

ASSOCIATIONS BETWEEN ENVIRONMENTAL NON-ESSENTIAL HEAVY METALS, ECOBIOCHEMISTRY AND HEALTH

**Mirela Ahmadi¹, Ioan Pet², Lavinia Stef², Narcisa Mederle¹, Cornelia Milovanov¹,
Gabi Dumitrescu², Marioara Nicula², Laura Iosefina Smuleac³, Raul Pascalau⁴,
Adrian Smuleac³, Dorel Dronca²**

¹*Faculty of Veterinary Medicine, Banat's University of Agricultural Sciences and Veterinary Medicine „King Michael Ist of Romania“ from Timisoara (BUASVM), Timisoara – 300645, Calea Aradului, no. 119, Romania*

²*Faculty of Bioengineering of Animal Resources, BUASVM Timisoara*

³*Faculty of Agriculture, BUASVM Timisoara*

⁴*International Relations Office, BUASVM Timisoara*

e-mail: ddronca@animalsci-tm.ro

Abstract

Environmental heavy metals should be a concern of the entire world due to its impact on the animal and human population. "Heavy metals" is a generic name used for metals characterized by relatively high atomic weight, density, and atomic number. Some of the heavy metals are essential nutrients for animals and humans, but when their ingested concentration exceeds the needs, their homeostasis is unbalanced and health status is impaired. Non-essential heavy metals are minerals that are harmful to the environment and living organisms. The environment is the main source of minerals provided by soil, water and air. Any deficiency or excess of minerals in the environment will be transferred to the living organisms. Plants, meat and water – are ingredients of humans' diet, and because of that, any overload affects the minerals' homeostasis that could lead to accumulation in target organs – mainly in the liver and kidney, also in the brain, heart, lungs, and other organs. Ecobiochemistry and xenobiochemistry are two complex sciences that are trying to find correlations between the biochemical processes related to the minerals' needs, intake, and excretion to assure a good health status.

Key words: environment, heavy metals, health

Introduction

Health status for animals and humans is a very complex subject that involves the environment, lifestyle, and biochemical characteristics. Lately, more and more concerns are related to the environment and pollution, in order to ensure a healthy environment for all living organisms. Thus, one major concern is focused on heavy metals, which are much spread and could suffer risk assessment due to the trophic transfer and/or biomagnification. "Heavy metals" is a generic name that characterizes natural chemical elements with high atomic mass (usually higher than 23) and high density (higher than 5g/cm³) [1]. Heavy metals are found wild spread, but their concentration in environment and organisms is relatively low. Ecobiochemistry as a term, was mention in a research experiment that studied the adenine nucleotides in the deep-water pelagic community as an estimator of energetic metabolism, and also it was mentioned in a USPA Program – which has studied sub-Antarctic habitats [2]. It's a science that evaluates the organisms' metabolic processes related to the quality of the living environment – which most of the time is assessed in order to found out if there is any contamination of air, water or soil. Thus, the main chemical reactions from animal and human organism are evaluated in terms of efficacy in the presence of excessive amounts of organic chemicals (ex. pesticides, insecticides) or inorganic chemicals (such as metals with toxicogenic potential), finally referring to the quality of soil, water and air.

Xenobiochemistry studies the foreign compounds in plants, animals or human organism, or studies the chemical compounds that are essential for the living organisms but are found in too high concentrations. Specialized functions in the body identify the presence of toxic substances or

essential substances in concentrations that exceed the tolerance of the body, block their absorption, and are transported to the liver to be annihilated. For example, heavy metals bind to various chelators which make them impossible to be absorbed, and thus their action is blocked, after which they are transferred to the renal function in order to be excreted through the urine [3]. The chelation process in the body is a very easy process and is often used by enzymes that have metal cofactors. These chelators have two or more chemical bonds between metal and the organic molecule, which are coordination bonds formed between metal ion and chelator. The strength of the coordination bond and the accessibility of chelation process are depending on various characteristics, such as: accessibility of the chelators and metal ions in the tissues; the metal ion and chelator concentration; the strength of the metal ion already bound to other chemicals; and the strength of the bound formed between the chelator and the metal ion. The most important chelators are metallothioneins and glutathione – enzymes that play the role of biomarkers, being involved in the cellular response of the presence of toxic heavy metals, in mobilization, transport and renal excretion (in urine). Dietary fibers can also help in detoxification processes, playing an alternative role in reducing the quantity of toxic metals in the body, absorbing chemicals and excreting them via digestive tract (in feces). USA (US Environmental Protection Agency, World Health Organization) and Canada (Environment Canada, Canadian Institute of Health Research, Canadian Poison Control Centers) developed and funded different divisions that are specialized in treatments using chelators regarding the most heavy metals exposure, such as: arsenic, cadmium, mercury, and lead among their population, especially for the children [4,5].

If we talk about the possibility of eliminating the heavy metals from the organism through chelation we must remember that along with the main elimination pathways (the renal and digestive pathways) it is necessary to take in consideration the excretion of these chelated substances also by sweat. But having in view that for any organism there are tolerance limits to concentrations of certain substances, we must emphasize that living organisms are capable of evolving over time and tolerating increasing amounts of pollutants [4].

Heavy metals in environment

The environment is a very important source for heavy metals, in which water plays a key role in translocation. Humans' activities could be also important factors that can influence the quantity of heavy metals from the environment. The heavy metals released in the eco-biosphere come from agriculture, industries, technologies, automotive and medical uses and applications. Proper use of these chemicals does not harm the environment, but we are increasingly witnessing disasters caused by improper use (quantitative and qualitative), uncontrolled discharges and pollution, that have serious consequences on the environment in the very long term.

Biomagnification is a process that occurs when some chemicals (such as heavy metals or organic pollutants) accumulate in the internal organs and tissues of plants, animals and/or humans. The biomagnification processes are characterized by bioaccumulation, biodilution and bioconcentration. Bioaccumulation is referring to accumulation on some chemicals along the trophic chain that lead to increased concentration in specific organs and tissues. Biodilution is the process in which the chemicals concentration is diluted due to an increase in trophic level [6].

Humans and animals are at the top of the trophic chain and from this point of view biomagnification has become a subject extensively studied in recent years. Biomagnification of toxic, polluting substances - such as heavy metals, increases the risk of serious diseases such as various types of cancer; liver, kidney and heart failure; birth disorders; and brain irreversible damage [7,8].

Environmental decontamination and de-pollution are the main target of environmental researchers, biologists, and biochemists, who are trying to find new solutions to reduce the degree of environmental contamination. Thus, recent studies have shown that a system that combines

functional bacteria with absorbent materials (sponge, cotton treatment) has a direct effect of removing copper, cadmium, and chromium; and indirectly on lead and chromium [9].

For decontamination of water polluted by heavy metals, there are more options to take into consideration, such as physical, chemical or thermal treatment, but the best and effective traditional solution remains the alkaline lime precipitation. This method is effective for treatment of contaminated wastewater where the heavy metals exceed 1g/L [10].

Phytoremediation is another method very useful for biodegradation of the heavy metals. There are some specific plants that have the ability to chemically transform the heavy metals into chemically bioavailable form for the plant, with the final effect of decreasing the concentration of metal pollutants or high concentrations of essential metals, in the soil. This method is a recent technology, being a cost-effective, efficient, safe ecologic method, and available for decontamination of soils and waters. The phytoremediation is a very good option to “clean” the environment of different chemical hazardous substances, with the help of some plants that are capable to upload thousands of ppm of heavy metals [11,12].

Ecobiochemistry and heavy metals

For living organisms, there are different essential minerals and even heavy metals – which are important for metabolic processes. Between the heavy metals, arsenic, cadmium, lead, mercury, and chromium have the highest toxicity, chromium being essential for carbohydrates metabolism – but in very small amounts. Regarding the quantitative needs of heavy metals in living organisms, they are necessary in trace amounts, less than 10ppm or even ppb. The quantity of heavy metals is significant for environmental pollution characterization, but it has to be taken into account their bioavailability that it is influenced by physical factors (such as temperature, absorption, sequestration, phase association) and chemical factors (water or lipid solubility, the chemical form, concentration, pH) [13].

The classification of minerals into heavy metals with toxic effect must be done careful because there are recent studies that have shown the beneficial effect of toxicogenic metals in the treatment of serious diseases, such as arsenic used as cancer cell apoptosis in the case of leukemia.

In the following we will make some references to toxic effects of some minerals with essential role in the human and animal organism.

Chromium is an essential trace element directly involved in carbohydrates and cholesterol metabolism. Lately, due to the technological food and feed processes, nutritional chromium intake is lower and thus become a very popular dietary supplement. The key role of chromium in the organism is to facilitate the intracellular access of glucose, involved in the processes of energogenesis. Also, chromium is taking part in lipid metabolism, and influence the cholesterol level into the bloodstream. Due to its implication in energy metabolism, chromium has become an important nutrient in the weight loss programs, and also in diabetic patients. From chemically point of view, chromium occurring in environment and organism in different valence states, as Cr^{2+} to Cr^{6+} , but Cr^{3+} compounds are the most stable, followed by Cr^{6+} . Hexavalent chromium is known as industrial pollutant, classified as carcinogenic. Cr^{3+} naturally occurs in soil, water, air and other biological sources. Ingesting or inhalation of chromium leads to reproduction damages, gastrointestinal irritation, anemia, liver and kidney failure, neurological and hematological damages [14].

Lead is a naturally mineral in the environment. Lately the industrial use of lead was significantly reduced, but the largest source of lead contamination is contaminated soil, dust and chips of old paint from deteriorated houses – especially for children [15]. In children there are many studies that demonstrated that lead exposure diminish the intelligence; leads to growth retardation; brain, kidney, and heart damages; gastrointestinal diseases, and disturb the central nervous system [16].

Cadmium has essential role in the metabolism of various microalgae from Diatomophyceae class [17]. Sedimentary rocks and marine phosphates accumulate the highest level of environmental

cadmium, in concentration of about 15mg/Kg [18]. Also some dietary products can be important sources of cadmium for human organism, such as crustaceans, mollusks, leafy vegetables, mushrooms, potatoes, seeds, grains, cacao powder, and organs like liver and kidney [19,20]. The metabolic pathways of cadmium toxicity is poorly known and understood, but researchers speculate that the main damage of cadmium is generation of reactive oxygen species inside the cells that lead to single-strain DNA, disrupting the DNA and proteins synthesis [21]. Cadmium quantitative determination from different biological samples can reflect the acute or chronic exposure. Thus, cadmium determination from blood reflects acute or recent exposure, while cadmium from urine reflects the chronic or accumulation of cadmium (usually the rate between cadmium/creatinine is calculated). Lately, due to the industrial applications, cadmium environmental contamination has dramatically increased.

In humans arsenic exposure is associated with carcinogenic and systemic health effects, and the main exposure source is the diet and drinking water, and much less important the soil and air. Arsenic contamination is associated with pesticides use, wood preserving technologies, semiconductor manufacturing, glass and ceramic factories and smelting [21]. The toxicogenic effects of arsenic are difficult to estimate because it is highly influenced by exposure dose, frequency and duration, by organism characteristics, by solubility, by its oxidation state, and by nutritional factors. Experimental studies demonstrated that exposure of trivalent arsenite (As^{3+}) is 2-10 times more toxic compared to pentavalent arsenate (As^{5+}) [22]. Experimental studies demonstrated that arsenic can also be used in the treatment of promyelocytic leukemia, which can be achieved by the administration of arsenic trioxide – compound approved for pharmaceutical use by the Food and Drug Administration which provide cancer cell apoptosis [23].

But the quantity and the chemical form of some heavy metals are the major characteristics in being necessary or harmful for organism. Most of these minerals have been demonstrated that have carcinogenic (antimony, arsenic, hexavalent chromium, cobalt, mercury, nickel, vanadium), teratogenic (arsenic), and mutagenic (arsenic, vanadium), allergenic (nickel), and/or endocrine-disrupting (cooper, selenium, silver, zinc) effect. Other less known heavy metals, such as thallium – are harmful to the nervous system – especially in children. Mercury, lead, tin, and thallium are toxic to the body, affecting the central nervous system, the bone marrow, the immune system, and also the heart, liver and kidney – organs that are involving in detoxification and excretion of excess or toxic chemicals [23].

Conclusions

Heavy metals are chemicals naturally present into the environment, and some of them are even essential for metabolic pathways.

Ecobiochemistry and xenobiochemistry are sciences that evaluate the metabolic processes from animal or human organisms, regarding the contamination from diet, soil, air, water. Biomagnification is the accumulation of some chemicals in internal organs, and could be characterized by bioaccumulation and biodillution.

Body chelation process and phytoremediation are the best methods to decontaminate the environment and the living organism.

Arsenic, cadmium, chromium, lead, magnesium, manganese, mercury, molybdenum – are considered heavy metals, but some of these are essential nutrients for animal and human organism, being involved in metabolic processes. The toxic effect of heavy minerals has to be evaluated related to other minerals, to the environment concentration, chemical form, bioavailability, temperature, pH, and also to the environmental type: water, soil or air.

References

[1] M. Koller, H.M. Saleh, Introductory Chapter: Introducing Heavy Metals, in Heavy metals, editors: H.M. Saleh, R.F.Aglan, Intechopen, 2018

[2] U.S. Antarctic Program, 2003-2004 USAP Field Season, Biology & Medicine, International collaborative expedition to collect and study fish indigenous to sub-antarctic habitats, 2003

[3] M.E. Sears, Chelation: Harnessing and Enhancing Heavy Metal Detoxification – A review, *Scientific World Journal* 2013 (2013) 219840.

[4] M.E. Sears, K.J. Kerr, R.I. Bray, Arsenic, cadmium, lead and mercury in sweat: a systemic review, *J. Environ. Public Health* 2012 (2012) 184745.

[5] Agency for Toxic Substances and Disease Registry, Toxicological Profile: Arsenic, 2007.

[6] K. Watanabe, M.T. Monaghan, Y. Takemon, T. Omura, Biodistribution of heavy metals in a stream macroinvertebrate food web: Evidence from stable isotope analysis, *Sci. Environ.* 394 (2008) 57.

[7] J. Liu, L. Cao, S. Dou, Trophic transfer, biomagnification and risk assessments for four common heavy metals in the food web of Laizhou Bay, the Bohai Sea, *Sci. Total Environ.* 670 (2019) 508.

[8] I.G. David, M.L. Matache, A. Tudorache, G. Chisamera, L. Rozylowicz, G.L. Radu, Food chain biomagnification of heavy metals in samples from the lower Prut Floodplain Natural Park, *Environmental Engineering and Management Journal* 11 (2012) 69.

[9] K. Yang, L. Zhu, Y. Zhao, Z. Wei, X. Chen, C. Yao, Q. Meng, R. Zhao, A novel method for removing heavy metals from composting system: The combination of functional bacteria and absorbent materials, *Bioresource Technology* 293 (2019) 122095.

[10] M.A. Barakat, New trends in removing heavy metals from industrial wastewater, *Arabian Journal of Chemistry* 4 (2011) 361.

[11] H. Ali, E. Khan, M.A. Sajad, Phytoremediation of heavy metals – Concepts and applications, *Chemosphere* 91 (2013) 869.

[12] N. Sarwar, M. Imran, M.R. Shaheen, W. Ishaque, M. Asif, M.A. Kamran, A. Matloob, A. Rehim, S. Hussain, Phytoremediation strategies for soils contaminated with heavy metals: Modifications and future perspectives, *Chemosphere*, 171 (2017) 710.

[13] Kabata-Pendia, Trace elements in soil and plants, 3rd edition, FL: CRC Press, 2001.

[14] Agency for Toxic Substances and Disease Registry (ATSDR), US Department of Health and Human Services, Atlanta, GA: Public Health Service, 2008.

[15] Agency for Toxic Substances and Disease Registry (ATSDR), Public Health Service, Atlanta, US Department of Health and Human Services, Toxicological profile of lead, 1999.

[16] S.J.S. Flora, G.J.S. Flora, G. Saxena, Environmental occurrence, health effects and management of lead poisoning, in Lead: Chemistry, analytical aspects, environmental impacts and health effects (S.B. Cascas, J. Sordo – Eds.), Netherlands: Elsevier Publication, 2006, pp. 158-228.

[17] T.W. Lane, M.A. Saito, G.N. George, I.J. Pickering, R.C. Prince, F.M. Morel, Biochemistry: A cadmium enzyme from a marine diatom, *Nature* 435 (2005) 7038.

[18] P.B. Tchounwou, C.G. Yedjou, A.K. Patlolla, D.J. Sutton, Heavy metals toxicity and the environment, *Molecular, Clinical and Environmental Toxicology* 101 (2012) 133.

[19] S. Satarug, J.R. Baker, S. Urbenjapoli, M. Haswell-Elkins, P.E. Reilly, A global perspective on Cd pollution and toxicity in non-occupationally exposed population, *Toxicol. Lett.*, 137 (2003) 65.

[20] C.M. Gallager, J.S. Kovach, J.R. Meliker, Urinary cadmium and osteoporosis in US women \geq 50 years of age: NHANES 1988-1994 and 1999-2004, *Environ. Health Perspect.* 126 (2008) 1338.

[21] P. Bhattacharya, A.H. Welch, K.G. Stollenwerk, M.J. McLaughlin, J. Bundschuh, G. Panaullah, Arsenic in the environment: biology and chemistry, *Sci. Total Environ.* 379 (2007) 109.

[22] M.P. Pothier, A.J. Hinz, A.J. Poulain, Insights into arsenite and arsenate uptake pathways using a whole cell biosensor, *Front. Microbiol.*, 9 (2018)

[23] P.B. Tchounwou, A.K. Patlolla, J.A. Centeno, Carcinogenic and systemic health effects associated with arsenic exposure – a critical review, *Toxicol. Pathol.* 31 (2003) 575.