



## **A Review on Heavy Metal Contamination in Herbals**

**Maruti Shelar<sup>1\*</sup>, Vaibhav Gawade<sup>2</sup> and Santosh Bhujbal<sup>1</sup>**

<sup>1</sup>*Department of Pharmacognosy, Dr. D. Y. Patil Institute of Pharmaceutical Sciences and Research, Pimpri, Pune 411018, India.*

<sup>2</sup>*Department of Pharmaceutical Chemistry, Dr. D. Y. Patil Institute of Pharmaceutical Sciences and Research, Pimpri, Pune 411018, India.*

### **Authors' contributions**

*This work was carried out in collaboration among all authors. Author MS designed the study, and wrote the first draft of the manuscript. Authors VG and SB managed the analyses of the study. Author SB managed the literature searches. All authors read and approved the final manuscript.*

### **Article Information**

DOI: 10.9734/JPRI/2021/v33i29A31561

Editor(s):

(1) Giulio Tarro, Foundation T. & L. de Beaumont Bonelli for cancer Research, Italy.

Reviewers:

(1) Sangeetha R K, Sri Ramakrishna Institute of Paramedical Sciences, India.

(2) Nguyen Thanh Giao, Can Tho University, Vietnam.

Complete Peer review History: <http://www.sdiarticle4.com/review-history/68200>

**Review Article**

**Received 01 March 2021**

**Accepted 06 May 2021**

**Published 15 May 2021**

### **ABSTRACT**

Nearly 70-80% of the world's population relies on non-conventional medicines, often derived from herbal plants, according to World Health Organization (WHO) figure. Medicinal plants are starting material for any herbal preparation such as herbal medicines, herbal teas, herbal oil etc. These preparations are being used worldwide due to their therapeutic potential and as they are considered to be safe as compared to allopathic medicines. Lead, cadmium, chromium, nickel, arsenic and mercury are the most common toxic metals that have become a matter of concern due to the reports of their contamination in various herbal preparations and herbal ingredients. Although the minimum acceptable limits have been laid out as safety concern. Heavy metal are evaluated by AAS, ICP-OES, ICP-MS, XRFS, HPLC, DPP, NAA, ASV and disposable sensor applications for achieving therapeutic efficacy and evolutions of heavy metal in herbals.

*Keywords: Heavy metals; detection methods; heavy metal toxicity; heavy metals limits.*

\*Corresponding author: E-mail: [marutishelar@rediffmail.com](mailto:marutishelar@rediffmail.com);

## 1. INTRODUCTION

Although there is no clear definition of heavy metals but density is considered to be the most defining factor. The term “heavy metals” refers to any metallic element that has a relatively high density and is toxic or poisonous even at low concentration. “Heavy metals” is a general collective term, which applies to the group of metals and metalloids with atomic density greater than 4 g/cm<sup>3</sup>, or 5 times or more, greater than water. The main threats to human health from heavy metals are associated with exposure to Lead, Cadmium, Mercury and Arsenic. Medicinal plants are starting material for any herbal preparation such as herbal medicines, herbal teas, herbal oil etc. These preparations are being used worldwide due to their therapeutic potential and as they are considered to be safe as compared to allopathic medicines. Lead, Mercury, cadmium, Nickel, chromium and arsenic are the most common toxic metals that have become a matter of concern due to the reports of their contamination in various herbal preparations and herbal ingredients [1].

The determination of trace elements, particularly heavy metals, in real matrices has received increasing attention in recent years. Their accumulation and distribution in a plant depends on the plant species, type of element – its chemical properties and bioavailability, soil characteristics (e.g., pH, amount of dissolved oxygen and trace elements) as well as on weather conditions. Excessive levels of heavy metals can be hazardous to plants as well, e.g. more than 100 ppm of Ni develops symptoms of toxicity; 60 ppm of Cu and 120 ppm of Zn are the critical toxic levels for plants for example, Peanuts are enormously responsive to Zn, and toxicity has been seen at levels as low as 12 ppm. Effects of heavy metals on plants result in growth inhibition, structural damage, and a decline of physiological and biochemical activities as well as the function of plants [2].

Many metals are essential to life, but in excess, these can be poisonous. The basic tenet of toxicology – “the dose makes the poison” – is still actual. Too little can lead to a deficiency; too much can result in adverse health effects [3].

### 1.1 Sources of Heavy Metal Pollution

Heavy metal pollution is mainly the result of human activities such as agriculture, mining, construction and industrial processes. Improper

waste disposal activities and overuse of pesticides were among the most significant sources of heavy metal pollution in the environment. Heavy metals in the environment are a health hazard due to their persistence, bioaccumulation and toxicity to plants, animals and human beings. Several health problems have been linked to overdose dietary supplements, including a decrease in the immune system, the heart dysfunction, fetal dysfunction, mental and psychiatric disabilities sensory behavior [4]. Pb and Cd are missing essential nutrients that are not needed in the human body or in plants, and which cause various bimolecular conflicts low performance results [5]. Although it is an important component of many enzymes, it is excessive Cu diet can cause dermatitis, high irritation respiratory tract, abdominal pain, nausea, diarrhea, vomiting, and liver damage [6]. While As and Hg knew damage the lung, nervous, kidney, and respiratory systems, e.g. and causing skin disease. It can also cause problems with the central nervous system, the liver, lungs, heart, kidneys and brain. It leads to hypertension, abdominal pain, skin rash, intestinal ulcer and so on associated with various types of cancer [7]. It is therefore necessary and urgent to do a comprehensive assessment of the risks of heavy metal pollution in herbal remedies. So, the study was done precisely heavy metal content in herbal medicine emerges it is necessary to continue testing and specifying the dosage of herbs formulas. This study examines pollution levels and health danger to humans caused by heavy metal especially on herbs medicines, which provide a basis for evidence on which you can continue to build preventive measures, set consistent standards, and controls external contamination. Investigations he raised recommendations that can reduce or eliminate quickly levels of heavy metals in pharmaceuticals.

In 2019 total of 60,107 cases of COVID-19 have been reported (85.20% of total cases) in China are treated with effective Chinese herbal remedies all stages of infection, including the management of significant symptoms, low rates of deterioration and death, speedy recovery and disease prevention February 17, 2020 (Ministry of Science and Technology, 2020).

### 1.2 Classification of Metals

- **Class 1 Metals** – metals of *significant* safety concern (which can become suspected human carcinogens).

- **Class 2 Metals** – metals of **low** safety concern (these are generally well tolerated at typical pharmaceutical exposure & may be nutritional trace metals).
- **Class 3 Metals** – metals of **minimal** safety concern (These have well established safety profile, no significant toxicity, well tolerated even at levels above the typical pharmaceutical exposure, typically ubiquitous in nature).

Generally heavy metals include lead (Pb), cadmium (Cd), zinc (Zn), mercury (Hg), arsenic (As), silver (Ag), chromium (Cr), copper (Cu), iron (Fe), and the platinum group elements.

In totality of circumstance heavy metal ores include sulphides, such as iron, arsenic, lead, lead-zinc, cobalt, gold, silver and nickel sulphides; oxides such as aluminium, manganese, gold, selenium and antimony. Some exist and can be recovered as both sulphide and oxide ores such as iron, copper and cobalt

### 1.3 Physiological Function

Sometimes heavy metals are important in physiological functioning of body for example Zinc is a 'masculine' element that balances copper in the body, and is essential for male reproductive activity. Zinc deficiency causes anemia and retardation of growth and development [8].

Calcium it is the chief element in the production of very strong bones and teeth in mammals.

Magnesium is an important electrolytic constituent of the blood, present in the blood plasma and body fluids interstitial and cell fluids. Arsenic has been reported to be a trace element of nutritional importance to humans but its functions in the biological system is not clear [9].

Heavy metals enter the body by various sources like they leach into underground waters, moving along water pathways and eventually depositing in the aquifer, or are washed away by run-off into surface waters thereby resulting in water and subsequently causing soil pollution. Poisoning and toxicity in animals occur frequently through exchange and co-ordination mechanisms. When ingested, they combine with the body's biomolecules, like proteins and enzymes to form stable bio-toxic compounds, thereby mutilating their structures and hindering them from the bio-reactions of their functions [10].

### 1.4 Poisoning and Toxicity

Heavy metal in excess amount shows poisoning and toxicity. The bio-toxic effects of heavy metals refer to the harmful effects of heavy metals to the body when consumed the following have been reported as general signs associated with cadmium, lead, arsenic, mercury, zinc, copper and aluminium poisoning: gastrointestinal (GI) disorders, diarrhoea, stomatitis, tremor, hemoglobinuria causing a rust-red colour to stool, ataxia, paralysis, vomiting and convulsion, depression, and pneumonia when volatile vapours and fumes are inhaled. The nature of effects could be toxic (acute, chronic or sub-chronic), neurotoxic, carcinogenic, mutagenic or teratogenic [11]. For example

**Cadmium-** is toxic at extremely low levels. The concentration of cadmium (Cd) varied according to from less than 0.1 mg/kg to 1.11. There was no detection of cadmium. Thirteen samples of mint. Maximum detected Cd concentrations in parsley, chamomile, basil, sage. The oregano and thyme levels were 0.21, 0.82, 1.11, 0.88, 0.35, 0.63 mg per kg<sup>-1</sup> respectively in humans, long term exposure results in renal dysfunction, characterized by tubular proteinuria. High exposure can lead to obstructive lung disease, cadmium pneumonitis, resulting from inhaled dusts and fumes. It is characterized by chest pain, cough with foamy and bloody sputum, and death of the lining of the lung tissues because of excessive accumulation of watery fluids. Cadmium is also associated with bone defects, viz; osteomalacia, osteoporosis and spontaneous fractures, increased blood pressure and myocardial dys functions. Depending on the severity of exposure, the symptoms of effects include nausea, vomiting, abdominal cramps, dyspnea and muscular weakness. Severe exposure may result in pulmonary edema and death. Pulmonary effects (emphysema, bronchiolitis and alveolitis) and renal effects may occur following sub chronic inhalation exposure to cadmium and its compounds.

**Lead-** The most significant toxin of the heavy metals and the inorganic forms are absorbed through ingestion by food and water, and inhalation. A notably serious effect of lead toxicity is its teratogenic effect. The lead (Pb) content in the samples analyzed. The range was between less than 1.0 and 23.52 mg/kg<sup>-1</sup>. The FAO/WHO overall allowable lead limits. The consumption of medicinal herbs is 10 mg per kg<sup>-1</sup>. Lead poisoning also causes inhibition of the synthesis

of hemoglobin; dysfunctions in the kidneys, joints and reproductive systems, cardiovascular system and acute and chronic damage to the central nervous system (CNS) and peripheral nervous system (PNS). Other effects include damage to the gastrointestinal tract (GIT) and urinary tract resulting in bloody urine, neurological disorder and can cause severe and permanent brain damage. While inorganic forms of lead, typically affect the CNS, PNS, GIT and other bio systems, organic forms predominantly affect the CNS. Lead affects children by leading to the poor development of the grey matter of the brain, thereby resulting in poor intelligence quotient. Its absorption in the body is enhanced by Ca and Zn deficiencies. Acute and chronic effects of lead result in psychosis.

**Zinc-** has been reported to cause the same signs of illness as does lead, and can easily be mistakenly diagnosed as lead poisoning. The samples ranged from 12.65 to 146.67 mg·kg<sup>-1</sup>. The FAO/WHO permits more than 50 mg/kg<sup>-1</sup>. Zinc is an important trace element that is suitable for growth, blood clotting, thyroid function, and protein as well DNA synthesis. Minor details are available on Zn poisoning; however, high availability of zinc beyond permissible limits is productive toxic effects on the immune system, blood lipoprotein levels, and the level of copper. Zinc is considered to be relatively non-toxic, especially if taken orally. The clinical signs of zinc toxicosis have been reported as vomiting, diarrhea, bloody urine, icterus (yellow mucus membrane), liver failure, kidney failure and anemia.

**Mercury-** is toxic and has no known function in human biochemistry and physiology. Inorganic forms of mercury cause spontaneous abortion, congenital malformation and GI disorders (like corrosive esophagitis and hematochezia). Poisoning by its organic forms, which include monomethyl and dimethylmercury presents with erethism (an abnormal irritation or sensitivity of an organ or body part to stimulation), acrodynia (Pink disease, which is characterized by rash and desquamation of the hands and feet), gingivitis, stomatitis, neurological disorders, total damage to the brain and CNS and are also associated with congenital malformation. As with lead and mercury, arsenic toxicity symptoms depend on the chemical form ingested. Arsenic acts to coagulate protein, forms complexes with coenzymes and inhibits the production of adenosine triphosphate (ATP) during respiration.

It is possibly carcinogenic in compounds of all its oxidation states and high-level exposure can cause death. Arsenic toxicity also presents a disorder, which is similar to, and often confused with Guillain-Barre syndrome, an anti-immune disorder that occurs when the body's immune system mistakenly attacks part of the PNS, resulting in nerve inflammation that causes muscle weakness.

**Copper-**The copper (Cu) concentrations varied in a wide range between 1.44 and 156.24 mg·kg<sup>-1</sup>. Copper is an important component of many enzymes, therefore to play a key role in many body processes including the use of iron, the elimination of free radicals, bone growth and tissue interaction, melanin production, and many others. Still, overreacting copper can cause dermatitis, upper respiratory tract irritation, abdominal pain, nausea, diarrhea, vomiting, and liver damage.

### 1.5 Heavy Metals and Ayurveda Medicines

Ayurveda has been practiced for over 5000 years and is based on the Vedic hypothesis that there are common principles underlying the microcosm (individual) and macrocosm (universe) and that man and the universe are composed of the same basic elements, and disease occurs if there is an imbalance [12]. Ayurvedic medicines are generally based on herbal products and Ayurvedic practitioners usually make up their own medicines. They may use individual herbal extracts or a mixture of herbal extracts with vegetable, animal and mineral products. The equilibrium of lead, copper, gold, iron, mercury, silver, tin and zinc are seen in Ayurveda as essential for normal functioning of the human body and an important component of good health; in addition, some products contain other heavy metals such as thallium and arsenic (Some Ayurvedic texts acknowledge that these heavy metals and potentially other components of Ayurvedic medicines could be associated with toxicity and there is a specific area within Ayurveda that deals with toxicity known as 'Vishagarvajrodhika Tantra'). There are often specific procedures recommended to 'detoxify' the metals in Ayurvedic products. These procedures include heating and cooling products in buttermilk, cow's urine, sesame oil and the use of 'mineral herbs' or other herbal products such as tamarind [13]. Some cases ayurvedic medicines may show toxicity due to improper purification process. Heavy metal poisoning

related to Ayurvedic medicines was in a patient in the UK and was reported in 1978. These include reports of heavy metal poisoning in both children and adults, fatalities due to lead poisoning and a report of lead poisoning in a pre-term infant due to trans-placental lead transfer from a mother using Ayurvedic medicines [14]. The WHO Provisional Tolerable Weekly Intake (PTWI) of lead is 25 µg/kg body weights, which is equivalent to 3.5 µg/kg body weight per day. If lead intake exceeds this amount, lead accumulation will occur [15].

## 2. METHODS FOR DETECTION OF HEAVY METALS

### 2.1 Inductively Coupled Plasma Mass Spectroscopy

It is based on measuring m/z ratio. It has high degree of atomization in argon plasma at 7000K this extreme temperature makes it far sorrier than graphite furnace as an atomization source fir atomic spectroscopy. It has wide linear dynamic range, high sample throughput multi element capability. ICP-MS (AES)-Identifies each metallic impurity more specific, quantifies each metallic impurity, higher sensitivity. Typical detection limits 0.01 – 1 Mg/L (ppb) in solution. Sample size as little as 10 mg. ICP Analyses is in use and well established. It gives better results and is affordable [16].

### 2.2 Atomic Emission Spectroscopy

It is usually coupled with optical emission spectroscopy. Sample is excited by absorbing thermal or electric energy and the radiation emitted by excited sample is studied. More over it is related to atomssolids, liquids are usually analysed. It can be used for analysis of about seventy elements at concentration level as low as 1ppm for example in *Artemisia vulgaris* (Mn 52.94±0.01, Zn 38.14±0.02, Fe 81.39±0.30, Cu 9.65±0.04, Cr 4.65±0.04) [17].

### 2.3 Atomic Absorption Spectroscopy

It is sensitive and has detection limit of 1ppm.it uses flame atomic absorption (F-ASS), and Graphite furnace (GF-ASS) method technique for atomization flame uses gas for high temperature production. The liquid sample are aspirated in the flame. In the graphite furnaces the temp achieved is 2000 °C. Detection limit of Cd by F-

ASS is 1µg/L and only 8ng/L by GF-ASS. Chemical analyses of heavy metals have traditionally been carried out mostly by atomic absorption spectrometry(AAS), graphite furnace-atomic absorption spectrometry(GF-AAS) possessing better detection capabilities, and currently, new high-cost technologies like inductively coupled plasma atomic emission spectrometry (ICP-AES)or inductively coupled plasma mass spectrometry (ICPMS)that are slowly replacing other analytical techniques. To check the presence of lead, cadmium, chromium, nickel, arsenic and mercury in two major ingredients (*Azadirachta indica* and *Curcuma longa*) of a polyherbal product. These ingredients were subjected to analysis by Atomic Absorption Spectrophotometer (AAS). The minimum limit of heavy metals detected in *Azadirachta indica* (Cd 0.17±0.03, Pb 0.15±0.02, Ni 0.15±0.02, Cr 0.08±0.01, As 0.20±0.03, Hg 0.31±0.04) and in *Curcuma longa* (Cd 0.1±0.04, Pb 0.17±0.04, Ni 0.10±0.02, Cr 0.25±0.03, As 0.18±0.02, Hg 0.24±0.03) [18].

### 2.4 X-Ray Fluorescence (XRF)

Is the emission of characteristic "secondary" (or fluorescent) X-rays from a material that has been excited by bombarding with high-energy X-rays or gamma rays .The phenomenon is widely used for elemental analysis and chemical analysis, particularly in the investigation of metals, glass, ceramics and building materials, and for research in geochemistry, forensic science and archaeology [19].

### 2.5 Anode Stripping Voltammetry

It is a simple method for the simultaneous determination of heavy metals in medicinal plants by differential pulse anodic stripping. It is a simple Volta-metric apparatus of hanging mercury electrode and platinum wire used as working and counter electrode. All potentially are measured against an Ag/Ag ClKCl reference electrode. Pure n2 was bubbled through the sample for 400s before the measurements. This method has higher sensitivity. The method gives good reproducible results. There is a rapid achievement of constant current during drop growth and clean surface generated. The sample preparation was carried out by dry ash 1.0g of finely pulverized plant sample for 2.5hr at 500°C. It shows some disadvantages as enlisted. There is electrode fouling phenomenon. The method is time consuming. As and Hg is

easily oxidized limited use as anode ( $E < +0.4V$ ) [20].

## **2.6 Thermolysis Coupled atomic Absorption Spectroscopy**

In this method subjected plant material or the formulation is heated to high temperature in a constant stream of dry air this results evolution of elementary Heavy metal vapor thermally released from molecular heavy metal species in the sample at high temperature was directed into the AA detector. The method not required pretreatment. There are less chances of contamination as no pretreatment required. This is the time saving method (4 min/one cycle). The continuous analysis can be made, no need of calibration. It has some limitation like only mercury can be detected. Simultaneous determination of heavy metals is not possible [21].

## **2.7 Synchrotron Radiation X-Ray Fluorescence Analysis**

Synchrotron radiation which emits x-rays in excitation of the electrons present in the molecules where they get excited to a higher energy level this is transient phase known as singlet phase. Singlet electrons have opposite spin. While returning back to ground state electrons emit energy in the form of fluorescence. Hence this phenomenon is used for quantitative determination of various elements. This method shows very high sensitivity, reproducibility in the results and detects wide range of elements. Limitation of these methods is it is expensive method. It requires skilled pretreatment. By this method non fluorescence elements cannot be detected [22].

## **2.8 Neutron Activation Analysis**

It is based on the principle that when materials are irradiated in nuclear reactor or in another neutron source, some of the items were converted into radioactive isotopes. Where comparison is made between the element's radio-activities irradiated simultaneously with some standards. It has very high sensitivity and selectivity. It is the most accurate method amongst new methods. It has high cost of analysis; exposure to radiation may be harmful for analyst. Time required for whole procedure is very high [23].

## **2.9 Electro-Thermal Atomic Absorption Spectroscopy (ETAAS) and Ultrasonic Nebulization System Coupled to Inductively Coupled Plasma Optical Emission Spectroscopy**

Sample is subjected for pretreatment by using flame, electro-thermal, plasma flow which results in the removal of biomaterials and availability of the elements. In atomic absorption spectroscopy the difference in the incident and emergent intensity of radiation is calculated by the means of photo-detectors and in case of atomic emission spectroscopy the amount of energy emitted by the elements is measured. In both methods the practical value is compared with standards which give the quantitative ideas of the elements present. It shows higher sensitivity than the flame atomic absorption spectroscopy, Simultaneous multi-element detection is possible and has well in results. It shows the interference of biomaterials is bound to take place. It is tedious experiment [24].

## **2.10 Disposable Electrochemical Sensor for Rapid Determination of Heavy Metals**

When sufficient negative potential is applied to an electrode dipped in metal solution a thin layer of metal is formed on it. Screen printing technology involves use of disposable electrode these were modified by coating them with desired metal and used as the working electrodes for stripping voltammetry. It has low analysis cost. It gives rapid and accurate results. It has very low detection [16].

## **2.11 Cold Vapor Atomic Absorption Spectrometry (CVAAS)**

This unique feature of mercury provides energy measurement with CVAAS without sample heat. In this way, the mercury in the sample is first reduced to a free atom state with a strong reducing agent, such as sodium borohydride or stannous chloride. Mercury vapor is absorbed in carrier gas and 253.7 nm of light are absorbed by atoms of mercury. Argon is widely used as a control gas; however, nitrogen or air can also be added. Absorption of atoms are recorded and a very high amount of absorption is used analyze mercury concentration. Methods of injecting flow can be used to make the process more efficient and reduce the cost of the reagents required in the scale to reduce the [25].

## 2.12 Graphite Furnace Atomic Absorption Spectrometry (GFAAS)

The atomized sample passes through a simple surface quickly as well only a small fraction of the nebulized vapor reaches the flame. Therefore, the process of making advanced models using graphite furnace for electric vaporization is used to improve analytical sensitivity. In graphite furnace atomic absorption (GFAA), the sample is first introduced directly to graphite tube. The sample is then heated to remove the solvent and matrix materials, and the remaining atomic sample GFAAS used for the analysis of lead, cadmium, concentration of copper, arsenic and mercury in four Chinese herbal remedies [26].

## 2.13 Atomic Fluorescence Spectrometry (AFS)

The spectrometry of Atomic fluorescence is different from that of atoms the absorption of spectrometry by means of the mechanisms used by the positive atoms from the underground condition and receiving the issued signals. In AFS, sample solution is first diluted in flame or non-flame cell, to then atoms are illuminated by a light source. Some atoms cause radiation exposure to radiation in the index of the detection device, and the atomic fluorescence is measuring detector. Similar to CVAAS, cold

atomic fluorescence spectrometry (CVAFS) can be used to determine mercury concentrations using cold mercury smoke at room temperature. Free mercury portable atoms are transported to the cell by a network company gas, such as argon. After that, mercury atoms rejoice with a bright source of ultraviolet light of length 253.7 nm. Excited atoms light up the energized as fluoresce. Fluorescence is omnidirectional and can be detected by a tube photomultiplier or UV photodiode detector. Atomic fluorescence spectrometry has been reported to determine arsenic and mercury in traditional Chinese injections [27].

## 2.14 Differential Pulse Polarography

As a component of voltammetry, differential pulse polarography (DPP) uses a mercury drop electrode as the active electrode. In the DPP strategy, the current is measured immediately before each possible change and the current difference is classified as potential work. The DPP can be used to study the tracking values of chemical detection limits in the sequence of Approximately 10<sup>-8</sup> M. Other heavy metals, including Pb, Cd, Zn, Cu and Fe, have been successfully identified and given to chamomile flowers and calendulea in a variety of pulse polarography [28].

Table 1. Example of medicinal plant and heavy metal contamination

Name of plants	Cd (ppm)	Pb (ppm)	Ni (ppm)	Cr (ppm)	As (ppm)	Hg (ppm)
<i>W.somnifera</i>	1.33±0.64	7.93±3.29	5.66±2.62	8.34±21.89	-	-
<i>R.communis</i>	1.58±0.07	10.63±2.44	8.10±2.92	14.26±1.28	-	-
<i>J.adhatoda</i>	0.99±0.29	5.12±2.06	4.09±1.47	5.30±2.50	-	-
<i>H.vulgare</i>	1.16±0.19	10.34±1.75	14.96±1.68	6.21±1.45	-	-
<i>C.arvensis</i>	1.23±0.54	3.15±0.87	2.60±0.98	1.20±0.08	-	-
<i>C.sativa</i>	1.66±0.64	10.57±2.46	15.18±1.08	29.49±2.93	-	-
<i>A.pungens</i>	1.45±0.80	9.89±2.96	7.97±1.67	17.74±1.56	-	-
<i>A.aspera</i>	0.59±0.41	9.28±1.66	5.90±0.92	1.48±0.90	-	-
<i>A.indica</i>	0.28±0.03	0.85±0.25	0.80±0.10	0.40±0.05	0.31±0.04	0.75±0.05
<i>C.longa</i>	0.19±0.05	0.30±0.05	0.75±0.15	0.23±0.03	0.20±0.03	-
<i>A.vulgaris</i>	Nd	Nd	4.35±0.01	4.65±0.04	-	-
<i>A.adscendens</i>	Nd	Nd	0.94±0.01	1.13±0.01	-	-
<i>G.aparine</i>	Nd	Nd	4.16±0.04	6.14±0.01	-	-
<i>M.pruiens</i>	Nd	Nd	3.18±0.02	0.27±0.01	-	-
<i>P.crispum</i>	-0.21 ± 0.07	-12.83 ± 0.97	-	-	-	-
<i>C.recutita</i>	-0.82 ± 0.02	5.37 ± 1.25	-	-	-	-
<i>O.basilicum</i>	0.13 ± 0.01	01 ± 0.28	-	-	-	-
<i>S.officinalis</i>	-0.88 ± 0.08	12.66 ± 1.54	-	-	-	-
<i>O.vulgare</i>	-0.35 ± 0.02	9.39 ± 1.77	-	-	-	-

Nd –Not determined

**Table 2. WHO and F.D.A limit of heavy metals**

Heavy metal contents	Permissible limits as per W.H.O & F.D.A
1. Lead (Pb)	10 ppm
2. Cadmium (Cd)	0.30 ppm
3. Arsenic (As)	10 ppm
4. Mercury (Hg.)	1 ppm
5. Zinc	0.50ppm

**Table 3. Plants Used in Indian system of medicine with minimum acceptable limits of heavy metals**

Name of herbs	Botanical name	Limits (in ppm)
Coleus	<i>Coleus forskohlii</i> Briq	20
Brahmi	<i>Bacopa monnieri</i>	20
Bhuiamla	<i>Phyllanthus amarus</i>	20
Bhringraj	<i>Eclipta alba</i>	20
Bhibhitaki	<i>Terminalia belerica</i>	20
Ashwagandha	<i>Withania somnifera</i>	20
Arjuna	<i>Terminalia arjuna</i>	20
Arachis Oil	<i>Arachis hypogaea</i>	10
Amra	<i>Mangifera indica</i>	20
Amalaki	<i>Embllica officinalis</i>	20
Kutki	<i>Picrorhizakurroa</i>	20
Kunduru	<i>Boswellia serrata</i>	20
Kalmegh	<i>Andrographis paniculata</i>	20
Haritaki	<i>Terminalia chebula</i>	20
Haridra	<i>Curcuma longa</i>	20
Guduchi	<i>Tinospora cordifolia</i>	20
Gudmar	<i>Gymnema sylvestre</i>	20
Guar Gum	<i>Cyamopsis tetragonolobus</i>	20
Gokhru	<i>Tribulus terrestris</i>	20
Garcinia	<i>Garcinia cambogia</i>	20
Vasaka	<i>Adhatoda vasica</i>	20
Tulasi	<i>Ocimum sanctum</i>	20
Sunthi	<i>Zingiber officinale</i> Rosc.	20
Shellac	<i>Laccifer lacca</i> Kerr	20
Shati	<i>Hedychium spicatum</i>	20
Punarnava	<i>Boerhaavia diffusa</i>	20
Pippali,	<i>Small Piper longum</i>	20
Pippali,	<i>Big Piper longum</i>	20
Maricha	<i>Piper nigrum</i>	20
Manjistha	<i>Rubia cordifolia</i>	20
Mandukaparni	<i>Centella asiatica</i>	20

### 3. CONCLUSION

Herbal contaminants made from heavy toxins lead to major safety issues due to the growing popularity of the population herbs in the world. Therefore, it is important to analyze heavy metals in both source material and end products to ensure that heavy metal standards do not exceed the required limits set by regulations. In this review, several of the most widely used and sensitive methods of analyzing heavy metals in medicinal plants are discussed, including AAS,

ICP-OES, ICP-MS, XRFs. Other widely used methods, their merits, and benefits are also discussed, such as HPLC, DPP, NAA, ASV and disposable sensor applications. With each analysis process, applications for the analysis of heavy metals in herbal medicine are discussed and the method of analysis.

### CONSENT

It is not applicable.



## ETHICAL APPROVAL

It is not applicable.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

## REFERENCES

1. Yap DW, Adezrian J, Khairiah J, Ismail BS, Ahmad-Mahir. The uptake of heavy metals by paddy plants (*Oryza sativa*) in Kota Marudu, Sabah, Malaysia American-Eurasian J. Agric. & Environ. Sci. 2009; 6(1):16-19. ISSN 1818-6769
2. Naithani V, Pathak N, Chaudhary M. Evaluation of heavy metals in two major ingredients of ampucare, International Journal of Pharmaceutical Sciences and Drug Research. 2010;2(2):137-141. DOI: 10.25004
3. Chinelo A, Ogochukwu E, Adaeze N. Heavy metal contamination of herbal drugs: Implication for Human health-a review, International Journal of Tropical Disease and Health. 2014;4(10): 1044-1058. DOI: 10.9734/IJTDH/2014/11481
4. Khan SK, Shah LH, Akhtar N. Comparative assessment of heavy metals in Euphorbia helioscopiaL, Pakistani Journal of Weed Science Research. 2008;14(1-2):91-100. Available:http://dx.doi.org/10.17582/journal.sja/2017/33.2.269.275
5. Kofi A, Rita A, Isaac K. The heavy metal contents of some selected medicinal plants sampled from different geographical locations, Pharmacognosy Research. 2013;5(2):103-108. DOI: 10.4103/0974-8490.110539
6. Błażewicz AB, Wiebod TS, Swiatek RL. Determination of heavy metals in aerial part of hyssop (*Hyssopus officinalis* L.) using High performance ion chromatography with the aid of a linear and non-linear weighted least-squares regression model, Polish Journal of Environmental Science. 2007;2:191-198.
7. Street RA. Heavy metals in medicinal plant products — An African perspective, South African Journal of Botany. 2012;82(67-74):254-629. Available:http://dx.doi.org/10.1016/j.sajb.2012.07.013
8. Pethkar AG, Agerwal PK. Biosorptive removal of contaminating heavy metals from plant extracts of medicinal value, Current Science. 2001;80(9):10. Available:https://doi.org/10.1155/2018/2568038
9. Luo L, Wang B, Jiang J, Martin F, Huang Q. Heavy metal contaminations in herbal medicines: Determination, Comprehensive Risk Assessments, and Solutions, Frontier Pharmacology. 2021;11:1-14. Available:https://doi.org/10.3389/fphar.2020.59533523
10. Kam PC, Liew S. Traditional Chinese herbal medicine and anaesthesia, review article, Anaesthesia. 2002;57:1083–1089. DOI: 10.1046/j.1365-2044.2002.02823.x
11. Dghaim R, Khatib S, Husna R. Determination of heavy metals concentration in traditional herbs commonly consumed in the United Arab Emirates, Journal of Environmental and Public Health. 2015;9(3):1-6. Available:http://dx.doi.org/10.1155/2015/973878
12. Jabeen S, Shah M, Khan S, Qasim H. Determination of major and trace elements in ten important folk therapeutic plants of Haripur basin, Pakistan Journal of Medicinal Plants Research. 2010;4(7):559-566. ISSN 1996-0875.
13. Rao MA, Kaur MK, Panda P. Comparative evaluation of standardisation parameters between wedelia genus species, International Journal of Pharma Sciences and Research. 2010;1(3):207-210. ISSN: 0975-9492
14. Hussain I, Khan L. Comparative study on heavy metal contents in *Taraxacum officinale*, International Journal of Pharmacognosy and Phytochemical Research. 2010;2(1):15-18. ISSN: 0975 4873.
15. Mohammad SA, Ziad H. Essential oil content and heavy metals composition of thymus vulgaris cultivated in various climatic Regions of Jordan, International Journal of Agriculture and Biology Print. 2009;1560–8530. ISSN Online: 1814–9596 08–203/AWB/2009/11–1–59–63.
16. Palchetti IM, Minunni M, Bilia AM, Vincieri F. Disposable electrochemical sensor for rapid determination of heavy metals in herbal drugs, Journal of Pharmaceutical

- and Biomedical Analysis. 2003;32(2):251-6.  
DOI: 10.1016/s0731-7085(03)00132-8
17. Huang R, Zhi X, Zhuang Y, Rong F, Xiao R, Frank S. Direct analysis of mercury in Traditional Chinese Medicines using thermolysis coupled with online atomic absorption spectrometry. *Talanta*. 2006;68:728-734.  
DOI: 10.1016/j.talanta.2005.05.014
18. Yamashita C, Saiki M, Vaconcellos MB, Sertie JA. Characterisation of trace elements in Casearia medicinal plants by neutron activation analysis. *Applied Radiation and Isotopes*. 2005;63:841-86.  
Available: <https://doi.org/10.1016/j.apradiso.2005.05.045>
19. Gomez MR, Cerutti S. Determination of heavy metals for quality control in Argentinian herbal medicines by ETAAS and ICP-OES, *Food and Chemical Toxicology*. 2007;45:1060-1064.  
DOI: 10.1016/j.fct.2006.12.013
20. Jesus E, Simabuco S, Anjos M, Lopes R. Synchrotron radiation X-ray fluorescence analysis of trace elements in Nerium Oleander or pollution monitoring, *Spectrochimica Acta Part B*. 2000;55:1181-1187.  
DOI: 10.1016/S0584-8547(00)00182-8
21. Lawrence SL, Drake R, Gary DR. Affinity distributions of lead ion binding to an immobilised biomaterial derived from cultured cells of *Datura Innoxia*, *Advances in Environmental Research*. 2002;32(10):6523-532.  
Available: <https://doi.org/10.1021/es970843z>
22. Mamani M, Aleixo M, Abrue M, Rath S. Simultaneous determination of cadmium and lead in medicinal plants by anodic stripping voltammetry, *Journal of Pharmaceutical and Biomedical Analysis*. 2003;37(4):709-713.  
DOI: 10.1016/j.jpba.2004.11.049
23. Iman AS, Sami AE, Neptune S. Assesment of lead in cosmetic products, *Regulatory toxicology and Pharmacology*. 2009;54(2):105-113.  
DOI: 10.1016/j.yrtph.2009.02.005
24. Xudong Y, Robert L, Zhiqian W. Analytical methods for heavy metals in herbal medicines, *Phytochemical Analysis*. 2014,2011;22:189-198.  
DOI: 10.1002/pca.1287
25. Yuan X, Koh H, Chui W. The analysis of heavy metals in Chinese herbal medicine by flow injection-mercury hydride system and graphite furnace atomic absorption spectrometry, *Phytochemical Analysis*. 2009;20(4):293-297.  
DOI: 10.1002/pca.1287
26. Chuang C, Chen K, Huang L, Lee P, Lin H. Determination of trace elements in some natural drugs by atomic absorption spectrometry, *Biological Trace Element Research*. 2000;76(3):235-244.  
DOI: 10.1385/bter:76:3:235
27. Yang L, Gao L, Zhang D. Speciation analysis of arsenic in traditional Chinese medicines by hydride generation-atomic fluorescence spectrometry. *Analytical Sciences*. 2003;19(6):897-902.  
Available: <https://doi.org/10.2116/analsci.19.897>
28. Taijun H, Zhengxing Z, Shanshi D, Yu Z. The determination of trace levels of selenium contained in Chinese herbal drugs by differential pulse polarography. *Talanta*. 1992;39(10):1277-1280.  
DOI: 10.1016/0039-9140(92)80237-8

© 2021 Shelar et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

*Peer-review history:*

*The peer review history for this paper can be accessed here:  
<http://www.sdiarticle4.com/review-history/68200>*