Journal of Molecular and Pharmaceutical Sciences Vol. 01, N°02 (02)

JMPS

Heavy metal contamination of medicinal plants

S. Derbal [1],*

[1] Pharmaceutical Sciences Research Center (CRSP), Constantine 25000, Algeria

Abstract. Medicinal plants are widely used in traditional medicine and in the pharmaceutical industry. These medicinal plants and their products can be contaminated by several contaminants with harmful effects on the consumer health. Heavy metals are among the most dangerous contaminants due to their toxic potential. Therefore, it is necessary to control the quality of these herbal products regarding heavy metal contamination in order to ensure the consumers safety. This review attempts to describe certain generalities on the contamination of medicinal plants by heavy metals, the admissible limits of this contamination established by the World Health Organization, the toxic effects of heavy metals on the human organism and finally the methods of preventing contamination and treatment of heavy metal poisoning.

Keywords: Medicinal plants, Contamination, Heavy Metals, Toxicity, Prevention

1 Introduction

Medicinal plants are commonly used as raw materials for self-administered pharmaceutical remedies and as complementary products. The plant parts used include seeds, berries, roots, rhizomes, leaves, bark and flowers. Thus, phytopharmaceutical products have been widely used since time immemorial side effects [1]. The expansion of the phytopharmaceutical industry is a direct indication of the growing importance of medicinal plants, of which 25% of modern drugs have been made from plants and their chemical analogues are now being synthesized and used in modern medicine [2]. Plants can accumulate trace elements, especially heavy metals, in and on their tissues due to their ability to tolerate potentially toxic ions in the environment [3]. Heavy metals are metals and metalloids with an atomic density greater than 6 g/cm3 such as cadmium (Cd), chromium (Cr), copper (Cu), mercury (Hg), nickel (Ni), lead (Pb) and zinc (Zn).

Factors that influence the accumulation and concentrations of heavy metals in a medicinal plant include atmospheric deposition, the bioavailability of heavy metals in the soil, the nature of the soil where the plant is grown, and the conditions of harvest and manufacture [4]. The concentration of these metals

* Corresponding author
Received July 03, 2022; accepted August 19, 2022

in plants can influence the composition and pharmacological activity of herbal medicines. Thus, these heavy metals can bind with pharmacologically active substances of herbal drugs can also influence the pharmacokinetics of the drug. The consumption of herbal drugs obtained from polluted sources will lead to serious health risks, especially if it results in exposure to Cd, Pb, Hg and As [5]. Therefore, the selection and quality assessment of plant material should be standardized.

When accumulated at lower concentrations, heavy metals have some health benefits. However, at higher levels they can be toxic and pose health risks [6]. Consumption of contaminated herbal products can lead to chronic accumulation of these metals in human organs which causes internal imbalances within the body [7]. In fact, heavy metals accumulated in tissues disrupt several metabolic processes by modifying the pro-oxidant/antioxidant balance and by interfering with the activity and function of several enzymes and hormones [8].

The purity issues of herbal products are also of great concern [9]. In order to ensure the optimal therapeutic benefits of herbal products, it is therefore important to monitor the quality of the raw materials with regard to their heavy metal content. Due to these health risks associated with heavy metals, WHO has established maximum admissibles values for heavy metals in herbal products [10]. In this review, we discuss some generalities on the contamination of medicinal plants and their products with heavy metals, the permissible limits of the contamination, as well as the medical implications of this contamination and ultimately the prevention strategies that can help ensure consumer safety. We present also some reports on this problem in different countries.

2 Generalities

Heavy metals are widely distributed in the environment from natural and various anthropogenic sources [11, 12]. The rapid industrialization and intensive agricultural activities over the past decades have resulted in the accumulation of various pollutants in the environment, mainly soil, which has led to the accumulation of heavy metals [13]. Waste from industrial processes is also a major source of their accumulation in the environment [14]. The application of different processes causing the mobility of heavy metals leads to the addition of these elements in the environment [15]. Also, the multiple industrial, domestic, agricultural, medical and technological applications of these metallic elements have led to their wide dissemination in the environment [16]. Being non-biodegradable, heavy metals accumulate in the environment and enters the food chain causing the impurity. This type of contamination presents risks to the environment as well as the human health [15].

The presence of heavy metals in plant tissues depends mainly on their availability and concentration in the soil [11]. Also, they be deposited directly on plant surfaces from the atmosphere [11] since the accumulation of heavy metals in many places in several parts of the troposphere constitutes a great danger for humans, creatures and vegetation [17].

Generally, metals such as Pb, Hg, Cu, Cd, As, Cr are highly toxic to the environment and affect ecosystem metabolism [17]. Lead is the most abundant heavy metal in the earth's crust [18]. Occupational and environmental exposure to this metal remains a serious problem in many developing and industrializing countries, as well as in some developed countries [18].

Although the popularity of herbal medicine is increasing rapidly around the world, the toxicity of heavy metals has a huge impact and importance on medicinal plants and consequently affects the quality of herbal raw materials, plant extracts, drug safety and marketing [12]. Ingestion of contaminated herbal and herbal drugs is considered as potential source of heavy metal toxicity to humans and animals [11]. There is a need to find ways to maximize consumer safety as there is evidence in various countries that toxic heavy metals and herbal medicines could be a serious health problem [19].

3 Admissible limits of contamination

According to the World Health Organization, the admissible limits for heavy metals in medicinal plants are: 0.3 ppm for Cadmium, 10.0 ppm for Lead, 10 ppm for Arsenic, 1.0 ppm for Mercury, 20.0 ppm for Cuprum, 50 ppm for Zinc [10].

4 Contamination reports

In India, a study on the chemical profile of certain heavy metals (Fe, Cu, Zn, Ni, Co, Cr, Pb, Hg and Cd) in the whole plant, fruit and rhizome of Bacopa monnieri, Hippophae rhamnoides and Dioscorea bulbifera, respectively, showed that most samples exhibited heavy metal profiles within allowable limits as established by regulatory authorities, with the exception of Cd and Hg in low elevation regions [20]. In Pakistan, a study was carried out to evaluate certain medicinal plants for their endogenous content of Pb, As, Cd, Hg and Zn; the results showed that they contain an acceptable quantity of heavy metals, the highest levels of which are Pb (0.229 µg/g), As (0.542 µg/g), Cd (0.036 µg/g), Hg (0, 0436 µg/g), Zn (0.209 µg/g) [21]. In another study, the contents of heavy metals in Thymus vulgaris L., Thymus serpyllum L. and Salvia officinallis L. cultivated in the south of Jordan were determined in the ranges of 1.26-32.03 ppm (Pb), 0.47-23.85 ppm (Ni), 7.66-13.23 ppm (Cu), 15.8-114.91 ppm (Zn), 141.3-756.17 ppm (Fe). Co was only detected in T. serpyllum, while Cd and Cr were not detectable in all samples studied. The highest content of Pb, Ni and Cu was detected in T. vulgaris (32.03 ppm, 23.85 ppm and 13.23 ppm, respectively). S. officinalis had the highest content of Zn (114.91 ppm) and Fe (756.17 ppm) [22].

In a study carried out in the Republic of Macedonia, the level of selected heavy metals (Zn, Cu, Fe and Cr) was determined in certain local plants (Urtica dioica L., Taraxacum officinale, Robinia pseudoacacia and Matricaria recutita). Results showed that all the metals were accumulated to greater or lower extents by all 4 plant species studied [23]. Medicinal and aromatic plants cultivated in

different regions of Austria were monitored for their content of Cd, Cu, Fe, Pb and Zn; the level of contamination by these toxic heavy metals was low since most samples contained less than 0.2 mg/kg of Cd and less than 1.5 mg/kg of Pb on a dry weight basis [24]. In a study carried out in Romania to determine the concentration of heavy metals (Pb, Cd and Hg) in certain medicinal plants (Chelidonium majus L., Crataegus monogyna, Artemisia absinthium L. and Hypericum perforatum); the authors reported that the highest contents were Pb (7.21 mg/Kg), Hg (0.005 mg/Kg) and Cd (0.128 mg/Kg) [25]. In Turkey, medicinal and aromatic plants were collected from herbalists in different districts and their heavy metal contents (Fe, Cu, Zn, Co, Cd, Cr, Ni and Pb) were measured; the results showed that some of the heavy metals are found at concentrations above the reported critical levels [26].

In Nigeria, leaves and dried roots of 5 medicinal plants (Ageratum conyzoides, Aspilia africana, Alchornea cordifolia, Amaranthus brasiliensis and Chromolaena odorata) were digested and analyzed using an atomic absorption spectrophotometer (AAS) for detecting the presence of Pb, Cd, Cr, Ni and Zn; the results showed that the concentrations of these heavy metals in the leaves and roots of plants taken from polluted soils were significantly higher than those obtained from unpolluted soils [27]. In sudan, the concentrations of certain heavy metals (Cd, Pb, Hg, Cu, Fe, Zn and Cr) were determined by several techniques in 33 medicinal plants used for the treatment of diabetes mellitus in traditional medicine. Cd, Pb and Hg were only found at traces of concentrations significantly well below global limits. However, high concentrations of Cr have been found [28]. In another study, a total of 303 samples of Egyptian spices and medicinal plants were analyzed for heavy metal contamination. The results revealed that the maximum heavy metal contents in the studied samples were 14.4 µg/g (Pb), 2.44 µg/g (Cd), 33.75 µg/g (Cr), 2.85 µg/g (Ni), 68.80 µg/g (Zn), 11.40 µg/g (Cu) and 1046.25 µg/g (Fe). On the other hand, Co was not detected in any of the analyzed plants [29].

5 Heavy metal toxicity

Due to their toxicity and their long persistence in nature, heavy metals can be accumulated in the trophic chain and cause dysfunction of the organism and deficiency of essential metals like Zn, Cu, etc. in humans and animals' tissues [12, 30]. Arsenic, cadmium, lead and mercury rank among the main heavy metals that are of health concern. They are inactive redox metals which show their toxic effects via binding to sulfhydryl groups in proteins and depletion of glutathione (an antioxidant) [11]. These metallic elements are considered to be systemic toxicants known to induce multiple organ damage, even at lower exposure levels [16]. Almost all of them are classified as carcinogenic to humans. For instance, arsenic, cadmium, chromium and nickel are classified as Group 1 carcinogens of the International Agency for Research on Cancer [14]. Arsenic poisoning is third in terms of prevalence and severity [31]. In addition, heavy metals have been to be mutagenic and teratogenic causing neurological problems, especially

in children [15]. Their toxicity depends on several factors, including dose, route of exposure and chemical species, as well as the age, sex, genetics and nutritional status of exposed individuals [16].

Heavy metals are necessary for various biological functioning, however, they become harmful in excess [32]. For example, manganese, copper, zinc and nickel are needed in exceedingly small quantities for optimal growth and biological processes of plants and animals. Nevertheless, high concentrations of these metals have strong toxic effects environment, humans, animals and plants [13].

Heavy metals induce oxidative stress by generating free radicals and reducing antioxidant levels. They cause also changes in proteins and DNA and inhibit their function which leads to cell death and increases the risk of cancer-related diseases [14, 32]. In addition, prolonged exposure to these metallic elements has been associated to the development of neurodegenerative diseases and various ocular pathologies such as glaucoma [33]. On the other hand, it should be noted that these heavy metals have therapeutic potential. For instance, some metals are used in the treatment of acute promyelocytic leukemia associated with retinoic acid. Also, magnesium oxide and zinc oxide are used against constipation and skin inflammation [34].

6 Prevention and treatment

In order to ensure the quality and safety of herbal medicines, cultivation and collection of medicinal plants in the immediate vicinity of industrial sites using these metals or sites where these metals have been inappropriately disposed of are strongly discouraged, because plants in these areas are subject to a high concentration of heavy metals. In addition, the screening of plant extracts, herbal products and medicinal plants for heavy metal contamination is of great medical importance and should receive maximum attention in phytotherapy [11].

Currently, there is no permanent and foolproof method to prevent entry of heavy metals into the food chain, but methods to reduce the intensity of the effects are available [30].

There are various methods of depolluting heavy metals but they have many limitations such as alteration of soil properties, high cost, disturbance of soil microflora and high demand for labor [13, 15]. Among these remedial methods, phytoremediation is relatively the most competent to solve this serious problem [15]. Phytoremediation is one of biological methods based on the use of plants (hyperaccumulators), as well as associated soil microbes to reduce the heavy metal content in contaminated soil [15]. This technology is accepted globally because it is efficient, cost effective and environmentally friendly [13, 15]. It is becoming an important tool for decontaminating soil, water and air by detoxification, extraction, hyperaccumulation and/or sequestration of contaminants [13].

Chelation therapy is a medical procedure commonly used to treat metal toxicity, it involves the administration of chelating agents to reduce, remove or degrade heavy metals [35]. Chelation is a chemical process that occurs when the

interaction between a central metal atom/ion and a ligand leads to the formation of a complex ring-shaped structure. Combination therapy with a chelating agent and an antioxidant led to improved outcome [32]. Kim et al [14] suggested that phytochelatin molecules and antioxidative phytochemical substances may be useful for the prevention of cancer induced by heavy metals.

For the treatment of heavy metal poisonings and the epidemiological tracing of accidental exposures, early detection of such poisonings is essential. A thorough history and physical examination are essential to arrive at an accurate diagnosis because the signs and symptoms of these poisonings are nonspecific [36].

Boron compounds (5-20 ppm) could be useful in the development of functional foods and medical raw materials effective in the treatment of heavy metal poisoning since they have an antigenotoxic and antioxidant effect against these poisonings [37].

7 Conclusion and perspectives

Heavy metals can cause serious and difficult abnormalities in the human body. Based on the data in this review, contamination of medicinal plants by these metallic elements is almost impossible to avoid, especially under certain conditions in contaminated environments. Many efforts have been made to determine the levels of heavy metals in medicinal plants and their products in various parts of the world. In order to ensure the consumers safety, the World Health Organization has established admissible limits of contamination for the heavy metals most dangerous to public health. To minimize or avoid the contamination of medicinal plants by these toxic compounds, it is necessary to apply depollution methods and chelation therapies against heavy metal poisoning.

References

1. Schulz V., Hansel R., Blumenthal M., Tyler V.E., Rational Phytotherapy: A Reference Guide for Physicians and Pharmacists. Rational Phytotherapy, (2004).
2. Rao M., Palada M., Becker B., Medicinal and aromatic plants in agroforestry systems. Agroforestry Systems, (2014), 61-62(1-3): 107-122.
3. Kabata-pendias A., Trace elements in soils and plants. CRC Press, New York, (2001).
4. Kalăc P., Svoboda L., A review of trace element concentrations in edible mushrooms. Food Chem, (2000), 69: 273-281.
5. Mishra S., Dwivedi S., Singh R., A review on epigenetic effect of heavy metal carcinogens on human health. Open Nutraceuticals J, (2010).
6. Schumacher M., Bosque M.A., Domingo J.L., Corbella J., Dietary intake of lead and cadmium from foods in Tarragona Province, Spain. Bull of Environ Contam Toxicol, (1991), 46: 320-328.
7. Weber G., Konieczyński P., Speciation of Mg, Mn and Zn in extracts of medicinal plants. Analytical and Bioanalytical Chemistry, (2003), 375: 1067-1073.

8. Rusyniak D., Arroyo A., Acciani J., Froberg B., Kao L., Furbee B., Heavy metal poisoning: management of intoxication and antidotes. In Molecular, clinical and environmental toxicology, Boston: Birkhauser, (Ed. A. Luch), (2010).
9. Mazzanti G., Battinelli L., Daniele C., Costantini S., Ciaralli L., Evandri M.G., Purity control of some Chinese crude herbal drugs marketed in Italy. Food Chem Toxicol, (2008), 46: 3043-3047.
10. WHO (World Health Organisation), WHO Guidelines for Assessing Quality of Herbal Medicines with Reference to Contaminants and Residues. World Health Organization, Geneva, (2007).
11. Ezeabara C.A., Okanume O.E., Emeka A.N., Okeke C.U., Mbaekwe E.I., Heavy Metal Contamination of Herbal Drugs: Implication for Human Health-A Review. International Journal of tropical disease health, (2014), 4(10): 1044-1058.
12. Chen Y.G., He X.L.S., Huang J.H., Luo R., Ge H.Z., Wo-lowicz A., Wawrzkiewicz M., G-ladysz-P-laska A., Li B., Yu Q.X., Ko-lodynska D., Lv G.Y., Chen S.H., Impacts of heavy metals and medicinal crops on ecological systems, environmental pollution, cultivation, and production processes in China. Ecotoxicology and Environmental Safety, (2021), 219: 112336.
13. Edao H.G., Heavy metals pollution of soil; toxicity and phytoremediation techniques. International Journal of Advanced Research and Publications. (2017), 1(1): 29-41.
14. Kim H.S., Kim Y.J., Seo Y.R., An Overview of Carcinogenic Heavy Metal: Molecular Toxicity Mechanism and Prevention. Journal of Cancer Prevention, (2015), 20(4): 232-240.
15. Devi P., Kumar P., Concept and Application of Phytoremediation in the Fight of Heavy Metal Toxicity. J. Pharm. Sci. Res., (2020), 12(6): 795-804.
16. Tchounwou P.B., Yedjou C.G., Patlolla A.K., Sutton D.J., Heavy Metals Toxicity and the Environment. EXS, (2012), 101: 133-164.
17. Raj A., Kumar A., Vaghasiya T.P., Multidisciplinary Approaches to Clean up Heavy Metal Contaminated Soil: A Review. Bull. Env. Pharmacol. Life Sci., (2021), 10(6): 53-65.
18. Tong S., von Schirnding Y.E., Prapamontol T., Environmental lead exposure: a public health problem of global dimensions. Bulletin of the World HealthOrganization, (2000), 78 (9): 1068-1077.
19. Ernst E., Toxic heavy metals and undeclared drugs in Asian herbal medicines. TRENDS in Pharmacological Sciences, (2002), 23(3): 136-139.
20. Sadhu A., Upadhyay P., Singh P.K., Agrawal A., Ilango K., Karmakar D., Singh G.P., Dubey G.P., Quantitative analysis of heavy metals in medicinal plants collected from environmentally diverse locations in India for use in a novel phytopharmaceutical product. Environ Monit Assess, (2015), 187(8): 542
21. Begum H.A., Hamayun M., Zaman K., Shinwari Z.K., Hussain A., Heavy metal analysis in frequently consumable medicinalplants of khyber paktunkhwa, Pakistan. Pak. J. Bot., (2017), 49(3): 1155-1160.
22. Abu-Darwish M.S., Essential Oils Yield and Heavy Metals Content of Some Aromatic Medicinal Plants Grown in Ash-Shoubak Region, South of Jordan. Adv. Environ. Biol., (2009), 3(3): 296-301.
23. Gjorgieva D., Kadifkova-Panovska T., Baeva K., Stafilov T., Metalic Trace Elements in Medicinal Plants from Macedonia. Middle-East J. Sci. Res., (2011), 7(1): 109-114.
24. Chizzola R., Michitsch H., Franz C., Monitoring of metallic micronutrients and heavy metals in herbs, spices and medicinal plants from Austria. Eur Food Res Technol, (2003), 216: 407-411.

25. Badea D.N., Determination of Potentially Toxic Heavy Metals (Pb, Hg, Cd) in Popular Medicinal Herbs in the Coal Power Plant Area. Rev. Chim., (2015), 66(8):1132-1136.
26. Esetlili B.Ç., Pekcan T., Çobanoglu O., Aydoğdu E., Turan S., Anaç D., Essential Plant Nutrients and Heavy Metals Concentrations of Some Medicinal and Aromatic Plants. Journal of Agricultural Sciences, (2014), 20: 239-247.
27. Awodele O., Popoola T.D., Amadi K.C., Coker H.A.B., Akintonwa A., Traditional medicinal plants in Nigeria—Remedies or risks. Journal of Ethnopharmacology, (2013), 150: 614-618.
28. Ebrahim A.M., Eltayeb M.H., Khalid H., Mohamed H., Abdalla W., Grill P., Michalke B., Study on selected trace elements and heavy metals in some popular medicinal plants from Sudan. J Nat Med, (2012), 66: 671-679.
29. Abou-Arab A.A.K., Abou Donia M.A., Heavy Metals in Egyptian Spices and Medicinal Plants and the Effect of Processing on Their Levels. J. Agric. Food Chem., (2000), 48(6): 2300-2304.
30. Ganeshamurthy A.N., Varalakshmi L.R., Sumangala H.P., Environmental risks associated with heavy metal contamination in soil, water and plants in urban and periurban agriculture. J. Hortl. Sci., (2008), 3 (1): 1-29.
31. Jain N., Chandramani S., Arsenic poisoning- An overview, Indian J Med Spec., (2018), 178(3): 1-3.
32. Kim J.J., Kim Y.S., Kumar V., Heavy metal toxicity: An update of chelating therapeutic strategies. Journal of Trace Elements in Medicine and Biology, (2019), 54: 226-231.
33. Vennam S., Georgoulas S., Khawaja A., Chua S., Strouthidis N.G., Foster P.J., Heavy metal toxicity and the aetiology of glaucoma. Eye, (2020), 34: 129-137.
34. Inoue K.I., Heavy Metal Toxicity. J Clinic Toxicol, (2013), S3: 007.
35. Sidhu G.P.S., Heavy Metal Toxicity in Soils: Sources, Remediation Technologies and Challenges. Adv Plants Agric Res, (2016), 5(1): 00166.
36. Graeme K.A., Pollack Jr C.V., Heavy Metal Toxicity, Part I: Arsenic and Mercury. The Journal of Emergency Medicine, (1998), 16(1): 45-56.
37. Turkez H., Geyikoglu F., Tatar A., SaitKeles M., Kaplan I., The effects of some boron compounds against heavy metal toxicity in human blood. Experimental and Toxicologic Pathology, (2012), 64: 93-101.