Ensuring the Safety of Indian Herbal Drugs: A Comprehensive Assessment of Heavy Metal Contaminations with Emphasis on Lead, Arsenic and Cadmium

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Abstract

Background

This study addresses the critical concern of heavy metal contamination in medicinal plants, with potential health risks such as renal failure and chronic toxicity. The World Health Organization advocates stringent control of heavy metals, including lead (Pb), arsenic (As), and cadmium (Cd), in herbal medicines to ensure safety, with recommended limits emphasizing their toxicity even at low concentrations (Pb: 10 mg/kg, As: 10 mg/kg, Cd: 0.3 mg/kg).

Methods and Results

Focusing on Shatavari (*Asparagus racemosus*), Ashoka (*Saraca asoca*), Ashwagandha (*Withania somnifera*), and Safed Musli (*Chlorophytum borivilianum*), this research, utilizing ICP-MS for heavy metals analysis, revealed Pb concentrations within safe limits across all samples, and As was absent in Shatavari and Ashoka samples. Cd concentrations in all drugs were below the 0.080 mg/kg limit of detection, highlighting the method's sensitivity.

Conclusion

The study affirms that heavy metal concentrations in the studied herbal drugs are within acceptable limits, reinforcing their safety. This research provides vital insights, emphasizing the necessity for ongoing monitoring and adherence to international standards in comprehensive pharmacological and toxicological evaluations, ensuring the well-being of consumers.

Introduction

Herbal medications have been utilized for the management and treatment of a broad variety of illnesses, including serious medical conditions for centuries. These medicinal products are reported to be among the most commonly traded products across the globe, have attracted a lot of attention in previous decades, and are projected to be in high demand going forward [1]. Products containing, medicinal plant or their parts such as bark, berries, leaves roots and flowers or their extracts that serve as active components meant for therapeutic purposes are classified as herbal medications by the WHO (World Health Organisation) [2].

Various ancient medicinal systems, including Chinese, Ayurvedic and Unani are based on medicinal plants. These systems of medicine produced some significant medications that continue to be in use nowadays [3]. medicinal plants might incorporate toxic metals due to environmental contamination and industrialization, previous application of fertilizers and pesticides. Higher heavy element accumulation has been observed in medicinal plants compared to any other plant [4].

Elements such as Chromium, Mercury, lead, and Arsenic that have a density higher than 4.5 g/cm3 are referred to as heavy metal elements. In the process of biomagnification, heavy metals may build up in the plants and eventually get to the human organs via contaminated herbal drug consumption, where they interfere with the normal activities of enzymes and proteins to the point of inactivation. Furthermore, it can accumulate in particular tissues and organs, where it might result in a range of poisoning symptoms. [5]. High amounts of these metals may occur in herbal drugs when used as active ingredients in medicinal preparations. lead and mercury were reported in various Chinese, Mexican, and Indian traditional medicinal systems [6] likewise, when the medicinal plants are cultivated in contaminated environments, such as sites where metal is mined and smelted [7].

The accumulation of heavy metals such as lead, arsenic and cadmium in herbal products is regarded as a serious problem of insignificant concern. The poor-quality control of these products causes health hazards Some products may contain dangerously high levels of toxic metals, which can lead to fatal consequences if consumed. [8]. The consumption of such products will result in adverse effects with symptoms such as renal failure, symptoms of chronic toxicity, and liver damage [9]. According to the stipulation of the World Health Organization lead, cadmium and arsenic other heavy metals must be controlled in medicines to ensure their safety [10].

International organizations recommend assessing therapeutic herbal drugs generated from medicinal plants for the concentration of heavy toxic metals in the raw materials as well as in the final products. The maximum allowed limits are set, prevalently Lead (10 ppm), cadmium (0.3 ppm) and arsenic (10 ppm). Even at low concentrations, Lead, Cadmium and Arsenic are toxic. No negative health effects resulting from their deficiency were reported [11]. Lead is toxic to the liver, heart, kidney and intestine. It can result in permanent behaviour and cognitive disabilities in children by distrusting the normal metabolism process of the nervous system. Its symptoms include mental confusion, convulsion, irritability, coma and death. It is among the widespread toxic metals [12]. Cadmium can cause damage to the Kidney, liver, brain, and many other vital organs of the human body [13] Arsenic causes myocardial injury, cardiomyopathy and cardiac arrhythmias by decreasing the activity of some antioxidant enzymes of the heart, other symptoms include behavioral abnormalities, memory loss, and confusion [14].

Evaluating the concentrations of heavy metals in herbal drugs is of paramount importance and needs to be performed to ensure conformity to the regulations that govern the level of these metals in herbal goods offered on the market. To solve this essential challenge, the current research utilizes Inductively Coupled Plasma Mass Spectrometry (ICP-MS), an innovative technique used in inorganic multi-element evaluation. This technology, which employs a quadrupole mass spectrometer, enables the fast and reliable determination of various elements, making it an effective and effective method of heavy metal identification and quantification [15]. While AFS (alternative methods like atomic fluorescence spectrophotometry), ICP-OES (inductively coupled plasma atomic emission spectrometry), UV-VIS (ultraviolet-visible spectrophotometry) and AAS (atomic absorption spectrophotometry) exist, the drawbacks of these techniques in detecting low-content constituents highlight ICP-MS' advantages, particularly in the setting of quality control evaluations of herbal drugs [16–18]. In this research, ICP-MS was utilized to detect and quantify heavy metals, namely Lead, Arsenic, and Cadmium, in selected herbal drug samples of Shatavari, Ashoka, Ashwagandha, and Safed Musli sold in Indian markets. The significance of this investigation lies in the analysis of these heavy metals in the drug samples thereby ensuring the safety of these herbal drugs for therapeutic use.

Materials and methods

Sample collection

Twelve herbal drug samples were chosen for analysis. Specifically, three samples were obtained for each herbal drug, namely Shatavari (*Asparagus racemosus* STV1, STV2, STV3, Ashoka (*Saraca asoca* AHK1, AHK2, AHK3), Ashwagandha (*Withania somnifera* ASH1, ASH2, ASH3), and Safed Musli (*Chlorophytum borivilianum* SAF1, SAF2, SAF3), each sourced from different reputable herbal drug companies across various locations in India (Fig. 1). All the samples were acquired in powdered form, ensuring a consistent and convenient state for analysis.

Reagents:

Ultra-pure reagents, including HNO_3 (Merck) and H_2O_2 (Fisher Chemicals), along with Milli-Q water (Qualigens, HPLC grade, Thermo Fisher Scientific India Pvt Ltd), were employed in the analysis. A stock solution of 100 mg/kg using Certipur® - Standards Reference (Inorganic Ventures) at a concentration was prepared. Subsequently, generated a series of final dilutions for working standards at concentrations of 2.0, 5.0, 10.0, 20.0, and 50.0 mg/kg, ensuring a minimum of five data points to achieve a linear calibration curve.

Digestion of The Samples:

Sample digestion by Microwave Reaction system (MRS). A precisely measured amount of 0.5 mg from the sample was placed into an MRS vessel. Subsequently, 5 mL of HNO_3 and 2 mL of H_2O_2 were carefully added to the MRS vessel, securely sealed, and acid blanks were prepared. The vessels, each identified by their unique numbers, were then securely placed into the Rotor. The microwave reaction system (Anton Paar) was initiated, activating the digestion program (Table 1). Upon completion of the digestion process, the vessels were removed and depressurized in the exhaust chamber. Following this, the vessels were washed with Milli-Q water, and the resulting samples were transferred into 1 mL volumetric flasks, adjusting the volume to 50ml with Milli-Q water. The samples underwent filtration using a 0.22 µm membrane filter, and the filtrate samples were aspirated into the ICP-MS for further analysis.

Table 1
Digestion Program

S/N	Temperature ^0C	Ramp Time (min)	Hold Time (min)
1	90	20	10
2	120	10	5.0
3	150	10	5.0
4	190	10	5.0
5	Cold down to 40^0C	-	-

Instrumentation:

Perkin-Elmer series (NEX 10N 2000) ICP-MS system was used for the simultaneous multi-element detection of Lead, Arsenic and cadmium. ICP-MS device operating parameters summarized in Table 2.

Table 2
ICP-MS device operating parameters

Parameter	Description / Value
Plasma gas	Argon
Makeup gas	Argon
Carrier gas (inner)	Helium
Plasma gas flow (Ar)	15 L/min
Radio frequency power (generator power)	1600watt
Radio frequency matching	1600watt
Generates temperature	24.3^{0}C
Injector	Sample injector part
Cones	Sample Cone, Skimmer Cone & Hyper Skimmer Cone
Nebulizer gas flow	0.851L/min
Background	< 3.0 cps
Short-term stability (in run)	1–3%
Long-term stability (in hours)	< 5%
Resolution m/z	0.7-1.0 amu
Spray chamber temperature	20 0C
Rinse time 45 sec	50 sec
Sample intake	35.0 rpm
Software	Syngistix

Results and Discussion

ICP-MS technology is one of the most sophisticated methods used in minerals and heavy metals detection and quantification. Its ability to analyze heavy metals at low concentrations distinguishes it compared to other methods in terms of reliability and sensitivity [19]. [19]. For this reason, quantitative and qualitative metal element analyses of plants were made with ICP-MS (Table 3).

Table 3
Illustrating herbal drugs sample collection locations

Shatavari (*Asparagus racemosus*)	**Ashoka** (*Saraca asoca*)	**Ashwagandha** (*Withania somnifera*)	**Safed musli** (*Chlorophytum borivilianum*)
STV1 Kottivakkam, Chenni Tamil Nadu	AHK1 Indore, Madhya Pradesh	ASH1 Ahmedabad, Gujarat	SAF1 Jaipur, Rajasthan
STV2 Coimbatore, Tamil Nadu	AHK2 Kelapur, Maharashtra	ASH2 jammu	SAF2 Bolangir, Odisha
STV3 Gandhi Nagar, Jammu	AHK3 Bangalore, Karnataka	ASH 3 Kottayam, Kerala	SAF3 Gurugram, Haryana
Shatavari STV, Ashoka: AHK, Ashwagandha: ASH, and Safed Musli: SAF			

Lead (Pb) has been found to have dangerous impacts on the health of humans, and its level in blood varies depending on age, physiological circumstances, and diet [20]. Lead levels of 100–1000 µg/L in blood have been linked to adverse effects on the neurological system, including mental retardation, headache, behavioral abnormalities, diarrhea, anemia, and tremors [21–22]. The World Health Organization (WHO) has established a limit of 10 mg/kg for lead in herbal medications [23].

In our study, the lead concentrations in Shatavari herbal drug samples STV2 and STV3 were found to be 0.264 and 0.451 mg/kg, respectively, while the lead level in STV1 was below the limit of detection (LOD). Similarly, Ashoka (*Saraca asoca*) samples (AHK1, AHK2, and AHK3) exhibited lead levels of 0.211, 0.230, and 0.096 mg/kg, respectively. Ashwagandha (*Withania somnifera*) samples revealed lead concentrations of 0.131 mg/kg (ASH1), 0.284 mg/kg (ASH2), and 0.523 mg/kg (ASH3). Notably, the lead concentrations in Ashwagandha were higher compared to those observed in Ashoka and Shatavari. Safed musli herbal drugs, exclusively processed from the *Chlorophytum borivilianum* medicinal plant, demonstrated elevated lead concentrations in comparison to other herbal drugs in our study. SAF 1 samples from Bolangir, Odisha, contained 0.659 mg/kg, with the highest lead concentration recorded in SAF3 from Gurugram, Haryana, at 1.166 mg/kg (Table 4).

Table 4
Illustrating lead, Arsenic and Cadmium Analysis of herbal drugs samples

Herbal drug /medicinal plant	**Samples**	**Lead mg/kg**	**Arsenic mg/kg**	**Cadmium mg/kg**
Shatavari (*Asparagus racemosus*)	STV1	< 0.080	< 0.080	< 0.080
	STV2	0.264	< 0.080	< 0.080
	STV3	0.451	< 0.080	< 0.080
Ashoka (*Saraca asoca*)	AHK1	0.211	< 0.080	< 0.080
	AHK2	0.230	< 0.080	< 0.080
	AHK3	0.096	< 0.080	< 0.080
Ashwagandha (*Withania somnifera*)	ASH1	0.131	< 0.080	< 0.080
	ASH2	0.284	0.410	< 0.080
	ASH3	0.523	< 0.080	< 0.080
Safed musli (*Chlorophytum borivilianum*)	SAF1	< 0.080	4.092	< 0.080
	SAF2	0.659	0.141	< 0.080
	SAF3	1.166	0.160	< 0.080

Previous studies have reported lead concentrations in plants ranging from 0.22 to 1.15 mg/kg [24]. Our findings fall within this range, with lead concentrations in the range of 0-1.166 mg/kg. Importantly, our results affirm that the observed lead concentrations are within the safe range, as they remain below the 10 mg/kg limit set by WHO. Exceeding this limit is associated with heightened toxicity and adverse health complications.

Arsenic (As) is often found in a variety of foods, including legumes, vegetables and herbs. Given its deadly nature, determining the level of human arsenic exposure is critical for successful management efforts [25]. In our study, arsenic was not detected in any of the Shatavari and Ashoka drug samples. However, arsenic was identified in the Safed musli (SAF) and Ashwagandha (ASH) samples. Specifically, SAF1, SAF2, and SAF3 Safed musli samples, as well as ASH3 Ashwagandha samples, exhibited arsenic concentrations of 4.2092, 0.141, 0.160, and 0.410 mg/kg, respectively.

It is noteworthy that the detected concentrations of arsenic in our study fall below the toxic level set by the World Health Organization (WHO). This indicates that the arsenic content in the analyzed herbal drugs is within the acceptable range, posing no immediate health risks to consumers. The absence of arsenic in Shatavari and Ashoka samples is reassuring, suggesting that these herbal drugs, derived from *Asparagus racemosus* and *Saraca asoca*, respectively, have minimal arsenic contamination. This is significant for consumers who rely on these herbal remedies, reinforcing their safety profile. For Safed musli and Ashwagandha samples that did show arsenic presence, the concentrations observed are well below the established toxic thresholds. The detailed analytical findings contribute to the understanding of arsenic variability in herbal drugs and underscore the importance of continual monitoring. The adherence to international standards, as exemplified by the compliance with WHO guidelines in this study, is paramount for ensuring the safety of herbal drugs. The results affirm that, in the context of arsenic, the herbal drugs analyzed remain within the safety limits, promoting consumer confidence in their usage.

Cadmium (Cd) exposure has several acute and chronic risks most notably the build-up of heavy metals in the kidneys, which can cause kidney disease. Lead (Pb) and cadmium poisoning have been reported to be associated with the usage of Chinese herbal medicines [26]. Consequently, the meticulous analysis of trace Pb and Cd in herbal medicines and their decoctions is essential for comprehensive pharmacological and toxicological evaluations.

In our study, all herbal drug samples exhibited cadmium concentrations below the limit of detection (LOD), set at 0.080 mg/kg (Fig. 2). This LOD is notably lower than the recommended threshold of 0.3 mg/g for medicinal plants [27]. The sensitivity associated with our analytical procedures is critical for properly identifying and quantifying even trace cadmium quantity. It is worth noting that plants mostly absorb cadmium via their roots [28]. The consistently low concentrations of cadmium across all samples are reassuring, suggesting that the herbal drugs analyzed are within a safe range concerning cadmium content. This observation aligns with established safety thresholds for medicinal plants, mitigating potential health risks associated with cadmium exposure.

The meticulous analysis of levels of Pb and Cd in herbal medicines is foundational for conducting robust pharmacological and toxicological evaluations. The data from our study, particularly the low cadmium concentrations, contribute valuable insights into the safety profile of the analyzed herbal drugs, bolstering their potential for use in traditional and alternative medicine.

The various levels of lead (Pb) and arsenic (As) found in herbal medication samples highlight the complexities of heavy metal dynamics in medicinal plants. This diversity can be attributable to a variety of causes, including environmental impacts, structural differences in plant morphology, and regionally diverse soil chemical compositions. Environmental variables have an important impact on the observed variability. As proven in prior investigations [29].

Conclusion

Our comprehensive study emphasizes the critical importance of monitoring heavy metal concentrations, particularly lead, arsenic, and cadmium, in herbal drugs. Elevated levels of these metals pose potential health risks, underscoring the need for continuous scrutiny and adherence to regulatory standards to ensure the safety of these products for human consumption. Our findings reveal that lead concentrations remain within acceptable limits, reinforcing the safety of the studied herbal drugs. The absence of arsenic in some samples, coupled with low concentrations in others, further validates the safety of Shatavari, Ashoka, Safed musli, and Ashwagandha within established regulatory frameworks. Additionally, the consistently low or undetected concentrations of cadmium in all samples further affirms the safety of these herbal drugs. Recognizing the complexity of environmental, anatomical, and soil-related factors influencing heavy metals absorption by medicinal plants, the need for ongoing research to unravel the intricate dynamics of heavy metal content in herbal medicines is paramount, ensuring their continued safety and efficacy in the realm of human health.

Declarations

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Competing Interests

The authors have non-financial interests to disclose.

Authors contribution

The study conceptualization and design were carried out by Munir Ibrahim and Ashok Kumar Bishoyi. Data curation, methodology and analysis were performed by Munir Ibrahim, Asmita Detroja, Avani Bhimani, Tirth Chetankumar Bhatt, JayKumar Koradiya. Data curation and analysis: Gaurav Sanghvi. Supervision of the research: Ashok Kumar Bishoyi. The first draft was written by Munir Ibrahim and revised by Ashok Kumar Bishoyi. All Authors approved the final manuscript.

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Figures

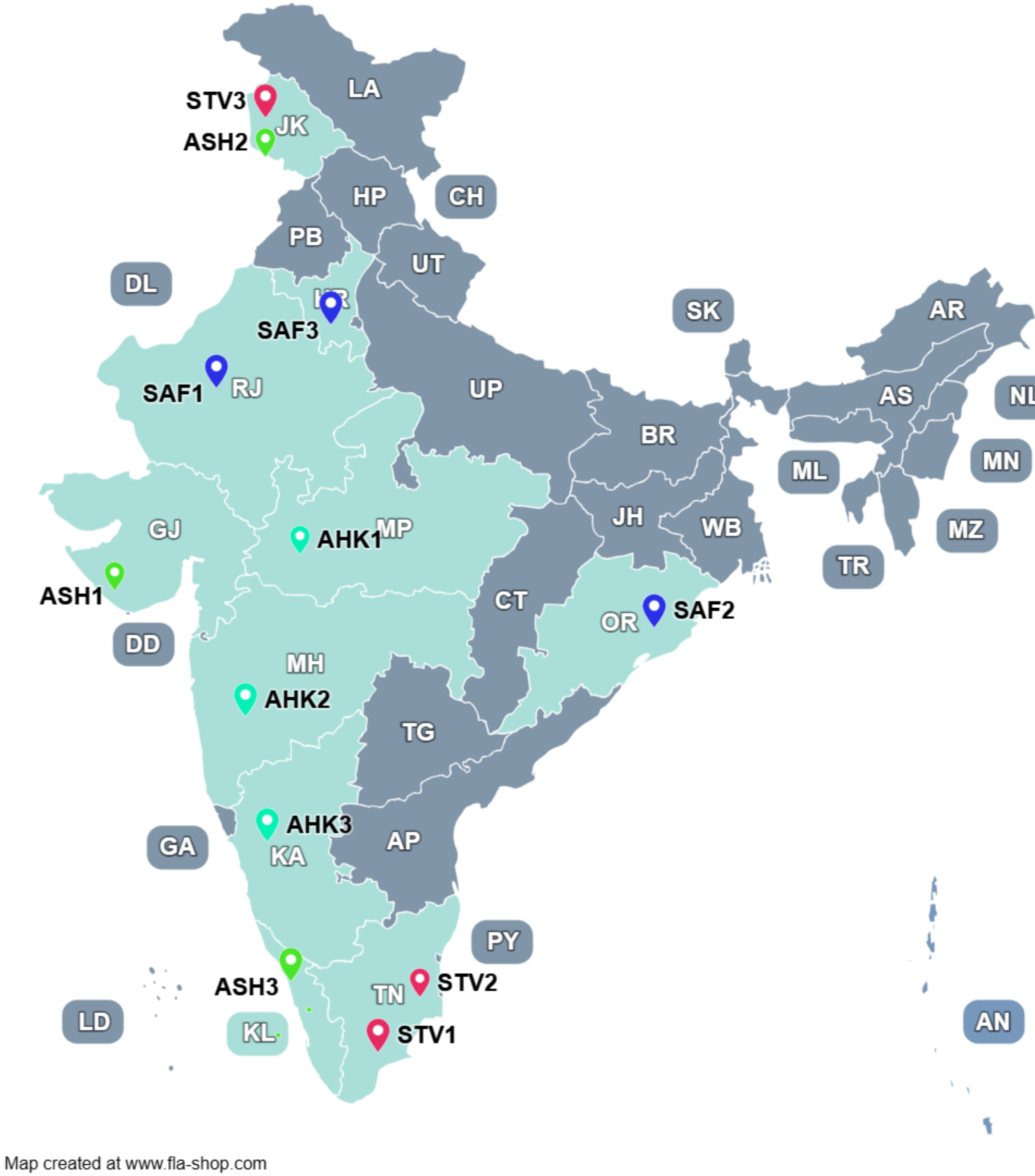

Figure 1

Illustrating locations of herbal drugs sample collection. (Shatavari STV, Ashoka: AHK, Ashwagandha: ASH, and Safed Musli: SAF, TN: Tamil Nadu, KL: Kerala, KA: Karnataka, MH: Maharashtra MP: Madhya Pradesh, GJ: Gujarat, RJ: Rajasthan, JK: Jammu and Kashmir, HR: Haryana, OR: Odisha)

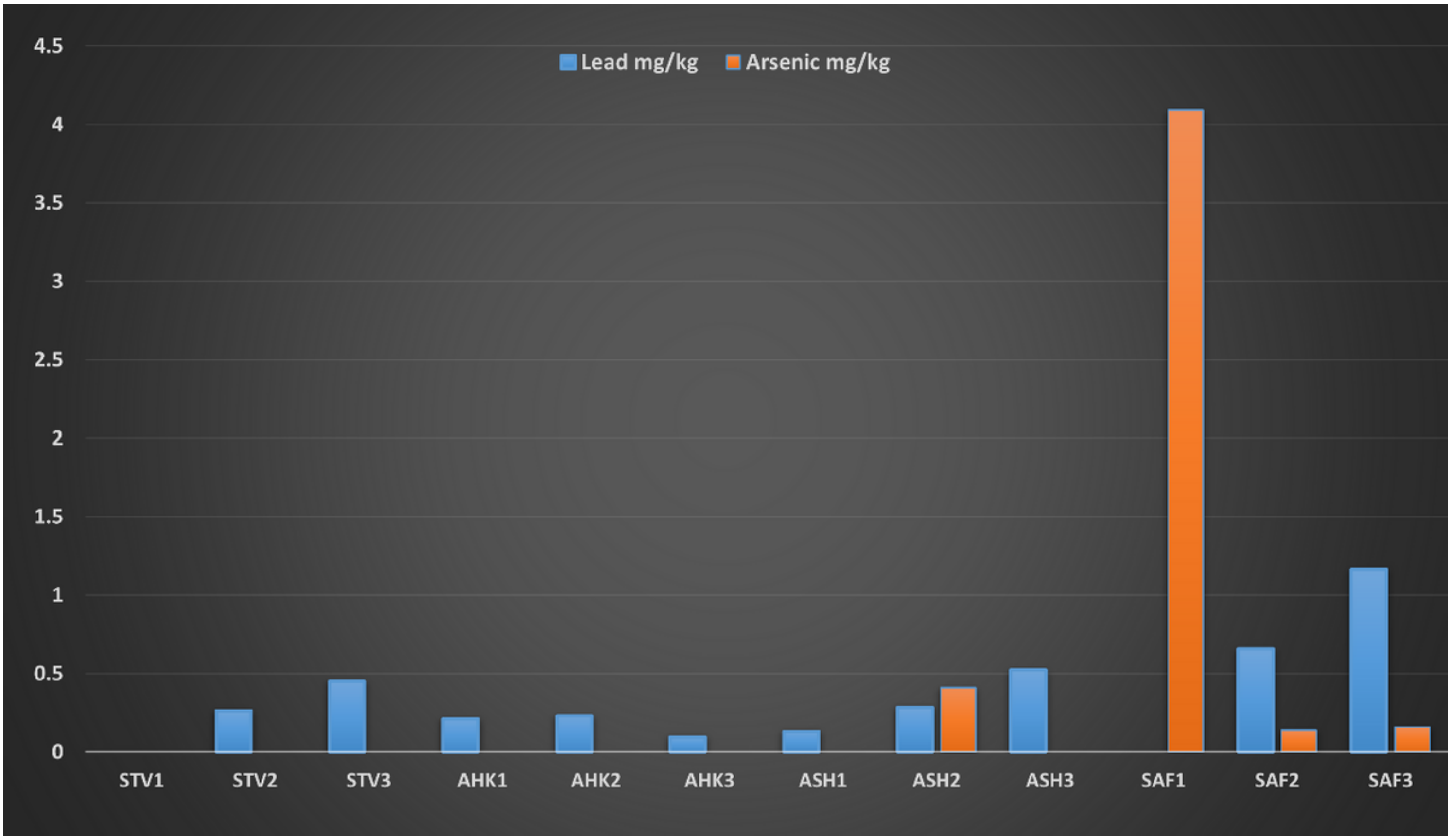

Figure 2

Illustrating concentrations of lead, Arsenic and Cadmium Analysis of herbal drugs samples (Shatavari STV, Ashoka: AHK, Ashwagandha: ASH, and Safed Musli: SAF)