Scientific Papers. Series B, Horticulture. Vol. LXVIII, No. 1, 2024
Print ISSN 2285-5653, CD-ROM ISSN 2285-5661, Online ISSN 2286-1580, ISSN-L 2285-5653

A GREEN APPROACH USED FOR HEAVY METALS REMOVAL FROM HUMAN BODY

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Abstract

Recent research has shown that the level of heavy metals in the human body is near 700 times higher than that of our ancestors. It is known that heavy metals do not degrade and are not broken-down by microorganisms and the period for their elimination from the body is very long. They can accumulate in the liver, brain, kidneys, muscles, bones, nails and hair. The World Health Organization highlights the risks of neurological, renal, liver, heart and bone diseases caused by heavy metals. The treatment for most heavy metal intoxications is chelating therapy, which can extend over a very long period of time and is quite costly. However, complementary treatments with medicinal plants have proven helpful to remove heavy metals by intensify diuresis, purifying the blood, through their depurative and hepato-protective role, etc. The paper presents the results of some publications in the field, focusing on the plants role in the human body detox.

Key words*: detoxification, lead, mercury, medicinal plants, morphological characters.*

INTRODUCTION

Heavy metals are found in the nature and they are essential to life, but they can become toxic through accumulation in organisms, being associated with environmental pollution, toxicity and adverse effects on biota.
Heavy metals are mostly defined in terms of high density and relative atomic mass (Kolller & Saleh, 2018).
Increasing urbanization and industrialization, mining, waste dumps, road traffic, etc., have contributed to the deterioration of the environment and depreciation of human health (Briffa et al., 2020; Yu et al., 2023).
Heavy metals' pollution has become a galloping worldwide problem that must be prioritized. Exposure to heavy metals can be done in different ways: inhalation, consume of contaminated food & water (Masindi & Muedi, 2018), skin touch and so on. As a direct consequence, several health problems may occur, such as: neurological & blood abnormalities, cardiovascular and neurological diseases, diabetes and various types of cancer. Also, heavy metals can interact with some elements, such as calcium, iron and zinc, affecting the body's normal metabolism (Lopez Alonso et al., 2004).
Since ancient times, medicinal plants have been used as remedies for various ailments, in most countries of the world, even if the active principles were not deeply known (Jamshidi-Kia et al., 2017).
Nowadays, the medicinal plants have an important place in traditional medicine or as adjuncts in classical medicine. There are numerous studies that state the pharmacological value of the medicinal plants and their role in body detoxification and alleviation of vary disorders (Luchian et al., 2017; Toma & Luchian, 2019; Toma et al., 2020; Luchian et al, 2021a; 2021b; Toma et al., 2022; Burzo and Badea, 2023).
This review aims to analyse the most aggressive and wide spread heavy metals and how they affect people's health, as well as the species of plants useful to remove or diminish them from the body, both from Romanian spontaneous flora and cultivated areas, their list not being exhaustive.

MATERIALS AND METHODS

An electronic search for literature was carried out using the following databases: PubMed, Google Scholar, Google, Scopus, Research Gate, Direct Science, Web of Science, Science Notes and Academic Journals. The present paper presents some of the most effective natural remedies in the elimination of heavy metals from the human body, knowing that their chelation treatment is difficult and with possible side effects.

The analysed papers provided pre-clinical research to those interested. In the case of antioxidants supplementation and the use of medicinal plants, the therapy with chelating agents is much more effective (Flora et al., 2008). Various studies, as those conducted by Amadi et al. (2019) and Mehrandish et al. (2019) reported mitigation of metal toxicity from whole, parts, or extracts of medicinal plants. The herbal treatments can lead to the elimination of heavy metals by intensifying diuresis, purifying the blood, through their depurative and hepato-protective activity (Algandaby et al., 2021; Sobhani et al., 2022).

RESULTS AND DISCUSSIONS

There are 35 metals under the attention of international health and environmental organizations - in order of increasing atomic number, as it's mentioned at https://science notes.org /list/ metals (In resources for authors: List of metals. (n.d.) Science Notes. Retrieved from: https://sciencenotes.org/ list-metals): lithium, beryllium, sodium, magnesium, aluminium, potassium, titanium, vanadium, chromium, manganese, iron, cobalt, nickel, copper, zinc, strontium, zirconium, niobium, molybdenum, palladium, silver, cadmium, indium, tin, cesium, barium, tungsten, iridium, platinum, gold, mercury, thallium, lead, bismuth, radium, uranium), of which 23 are heavy metals as it is mentioned in the paper of Tchounwou et al. (2012): aluminium, antinomy, arsenic, barium, beryllium, bismuth, cadmium, gold, indium, lead, lithium, mercury, nickel, platinum, silver, strontium, tellurium, thallium, tin, titanium, vanadium, uranium and zirconium), because their specific weight (S.W.) is at least 5 times higher than that of water (S.W.=1 N/m^3). Some heavy metals, such as iron, copper, magnesium and zinc, are essential in carrying out metabolic processes, but only in accurate amounts. Among the most toxic and widespread heavy metals with a serious impact on human health are mentioned: arsenic (S.W.=5.7 N/m^3), cadmium (S.W.=8.6 N/m^3), mercury (S.W.= 13.5 N/m^3) and lead (S.W.=11.3 N/m^3). Heavy metals do not decompose themselves, being extremely difficult to be removed and, once accumulated, their concentration per unit mass increases in the body.

Arsenic (As) is an extremely toxic metalloid for human beings, coming from natural and anthropogenic sources (Lim et al., 2014), e.g. industry, pesticide manufacturing, etc. The people can be exposed to arsenic by drinking, inhaling or direct contact, etc. High As concentrations were found in the plasma and cerebrospinal fluid of patients with Alzheimer's and Parkinson's diseases (Cheng et al., 2007). Arsenic generates reactive oxygen species (ROS), which cause cell damage followed by death. For this reason, arsenic compounds were used in ancient times to treat malaria, cancer, plague, and syphilis (Khan et al., 2022). However, several studies have shown the link between arsenic exposure and the onset of certain diseases & disorders. Long-term exposure to inorganic arsenic may cause various cardiovascular disorders, such as atherosclerosis, hypertension, ischemic heart diseases and ventricular arrhythmias (Tsai et al., 2001; Balakumar & Kaur, 2009). Prolonged As exposure can decrease insulin sensitivity, responsible to induce type II diabetes (Paul et al., 2007). Other imbalances produced by arsenic could be: hearing problems, blood abnormalities, venous insufficiency, fatigue, headaches, dermatitis, salivation overflow, hair loss, nails damage, kidney & liver diseases (Hedayati, 2016) and cancer (Majumdar, 2017). Carcinogenic effects of arsenic on lungs, liver, bladder, kidneys and skin are well known (Waalkes et al., 2004). Some medicinal plants, used single or in combination with synthesis medicines, can realize a synergistic effect in the chelation process (Muthumani & Prabu, 2012; Das & Chaudhur, 2014; Gupta et al., 2015; Miltonprabu & Sumedha, 2015, Mohaddese, 2021). Various studies have been done high-

lighting the role of flavonoids, stilbenoids (Mishra et al., 2022) and other kinds of bio-compounds in the alleviation of arsenic toxicity (Bjorklund et al., 2020, Khan et al., 2022). Bhattacharya (2017) stated that some medicinal plants can help in the amelioration from sub-chronic As toxicity through their antioxidant properties. Thus, *Trichosanthes dioica* fruit possessed remarkable alleviative effects due to its content of quercetin and vitamin C against arsenic induced myocardial toxicity (Bhattacharya et al., 2014). The ethanolic extract of *Hippophae rhamnoides* and *Triticum aestivum* worked in the same direction based to their anti-oxidant value (Lakshmi et al., 2015). *Mentha piperita* extract showed significant alteration in lipid peroxidation and free radicals scavenging by redu-cing genotoxicity and exhibiting hepato-protective and nephro-protective effects (Sharma et al., 2007). Vineetha et al., (2014) highlighted the protective role of polyphenols found in the apple peel, in case of heart injury produced by the action of arsenic trioxide. The extract of *Vitis vinifera* seeds, protects the liver (Li et al., 2015) and *Viscum album* extracts has reduced the elevated plasma levels of liver enzymes and clastogenicity induced by sodium arsenite in rats (Adegboyega & Odunola, 2012). The *Zea mays* extracts might protect rats from accumulation of arsenic in different tissues and oxidative stress, which is reflected by the increasing the glutathione concentration in those tissues (Chowdhury et al., 2009). *Spinacia oleracea* is a rich source of antioxidants and micronutrients, which could be a good solution for the management of arsenicosis (Umar, 2007). Some bio-compounds found in garlic, mainly the allicin used in aqueous extracts, appeared to be very helpful in arsenic toxicity (Chowdhury et al., 2008).

About 13,000 tons of **cadmium (Cd)** are produced annually worldwide, mainly for nickel-cadmium batteries, pigments, chemical stabilizers, various alloys. Chronic Cd exposure suppresses serotonin and acetylcholine levels, and its inhalation triggers the development of lung cancer. Also, direct Cd contact can proliferate prostatic lesions, including adeno-carcinoma. Cadmium toxicity affects the digestive tract, kidneys, liver, lungs, pancreas, brain, testicles, urethra, heart and central nervous system. Among the diseases due to cadmium poisoning are listed: hypertension, osteoporosis, anaemia, hair loss, non-hyper-trophic emphysema, cell apoptosis (Hernández-Cruz et al., 2022; Zhang et al., 2023; Oosterwijk, 2023) which can lead to coma and even death (Satarug et al., 2003). Cadmium is also known to cause deleterious effects by deactivating DNA repairing (Genchi et al., 2020; Mc Murray & Tainer, 2003). Using garlic (*Allium sativum)* extract, some researchers demonstrated Cd reduction in rats (Sadeghi et al., 2013). Other studies showed that garlic is a successful agent of Cd chelation (Boonpeng et al., 2014) and the *Aronia melanocarpa* anthocyanins as well (Mężyńska et al., 2019; Smereczański et al., 2023). Bamidele et al. (2012) noticed that Cd toxicity effects were significantly controlled by methanolic extract of *Momordica charantia* and good results were obtained by the use of *Solanum tuberosum* extract (Lawal et al., 2011). Moreover, when coriander (*Coriandrum sativum*) was introduced as a supplement, together with garlic and *Chlorella* algae in the diets of *Prussian* carp (*Carassius gibelio*), the protection against kidney damage from Cd exposure was observed (Nicula, 2016). Essential polyphenols found in grape and apple showed a protective action in case of rat's kidney injury due to cadmium poisoning (Handan et al., 2020). The bio-compound oryzanol from *Oryza sativa* protects against acute Cd-induced oxidative damage in mice testicles (Spiazzi et al., 2013). Suliman (2017) has studied the effect of *Arctium lappa* against Cd genotoxicity and histopathology in kidney. Extract of *Nasturtium officinale* have protective effect on arsenic-induced damage of blood cells (Zargari et. al., 2015). Other scientific papers showed that Cd induced arterial and cardiac injuries could be significantly reduced by introducing soybean supplementation in the diet (Pérez Díaz et al., 2013).

Mercury (Hg) is a very toxic heavy metal which is widely dispersed in the nature (Bernhoft, 2012). Human Hg exposure is caused by its release from dental amalgam, vaccines, consumption of contaminated fish and seafood or through occupational exposure. Atmospheric Hg exposure can occur through volcanic activity, mining, etc. Elemental, inorganic and organic forms of mercury (Abdel-Salam et al.,

2018) exhibit toxicologic characteristics including neuro and nephrotoxicity (Zalups, 2000), gastro-intestinal toxicity with ulceration and haemorrhage, reduced sensory abilities, anorexia, fatigue, irritability and excitability, cardiovascular disease, hypertension, respiratory, immune and reproductive disorders. Hg toxicity also induces a number of stress proteins (Papaconstantinou et al., 2003) and can affect human health by causing severe changes in tissues (Zahir et al., 2005). Mercury leads to the formation of reactive oxygen species, causing DNA damage, but can also lead to carcinogenesis (Flora and Pachauri, 2010). Bulb extract of *Allium sativum* is very useful in blood disorders, such as the peripheral leukocytes damage (Abdalla et al., 2010) and brain damage (Bhattacharya, 2018) induced by Hg poisoning, due to the antioxidant potential, done by its high amount of polyphenols. *Rheum palmatum* (rhubarb) root extract, in particular, its anthraquinones, have been used with good results in kidney Hg damage on rats (Gao et al., 2016), showing significant declines of serum creatine & urea nitrogen values and increases of total protein albumin in treated groups. Seven days oral administration of *Eruca sativa* seeds extract highlighted an antioxidant, protective and curative renal activity on Hg-induced nephrotoxicity on rats (Alam et al., 2007). Kavitha et Jagadeesan (2006) evaluated the renal functions at mercury intoxicated rats, proving how kidney parameters reached to near normal after administration of fruit extract of *Tribulus terrestris* for seven days. The consumption of wormwood (*Artemisia absinthium)* aqueous extract during four weeks restored the enzymes activities perturbed by exposure to lead, offering a protective action against lipid peroxidation. In fact, the dried leaves and stem of wormwood were grinded in a blender with water and then centrifugated to eliminate the solid waste. The sterile aqueous extract was finally obtained by a series of filtrations and then orally administrated to rats (200 mg per every kg of body weight), as appears in the study of Kharoubi et al. (2008). Same extract showed also a protective action in brain dysfunction induced by $HgCl_2$ (Hallal et al., 2016). Abdel-Salam et al. (2018) studied the effect of dandelion (*Taraxacum officinale)* and *Coriandrum sativum*. The coriander, called, also, cilantro is a popular culinary and medicinal herb which is very recommended in heavy metals detox, mainly mercury and lead (Rafati-Rahimzadeh et al., 2017), as well as *Viola tricolor*. Their mechanism is to enhance the Hg excretion (Abascal & Yarnell, 2012), improving its clearance in a number of patients poisoned with heavy metals (Mehrandish et al., 2019). Coriander ethanolic extract is highly effective to take out the mercury stored at the brain level. *Urtica dioica* is also found to be protective at the level of different organs in case of mercury poisoning (Jaiswal et al., 2022), including the brain, liver, lungs, kidney, ovary (Siouda & Abdennour, 2015). Alfalfa (*Medicago sativa*) extract, by its nutritional and antioxidative activities, could also decrease the Hg toxicity-induced and could improve the structure and function of the kidney and liver (Raeeszadeh et al., 2021). *Allium ursinum* is indicated for binding heavy metals using sulphur compounds to eliminate them through kidneys; an important compound is the glutathione peptide which is responsible for the detoxification of free radicals and their neutralization in the human body (Sobolewska et al., 2015).

Lead (Pb) is a heavy metal used in different industrial plants and emitted from some petrol motor engines, batteries, radiators, waste incinerators, and residual water (Manisalidis et al., 2020). Lead poisoning, called saturnism (Montes-Santiago, 2013) is correlated with the bluish tinge of the skin around lips, eyes, gums and nail beds. This colour represents the sign of cyanosis. It may not appear until oxygen saturation falls below 85%. The blue colour of cyanosis means that organs, muscles and other body tissues do not receive enough amount of oxygen to operate properly. The cyanosis symptoms are due to drugs overdose or poisoning, including heavy metals toxicity, heart & lung injuries or some autoimmune diseases. The lead poisoning can generate brain damage, even in animals' liver, kidneys (Aziz et al., 2012), bones and diseases of the digestive system, central nervous system (Saleh et al., 2019), and the reproductive system (Abdou et al., 2006), causing metallic taste, weight loss and headaches, insomnia and metabolic dysregulation of vitamin D (Mutter et al., 2010). Children are extremely sensitive even to minimal doses of lead, being highly neurotoxic

(Assi et al., 2016) and it causes hearing loss, hyperactivity, aggressiveness, learning difficulties, impairment of memory (Soodi et al., 2008) and even mental retardation (Farhat et al., 2013). *Ginkgo biloba* is one of the herbal remedies used as a complementary treatment for lead-poisoned patients, by reducing the oxidative stress and elevating the glutathione level (Tunali-Akbay et al., 2007). The aqueous extract of coriander seeds was effective in normalizing the adverse effects of lead induced nephrotoxicity (El-Masry et al., 2016). Several natural products involved in nephroprotection (Sri Laasya et al., 2020), such as phenolics and flavonoids, can reduce renal damage, lipid peroxidation, urea and creatinine reduction (Gholamine et al., 2021) by decreasing the oxidative stress and protecting the liver (Kükner et al., 2021; Mahmoud et al., 2023). Other researches showed highly protective effect of *Aquilegia vulgaris* against lead acetate-induced oxidative stress in rats (El-Nekeety et al., 2009*).* Cilantro has a wide range of healing and body detox properties by removing toxic residues, such as lead, and excreting them (Tellez-Lopez et al., 2017). *Coriandrum sativum* extract has an extensive application in treating pathological situations of nervous tissues, nervous disorders affected by heavy metals toxicity (Ghosh et al., 2017). Coriander showed, also, encouraging results as chelation and poisoning reduction in animal studies, in case of lead intoxication (Velaga et al., 2014). Ghanem et al. (2008) demonstrated that *Cynara scolymus*, due to its volatile constituents is useful to fight against lead toxicity, especially at liver & kidney level. Falah (2012) has also reported that *Ficus carica* rendered hepatoprotective effects in animal studies. Waggas (2012) showed that grape seed extract (*Vitis vinifera)* alleviate neurotoxicity and hepatotoxicity induced by lead acetate in male albino rats. *Rosmarinus officinalis* was very helpful to treat the lead injuries at the level of liver and kidney (Mohamed et al., 2016). Ishiaq et al. (2011) stated that lycopene, the valuable antioxidant found in tomato fruit, may improve the enzymatic activity in case of kidney Pb damage, while Jarad (2012) stated that freshly prepared aqueous extract of *Allium sativum* alleviated the liver Pb damage. Chinthana and Ananthi (2012) have reported that the neurotoxicity induced by lead in albino mice could be significantly reduced by administration of *Solanum nigrum* extract. Ethanolic extract of *Tagetes erecta* balanced the antioxidants' level and decreased lipid peroxidation in Pb intoxicated rats (Adikwu et al., 2013). Some plants can reduce the bio-availability and gastrointestinal absorption of heavy metals by increasing gastro-intestinal motility, so that a faster excretion of toxic substances is achieved through stool. Due to this fact, the people with regular use of herbal products can significantly reduce the absorption of heavy metals (De Smet et al., 1992). In the traditional Chinese medicine, the roots of *Arctium lappa* (the burdock) are considered a blood detoxifying agent (Raeeszadeh et al., 2021). In an Egyptian study conducted by Algandaby et al. (2021) seven medicinal plants (*Arctium lappa* - roots, ratio 20:100, *Coriandrum sativum* - leaves, ratio 10:100, *Olea europaea* - leaves, ratio 15:100, *Silybum marianum* - fruits, ratio 20:100, *Tribulus terrestris* - shoots, ratio 20:100, *Urtica dioica* - shoots 15:100) were used as chelating compounds to alleviate toxicity of heavy metals. The formula was administrated six months, half an hour before meal (near 10 g of herbal mix at 200 ml boiled water once a day or half dose twice a day). The potentiality of plant extracts to mitigate heavy metal toxicity in animals and humans is attributed to their antioxidant properties of the phytochemicals present in these extracts. Bilberry (*Vaccinium mirtylus*) anti-oxidants can scavenge free radicals and chelate the metallic ions (Mazza et al., 2002). The antioxidative mechanisms of silymarin found in *Silybum marianum* include the inhibition of reactive oxygen species (ROS), direct scavenging of free radicals' actions and ion chelation (Surai, 2015), being a supporting treatment in liver curing (Gillessen and Schmidt, 2020). The red clover (*Trifolium pratense*) aids in blood purification and also help to stimulate bile production, having the ability to remove heavy metals and toxins from the body (Nelsen et al., 2002). Sorrel (*Rumex crispus* and *Rumex acetosa)* is likewise an excellent detoxifying herb that helps with the digestion of fats and gentle elimination of heavy metals (Mostafa et al., 2011). The ripe berries of *Mahonia aquifolium* are known to enhance liver functions, bile production and

blood purification (He and Mu, 2015). Vary authors highlighted the powerful role in body detox from heavy metals played by the medicinal plants, such there are: *Equisetum arvense* - lead detoxification (Pant et al, 2015), *Petroselinum crispum* - cadmium neurotoxicity (Maodaa et al., 2016), *Solidago virgaurea* - general detox (Fursenco et al., 2020), as well as *Foeniculum vulgare* (Al-Snafi, 2018), *Thymus* sp. (Afonso et al., 2020), *Oregano* sp. (Velickovic et al., 2014) and *Ocimum* sp. (Cohen, 2014) having strong antioxidative and detoxifying properties.

CONCLUSIONS

This review analyses the main species of plants used to remove heavy metals from the body or to mitigate their injuries at cell level.

The mentioned species of this paper belong to Romanian spontaneous flora and cultivated area, as well.

Trifolium pratense, *Rumex* sp., *Equisetum arvense*, *Solidago virgaurea, Thymus* sp., *Oregano* sp., *Ocimum* sp. show very strong antioxidative and detoxifying properties.

To counteract arsenic poisoning, the studies recommend the use of some spontaneous and cultivated plants, such as: *Trichosanthes dioica, Hippophae rhamnoides, Triticum aestivum, Mentha piperita, Viscum album, Zea mays, Spinacia oleracea, etc.*

Cadmium toxicity can be reduced by herbal remedies based on some medicinal and cultivated plants, as there are: *Aronia melanocarpa, Momordica charantia, Solanum tuberosum, Oryza sativa, Arctium lappa, Nasturtium officinale,* etc.

Mercury poisoning can be mitigated with the help of some plants, such as: *Allium ursinum*, *Rheum palmatum*, *Eruca sativa, Tribulus terrestris*, *Artemisia absinthium, Taraxacum officinale*, *Coriandrum sativum, Urtica dioica*, *Medicago sativa*, etc.

To alleviate lead body's damage, some plants can be used as complementary treatment: *Viola tricolor, Allium sativum, Rosmarinus officinalis, Cynara scolymus*, *Ginkgo biloba, Tagetes erecta, Silybum marianum, Vaccinium mirtylus*, *Vitis vinifera,* etc.

Re-discovery of natural herbal remedies represents increasingly obvious research of modern humans, and the "return to the nature" is the act of finding internal balance and healing.

By corroborating the data of some valuable publications in the field, the current review makes a first national inventory of spontaneous and cultivated plants and of herbal remedies valid for human body detox of heavy metals.

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