

Toxic metals in ayurvedic preparations from a public health lead poisoning cluster investigation

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ABSTRACT

Background: Herbal formulations, traditional medicine, and complementary and alternative medicine are used by the majority of the world's population. Toxicity associated with use of Ayurvedic products due to metal content is an increasingly recognized potential public health problem.

Objectives: Report on toxic metals content of Ayurvedic products obtained during an investigation of lead poisoning among users of Ayurvedic medicine.

Methods: Samples of Ayurvedic formulations were analyzed for metals and metalloids following established US. Environmental Protection Agency methods.

Results: Lead was found in 65% of 252 Ayurvedic medicine samples with mercury and arsenic found in 38 and 32% of samples, respectively. Almost half of samples containing mercury, 36% of samples containing lead and 39% of samples containing arsenic had concentrations of those metals per pill that exceeded, up to several thousand times, the recommended daily intake values for pharmaceutical impurities.

Conclusions: Lack of regulations regarding manufacturing and content or purity of Ayurvedic and other herbal formulations poses a significant global public health problem.

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Introduction

Ayurveda is one of the oldest and most widely practiced traditional Indian systems of medicine which has, along with other complementary and alternative medicine (CAM) systems, grown in popularity in Western nations in recent years. According to the World Health Organization (WHO), up to 80% of the world's population relies on traditional medicine for their healthcare needs with between 35 and 75% of developed countries' populations reporting use of CAMs [1–3]. Contrary to allopathic medicine the manufacturing of and access to CAMs are poorly regulated. Ayurvedic medicines in Western countries are potentially available without medical consultation through ethnic markets, health food stores, Ayurveda practitioners, self-importation, and/or Internet [4–6].

Ayurvedic formulations are based on herbal products but often include toxic metals and other elements as part of the *Rasa Shastra* practice [5,7,8]. These elements are used intentionally, as Ayurvedic tradition holds that lead, mercury, copper, gold, iron, silver, tin, and zinc may help restore good health and normal function to the human body [9–11]. Arsenic, aluminum, cadmium,

chromium, and nickel may be found in Ayurvedic products as well [5,7,12,13]. It is estimated that over 20% of the Ayurvedic medications manufactured and distributed by U.S. and Indian companies contain toxic metals such as lead, mercury, and/or arsenic [5,14].

The contamination of herbal formulations with toxic metals poses potential health risks. Several cases of metal toxicity have been reported following the use of Ayurvedic products primarily associated with lead, mercury, and arsenic. These include reports from the United States, Canada, England, New Zealand, and India [6,15–24]. Recent epidemiological studies show that these products can become a significant public health issue [6].

This manuscript presents analytical results of levels of toxic metals in samples of Ayurvedic products obtained during an investigation of a lead poisoning outbreak in a small community in mid-western United States.

Methods

The details of this investigation, including recruitment of participants and results of blood lead and mercury levels have been described previously [6]. In short, one

of the authors was contacted by the family of a local resident who presented with symptoms of plumbism that worsened after travelling to an Ayurvedic clinic in India. This patient lived in a small community where a subset of residents adhere to Ayurvedic medicine and had obtained herbal supplements and medicines from the same Ayurvedic clinic in India. This community was reached out to by placing advertisements in local newspapers and an email campaign coordinated between the clinic in India and the authors, offering community members to have their blood tested for lead and mercury and to have samples of Ayurvedic products analyzed for metals content. One hundred and fifteen individuals participated in this study.

The samples were analyzed for levels of heavy metals including silver (Ag), barium (Ba), cadmium (Cd), chromium (Cr), mercury (Hg), nickel (Ni), and lead (Pb), and metalloids including arsenic (As) and antimony (Sb). These elements are considered impurities with potential adverse health effects including cancers and possible death when ingested in large doses. Reference standard recommendations for daily oral intake limits have been issued for these elements by various regulatory and public health agencies and institutions in the United States and in Europe (Table 1).

The samples were prepared for analysis based on the U.S. Environmental Protection Agency's (EPA) Method 3050B for acid digestion of sediments, sludges, and soils [25]. Samples were homogenized with 0.5–1.0 g of substance and weighed out for digestion initially with nitric acid (Fisher Scientific, Trace Metal Grade) for 2 h at 95 °C and further by addition of 30% hydrogen peroxide (Fisher Scientific Reagent Grade) until digestion was complete. Cool digestates were transferred to 100 mL volumetric flasks and diluted to volume prior to analysis. Elemental content per pill was determined based on the U.S. EPA Method 6020B for inductively coupled plasma-mass spectrometry [26] and using an Agilent 7500 Series ICP-MS. This method is an EPA validated method for the determination of elements by ICP-MS in solid matrices. Method specific quality control samples included initial and continuing calibration verification samples, laboratory fortified blank, quality control samples (second source), and Laboratory Control Samples (in triplicate) using a commercially available quality control material with known elemental values in soil from ERA of Golden, CO (Metals in Soil Lot No. D067–540 Catalog No. 540) for this study. All recoveries and precision measurements were within acceptable limits. The Method Detection Limits (MDLs) for studied elements were as follows: Ag – 1.9 mg/kg, Ba – 0.4 mg/kg, Cd – 1.1 mg/kg, Cr – 1.3 mg/kg, Hg – 3.6 mg/kg, Ni – 0.4 mg/kg, Pb – 0.4 mg/kg, As – 3.1 mg/kg, Sb – 0.8 mg/kg.

Results were expressed in mg/kg of substance. Reference values were converted from microgram to milligram (1 µg = 0.001 mg) where necessary to calculate

the proportion of samples exceeding the recommended daily intake values. The United States Pharmacopeia Convention (USP) reference standard was chosen for comparison as it provides daily exposure value recommendations for pharmaceutical impurities. Study participants provided the names of Ayurvedic products. Elemental content per pill was calculated assuming 500 mg of substance per pill and using the following formula: content of heavy metal(-loid) in mg/kg of herbal product × 500 mg (0.0005 kg) pill.

Measures of central tendency including median and range were used to present the aggregate results of chemical analyses with summary analysis carried out in Microsoft Excel 2013.

Results

Two hundred and fifty-two samples of Ayurvedic products and herbal supplements were analyzed between the first and third quarter of 2011. Lead was the most common element found in 65% ($N = 164$) of all samples with maximum level of 43,200 mg/kg. However, half of the samples had Pb levels of 4.9 mg/kg and below (Table 2). Mercury and arsenic were each found in over one-third of the samples with median level of 53.0 mg/kg and 8.4 mg/kg and maximum levels of 279,000 mg/kg and 44,800 mg/kg of product, respectively. Antimony, barium, chromium, nickel, and silver were each found in less than one-fifth of the samples. Cadmium was present in only one product analyzed in this study.

The proportion of samples with elemental content per pill exceeding the USP's recommended oral Permissible Daily Exposure (PDE) in mg/day based on a 50 kg person and assuming a 500 mg weight of each pill with minimal dosage of one pill per day is also presented in Table 2. Almost half of the Ayurvedic products with mercury found in the analysis had elemental content per pill exceeding the PDE of 0.03 mg/day. Lead and arsenic in doses per pill exceeding those recommended by the USP (0.005 and 0.015 mg/day, respectively) were found in over one-third of the products analyzed in this study. The single sample that had cadmium detected was at a level exceeding the PDE reference value. No products with doses exceeding the oral PDE per pill were found for antimony, barium, chromium, and nickel in this study.

The list of Ayurvedic supplements by product family name with highest elemental content per pill is presented in Table 3. *Indukantham* tablets contained the highest levels of lead of all the samples with lead detected in the study. *Swarna Bhasma* was found to have the highest levels of three of the elements under analysis including arsenic, antimony, and silver. The highest level of mercury was detected in *Brihat Vatchintamani Ras*, while barium was found in highest doses in the *Saubhagya* product family. *Shulagna* products had the highest levels of chromium and nickel, and cadmium was found in

Table 1. Analyzed elements with oral exposure primary target organ/system and corresponding U.S. and European reference values for daily oral intake.

Element	Primary target organ/system	Reference values for daily oral intake (foodstuffs and medicines)				
		FDA	USP	SWDTEA	EFSA	JECFA
Ag	Skin, nervous ^c , cardiovascular ^a	-	0.15	-	-	-
As	Skin, nervous, cardiovascular, gastrointestinal, hepatic. Carcinogenic to humans (Group 1 IARC)	-	0.015 ^a	0.01 ^{ad}	-	-
Ba	Hematologic, gastrointestinal, renal ^e	-	1.4	-	-	-
Cd	Renal, skeletal, gastrointestinal, hepatic. Carcinogenic to humans (Group 1 IARC)	-	0.005	0.0041	0.0025	0.0058
Cr	Gastrointestinal, immunologic, hematologic ^c , reproductive ^c . Carcinogenic to humans ^b (Group 1 IARC)	-	11.0	0.0082 ^b	-	-
Hg	Renal, central nervous system, respiratory, cardiovascular, gastrointestinal, hematologic, musculoskeletal, hepatic, endocrine ^e	-	0.03 ^a	-	0.004 ^a 0.0013 ^c	0.004 ^a 0.0016 ^c
Ni	Gastrointestinal, nervous, cardiovascular, hematologic ^c reproductive ^c , renal ^c . Carcinogenic to humans (Group 1 IARC)	-	0.2	-	0.0028 ^f	-
Pb	Nervous, renal, hematologic, endocrine, gastrointestinal, cardiovascular, reproductive, skeletal, developmental	0.075	0.005	0.015	-	-
Sb	Gastrointestinal, hepatic ^c , hematologic ^e	-	1.2	-	0.04 ^g	-

Abbreviations: FDA – US Food and Drug Administration; USP – United States Pharmacopeial Convention; SWDTEA – Safe Drinking Water and Toxic Enforcement Act of 1986 (California Proposition 65); EFSA – European Food Safety Authority; JECFA – Joint Food and Agriculture Organization (FAO)/World Health Organization (WHO) Committee on Food Additives; IARC – International Agency for Research on Cancer.

^aInorganic compounds.

^bHexavalent compounds.

^cMethylmercury

^dAll routes of exposure except inhalation.

^eIn animal models.

^fTolerable Daily Intake (TDI) (mg/kg body).

^gTolerable Daily Intake (TDI) (mg/kg food/day).

Table 2. Distribution of heavy metals and metalloids in Ayurvedic products and proportion of samples with elemental content per pill exceeding USP's PDE (total *N* = 252 samples).

Element	<i>N</i> (%) > MDL ^a	Median (mg/ kg of herbal product)	Range (mg/kg of herbal product)	<i>N</i> (%) > PDE ^b
Pb	164 (65.1)	4.9	0.46–43,200	59 (35.8)
Hg	97 (38.5)	53.0	0.8–279,000	48 (49.5) ^d
As	82 (32.5)	8.4	1.0–44,800	32 (39.5) ^d
Ba	38 (15.1)	24.5	5.8–118.0	0 (0)
Cr	35 (13.9)	4.7	2.0–35.0	0 (0)
Sb	25 (9.9)	6.7	1.1–72.0	0 (0)
Ni	12 (4.8)	7.9	5.5–16.0	0 (0)
Ag	7 (2.8)	200.0	13.0–330.0	1 (14.3)
Cd	1 (0.4)	–	4.7 ^c	1 (100)

^aMethod Detection Limit.^bOral Permissible Daily Exposure (PDE) for drug products – based on a 50 kg person (mg/day).^cSingle specimen.^dPDE for inorganic compound.**Table 3.** Ayurvedic products with the highest elemental content per pill.

Element	Product	Content per pill (in mg/0.5 g pill)
Pb	Indukantham	21.6
Hg	Brihat Vatchintamani Ras	139.5
As	Swarna Bhasma	22.4
Ba	Saubhagya	0.06
Cr	Shulagna	0.02
Sb	Swarna Bhasma	0.04
Ni	Shulagna	0.01
Ag	Swarna Bhasma	0.17
Cd	Arbudari	0.02

only one sample, a product under the Ayurvedic name *Arbudari*.

Discussion

This study found levels of lead, mercury, arsenic, silver, and cadmium in samples of Ayurvedic products obtained from Ayurvedic medicine consumers to exceed the recommended daily oral exposure intake values for these metals in the United States in approximately 50% of the samples tested. In the case of lead, mercury, arsenic, and cadmium, there were samples exceeding the recommended daily oral exposure by a factor of several thousand. These reference values have been established primarily for pharmaceutical impurities and herbal products and are not monitored or regulated by any federal agency in the United States. As a result of this lack of oversight, metal toxicity from herbal formulations may pose a significant public health problem in this country as well as across the globe. This study adds to the body of knowledge suggesting a need for regulatory policies to address the contamination of herbal products and or supplements.

In addition, the content of the metals varies between products and this study found some of the same Ayurvedic products from the same provider to have

different levels of the same elements, one example being the *Indukantham* tablets with lead and mercury content ranging from 43 to 43,200 mg and 13 to 950 mg per kg of substance respectively. As these formulations are prepared by hand, by small purveyors, consistency, purity, and potential toxicity issues are quite evident. The widespread use and growing popularity of herbal formulations globally makes this a potentially large-scale global public health concern.

One tenet of Ayurveda is that the metals used in the manufacturing of herbal supplements are non-toxic for ingestion, a result of “defanging” using traditional detoxification process [10,27]. Numerous case reports and epidemiological studies of clinically significant heavy metal poisonings from several countries have shown the detoxification process to be ineffective [6,15–24].

The frequency and duration of intake of herbal medications and supplements have not been described well in the literature. Common practice, especially among elderly, is to combine allopathic medications with herbal supplements without any consultation or supervision [28,29]. This study made a conservative assumption for intake of one 500 mg pill of herbal formulations per day to calculate the toxic metal burden on adherents to Ayurvedic medicine. These assumptions may have underestimated the actual daily intake of metals as interviews with study participants showed these products are often taken in combination with other herbal formulations (range for this study 2–20). An example was the study individual reporting taking up to 18 different herbal formulations per day in addition to the *Indukantham* tablets found to have the highest content of lead and *Shulagna* tablets with the highest levels of chromium and nickel found in this study. These findings warrant further epidemiological research.

This study was a public health intervention conducted in response to an individual's concern over the heavy metal content of self-imported Ayurvedic products. This individual lived in a small community in mid-western United States where many of town residents obtained Ayurvedic products from the same clinic in India and/or from local importers. Educational and medical screening campaigns were conducted in this community, with collaboration from the clinic in India that sent an email to all their international patients detailing our concern regarding metal content of their products. One hundred and fifteen individuals responded and were screened with treatment options offered where clinically indicated. Additional surveys were distributed after the study to further educate the community members about the health effects of heavy metal poisoning. Results of this epidemiological investigation have been published previously [6] and this report presents findings from the laboratory analysis of the Ayurvedic product samples collected throughout this investigation.

This study did not conduct metals speciation analysis of the Ayurvedic products. Some of the PDE value recommendations have been issued for different chemical species of metals, such as inorganic arsenic and elemental mercury, methyl mercury, or hexavalent chromium. Although different species of the same metal may differ in physicochemical and biochemical characteristics, due to oxidation state and solubility, all species can potentially induce a range of adverse health effects depending on bioavailability and dose [30]. The results of this study have implications for further toxicological research and show a need for additional analytical resources to provide for speciation analysis of the herbal products.

Human participant protection

The Human Subjects Research protocol was waived as this study was part of a public health response to heavy metals poisoning.

Disclosure statement

No potential conflict of interest was reported by the authors.

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