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Cadmium, mercury and lead in medicinal herbs in Brazil

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Abstract

Samples of herbal medicine used in Brazil were analyzed, after nitric digestion, for the content of cadmium, mercury and lead, by atomic absorption spectrophotometry. Fifteen samples of ginkgo biloba *(Ginkgo biloba*), 13 of celastraceae (*Maytenus ilicifolia*), 14 of cascara buckthorn (*Rhamnus purshiana*), 13 of eggplant (*Solanum melongena*), 15 of horse chestnut (*Aesculus hippocastanum*), 13 of Brazilian ginseng (*Pffafia glomerata*), 17 of centella asiatic (*Hydrocotyle asiatica*), 13 of guarana (*Paullinia cupana*), 12 of artichoke (*Cynara scolymus*) and five samples of chlorella (*Chlorella pyrenoidosa*) were analyzed. Cadmium, mercury and lead were not detected (limit of quantifications of 0.20, 0.01 and 2.0 mg/kg, respectively) in any sample of artichoke, eggplant and guarana. Cadmium was found in samples of the other medicinal herbs at levels up to 0.74 μg/g and mercury up to 0.087 μg/g. Three samples of horse chestnut contained 153, 156 and 1480 μg Pb/g, while the highest concentration found in the other samples analyzed was 22 μg Pb/g. The estimated lead intake through the consumption of horse chestnut reached 440% of Provisional Tolerable Weekly Intake (PTWI), and might be of concern to consumers if the medicine was taken on a long-term basis. Cadmium and mercury exposure through the herbal medicines does not appear to be of health concern.

Keywords: Lead; Mercury; Cadmium; Medicinal plants; Herbal medicines

1. Introduction

The use of medicinal plants in therapeutics or as dietary supplements goes back beyond recorded history, but has increased substantially in the last decades (Woods, 1999; Khan et al., 2001; WHO, 2002). However, the safety of their use has recently been questioned due to the reports of illness and fatalities (Stewart et al., 1999; Ernst, 2002). Poisonings associated with the presence of toxic metals in medicinal plants were reported in Asia, Europe and the United States (Olujohungbe et al., 1994; Dunbabin et al., 1992; Kakosy et al., 1996; Markowitz et al., 1994).

Plants can contain heavy metals from their presence in the soil (including contamination of the plant material with soil), water or air (McLaughlin, 1999). High levels of toxic metals can occur in medicinal preparations when they are used as active ingredients, as in the case of Pb and Hg in some Chinese, Mexican and Indian medicines (Levitt, 1984; Chan et al., 1993) or when the plants are grown in polluted areas, such as near roadways or metal mining and smelting operations (Pip, 1991). In addition, high levels can be found when agricultural expedients are used, including cadmium-containing fertilizers, organic mercury or lead based pesticides, and contaminated irrigation water (Abou-Arab et al., 1999). Chronic exposure to cadmium can cause nephrotoxicity in humans, mainly due to abnormalities of tubular re-absorption (Nordberg, 1999). Lead and mercury can cause adverse effects on the renal and nervous systems and can cross the placental barrier, with potential toxic effects on the fetus (Tong et al., 2000; WHO, 2003).

Brazil has a high diversity of plants used as medicine. Recently, 228 species of medicinal plants were reported in use by the local population of a single village of the country (Amorozo, 2002). In this work, we analyzed 130 samples of the most commonly consumed medicinal plants by the population of the Federal District, Brazil, for the presence of cadmium, mercury and lead. Also, the potential risk of the chronic use of these medicaments containing detectable levels of the toxic metals was evaluated.

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2. Materials and methods

2.1. Chemicals and instrumentation

HNO_3 65% (max. 0.0000005% Hg); standard solutions of mercury ($Hg(NO_3)_2$, 1000 mg/l, in 0.5M HNO_3), lead (1.000g of $Pb(NO_3)_2$ in H_2O) and cadmium (1.000 g of $CdCl_2$ in H_20); and $NaBH_4$ for reduction (>96% purity) were purchased from Merck (Darmastadt, Germany). Distilled-deionized water was used for all analytical work. All glassware was washed with 2% Extran solution, soaked in 3N HCl for 24 h, and rinsed with distilled-deionized water before use. The atomic absorption spectrophotometer (AAS) AA7000 BC, coupled with hydride generator GH 3000 and hole cathode lamps for Hg, Pb and Cd, was from Instrumentos Científicos C.G. LTDA (São Paulo, Brazil).

2.2. Samples

One hundred and thirty samples of powdered dry or dried extract of the plants were donated by local stores. Table 1 shows the plant names, the part of the plant used, the therapeutic use and the recommended dose, the form and origin of the sample analyzed. The samples (approximately 100 g) arrived in the laboratory in plastic bags and were kept at room temperature until analyzed.

2.3. Cadmium, mercury and lead determination

The protocol used to determine the metals in the plant material is a modification of the method proposed by Chow et al. (1995). In summary, 2 g of the sample was transferred to a 100 ml Nessler tube, where 15 ml of 10% HNO_3 v/v were added and left in water bath at 100 °C for 3 h. For mercury analysis, the digested solution was analyzed by cold vapor AAS after reduction with $NaBH_4$. For cadmium and lead, the digested sample solutions were treated twice under reflux with concentrated HNO_3 before determination by flame AAS. Each sample was analyzed in duplicate. The metals were quantified against standard curves prepared at the day of the analysis. The limits of quantification (LOQ) of the method were 0.01 μg/g for mercury, 2 μg/g for lead and 0.2 μg/g for cadmium.

3. Results

3.1. Levels of cadmium, mercury and lead in the medicinal plants

Table 2 shows the concentrations of the metals in the plants. None of the 38 analyzed samples of artichoke, eggplant or guarana contained detectable levels of cad-

Table 1
Plants used as medicines in Brazil

Common name	Botanical name	Part used	Recommended therapeutic use	Dose (g/week)[a]	Form of the sample	Origin of the sample
Artichoke	*Cynara scolymus*	Leaves or root	Decrease cholesterol level, prevention of arteriosclerosis and cardiac diseases	1.4–7.0	Dried extract	Brazil
Eggplant	*Solanum melongena*	Fruit	Decrease cholesterol level	4.2–8.4	Dried extract	Brazil
Guarana	*Paullinia cupana*	Seed	Depression, fatigue, stimulant, gastrointestinal problems, migraine	14–70	Dried powder	Brazil
Cascara buckthorn	*Rhamnus purshiana*	Barks	Laxative, appetite stimulant	4.2–7.0	Dried powder	Germany and USA
Horse chestnut	*Aesculus hippocastanum L.*	Seed, fruit	Chronic venous impairment, edema, anti-inflammatory,	4.5	Dried powder	France and Germany
Centella Asiatic	*Hydrocotyle asiatica*	Leaves, barks	Dermal lesions, hypertension, healing	1.8–7.0	Dried powder	Brazil, India. France
Clorella	*Chlorella pyrenoidosa*	Algae	Dietary supplement, immune modulator, anti-tumor,	6.3–8.4	Dried powder	Korea, USA, Taiwan
Celastraceae	*Maytenus ilicifolia*	Leaves and stems	Anti tumor, contraceptive, anti-asthmatic and anti-septic, ulcer, gastrointestinal and hepatic diseases	2.8–5.6	Dried powder	Brazil
Ginkgo biloba	Ginkgo biloba	Leaves	Circulatory activity, against memory lost, cellular aging, cerebral edema	0.8–1.1	Dried extract and powder	China, Germany
Brazilian ginseng	*Pffafia glomerata*	Root	Pressure control, hypoglycemic action, nervous system activator, increase the blood flux	35–70	Dried powder	Brazil

[a] In capsule form. Daily dose reported by Teske and Trentini (1997), multiplied by 7.

Table 2
Concentration of cadmium, mercury and lead in the medicinal herbs, in μg/g

Medicinal plant (samples analysed)	Concentration or concentration range (number of samples) (mean/median)[a]		
	Cd	Hg[b]	Pb
Artichoke (12)	<0.20 (12) (0.10/<0.10)	<0.01 (12) (0.005/<0.005)	<2.0 (12) (1.0/<1.0)
Eggplant (13)	<0.20 (13) (0.10/<0.10)	<0.01 (13) (0.005/<0.005)	<2.0 (13) (1.0/<1.0)
Guarana (13)	<0.20 (13) (0.10/<0.10)	<0.01 (13) (0.005/<0.005)	<2.0 (13) (1.0/<1.0)
Cascara buckthorn (14)	<0.2 (14) (0.10/<0.20)	<0.01 (11), 0.01–0.02 (3) (0.007/<0.005)	<2.0 (12), 2.7, 4.0 (1.3/<1.0)
Horse chestnut (15)	<0.20 (14) 0.61 (0.13/<0.10)	<0.01 (12), 0.02–0.06 (3) (0.01/<0.005)	<2.0 (8), 2.1–8.2 (3), 153, 156, 1480 (122/<1.0)
Centella asiatic (17)	<0.20 (4), 0.22–0.74 (13) (0.38/0.39)	0.01–0.04 (17) (0.023/0.02)	<2.0 (2), 2.0–11.7 (15) (3.6/3.0)
Clorella (5)	<0.20 (5) (0.10/<0.10)	<0.01 (3), 0.01 (2) (0.008/<0.005)	<2.0 (5) (1.0/<1.0)
Celastraceae (13)	<0.20 (12), 0.49 (0.13/<0.10)	0.02–0.08 (13) (0.029/0.02)	<2.0 (12), 14.4 (2.0/<1.0)
Ginkgo biloba (15)	<0.20 (15) (0.10/<0.10)	<0.01 (5), 0.01–0.09 (10) (0.043/0.06)	<2.0 (10), 2.4–22.1 (5) (3.1/<1.0)
Ginseng (13)	<0.20 (11), 0.25–0.31 (2) (0.13/<0.10)	<0.01 (12), 0.01 (0.005/<0.005)	<2.0 (13) (1.0/<1.0)

[a] Considering the samples with non detected level, at 1/2 LOQ for each metal.
[b] Total mercury

mium (<0.2 μg/g), mercury (<0.01 μg/g) or lead (<2.0 μg/g). Centella asiatic was the plant with the highest percent of samples with metal concentrations above the limit of quantification. All 17 analyzed samples contained detectable levels of mercury, 88% contained detectable levels of lead and 76.4% contained detectable levels of cadmium. Mercury was the metal most often detected in the plants samples (38% of the samples), followed by lead (23%) and cadmium (13%).

Cadmium concentrations varied from <0.20 to 0.74 μg/g. Centella asiatic was the only plant which had median values of cadmium and lead above the limits of quantification (0.39 and 3.0 μg/g, respectively). The levels of mercury varied from <0.01 to 0.09 μg/g with ginkgo biloba containing the highest mean and median levels (0.043 and 0.06 μg/g, respectively). The levels of lead in the samples varied from <2.0 to 1480 μg/g with horse chestnut having the highest concentrations.

3.2. Calculated intake of cadmium, mercury and lead

Weekly metal intakes through consumption of the medicinal plants were calculated by multiplying the maximum recommended dose of each product (Table 1) by the mean, median and maximum levels of the metals found in the plants (Table 2). The results are shown in Table 3. The maximum intake (using maximum dose and maximum metal concentration) reached 22 μg/week of cadmium and 0.70 μg/week of mercury. The intakes of both Cd and Hg were higher for the consumption of ginseng due to the high recommended dose for this medicinal plant (up to 10 g/day). High intakes of lead, up to 6630 μg/week, were found for the consumption of horse chestnut.

4. Discussion

4.1. Cadmium

One sample of horse chestnut, celastraceae and ginseng and 11 samples of centella asiatic had concentrations of cadmium exceeding the limit of 0.3 μg/g recommended for medicinal plants (WHO, 1999). Plants absorb cadmium from the roots (Pip, 1991; McLaughlin et al., 1999) and the morphology of centella asiatic, a slender trailing herb from which the leaves are used to prepare the medicines (WHO, 1999), can partially explain the high percentage of samples of this plant containing cadmium (76%).

The concentrations of cadmium found in this work were similar to the ones described in other parts of the world. In Italy, 79 samples of various herbal medicines had concentrations ranging from 0.01 to 0.75 μg/g, with higher levels reported in cinchona extracts (De Pasquale et al., 1993). In Egypt, 10 samples of peppermint, chamomile, anise, caraway and tilio had 0.05–0.30 μg/g (Abou-Arab et al., 1999). Levels of cadmium in 21 ginseng products purchased in the United States, Europe and Asia varied from 0.008 to 0.12 μg/g (Khan et al., 2001).

The estimated maximum weekly intake of cadmium after consumption of the maximum recommended therapeutic dose of the medicinal plant (Table 3), would reach up to 5% (from ginseng) of the FAO/WHO Provisional Tolerable Weekly Intake (PTWI) of 7 μg/kg body weight (JECFA, 2003) or 420 μg/person. Human exposure to cadmium from the diet and drinking water can reach up to 60% of PTWI in some regions of the

Table 3
Possible intake of cadmium, mercury and lead through the consumption of the maximum recommended dose of the medicinal herb

Medicinal plant	Intake, μg/week[a]								
	Cadmium			Mercury			Lead		
	Mean	Med.	Max.	Mean	Med.	Max.	Mean	Med.	Max.
Artichoke	0.7	0.7	0.7	0.04	0.04	0.04	7.0	7.0	7.0
Eggplant	0.84	0.84	0.84	0.04	0.04	0.04	8.4	8.4	8.4
Guarana	7.0	7.0	7.0	0.35	0.35	0.35	70	70	70
Cascara buckthorn	0.70	0.70	0.70	0.05	0.04	0.14	9.1	7.0	18.9
Horse chestnut	0.58	0.45	2.7	0.05	0.02	0.27	547	4.5	6630
Centella asiatic	2.7	2.7	5.2	0.16	0.14	0.28	25,2	21	81.9
Clorella	0.84	0.84	0.84	0.07	0.04	0.08	8.4[a]	8.4[a]	8.4[a]
Celastraceae	0.73	0.56	2.7	0.16	0.11	0.45	11.2	5.6	80.6
Ginkgo biloba	0.63	0.63	0.63	0.27	0.38	0.57	19.5	6.3	139
Ginseng	9.1	7.0	22	16.3	0.35	0.70	70	70	70

[a] Calculated by multiplying the residue level (Table 2) by the maximum dose of the medicinal drug (Table 1).

world (Baht and Moy, 1997; WHO, 1993), and the possible contribution from medicinal herbs might be significant. For instance, renal dysfunction would be expected in sensitive population groups at cadmium exposure levels half of the present PTWI (Nordberg, 1999).

4.2. Mercury

The highest concentration of mercury, as total mercury, found in this study, 0.09 μg/g in ginkgo biloba (Table 2), is much lower than the limit of 0.5 μg Hg/g recommended in drugs, including from plants, in Singapore (Chow et al., 1995). Vega-Carrillo et al. (1997) found mercury at similar levels (<0.01 to 0.08 μg/g) in 30 plants used in traditional medicine in Mexico and mercury was not detected (<0.001 μg/g) in 21 samples of ginseng products (capsule and tincture) in another study (Khan et al., 2001).

The higher estimated weekly intake of mercury (0.70 μg/person) was found for the only ginseng sample with detectable residues, and is insignificant when compared with the PTWI of 5 μg/kg body weight for total mercury (JECFA, 2000), or 300 μg/person. Mercury exposure for the general population occurs mainly from consumption of fish, as methyl mercury (Baht and Moy, 1997; Barbosa, 1997) and possibly from dental amalgam fillings (WHO, 2003), and it is unlikely that the exposure through medicinal herbs will affect human health.

4.3. Lead

Lead was detected only in samples prepared with the leaves, fruits or barks of the plants (cascara buckthorn, horse chestnut, centella asiatic, celastraceae and ginkgo biloba), what agrees with the fact that lead in plants is due mainly to aerial deposition or absorption by their external parts (Albertine et al., 1997; McLaughlin et al., 1999). Six samples analyzed exceeded the maximum recommended limit of 10 μg Pb/g (WHO, 1999). The horse chestnut tree can reach 35 m high (WHO, 1999), which probably favors the exposure of its fruits to contaminated air and explains the high lead concentrations found in the samples from this plant (up to 1480 μg Pb/g). Much lower concentrations (<0.001 to 2.6 μg Pb/g) were found in medicinal plants in Italy, Egypt and United States (De Pasquale et al., 1993; Aboub-Arab et al., 1999; Khan et al., 2001).

The estimated weekly intake of lead after consumption of the maximum recommended therapeutic dose exceeds the PTWI of 25 μg/kg body weight (JECFA, 2000), or 1500 μg/person, for the horse chestnut sample containing the highest concentration (by 4.4 times). The consumption of the horse chestnut samples with 153 and 156 μg/g lead would contribute with up to 47% of PTWI and the maximum intake for the other plants analyzed reached 9% of the toxicological parameter (Table 3). Lead is the most ubiquitous toxic metal in the environment, and in many countries the intake from the diet can approach or exceed the PTWI (Baht and Moy, 1997). Increased industrialization and persistence of lead in the environment requires constant monitoring of all sources of human exposure, including medicinal herbs.

5. Conclusions

The population growth in the developing world and the increasing interest in the industrialized nations have greatly expanded the demand for medicinal plants and their products. Approximately 80% of the world population use the medicinal plants (Woods, 1999). In Brazil, as in most countries (Khan et al., 2001), the standard quality control of these products is not always enforced, and their quality, efficacy and safety is unclear. The results of this study show the need for a systematic control of toxic heavy metals in plants used as medicines. In particular, investigations on the lead levels in horse chestnut, either by producer countries or importers, should be carried out.

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References

Abou-Arab, A.A.K., Kawther, M.S., El Tantawy, M.E., Badeaa, R.I., Khayria, N., 1999. Quantity estimation of some contaminants in commonly used medicinal plants in the Egyptian market. Food Chemistry 67, 357–363.

Albertine, S., Oetterer, M., Prado Filho, L.G., 1997. Source of contamination and toxicology of lead. Boletim da SBCTA 31, 137–147.

Amorozo, M.C.M., 2002. Use and diversity of medicinal plants in Santo Antonio do Leveger, MT, Brazil. Acta Botanica Brasileira 16, 189–203.

Baht, R.V., Moy, G.G., 1997. Monitoring and assessment of dietary exposure to chemical contaminants. Rapport Trimestriel de Statistiques Sanitaires Mondiales 50, 132–148.

Barbosa, A.C., 1997. Mercury in Brazil: present or future risk? Journal of the Brazilian Association for Advanced Science 49, 111–116.

Chan, T.Y.K., Tomlinson, B., Critchley, A.J.H., 1993. Chinese herbal medicines revisited: a Hong Kong perspective. The Lancet 342, 1532–1534.

Chow, P.Y.T., Chua, T.H., Tang, K.F., 1995. Dilute acid digestion procedure for the determination of lead. Copper and mercury in traditional Chinese medicines by atomic absorption spectrometry. Analyst 120, 1221–1223.

De Pasquale, A., Paino, E., De Pasquale, R., Germano, M.P., 1993. Contamination by heavy metals in drugs from different commercial sources. Pharmacological Research 27, 9–10.

Dunbabin, D.W., Tallis, G.A., Popplewell, P.Y., 1992. Lead poisoning from Indian herbal medicine. Medical Journal of Australia 157, 835–836.

Ernst, E., 2002. Toxic heavy metals and undeclared drugs in Asian herbal medicines. Pharmacological Sciences 23, 136–139.

JECFA, 2000. Joint FAO/WHO Expert Committee on Food Additives. Fifty-fifth Meeting. Summary and Conclusions. World Health Organization, Geneva.

JECFA, 2003. Joint FAO/WHO Expert Committee on Food Additives. Sixty-first Meeting. Summary and Conclusions. World Health Organization, Geneva.

Kakosy, T., Hudak, A., Naray, M., 1996. Lead intoxication epidemic caused by ingestion of contaminated ground paprika. Journal of Toxicology-Clinical Toxicology 34, 507–511.

Khan, I.A., Allgood, J., Walker, L.A., Abourashed, E.A., Schelenk, D., Benson, W.H., 2001. Determination of heavy metals and pesticides in ginseng products. Journal of AOAC International 84, 936–939.

Levitt, C.M.D., 1984. Sources of lead poisoning. Journal of the American Medical Association 252, 3127–3128.

Markowitz, S.B., Nenez, C.M., Klitzman, S., 1994. Lead poisoning due to hai ge fen: the porphyry content of individual erythrocytes. Journal of the American Medical Association 271, 932–934.

McLaughlin, M.J., Parker, D.R., Clark, J.M., 1999. Metals and micronutrients—food safety issues. Field Crops Research 60, 143–163.

Nordberg, G., 1999. Excursions of intake above ADI: case study on cadmium. Regulatory. Toxicology and Pharmacology 30, S57–S62.

Olujohungbe, A., Fields, P.A., Sandford, A.F., 1994. Heavy metal intoxication from homeopathic and herbal remedies. Postgraduate Medical Journal 70, 764–769.

Pip, E., 1991. Cadmium, Copper and Lead in soils and garden produce near a metal smelter at Flin Flon, Manitoba. Bulletin of Environmental Contamination and Toxicology 46, 790–796.

Stewart, M.J., Moar, J.J., Steenkamp, P., Kokot, M., 1999. Findings in fatal cases of poisoning attributed to traditional remedies in South Africa. Forensic Science International 101, 177–183.

Teske, M., Trentini, A.M.M., 1997. Compêndio de Fitoterapia, third ed. Herbarium, Paraná, Brasil.

Tong, S., von Schirnding, Y.E., Prapamontol, T., 2000. Environmental lead exposure: a public problem of global dimension. Bulletin of the World Health Organization 78, 1068–1077.

Veja-Carrillo, H.H., Iskander, F.Y., Manzanares-Acura, E., 1997. International Journal of Environmental Analytical Chemistry 66, 95–105.

WHO, 1993. Guidelines for Drinking-water Quality. Recommendations, Vol. 1, second ed.. World Health Organization, Geneva.

WHO, 1999. Monographs on Selected Medicinal Plants. Vol. 1. World Health Organization, Geneva.

WHO, 2002. Drug Information. Herbal Medicines. Vol. 16. World Health Organization, Geneva.

WHO, 2003. Elemental Mercury and Inorganic Mercury Compounds: Human Health Aspects. Concise International Chemical Assessment Document 50. World Health Organization, Geneva.

Woods, P.W., 1999. Herbal healing. Essence 30, 42–46.