxic Substances & Disease Registry (ATSDR, 2006) in 54 kinds of Chinese herbal medicine sold in the United States. Especially, we measured metal concentrations by medical use parts, radix (root), rhizoma (plant stem) cortex (plant outer layer), pericarpium (dried tangerine peel), fructus (fruit), lignum (woody tissue), semen (seed), folium (leaf), and herba (herb).

MATERIALS AND METHODS

Sample collection

The crude samples used for Chinese herbal medicine were collected from Chinese markets in New York, Los Angeles, and Washington D.C. areas between October and September, 2001. Each sample was obtained from each city (three samples per individual herbal medicine). The list of Chinese herbal medicine products by medical use parts was presented in Table 1. We determined metals concentrations from 13 radix, 9 rhizoma, 7 cortex, 2 pericarpium, 7 fructus, 1 lignum, 6 semen, 3 folium, and 6 herba, a total of 54 herbal products. Some of samples were not collected in all three cities which made a total of 143 samples rather than 162.

Reagents

All reagents were of analytical reagent grade. High purity de-ionized water (Milli-Q system, Millipore, USA) was used throughout. Analytical reagent nitric acid (Merck, 70%) was used after additional purification by sub-boiling distillation in quartz steal. Plastic bottles and glassware were cleaned by soaking in 20% (v/v) HNO_3 for 24 h. This material was then rinsed three times with de-ionized water.

Sample preparation and analyses

The samples were freeze-dried and then ground, homogenized and sieved (d ≤ 175 μm) before analyses. Samples with excessive concentrations of metals were diluted with spectral-grade graphite. Sample pretreatment and analytical methods were done using a modification of the methods of US EPA procedures and Goulle et al. and Mortada *et al.*'s studies (EPA US, 1981; Goulle *et al.*, 2005; Mortada *et al.*, 2002). In addition, the whole analytical procedure, from sampling to final analytical determinations, was carried out according to a pre-established quality assurance protocol (Cubadda et *al.*, 2003). Briefly, this included the use of powder-free gloves and non-contaminating equipment for sample collection and handling, sample storage in brand-new jars of high-density polyethylene previously submitted to a decontaminating acid treatment, sample transport in plastic envelopes in order to protect the jars from dust and aerial contamination, and sample treatment carried out by trained personnel under clean room conditions. Once in the laboratory, samples were stored at room temperature in the dark until analysis in less than 15 days.

Preparation for arsenic, cadmium and lead: Prepared samples were treated using 65 ml of cleaning solution (186 ml of ethyl alcohol, 93 ml of acetone and 371 ml of n-hexane to 1L volumetric flask) for 12 h. Each aliquot (0.1 – 0.2 g) from well homogenized samples was moved to a digestion vessel. The aliquots were mixed with 10 ml of 1:1 HNO_3, and then covered with a watch glass. Treated samples were heated to 95 ± 5°C and refluxed for 10 to 15 min without boiling. After adding 5 ml of concentrated HNO_3, the samples were allowed to be cool and were refluxed for 30 min. This step was repeated until no brown fume

Table 1. Mmetal concentrations in individual Chinese herbal medicine products

Medical Use Parts	Scientific Name	Mean (SD)*, μg/g			
		As	Cd	Hg	Pb
Radix	Aconiti Iateralis Preparata Radix	0.11(0.02)	ND	0.81	ND
	Asari Herba Cum Radice	1.36(0.58)	1.73(1.48)	0.19	10.39(9.71)
	Rehmanniae Radix Preparat	0.29(0.05)	ND	0.17(0.08)	ND
	Ginseng Radix	0.41(0.02)	ND	0.18(0.03)	2.09
	Paeoniae Radix Rubra	0.20	ND	0.12(0.02)	ND
	Scrophulariae Radix	0.17(0.04)	ND	0.45	4.23(0.84)
	Angelicae Sinens Radix	0.19	0.45	ND	ND
	Ophiopogonis Radix	0.50(0.49)	ND	0.24	2.65
	Aucklandiae Radix	0.09	0.34	0.09	2.26
	Paeoniae Radix Alba	0.14	ND	ND	4.45
	Rehmanniae Radix	0.49	ND	0.12	ND
	Rehmanniae Recens Radix	0.67	ND	0.23	ND
	Astragali Radix	0.13	ND	0.21	ND
Rhizoma	Pinelliae Rhizoma	0.10(0.04)	ND	0.14(0.03)	ND
	Atractylodis Macrocephalae Rhizoma	0.20(0.11)	ND	0.234(0.09)	ND
	Dioscoreae Rhizoma	0.54(0.43)	ND	0.26(0.18)	3.12(0.35)
	Atractylodis Japonicae Rhizoma	0.57(0.09)	0.54(0.40)	0.12	2.35
	Cyperi Rhizoma	0.13	0.25	0.15	ND
	Coptidis Rhizoma	0.27(0.12)	0.46(0.23)	0.35	3.61(0.34)
	Polygonati Rhizoma	0.46(0.15)	ND	0.30(0.18)	6.50
	Cnidium Officinale Makino	0.27(0.04)	0.47(0.05)	0.31(0.16)	ND
	Chuanxiong Rhizoma	0.15	N.D	0.14	ND

Table 1. (continued)

Medical Use Parts	Scientific Name	Mean (SD)*, μg/g			
		As	Cd	Hg	Pb
Cortex	Taxilli Ramulus	0.11(0.05)	ND	0.29(0.18)	2.45(0.54)
	Mori Radicis Cortex	0.17(0.07)	ND	1.16(0.35)	2.63
	Cinnamomi Cortex	ND	0.34(0.18)	0.48(0.01)	2.19
	Magnoliae Officinals Cortex	0.17(0.14)	ND	0.87	8.51(6.66)
	Eucommiae Cortex	0.26(0.11)	ND	ND	5.37(2.60)
	Lycii Radicis Cortex	0.50(0.40)	ND	0.28(0.18)	2.46
	Moutan Radicis Cortex	0.30	0.28	ND	ND
Pericarpium	Citri Reticulatae Pericarpium	0.34(0.14)	ND	0.16(0.08)	4.01(0.21)
	Citri Reticulatae Virdie Pericarpium	0.33(0.12)	ND	0.12	ND
Fructus	Amomi Fructus	ND	ND	0.18(0.13)	ND
	Crataegii Fructus	0.14(0.10)	ND	0.48(0.38)	2.21
	Corni Fructus	0.08(0.01)	ND	0.20(0.12)	2.34
	Schisandrae Fructus	0.25(0.17)	ND	0.29(0.20)	ND
	Ponciri Seu Aurantii Immaturus Fructus	0.66(0.80)	ND	0.13	12.27(16.57)
	Gardeniae Fructus	0.24(0.18)	ND	0.10	ND
	Chaenomelis Fructus	0.61(0.70)	ND	0.33	ND
Lignum	Sappan Lignum	0.18	ND	0.19(0.01)	ND
Semen	Tritici Levis Semen	ND	ND	0.22(0.15)	ND
	Phaseoli Semen	0.09	ND	0.27	ND
	Armeniacae Amarum Semen	0.58	ND	ND	ND
	Persicae Semen	0.08	ND	ND	ND
	Glycine Semen Nigrum	ND	0.33	0.14	ND
	Sesami Semen Nigrum	ND	ND	0.20	ND
Folium	Perillae Folium	1.53(0.58)	0.30(0.05)	0.25(0.22)	6.80(1.38)
	Artemisiae Argui Folium	0.52(0.17)	0.35(0.08)	0.27(0.07)	6.86(1.99)
	Biotae Cacumen	0.42(0.35)	ND	0.30	7.39(3.69)
Herba	Ephedrae Herba	0.15(0.10)	ND	0.84	ND
	Leonuri Herba	2.37(1.32)	ND	0.51(0.70)	19.20(15.52)
	Artemisiae Capillaris Herba	1.91(1.78)	1.02(0.49)	0.17	6.34(1.99)
	Ramulus Uncariae Cuny unicis	0.17(0.01)	0.24	0.18(0.09)	3.46
	Akebiae Caulis	0.12(0.05)	ND	0.08	2.99
	Menthae Herba	0.54(0.04)	ND	ND	3.54(1.09)

ND, not detected.
Detection Limit : As(ug/g) < 0.059 , Cd(ug/g) < 0.230 , Pb(ug/g) < 2.023 , Hg(ug/g)< 0.074
*Results from three individual samples collected from each store in New York, Los Angeles, and Washington DC area. No standard deviation was reported if metals were not detected in two of three samples.

was given off by the sample, showing the complete reaction with HNO_3. Using a ribbed watch glass, the solution was evaporated to approximately 5 ml at 95 ± 5°C for two hours. The samples were cooled again and 3 ml of 30% H_2O_2 was added. In order for the peroxide reaction the vessels were covered with a watch glass and placed on the heat source for warming until effervescence subsides. Then peroxide solution was added in 1 ml aliquots. The aliquots were warmed until the effervescence was minimal. The aliquots were covered with a ribbed watch glass. The acid-peroxide digestate of the

Table 2. Operating conditions of ICP-MS

Spectrometer	Ultramass 700*
Nebulizer	Babington
Spray chamber	Scott, 2°C
rf power	1300 W
Sampling depth	6.4 mm
Plasma gas flow rate	15.0 L/min
Auxillary gas flow rate	1.0 L/min
Nebulizer gas flow rate	1.05 L/min
Sampler	0.5 mm, Ni
Skimmer	0.5 mm, Ni
Integration time	0.3 s/channel (three channels per mass)
Repetitions	5

*Model : 820-MS made by Varian, Australia

aliquot was heated until the volume was reduced to approximately 5 ml. The solution was covered over the bottom of the vessel at all times. After cooling, it was diluted to 50 ml with water. The particulates in digestates were then removed by filtration. The filtered samples were analyzed by inductively coupled plasma-mass spectrometry (ICP-MS, Varian Ultramass 700, Australia) with a cross flow nebulizer. Operating conditions are shown in Table 2.

Preparation for mercury: Prepared samples were treated by using 65 ml of cleaning solution (186 ml of ethyl alcohol, 93 ml of acetone and 371 ml of n-hexane to 1L volumetric flask) for 12 h. Each aliquot (0.1 – 0.2 g) from well homogenized samples was placed in the bottom of a BOD bottle. The aliquots (0, 1, 3, 5 ml) of mercury working standard containing 0 – 5 μg/L of mercury were transfer to a series of BOD bottles. The reagent water (5 ml) and concentrated sulfuric acid (5 ml) were added to the aliquots of standard and sample. Also 2.5 ml of concentrated Nitric acid was added to them and then they were heated for two minutes at 95 ± 3. After cooling, samples and standard were added by 15 ml 5% potassium permanganate solution and mixed. They were heated for 30 minutes at 95 ± 3 After cooling, they were mixed with sodium chloride-hydroxylamine hydrochloride to reduce the excess permanganate. The standard and sample were diluted to 100 ml with de-ionized water. The particulates in digestates were removed by filtration. The filtered samples and standards were analyzed by mercury analyzer (Cetac, M-6000A, USA).

Data analysis

We calculated the proportion of herbal medicines containing metals by medical use parts. Arithmetic mean (standard deviation, SD) and median were calculated for each individual medicine and by medical use parts. We also calculated the proportion of herbal medicines whose concentrations exceeded the regulatory standards for arsenic (2 μg/g), cadmium (0.3 μg/g) and lead (10 μg/g) recommended by World Health Organization (WHO)(WHO, 1996), and for mercury (0.2 μg/g) adapted by China (Chinese Pharmacopoeia Commission, 2005).

RESULTS

Metal concentrations of arsenic, cadmium, mercury and lead in individual herbal medicine products were presented in Table 1. For arsenic, *Leonuri Herba* (2.37 ± 1.32 μg/g), *Artemisiae Capillaris Herba* (1.91 ± 1.78 μg/g), *Perillae Folium* (1.53 ± 0.58 μg/g), and *Asari Herba Cum Radice* (1.36 ± 0.58 μg/g) showed relatively high concentrations. *Asari Herba Cum Radice* (1.73 ± 1.48 μg/g) and *Artemisiae Capillaris Herba* (1.02 ± 0.49 μg/g) contained high concentrations of cadmium. For mercury, many herbal products appeared to have higher concentrations than the allowed standard limit (0.2 mg/g), especially, *Mori Radicis Cortex* contained 1.16 ± 0.35 μg/g of mercury. For lead, *Leonuri Herba* (19.20 ± 15.52 μg/g), *Ponciri Seu Aurantii Immaturus Fructus* (12.27 ± 16.57 μg/g) *and Asari Herba Cum Radice* (10.39 ± 9.71 μg/g) showed relatively high concentrations.

Table 3 presents metal concentrations by medical use parts. A total of 101 (71%), 77 (54%), 50 (35%) and 26 (18%) of 143 herbal medicine products

Table 3. Metal concentrations in Chinese herbal medicine products by medical use parts

Metal	Medical part (No. sample)	No (%) of samples detected	Concentrations (mg/g)			No (%) of samples above the standards*
			Mean (SD)	Median	Range	
As	Radix (31)	21 (68)	0.44 (0.47)	0.25	0.09 - 2.03	1 (3.2)
	Rhizoma (24)	20 (83)	0.33 (0.23)	0.26	0.06 - 0.99	0
	Cortex (19)	15 (79)	0.25 (0.22)	0.19	0.07 - 0.96	0
	Pericarpium (6)	6 (100)	0.33 (0.12)	0.28	0.23 - 0.50	0
	Fructus (20)	13 (65)	0.35 (0.46)	0.13	0.07 - 1.58	0
	Lignum (3)	1 (33)	0.18	0.18	0.18	0
	Semen (15)	3 (20)	0.25 (0.29)	0.09	0.07 - 0.58	0
	Folium (9)	9 (100)	0.82 (0.64)	0.69	0.21 - 1.98	0
	Herba (16)	13 (81)	0.96 (1.26)	0.22	0.07 - 3.62	3 (18.8)
	Total (143)	101 (71)	0.46 (0.61)	0.25	0.06 - 3.62	4 (2.8)
Cd	Radix (31)	5 (16)	1.19 (1.27)	0.50	0.34 - 3.36	5 (16.1)
	Rhizoma (24)	8 (33)	0.46 (0.21)	0.40	0.25 - 0.81	5 (20.8)
	Cortex (19)	3 (16)	0.32 (0.09)	0.28	0.26 - 0.42	1 (5.3)
	Pericarpium (6)	0	ND	ND	ND	0
	Fructus (20)	0	ND	ND	ND	0
	Lignum (3)	0	ND	ND	ND	0
	Semen (15)	1 (7)	0.33	0.33	0.33	1 (6.7)
	Folium (9)	5 (56)	0.32 (0.06)	0.30	0.26 - 0.41	2 (22.2)
	Herba (16)	4 (25)	0.82 (0.56)	0.75	0.24 - 1.55	3 (18.8)
	Total (143)	26 (18)	0.61 (0.65)	0.39	0.24 - 3.36	17 (11.9)
Hg	Radix (31)	15 (48)	0.23 (0.18)	0.20	0.08 - 0.81	8 (25.8)
	Rhizoma (24)	15 (63)	0.23 (0.12)	0.17	0.08 - 0.43	6 (25.0)
	Cortex (19)	9 (47)	0.59 (0.40)	0.48	0.16 - 1.41	7 (36.8)
	Pericarpium (6)	3 (50)	0.15 (0.06)	0.12	0.10 - 0.21	1 (16.7)
	Fructus (20)	13 (65)	0.27 (0.22)	0.15	0.09 - 0.89	6 (30.0)
	Lignum (3)	2 (67)	0.19 (0.01)	0.19	0.18 - 0.20	1 (33.3)
	Semen (15)	6 (40)	0.20 (0.08)	0.17	0.11 - 0.33	2 (13.3)
	Folium (9)	5 (56)	0.27 (0.12)	0.30	0.10 - 0.41	4 (44.4)
	Herba (16)	9 (56)	0.35 (0.43)	0.15	0.08 - 1.31	3 (7.9)
	Total (143)	77 (54)	0.29 (0.26)	0.20	0.08 - 1.41	38 (26.6)
Pb	Radix (31)	9 (29)	5.67 (6.07)	3.64	2.09 - 21.42	1 (3.2)
	Rhizoma (24)	7 (29)	3.70 (1.34)	3.37	2.35 - 6.50	0
	Cortex (19)	10 (53)	4.84 (4.29)	3.15	2.07 - 16.06	1 (5.3)
	Pericarpium (6)	2 (33)	4.01 (0.21)	4.01	3.86 - 4.16	0
	Fructus (20)	5 (25)	8.27(12.93)	2.51	2.21 - 31.40	1 (5.0)
	Lignum (3)	0	ND	ND	ND	0
	Semen (15)	0	ND	ND	ND	0
	Folium (9)	9 (100)	7.01 (2.22)	7.03	3.17 - 10.04	1 (11.1)
	Herba (16)	8 (50)	8.07 (9.16)	4.62	2.77 - 30.17	1 (6.3)
	Total (143)	50 (35)	6.05 (6.22)	3.78	2.07 - 31.40	5 (3.5)

ND, not detected.
*Regulatory standards for As, Cd, and Pb recommended by World Health Organization(WHO) are 2 μg/g, 0.3 μg/g, 10 μg/g, respectively. The standard for Hg used in this study (0.2 μg/g) is the legally allowed limit adapted by China.

contained detectable concentrations of arsenic, mercury, lead and cadmium, respectively. Cadmium was not detected among pericarpium, fructus, and lignum parts. Lead was not detected among semen and lignum parts. Folium had the highest median concentrations of arsenic (0.69 μg/g) and lead (7.03 μg/g). Herba and cortex showed the highest median concentrations of cadmium (0.75 μg/g) and mercury (0.48 μg/g), respectively. Further, herba had the highest mean concentration of arsenic (0.96 μg/g) and three of four samples that exceeded the regulatory standard of arsenic were from herba. Overall, 27% and 12% of 143 herbal medicines analyzed exceeded the regulatory standards for mercury and cadmium, respectively. In particular, more than 30% of folium, cortex and fructus seemed to be highly contaminated by mercury. Less than 4% of samples contained higher concentrations of arsenic and lead above the regulatory standards.

Some of notable factors causing metals in herbs are from existing metal concentrations in the earth's crust, soil and water quality, as well as environmental pollution such as atmospheric pollution (Peter, 1999).

Even for the same type of herbs, the level of contamination is dependent of environmental contamination of cultivating and producing areas (Wei *et al.,* 2005). The contamination level can vary between the parts of herb, such as seed, stem, root, leaves, or the whole herb. The level of contamination depends on the degree of absorption of atmospheric pollution and soil metal contents. If the part of herbs comes from under the ground, then the contamination is caused by the quality of soil and water.

Contamination can also occur during the circulation stage after the cultivation and harvest. An intentional or unintentional contamination can occur during the primary processing, packaging, storing, transporting, and other means (KFDA 2006).

The metal concentration can vary by numerous contributing factors of contamination and the part of herb used for medicinal purpose, yet there is no prior study conducted on the topic.

Various factors can lead to non-systematic results of metal contamination, and further specific studies should be followed.

In this study, we determined metals concentrations in 54 different kinds of Chinese herbal medicine widely used in the United States and other countries. We analyzed 4 important metals, arsenic, cadmium, mercury and lead, because they are widely distributed in the farming or rural areas and because they are known to pose the most significant potential threat to human health and prioritized by the Environmental Protection Agency and the Agency for Toxic Substances & Disease Registry (ATSDR, 2006). This is the first study to measure metal concentrations by medical use parts, such as radix, rhizoma, cortex, etc.

Arsenic, cadmium and lead were found in higher concentrations in herba and folium than other parts. Radix and rhizoma, root and stem of plants, also showed modest concentrations of all metals.

Mercury was found in higher concentrations in cortex. On the other hand, pericarpium, fructus, lignum and semen appeared to contain low concentrations of metals.

The regulatory standards for metals in traditional Chinese or Ayurvedic herbal medicine have not been established. We, therefore, used the recommended maximum limits for arsenic (2 μg/g), cadmium (0.3 μg/g) and lead (10 μg/g) by WHO (WHO, 1996) and for mercury (0.2 μg/g) by China (Chinese Pharmacopoeia Commission, 2005), and calculated the proportions of samples above these regulatory standards. We found 27%, 12%, 4%, and 3% of 143 samples were above the recommended limits for mercury, cadmium, lead and arsenic, respectively. The proportion for lead in our study is lower than that conducted in California where 24 products of 251 Asian patent medicines (10%) contained greater than 10 μg/g (ppm) (Ko, 1998). This California study also showed extremely higher ranges of arsenic (20.4 to 114,000 μg/g) and mercury

(22.4 to 5070 μg/g) concentrations. A recent study conducted in Singapore has reported that 2.1%, 1.4% and 0.6% of traditional Chinese medicine products tested (a total 3,320) were detected to contain mercury, arsenic and lead, respectively, in excess (Yee *et al.*, 2005). The legally allowed limits for mercury, arsenic, and lead in Singapore are 0.5 μg/g, 5 μg/g, and 20 μg/g, respectively (Wei *et al.*, 2005). If the Singapore's limits are applied in our study, 7 (4.9%) and 3 (2.1%) samples were above the limits for mercury and lead, and no sample exceeded the limit for arsenic. This suggests that the prevalences of mercury and lead contamination in Chinese herbal medicines in the United States are slightly higher than those in Singapore. However, Singapore's and our studies both suggest that mercury is the most contaminated metal in traditional Chinese medicines. In addition, although the regulatory standard for cadmium is not well established in many countries, our results suggest that Chinese herbal medicines sold in the United States are relatively contaminated by cadmium.

Sub-chronic and chronic exposure to mercury and mercury compounds may damage the nervous and renal systems and developing fetus depending on the form of mercury (ATSDR, 1999a). Effects on brain functioning may result in irritability, shyness, tremors, changes in vision or hearing, and memory problems (ATSDR, 1999a). The most extensive episodes of mercury poisoning have resulted from contamination of bread made from cereal grains treated with alkyl-mercury fungicides (Hu, 2008). We do not know how exactly the herbal medicines sold in the United States are contaminated by mercury, but fungicides used for culturing in those herbal plants may be one of reasons.

The health effects of chronic cadmium exposure are mainly of concern with respect to toxicity to the kidneys. Cadmium can damage the proximal tubules of each nephron which is manifested by leakage of low molecular weight proteins and essential ions, such as calcium, into urine, with progression over time to frank kidney failure (Wittman, 2002). Cadmium exposure may promote skeletal demineralization and increase bone fragility and fracture risk resulting from loss of calcium in the kidneys *(Clarkson et al.*, 1976). Cadmium is also a carcinogenic metal (ATSDR, 1999b).

Although small proportions of herbal medicine products were above the regulatory limit for arsenic (3%), more attention should be paid to the fact that more than 70% of samples analyzed contained arsenic. Chronic exposure to low-levels of arsenic may cause skin hyperpigmentation and skin cancer, peripheral nerve damage manifesting as numbness, tingling, and weakness in the hands and feet, diabetes, and blood vessel damage resulting in a gangrenous condition affecting the extremities (Col, 1999).

The toxicity of lead is also well recognized. Long-term exposure to low-level lead has been associated with increased risk of neurologic dysfunction including cognitive decline, cardio-vascular disease including hypertension and renal impairment (Hu *et al.*, 2007). Lead poisoning associated with use of traditional remedies has consistently been reported. According to a recent report by the Centers for Disease Control and Prevention, a total of 12 cases of lead poisoning among adults in five states during 2000 - 2003 were associated with Ayurvedic medications (CDC, 2004). This suggests that lead exposure from traditional medicines is still a concern.

CONCLUSION

In summary, a total of 18% (cadmium) to 71% (arsenic) of 143 Chinese herbal medicine products contained metals. Mercury and cadmium were detected in high concentrations above the regulatory standards in 27% and 12% of 143 products analyzed. Herba and folium (leaves of herbal plants) appears to be the most contaminated parts from metals, whereas pericarpium, lignum and semen (outer layers and seeds) seem to be less contaminated. This suggests metal contamination in herbal medicine is different by medical use parts.

It is not clear whether our samples were contaminated by the metals during cultivation or adulterated in the manufacturing process. Because Chinese traditional medicines are imported into the United States as “food”, they are not subject to the law as strict as drugs manufactured domestically or imported into the United States. Furthermore, as indicated by Saper *et al*., dietary supplements imported from other countries are not regulated for toxic metals by the Dietary Supplement Health and Education Act (DSHEA) (Saper *et al*., 2004). The present study provides further evidence that efforts to protect people using traditional remedies from metal intoxication should be made to enforce the regulatory standards (e.g., DSHEA).

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