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Review

The Content of Heavy Metals in Medicinal Plants in Various Environmental Conditions: A Review

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Abstract: Nowadays people are becoming poisoned through the consumption of herbal remedies that comprise heavy metals (HMs) worldwide. It is possible for HMs to be present in pharmaceutical herb materials coming from anthropogenic activities like agriculture, industrial waste, and natural sources. In various ethnic groups, there is evidence that contaminants were purposefully added in the belief that they had some sort of therapeutic benefit. HM toxicity of medicinal plant products has been linked to a wide range of adverse health effects, causing dysfunction of the liver, kidney, and heart, and even death. Natural plant-based products established around the world have progressed to the point that they now combine a variety of synthetic products for their purported medical benefits. This assessment focuses on the impacts of HMs on plants, sources of HMs, herbal sample collection, and identification techniques, especially in medicinal plant samples. At the same time, it focuses on the sociocultural applications of HMs as well as the dangers associated with their usage in conventional therapies. It is necessary to implement appropriate regulation and monitoring systems for natural supplements due to the prevalence of hazardous HMs.

Keywords: heavy metals (HMs); herbal plants; atomic absorption spectroscopy; X-ray florescence; neutron activation analysis; anodic stripping voltammetry

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1. Introduction

Currently, despite significant advances in the field of chemical synthesis, the interest of scientific medicine in herbal medicines remains high. Every third medicinal product on the world market is made of plant-based raw materials [1]. In some pharmaceutical groups, the share of herbal medicinal products is even higher; for example, about 70% of drugs used to treat cardiovascular diseases are plant-based [2].

In the Russian Federation, about 40% of the total number of medicinal products used in practical medicine are herbal medicinal products [3]. Their advantages over synthetic drugs are a wide spectrum of action, relatively low cost, high bioavailability, low toxicity when used rationally, lower likelihood of side effects, and the possibility of long-term use [1,4]. At present, interest in the study of medicinal herbs continues to increase. This is reflected in the number of relevant publications, which more than tripled from 2008 to 2018 (from 4686 to 14,884 publications) [5].

According to the World Health Organization (WHO), the share of herbal medicines will reach 60% in the near future [4]. An important problem that limits the possibilities of using medicinal herbs in medicine is the continuing reduction of territories that are not exposed to anthropogenic pressure. In this regard, it is not always possible to harvest medicinal plant materials only in environmentally clean areas. Therefore, one of the urgent issues in modern pharmacy is to analyze the possibility of using plants growing under technogenic pressure for medicinal purposes. This problem is of particular significance in Russia, as a major share of medicinal plant materials is harvested in the European part of the country, which is populated and industrialized [6].

Medicinal plant materials harvested under such conditions can be a source of various toxicants entering the human body, primarily heavy metals (HMs), as well as pesticides, nitrates, and other xenobiotics, and damage human health [7,8]. A good example of this is the study by Buettner et al. [9] that found a 10% increase in lead concentration in the blood of females who took herbal dietary supplements for a month compared the control group. Lead concentration in the blood of females who used Ayurvedic plants and plants of traditional Chinese medicine was more than 24% higher than that in the control group [9]. Similar results were obtained in epidemiological studies conducted in Taiwan [10]. Therefore, the present study aimed at systematizing and analyzing information on the content of HMs in medicinal plant materials and herbal medicinal products.

2. Heavy Metals, Medicinal Herbs, and Regulatory Documents

The common HMs in the environment are lead, cadmium, and mercury, and their major sources are vehicles, industrial and thermal power plants, waste incinerators, and agricultural production [11–14]. Plants, especially trees, act as a barrier to the spread of HMs. A comparative analysis of approaches to regulation of HMs in medicinal plant materials and herbal medicinal products adopted in Russia, Europe, the United States, and Asian countries were carried out. For this purpose, the current editions of the Russian, European, American, and Asian pharmacopoeias, as well as international standards, have been studied (Table 1).

According to the current *State Pharmacopoeia of the Russian Federation* (14th edition), the content of lead in medicinal plant materials and herbal medicinal products should not exceed 6.0 mg/kg; for cadmium—1.0 mg/kg; for mercury—0.1 mg/kg; and for arsenic—0.5 mg/kg [15]. The content limits of HMs in medicinal plant materials are similar to those for dry herbal dietary supplements and are less stringent than similar requirements for fruits, berries, and drinks (Table 1). A comparative analysis of the regulatory documentation in various countries has found that the requirements for the environmental safety of medicinal plant materials and herbal medicinal products differ significantly.

Table 1. Permissible concentrations of heavy metals according to regulatory documents in different countries.

Food Items and Medicinal Plant Materials	Regulatory Document	Permissible Concentrations (mg/kg)			
		Pb	**Cd**	**Hg**	**As**
Medicinal plant materials and herbal medicinal products	Russian pharmacopoeia [15]	6.0	1.0	0.1	0.5 (Laminaria 90)
Herbal medicines, medicinal herbs	European pharmacopoeia [16]	5.0	1.0	0.1	There are no general regulations (Laminaria 90)
Herbal medicines	United States pharmacopeia [17]	5.0	0.5	1.0 (total) methyl mercury 0.2	Non-organic 2.0
Medicinal plant materials and herbal medicinal products	Eurasian Economic Union pharmacopeia [18,19]	6.0	1.0	0.1	0.5
Medicinal plant materials (underground organs)	Pharmacopoeia of the People's Republic of China [20]	5.0	0.3	0.2	2.0
Herbs consumed by humans	World Health Organization [21]	10.0	0.3	–	1.0

Traditional Chinese herbal medicines	ISO international standards [7]	10.0	2.0	3.0	4.0
Medicinal herbal preparations	Ayurvedic pharmacopoeia [22]	10.0	0.3	1.0	3.0
Medicinal herbal preparations	Thai pharmacopoeia [7]	10.0	0.3	–	4.0
Medicinal plant materials	Korean pharmacopoeia [7]	5.0	0.3	0.2	3.0
Traditional medicine products	Singapore Health Sciences Authority [23]	20.0	–	0.5	5.0

The Russian standard for lead is lower than that recommended by World Health Organization and the International Organization for Standardization (ISO) (10 mg/kg). Nevertheless, it is slightly higher than the corresponding standard set by the European, American, and Chinese pharmacopoeias (5 mg/kg). For cadmium, the standard established by the Russian pharmacopoeia is similar to the European one and is more than three times higher than those recommended by WHO and many Asian countries (0.3 mg/kg). Interestingly, in the recent edition (2020) of the Chinese pharmacopoeia, the maximum permissible concentration (MPC) for cadmium was changed from 0.3 mg/kg to 1.0 mg/kg [7,23].

This is an illustrative example of a trade-off between safety for human health and the need to use medicinal herbs that grow in a particular region.

The WHO, Russia, and a number of countries have similar requirements for mercury concentration; however, in the Chinese and Indian pharmacopoeias, the MPC is 10 times higher, while the American pharmacopoeia separately regulates the content of methylmercury. The Russian pharmacopoeia imposes the most stringent requirements for arsenic concentrations; the regulatory documents of other countries set standards that exceed the Russian ones by 2–8 times. When comparing the methods for analyzing medicinal plant materials for HMs, it has been revealed that they do not always correspond to each other, which may explain the difference in maximum permissible concentration (MPC) values. Thus, in foreign pharmacopoeias, the arsenic concentration in medicinal plant materials and herbal medicinal products is determined by decomposition in closed vessels, which eliminates the loss of the element at the stage of sample preparation.

There are a number of imperfections in the methods for determining HMs given in the current *State Pharmacopoeia of the Russian Federation* [15]. The incorrectness of using standard samples to analyze medicinal plant materials and herbal medicinal products, in which HMs are found the form of inorganic salts and are not associated with organic compounds, was noted [24]. According to the authors, it is advisable to use standard samples of plant materials certified for the content of HMs, as the organic matrix has a significant influence on measurement results. In addition to the listed metals, the concentration of copper is regulated in China and Singapore, and the content of nickel is regulated in European countries. The introduction of MPCs for these metals, as well as zinc, iron, and manganese, possibly taking into account the regional characteristics of industrial activities, is also a pressing issue in Russian Federation. Another aspect to consider is the part of the plant used in pharmacy. The *State Pharmacopoeia of the Russian Federation* [15] imposes uniform requirements on the content of toxicants for all types of plant materials. In the Chinese pharmacopoeia [20], the standards for HM contents in underground organs are set separately, which is logical, because when growing on polluted soil, many species are able to limit the supply of xenobiotics to the aerial part, especially to the generative organs.

There is large number of publications that analyzes the regional features of HMs' accumulation in medicinal herbs [6,24–32]. For example, the environmental purity of *Cichorium intybus* L. in the Trans-Ural region of the Republic of Bashkortostan (Russia) has been assessed according to the MPCs of chemical elements in feed for farm animals and feed additives (5 mg/kg Pb, 0.3 mg/kg Cd) [31]. The authors have concluded that it is inappropriate to harvest the raw material under study as a medicinal plant material due to the excess of cadmium concentration by 3.0–6.5 times. However, by the current MPC for medicinal plant materials safety assessment, the results would have been different. Although the content of HMs in plants depends on the intensity of contamination in the harvesting area, a general conclusion about the unfavorable environmental situation is not enough to assess the possibility of growing medicinal herbs in a particular area. The safety of 51 samples of *Tanacetum vulgare* L. flowers, harvested in urban and agroecosystems of the Voronezh region, was established with respect to the content of HMs and arsenic [6]. The roots of *Taraxacum officinale* F.H. Wigg. plants growing in the Voronezh region near roads and railways were also found to be safe, while in the samples collected near a thermal power plant and a chemical enterprise, an excess of arsenic was recorded [6]. The aboveground parts of *Artemisia frigida* Willd. and *Artemisia jacutica* Drob. growing in the Republic of Buryatia, as well as *A. frigida* growing in Mongolia, had lead and cadmium concentrations within the normal range (except for the year in which forest fires occurred) [33]. It was found that *Plantago major* L. leaves harvested in the park area of the central part of the city of Kursk (Russia) were environmentally safe, while in the industrial area the concentration of lead in these medicinal plant materials was 20.5 times the MPC [34]. The content of HMs in medicinal plant materials growing in the Grodno region (in the Republic of Belarus) did not exceed the MPC [29]. This applied to both wild (*Vaccinium vitis-idaea* L., *Vaccinium myrtillus* L., *Elytrigia repens* (L.) Nevski, *Artemisia absinthium* L., *Hypericum maculatum* Crantz, *Angelica sylvestris* L.) and cultivated (*Calendula officinalis* L., *Chamomilla recutita* (L.) Rauschert, *Aesculus hippocastanum* L., *Paeonia anomala* L.) plants.

In Russia, wild-growing medicinal herbs are mainly used in pharmacy, in contrast to Europe and Asia. A significant number of studies were carried out in China. This can be attributed to the popularity of traditional medicine in the country: medicinal herbs were used to treat as many as 85.2% of COVID-19 (60,107 cases), yielding positive results at all stages of the disease [35]. In 2021, the results of a large-scale study on the analysis of HM contents in plant raw materials purchased at the major medicinal plant markets in China were published (1773 medicinal plant material samples were analyzed). In 541 samples, the content of HMs exceeded the MPC, of which 75 samples demonstrated excess content of two metals, 24 samples demonstrated excess content of three HMs, and 9 samples demonstrated excess content of four HMs. The highest concentration of copper was found in *Schisandra chinensis* (Turcz.) Baill. plant material (34.01 mg/kg), the highest arsenic concentration in *Plantago asiatica* L. (14.53 mg/kg), the highest cadmium concentration in *Curcuma longa* L. (6.20 mg/kg), the highest mercury concentration in *Chrysanthemum indicum* L. (8.69 mg/kg), and the highest lead concentration in *Tetradium ruticarpum* (A.Juss.) T.G.Hartley (50.11 mg/kg) [35].

A similar study was conducted in the United Arab Emirates [36]. A total of 81 medicinal plant samples (*Petroselinum crispum*, *Ocimum basilicum*, *Salvia officinalis*, *Origanum vulgare*, *Mentha spicata*, *Thymus vulgaris* and *Matricaria chamomilla*) purchased from Dubai markets were analyzed. The authors claim that 29% of the samples exceeded the MPC for cadmium compared to the WHO standard (0.3 mg/kg). If the assessment had been carried out according to the Russian standards (1.0 mg/kg), the concentration of cadmium would have exceeded the MPC only in the *Ocimum basilicum* plant. The results for lead were similar: its concentration in the analyzed samples varied from less than 1.0 to 23.52 mg/kg, and in 64% of the samples it exceeded the MPC established by the WHO (10 mg/kg), while in Russia a more stringent lead concentration standard of 6.0 mg/kg was adopted.

A number of studies have focused on the analysis of HM contents in pharmacy medicinal plant materials. The average contents of lead, cadmium, zinc, copper, and nickel in *Hypericum perforatum* L. and *Achillea millefolium* L. harvested in the vicinity of Dubna turned out to be significantly lower than those for samples purchased in the pharmacy network in the same city [37]. Similar results were obtained in India for various species of *Berberis* L.: market samples were found to be more contaminated with HMs (at a level exceeding the MPCs set by the WHO) [38]. The study of 26 samples of *Ginkgo biloba* L.-based products purchased in pharmacies in the capital of Mexico found that the contents of lead, arsenic, and cadmium in dietary supplements and medicinal plant materials were higher than in herbal preparations, and in some cases the concentrations of lead and arsenic exceeded the recommended daily allowances (10 µg/day) [39].

When assessing the environmental safety of medicinal plant materials, much attention was given to cadmium and lead determination, while mercury and arsenic were much less studied, which was due to the labor-intensive nature of the methods for their determination. However, even if a medicinal plant material contains metals in quantities not exceeding the MPCs, their presence can pose a potential threat to health due to their ability to accumulate, which can be observed in cases of long-term use of herbal decoctions, infusions, and teas in order to prevent diseases. This reality necessitates long-term studies to track the risk. Numerous works showed the content of HMs in leaves under conditions of pollution, whereas other types of plant materials (flowers, fruits, underground organs, bark) are often used to manufacture medicines, and different organs of the same plants are known to respond unequally to the effects of toxicants [14]. This makes it expedient to conduct a comparative analysis of the metal content in different organs of each type of HM.

The Russian pharmacopeia provides a single value on the content of metals in medicinal plant materials and herbal medicinal products that does not take into account the type of extractant, the dosage form, or production technology peculiarities. The standards for the total content of HMs in tinctures (not more than 0.001%) and extracts (not more than 0.01%) are set separately [15]. The colorimetric method is used, i.e., the whole range of HMs, including essential ones, is determined. In Russia, there are many fewer studies of HM concentrations in various dosage forms and the consequences of their impact on the human body than studies of their contents in plants. The studies of pharmaceutical herbal medicines do not provide information on the concentrations of toxicants in the raw materials the herbal medicinal products are made of. This does not allow tracing metals' migration from the plant to the medicinal product.

When studying the safety of medicinal herbs, the transfer of HMs from the plant material to various dosage forms is of great importance; the literature data on this issue are contradictory. In the case of wild *Rosa* spp., *Vaccinium subg. Oxycoccus*, *Glycyrrhiza glabra*, *Zingiber officinale*, and *Aronia melanocarpa*, it was shown that 15–96% of the HMs was transferred to the extract, the maximum transition being recorded for mercury (from 60 to 96%), and the minimum for arsenic (from 24 to 37%) [3]. Potassium, magnesium, sodium, strontium, cadmium, and nickel were found (the leaves of *Plantago major* L. were taken as an example) to transfer to decoctions to a large extent; copper, lead, and iron were characterized by a low degree of extraction [40]. When analyzing raw plant materials representing 16 species of various morphological groups and their herbal preparations, the transition of HMs into tinctures and liquid extracts (alcohol extracts) was found to be significantly lower compared to infusions and decoctions (water extracts) [41]. In 197 samples of herbal medicinal products obtained from various morphological parts of plants (powders, collections, liquid, and solid extracts) lead, cadmium, mercury, and arsenic showed low degrees of extraction from plant material when obtaining extracts and tinctures [24]. *Hypericum perforatum* L. is a super-concentrator of cadmium; however, the maximum extraction into decoctions did not exceed 23%, and 5% of its content in the herb into tinctures, which was due to the formation of physiologically inactive complexes, with lead extraction being 45–70% in decoctions and 30–60% in tinctures [26]. The minimum extractability of HMs, regardless of the extractant, was observed in the dustiest plants (with a higher content of total ash and residue insoluble in 10% HCl); apparently, some HMs in strongly bound forms were found in fine soil particles deposited on the surface of plants [26].

When assessing environmental safety, the dosage and duration of particular drugs' use are important. To this end, international publications calculated indicators such as health risk index, target hazard quotient, hazard index, cancer risk, non-carcinogenic risk assessment, and average daily intake [27,28,32,42]. Russian researchers were most often limited to comparing the HMs' content with the requirements of regulatory documentation. The environmental safety and pharmaceutical value of MHs growing in Donbass under various levels of anthropogenic pressure were analyzed [30]. It was revealed that the concentrations of cadmium, lead, and mercury in the medicinal raw materials of *Sorbus aucuparia* L., *Sorbus intermedia* (Ehrh.) Pers, *Rosa lupulina* Dubovik, *Crataegus fallacina* Klokov, and *Sambucus nigra* L., growing in the urban environment of Donbass, did not exceed the MPCs for medicinal plant materials, even for plants of first-row planting along urban highways with heavy traffic, and the contents of active substances met the requirements of regulatory documentation.

In places where plant material was harvested, soil samples were also collected, the mobile (the most accessible to plants) forms of HMs were determined, and the coefficients of biological accumulation (CBA) equal to the ratio of the toxicant content in the plant to that in the soil were calculated [11]. This made it possible to reveal disproportions between HM contents and CBAs, with the barrier function of the plant root system and the species specificity of plants in relation to specific metals being of major importance. It was found that the CBAs of cadmium and lead for most of the studied fruits and flowers under pollution conditions decreased, indicating the ability of plants to limit metal intake into the generative organs. The content of mercury in all analyzed soil samples was minimal; however, higher concentrations of mercury were found in plants, indicating its aerotechnogenic intake into aboveground organs. Nevertheless, when studying the leaves of *Cotinus coggygria* Scop. harvested in Donbass under the same conditions, completely different results were obtained [30]. The content of lead in the leaves of *C. coggygria* from the control (conditionally ecologically clean) territory was minimal, while in the urbanized environment it was 54 mg/kg, which was nine times higher than the MPC. It should be noted that CBA for lead in *C. coggygria* leaves under conditions of severe technogenic pollution was 19.3, which indicated its vigorous accumulation. The increase in lead concentration in the leaves of *C. coggygria* was more pronounced than the increase in its content in the soil. Thus, based on the results obtained in the study of several plant species, it is impossible to make general conclusions about the suitability of a particular area for harvesting medicinal plant materials. It is necessary to continue studying the characteristics of each individual type of MH in the conditions of a particular urbanized region.

HMs affect the quality of medicinal plant materials, thus indirectly causing a change in the contents of active substances. The concentration of biologically active substances in plants varies species-specifically, largely depending on how much one or another group of substances contributed to the antioxidant system of a particular species. Under conditions of technogenic pressure in most of the studied species, increases in the concentrations of hydroxycinnamic acids, anthocyanins, flavonoids, and carotenoids in contrast to decreases in the levels of tannins, free organic acids, and sugars has been revealed.

In other words, there is a decrease in the content of primary metabolites (which may indicate inhibition of their biosynthesis and/or intensive consumption) and an increase in the concentration of secondary metabolites known for high antioxidant activity and the ability to chelate HMs. The concentrations of those groups of phenolic compounds that are most effective for adapting a particular species to the technogenic environment (and probably make a significant contribution to its antioxidant system) increase in contrast to decreases in the contents of other phenolic compounds, which is due to the common way of their biosynthesis. In reference to the foregoing, when studying medicinal herbs growing in an anthropogenically transformed environment, it is necessary to study their pharmaceutical value along with the assessment of environmental safety.

3. Impact of Heavy Metal on Herbal Plants

Soils have become a significant source of HM pollution and possess a high conversion of ion capability. Certain important HMs become crucial elements which are required in extremely low quantities for proper development of plant [43]. Such HMs play a lead role in physiochemical processes in plants. Plant roots absorbs HMs from soil by the phenomenon of diffusion [44]. These HMs dissolve into their complex structures around the surface of root tissues and are taken up through the apoplast and symplast mechanisms

[45]. In contrast, Fe is a biological molecule that is rapidly reduced and oxidized in a wide range of biological reactions.

It is also a crucial mediator for metabolic catalysts that participate in respiration, photosynthesis, and nutrient absorption [46]. At the cellular level, several unique metal transporters like IRT1(Fe, Zn, Mn, and Cd transport), ZIP (Zn transport), and NRAMP (Ni transport) are found on the biological membrane. Several HMs like Co, Cu, Fe, Mn, Ni, and Zn in small amounts are vital for plants. These HMs are necessary for the induction of morphological and metabolic process, the regulation of photosynthesis, the synthesis of chlorophyll, a high rate of the production of bioactive compounds, transpiration, protection of DNA, distraction of ROS, and enhancing nitrogen fixation in plants [47]. However, a high amount of HMs causes lipid peroxidation, ROS generation, and DNA damage. Several studies have found that higher concentrations of Zn have a negative impact on plant development and metabolism [48]. Additionally, according to Arora et al. [49], an increase in plant Fe^{2+} levels triggers the formation of free radicals that destroy protein molecules, DNA, and membranes (Figure 1).

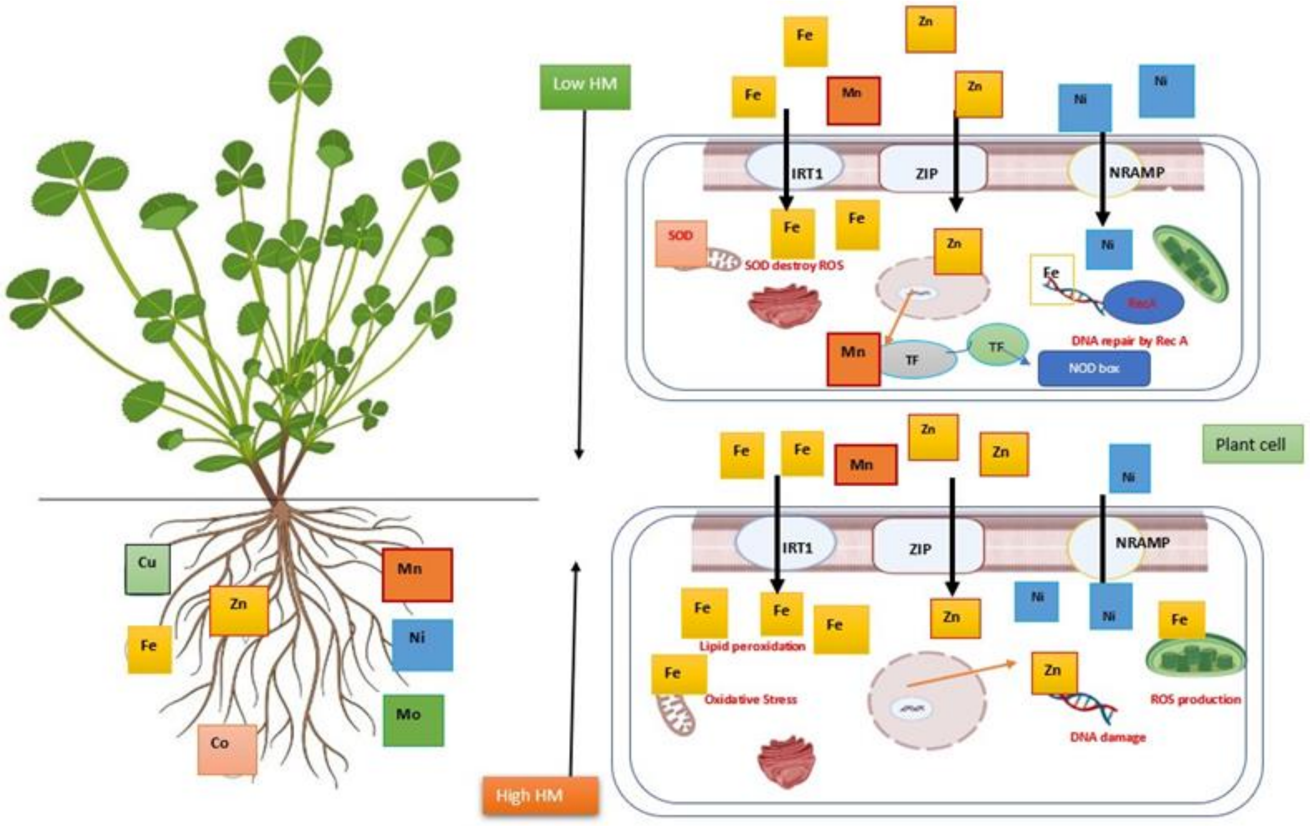

Figure 1. Impact of heavy metals' contribution to the creation of proteins, nucleic acids, photosynthesis pigments, and cell membrane function and structure at low concentrations [50]. Mn enhances antioxidant capacity [51], while Fe increases N_2-fixation and DNA repair [52]. At high concentrations, it causes conversion of numerous significant functional groups, lipid peroxidation (LPO), mitochondrial dysfunction, ROS production, and biochemical disruption via changing enzymatic activity [53,54].

The major causes of HM pollution are anthropogenic activities like resource extraction, agricultural production, construction, industrial activities, inadequate garbage management processes, and excessive use of agrochemicals (Figure 2). HMs enter the environment through these activities and accumulate in living systems. These HMs are toxic in nature and cause several chronic illnesses like weakened immunity, cardiac instability, neonatal disorders, psychological disorders, and sensorimotor behavior issues [55]. Several HMs like Pb, As, Hg, and Cd are not required by plants or the human body, and they also cause a variety of health complications associated with the brain, liver, lungs, heart, kidneys, and nervous system, including hypertension, abdominal pain, rashes, intestinal ulcers, and other symptoms linked to various cancer types [56,57]. Although copper is a major element in several enzymatic reactions, consuming excess amounts of it can lead to internal organ injury but also induce skin infections, elevated lung tissue inflammation, abdominal discomfort, nausea, vomiting, and diarrhea [58].

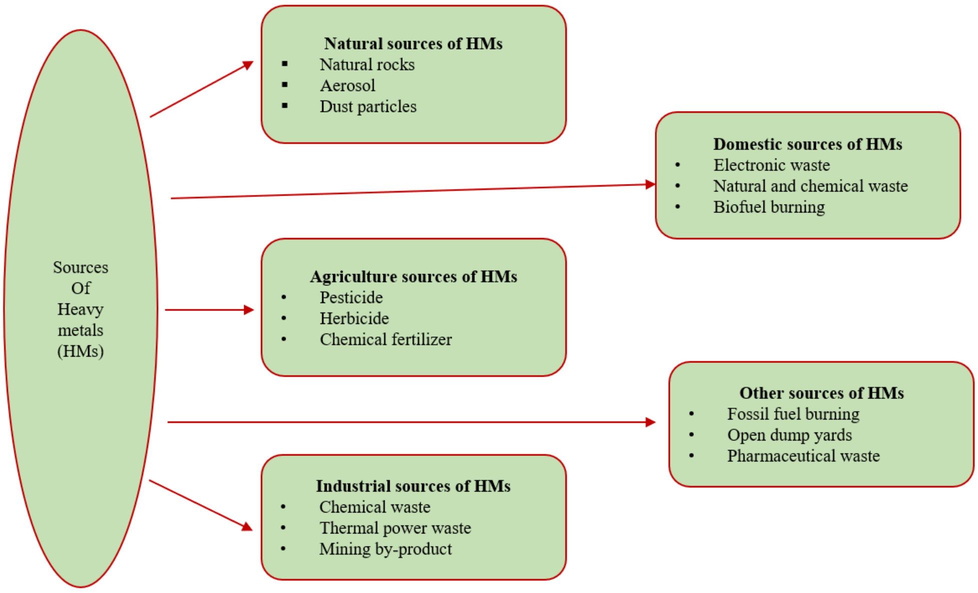

Figure 2. Various sources of heavy metals.

As they are known to cause harm, it is critical and urgent to conduct a thorough investigation into the dangers of metal contamination in medicinal herbs. As a result of the survey's exact methodology, it is now clear that more screening and dosing frequency guidance for herbal medicines is required. This research explored pollutant levels and their risks, particularly when they are present in herbal remedies. The results serve as a groundwork for future research into preventative methods, uniform guidelines, and exogenous contaminants. Research studies conducted have led to suggestions that can rapidly lower or completely remove HM contents in active pharmaceutical ingredients.

4. Herbal Sample Preparation

The processing of samples is an essential step throughout the examination of HM components. The choice of an appropriate technique for sample processing is one of the most critical factors in determining the precision of the measurement. The perfect method for preparing samples is one that does not produce any pollutants, does have a high response time, is easy to use, offers enhanced exactness, and works quickly. Even during the process of sample pre-treatment, there is an assortment of variables that need to be carefully considered. Some of these variables include the physical and chemical features of the matrix, the number of samples, the state of the samples, the composition of the compound that needs to be examined, as well as the estimated accuracy. There are three basic methods for sample processing: wet digestion, the ashing method, and direct injection (Figure 3) [59].

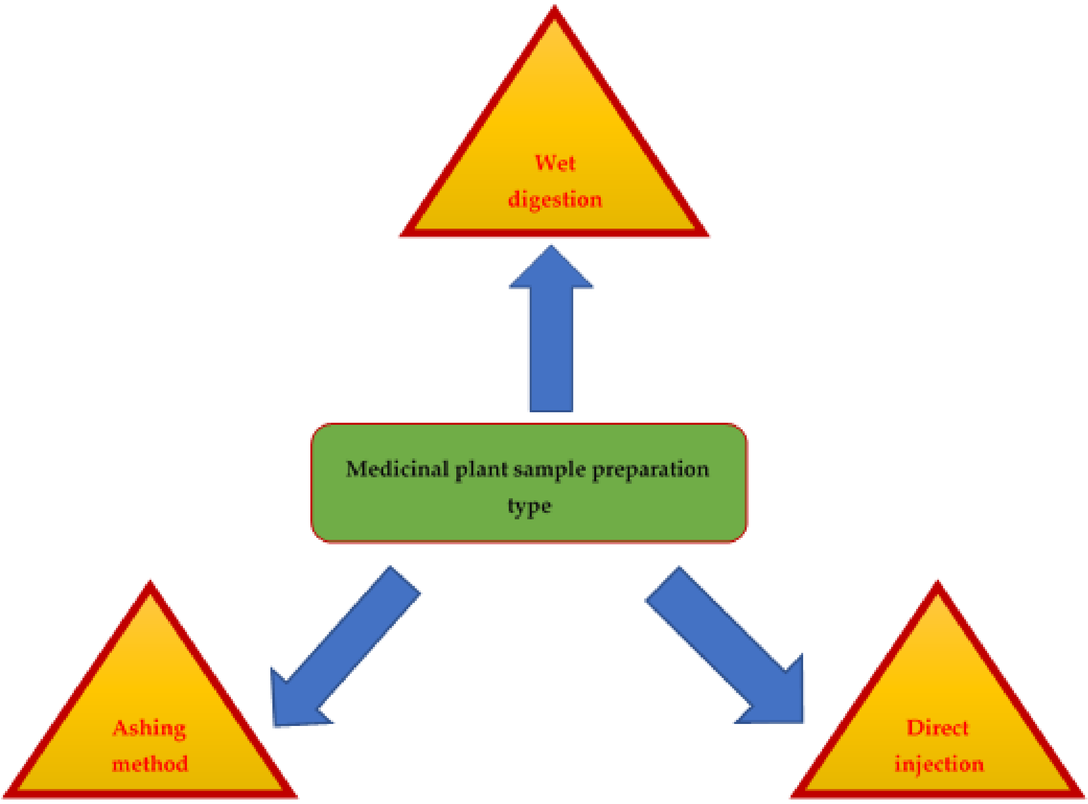

Figure 3. Methods of herbal sample preparation for heavy metal detection.

5. Detection Method of the Heavy Metals in Medicinal Plants

There are several techniques like inductively coupled plasma mass spectrometry (ICPMS), atomic emission spectroscopy (AES), X-ray fluorescence (XRF), neutron activation analysis (NAA), anodic stripping voltammetry (ASV), thermolysis-coupled atomic absorption spectroscopy (TCAS), atomic absorption spectrometry (AAS), and graphite furnace atomic absorption spectrometry (GFAAS) which are used for the quantification of the HMs in herbal plant samples (Figure 4).

5.1. ICPMS

ICPMS detects the HMs on the basis of m/z ratio measurement. As an atomization source for atomic spectroscopy, it is significantly more difficult to use than a graphite furnace due to its high degree of atomization in argon plasma at 7000 K. This method possesses a maximum output capacity of multi-element detection ability in a broad range. ICPMS and AES can identify numerous metallic pollutants in an extra-specific way and can quantify an impurity with a significantly greater degree of sensitivity. The typical detection limits in a solvent are between 0.01 and 1 ppm. The mass of the study sample can be as low as 10 mg. ICPMS assessments are currently being performed and have a solid foundation. It is cost-effective while also producing superior outcomes [60].

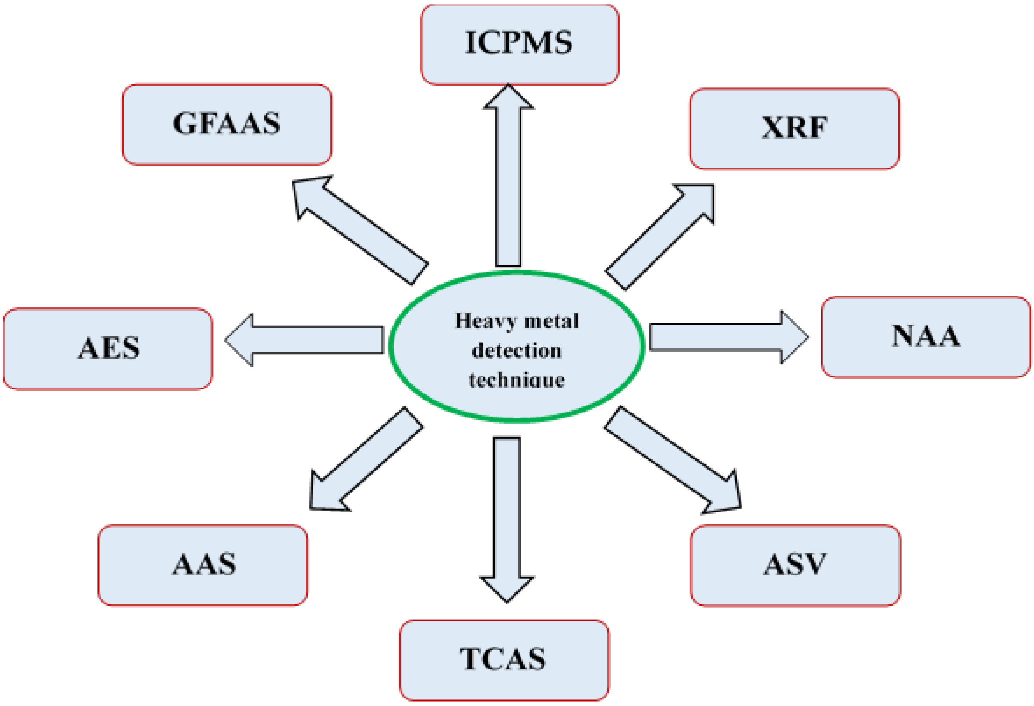

Figure 4. Techniques of heavy metal detection in herbal samples.

5.2. AES

The majority of the time, this method is combined with optical emission spectroscopy. The material is made to become stimulated through the absorption of either a thermal or electrical charge, and then the emission that the agitated material gives off is investigated. Additionally, this method is connected to a solid; however, fluids are often the samples that are examined. It is able to analyze over 70 different elements at dosages as low as one part per million (ppm) [61].

5.3. XRF

When a specimen comes into contact with high-energy X-rays or gamma rays, it emits "secondary" (or fluorescent) X-rays with a unique spectrum. This technique is used in geochemical analyses, toxicology, as well as paleontology. It is also adopted in the analysis of elements and chemicals, specifically in the study of metallic materials, glass, ceramic materials, and construction materials [62].

5.4. NAA

The NAA method is used for determination of the heavy metals present in an herbal material by analyzing the energy and intensity of rays (mostly gamma rays) generated through immediate radiation or radionuclide decay. This method makes use of neutron bombardment [63]. NAA need not require material processing beforehand. Because it is an excitation research methodology, it involves bombarding atoms as well as neutrons produced by reactors, accelerators, or isotope neutron sources; as a result, it is ideal for the qualitative and quantitative measurement of the compositions and occurrences of various elements [63]. In addition to this, NAA is sensitive to a wide variety of elements, and this sensitivity enables it to precisely estimate the levels of trace elements present in a wide variety of samples, including MPs. The use of NAA is important for the rapid identification of the various components of MPs.

5.5. ASV

By using differential pulse anodic stripping, it is a straightforward procedure to simultaneously determine the contents of heavy metals in pharmaceutical herbs. The specimen is prepared through the dry ashing approach, in which 1 g of fine powdered plant matter is kept at 5000 °C for 2.5 h. A hanging mercury electrode and platinum wire are employed as the functioning and countering electrodes in this straightforward voltametric device. These potentials are assessed in relation to a reference electrode made of Ag/Ag Cl and KCl. Prior to the analysis, pure N_2 is bubbled throughout the specimen for 400 s. The ASV approach is more sensitive. This technique yields accurate, repeatable outcomes. It has several drawbacks, like fouling, and it is time-consuming. Its use is constrained, as electrodes (E + 0.4 V) of As and Hg are readily oxidized [64].

5.6. TCAS

According to this procedure, plant materials or herbal products are heated. When the herbal sample is heated to a high temperature, the atomic absorption (AA) detectors are used to analyze HM vapors which have been thermally liberated from molecular HMs of the herbal sample. The procedure does not require any pre-processing of herbal samples. This procedure requires less time than other ones (four minutes every cycle). There is no requirement for calibrating, allowing for continuous testing to be performed. It has a few limitations, such as it only being able to identify Hg. HM level assessments cannot to be performed simultaneously [65].

5.7. AAS

AAS is a common technique of spectrum analysis that is used for both quantitative and qualitative analyses of the HMs present in MPs. Specific analysis of a wide spectrum of elements like Cd, Ni, Pb, and Zn in either solid or liquid specimens is possible with the help of such a technique [66]. In AAS, components such as a beam of light, atomizer, splitter, and detection system are implemented [67]. Although significant strides have been made in the advancement of technology for the identification of heavy metals, AAS is still widely used.

5.8. GFAAS

In GFAAS, an herbal sample is first introduced directly to the graphite tubes in the equipment known as a graphite furnaces. Here only a small portion of the nebulized vapor actually makes it to the flame after the atomized sample has quickly passed through a straightforward surface. Therefore, in order to boost the analytic sensitivity, advanced models employing graphite furnaces for electrical vaporization were utilized. The residual atomic samples of herbs are again employed by GFAAS, which detects the presence of lead and cadmium and the concentrations of copper, arsenic, and mercury in the herbal materials after the solvent and matrix materials have been removed using heat [68].

6. Conclusions

Herbal medicines are an important part of the modern pharmaceutical market worldwide. In order to expand the possible harvesting areas for medicinal plant materials, it must be taken into account that contamination of medicinal plant materials and herbal preparations can occur during storage and manipulation, so safety must be monitored throughout the entire manufacturing process, from harvesting to market. Studies by scientists from different countries show the potential use of plants growing under conditions of technogenic pressure for pharmaceutical purposes. However, it is necessary to continue fundamental and applied research of medicinal plants growing under varying intensities of anthropogenic pressure, taking into account regional characteristics. To date, the problem of setting standards for HM contents in medicinal plant materials in the territory of Russia has not been completely resolved. It is necessary to develop standards for the contents of toxicants in various medicinal products, taking into account the peculiarities of the manufacturing technology, as well as the permissible concentrations of other metals such as zinc, copper, nickel, manganese, and iron in medicinal plant materials and herbal medicinal products. The use of indicators that take into account the dose and frequency of use in assessing the environmental purity of plant raw materials or plant-based preparations will reduce the risk of excessive intake of HMs into the human body.

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