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Paper

Are Ayurvedic medications store house of heavy metals?

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Ayurvedic formulations are widely used and perceived as safer medicine and subjected to be self-prescribed. However, recent reports have demonstrated adulterating these drugs with toxic quantities of heavy metals. To study the magnitude of the problem in Indian-manufactured Ayurvedic medications, we randomly collected common over-the-counter Ayurvedic preparations from the licensed Ayurvedic shops in the local markets of Chandigarh in 2017. The samples were analyzed to identify and quantify eight metal ions, including mercury, arsenic, lead, cadmium, zinc, iron, copper, and chromium, using inductively coupled plasma mass spectrometry in Postgraduate Institute of Medical Education and Research, Chandigarh. The permissible limit set by the Food and Agriculture Organization/World Health Organization (FAO/WHO) for herbal medicines was followed to define the high metal concentrations. Out of 43 Ayurvedic preparations, 42 were analyzed. Heavy metals were detected in all formulations. The median (range) concentrations (in μg/g or mg/kg) of the metals were quantified as follows- mercury, 13.52 (0.00–61 095.99); arsenic, 0.00 (0.00–1038.83); lead, 1.40 (0.00–57.09); zinc, 84.2200 (26.48–22 519.03); iron, 1356.21 (128.24–136 835.25); copper, 17.1450 (0.00–12 756.86) and chromium, 20.9050 (0.00–2717.58). The metal contents above the FAO/WHO-mandated limit for zinc, mercury, arsenic, and lead were detected in 35, 29, 6, and 2 formulations, respectively. All medications contained detectable quantities of zinc and iron. Copper was detected in all except one. Cadmium was not found in any sample. Ayurvedic medications have a high prevalence of heavy metals. An evaluation of the sources of contamination and the necessary drug safety regulations are required.

Key words: Ayurvedic; metals; herbal; toxicity; lead; arsenic; mercury; zinc.

Introduction

Ayurvedic medicines are widely used, and over the past decades, their popularity has surprisingly been on the rise, with an estimated global market of ~5000 million US dollars per year [1]. These medications primarily comprise herbal (derived from natural plants), metallic preparations, and animal products. Worldwide, Ayurvedic medicine is principally referred to as complementary and alternative medicine and is mainly used when conventional medicine has limited or no efficacy or causes significant adverse effects [1]. In the low-middle income countries (LMIC), it is also used as a cheaper alternative to conventional medicine. Because of their "natural" origin and use for a long time, Ayurvedic medicine is perceived as safer medicine and subjected to be self-prescribed. Moreover, herbal preparations usually do not undergo the same rigorous testing as conventional medicine and are not evaluated for safety and effectiveness by the US Food and Drug Administration [2, 3]. Therefore, following the dictum "absence of evidence is not evidence of absence," the adverse effects and pharmacokinetic interactions of herbal medicine might be underreported rather than uncommon.

Trace minerals such as zinc, gold, silver, iron, copper, magnesium, manganese, and chromium are required to carry out specific biochemical reactions in the human body; however, they can exert toxic effects at high levels of exposure. Heavy metals such as lead, arsenic, mercury, and cadmium are xenobiotics and may cause toxicity even at low-level exposure [4–6]. Because the metals (*bhasmas*) are emphasized as essential for the proper biological functions in *rasa shastra Ayurveda*; they are added intentionally after "purification" (*shodhana*) in the formulations [7]. However, many recent reports have demonstrated adulterating herbal medicines with toxic quantities of heavy metals [8–10]. Besides the manufacturing processes (i.e. the addition or mixing of metals), the potential sources of toxicity remain environmental, i.e. conditions in which the herbs are grown, collected, dried, stored, or transported [2–5]. Heavy metals are considered the major environmental pollutants because of massive environmental contamination due to industrialization or urbanization and their toxicity, intrinsic stability, and bioaccumulation nature [11, 12]. The increasing prevalence of heavy metals in herbal preparations might be attributed to heavy metal pollution [13, 14].

Though Ayurveda has been practiced for more than 5000 years in India, Indian studies documenting the

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prevalence of metals in Ayurvedic pharmaceuticals are limited [7, 15, 16]. This study aims to determine the prevalence of heavy metals in common over-the-counter Ayurvedic medications in Chandigarh, an urban city in north India.

Material and methods

The commonly used Ayurvedic medications were collected from the licensed Ayurvedic shops in the local markets of Chandigarh (India) in 2017. The selection was random and based on high selling and popularity among the local public, including the various categories according to their actions or indications. We tried to obtain at least two medications of the same class (indication) to preserve the assumption of independence of observations. Samples were stored in pharmacy plastic bags and labeled with a numerical identification to make the laboratory team blind for the sample identity.

The samples were processed in the laboratory of the Department of Pediatric Biochemistry, Advanced Pediatric Center, Postgraduate Institute of Medical Education and Research, Chandigarh, a large academic medical institute in north India. The analysis was performed to identify and quantify eight metal ions, including mercury, arsenic, lead, cadmium, zinc, iron, copper, and chromium, using inductively coupled plasma mass spectrometry with Agilent Technologies 7700 series instrument (Agilent 7700 ICP-MS™). For microwave digestion, 10 μg of the sample was weighed into a digestion vessel, followed by the addition of 2 ml of concentrated nitric acid, 0.5 ml of hydrogen peroxide and 10 ppm of gold solution. All quality control, assurance, and safety measures were adequately undertaken.

The concentration of heavy metals was expressed in units of mg/kg or μg/g (ppm). The permissible limit set by the Food and Agriculture Organization of the United Nations and World Health Organization (FAO/WHO) for herbal medicines was followed, i.e. 10 μg/g for arsenic and lead, 1 μg/g for mercury, 0.3 μg/g for cadmium, and 50 μg/g for zinc [17]. The permissible limit for lead, mercury, and cadmium is the same mandated by Indian guidelines from the Department of Ayurveda, Unani, Siddha, and Homeopathy (AYUSH); however, a lower limit is set for arsenic (3 μg/g) [18]. The regulatory limit of FAO/WHO or AYUSH for iron, copper, magnesium, and chromium in medicinal herbs has not been established yet [17, 18].

For analysis, the data were fed in Microsoft Excel 2007. The discrete data were recorded as frequency (n) or percentage (%), and continuous data as median with range.

Results

A total of 43 Ayurvedic formulations were randomly selected. Indications of the medications and the metals (*Bhasma*) mentioned on the label are summarized in Table 1. Rejuvenation tonics and anti-inflammatory were the common categories ($n = 7$, each). However, only 8 of 43 had a single indication, and the majority could be used in several common conditions. Out of 42, 13 were a single ingredient, two had two components, and the rest ($n = 28$) had three or more (up to 30). All medications were prescribed twice or thrice daily doses for weeks or months to the users. 27.9% ($n = 12$) Ayurvedic formulations had listed heavy metals on the label, including seven had single metal, two had two metals, and two had three metals (Table 1).

Forty-two samples were analyzed, and one was excluded due to technical difficulties. The prevalence of heavy metals in the Ayurvedic formulations tested in this study is shown in Table 2 (and Supplementary Table 1). All medications contained detectable quantities of zinc and iron. Copper was detected in all except one. Cadmium was not found in any product. All except one preparation had at least one metal with a concentration higher than FAO/WHO permissible limit, most prevalent being zinc ($n = 35$) and mercury ($n = 29$). About 73.8% formulations contained above-limit levels of mercury, arsenic, or lead.

Discussion

Our study found a high prevalence of heavy metals in a random sample of commonly used Ayurvedic medicines in north India. We detected heavy metals in all formulations, although only 28% of Ayurvedic products had listed metals on their labels. The metal concentrations above the FAO/WHO and AYUSH-mandated limit for zinc, mercury, and/or arsenic are seen in all except one formulation. Detectable levels of zinc, iron, copper, and chromium were almost universally present. Cadmium was not detected in any sample.

Metals after purification in the *rasa shastra* are considered therapeutic without adverse effects. The high prevalence and toxic concentrations of heavy metals in our report and similar studies might have resulted from environmental contaminations of the herbal plants (e.g. heavy metal pollution) or manufacturing processes with incidental or intentional mixing of the metals [8–10, 19–22]. Furthermore, Ayurvedic pharmaceuticals are also not closely regulated for safety, and enforcement of related laws is considerably less strict in LMIC than in the developed world [23, 24]. Heavy metals, i.e. lead, arsenic, and mercury rank the top three in the hazardous substance list of the US Agency for Toxic Substances and Disease Registry (ATSDR) [6, 11]. Detectable levels of these metals were prevalent in our samples, supporting the recent worldwide observations [8–10, 20–22].

The lead remained the leading heavy metal detected in Ayurvedic preparations manufactured in the western world, whereas mercury was more frequently reported in Indian-manufactured products, like in this study [9, 10, 15, 16]. At least two out of three formulations had higher than regulatory limits of mercury in our sample. Chronic ingestion of mercury is linked to neurological

Table 1. Ayurvedic pharmaceuticals ($n = 43$) with their action or indication of use, the number of collected samples and heavy metal listed on the label

SN	Indication/action	*n*	Metals listed
1	Rejuvenator tonic	7	Zinc ($n = 2$), gold ($n = 2$), silver ($n = 2$), tin ($n = 1$), magnesium ($n = 1$)
2	Anti-inflammatory for joint disease	7	Mercury ($n = 1$)
3	Aphrodisiac	5	–
4	Digestive system abnormality	4	–
5	Liver dysfunction	3	Manganese ($n = 1$), mica ($n = 1$), copper ($n = 1$), iron ($n = 1$), mercury ($n = 1$)
6	Hemorrhoids	3	–
7	Immunomodulator	3	–
8	Menstrual problem	3	Iron ($n = 1$)
9	Anti-diabetic	2	–
10	Nervous system abnormality	2	Mercury ($n = 1$)
11	Anti-obesity	2	Mica ($n = 1$)
12	Renal stone disease	2	–

Table 2. Prevalence of the heavy metals in the Ayurvedic medications ($n = 42$)

SN	Heavy metals	Median (range) ppm (μg/g) or (mg/kg)	Values (*n*) higher than permissible limit[a]	Undetectable (0.00) level
1	Mercury	13.52 (0.00–61 095.99)	29	13
2	Arsenic	0.00 (0.00–1038.83)	6	36
3	Lead	1.40 (0.00–57.09)	2	8
4	Zinc	84.2200 (26.48–22 519.03)	35	0
5	Iron	1356.21 (128.24–136 835.25)	NA	0
6	Copper	17.1450 (0.00–12 756.86)	NA	1
7	Chromium	20.9050 (0.00–2717.58)	NA	4
8	Cadmium	0.00 (0.00–0.00)	0	42

[a]The permissible limit set by the FAO/WHO for herbal medicines was followed, i.e. 10 μg/g for arsenic and lead, 1 μg/g for mercury, 0.3 μg/g for cadmium, and 50 μg/g for zinc. The permissible limit for iron, copper, magnesium, and chromium in medicinal herbs has not been established yet. NA: not applicable.

and renal adverse effects. Although toxic lead contents were relatively less prevalent in our sample than previously reported, it remains the most hazardous toxicant [6, 11]. Much clinical toxicity from Ayurvedic drugs has been attributed to their toxic lead content, affecting multiple organs (e.g. gastrointestinal, hematological, neurological, or cardiovascular system; [8–10, 25–27]). Chronic exposure to arsenic is associated with many conditions, including cancers, reported with herbal drugs [4–6, 25]. Cadmium exposure, listed at sixth place in ATSDR, has been observed after herbal medicine intake. However, it was not detected in our Ayurvedic products. The explanation for the variation of heavy metals concentrations in different origin herbal preparations is not clear; however, variation in the regional heavy metal pollution might play a role [13, 28–31].

All samples contained zinc and iron. These metals are essential trace elements for human physiology; however, chronic ingestion causes many adverse effects. Immune dysfunction and hypo-proliferative anemia may occur with long-term zinc exposure. Chronic iron toxicity can manifest with gastrointestinal upset or increased susceptibility to infections (e.g. malaria, mucormycosis; [32]). Excess zinc has also been linked to mucormycosis [32, 33]. Copper and chromium were prevalent in our formulations. These metals are primarily non-toxic, but higher doses can cause liver, kidney, or brain abnormalities.

Although properly made Ayurvedic medications are believed to be a great boon to humanity, being helpful to prevent and treat various disorders, the potential for toxic metal exposure is increasingly evident. Because our sample formulations were prescribed twice or thrice daily doses for weeks or months, the resultant chronic exposure leads to bioaccumulation. The products contain heavy metals not listed on the label and may have a metal "substitution" (the labeled metal might not even be present). The herbal medicine users may develop undiagnosed or subclinical toxicity. Moreover, many of them do not report the herbal use to the clinicians. Thus, when asking patients about their medication use, clinicians should ask directly about Ayurvedic or herbal medicines and look for the specific signs of metal toxicity. Early recognition and the termination of exposure are essential components of the management of metal toxicity.

Although we had a reasonable sample size with multi-element detection, a single-center observation limits the generalizability of the results. Our study did not address the potential sources of increased toxic heavy metal contents. Because environmental contamination remains an essential factor, as almost every food product has hazardous chemicals (including heavy metals), a large

multicenter study with matched control might clarify any contribution of heavy metal pollution.

Conclusion

Our study highlights the concern about the potential heavy metal toxicity of Ayurvedic medications. Heavy metals are prevalent in Indian-manufactured Ayurvedic preparations, and mercury, arsenic, and zinc are typical toxic-metal contents. The nature and amount of the metals may not be recognized by the ingredient listed on the pharmaceutical label. These results call for evaluating the sources of toxic metal concentrations, e.g. environmental contamination (including heavy metal pollution) or manufacturing processes, and the necessary regulations for the safety of Ayurvedic medications.

Supplementary data

Supplementary data is available at *TOXRES Journal* online.

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Conflict of interest statement

None declared.

Authors' contributions

AB: Conceptualization (lead); Data curation; Methodology; Formal analysis (supporting); Writing-original draft (supporting); and Writing-review & editing (supporting).

AKP: Conceptualization (supporting); Formal analysis (lead); Writing-original draft (lead); and Writing-review & editing (lead).

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