The pollution with heavy metals is a risk factor on the quality of life, being mostly based on human activities related to mining, burning of fossil fuels, pesticides using, production of batteries, smelting of metals etc. [1]. The effects of heavy metals pollution are different among organization types, and between various species. The consequences are difficult to be established on a short term, being affected not just the elements from the base of the ecosystem, but also the superior organisms. Humans and animals are on the risk due to various ways of contamination, most commonly respiratory and digestive. By affecting the food chain, the contamination with heavy metals poses a threat to the safety and security of the consumer, significant on the long-term. The defining of heavy metals was a special concern of specialists up to now, in most of the cases being tried analogies with their consumer, significant on the long-term. The defining of heavy metals poses a threat to the safety and security of the consumer, significant on the long-term. The defining of heavy metals was a special concern of specialists up to now, in most of the cases being tried analogies with their consumer, significant on the long-term.
pollution due to a worldwide restriction in use for this type of fuel. However, according to a WHO study reviewed by [11], at the end of 1980’s the combustion of leaded petrol contributed with 80-90% of air lead pollution.

Cadmium (Cd) is a heavy metal (8.65 g/cm³) naturally found in zinc ores: 5 wt% Cd in sphalerite or zinc blende [Zn(S),S], and 4.5 wt% Cd in smithsonite or zinc carbonate (ZnCO₃) [12]. The largest emissions of atmospheric cadmium are due to the steel industry and waste incineration, followed by volcanic action and zinc production [4, 13]. Large amounts of Cd, as well as Pb and Hg found in nature, may be attributed to various activities in the construction industry such as those related to cement obtaining in which particles of dust are released in atmosphere and carried by the wind in neighboring regions. The process of cement obtaining is energy consuming requiring coal burning. The resulted combustion gases contain particles of heavy metals and also represent an important source in this regard [14, 15]. However, the coal combustion is not a process found only in the cement industry; the power plants are based on coal burning and any other industrial activity, which involves this process, is a presumed source of pollution with various heavy metals.

Mercury (Hg) is a naturally occurring element (13.59 g/cm³), directly mobilized by humans through mining activities. Cinnabar, (Hgs) is the primary mineralogical source of mercury which forms a bright red pigment, vermilion, when powdered, being used in the process of precious metals extraction (Au, Ag), in the manufacturing of various products such as chlorine-alkali paints, electronic devices or various instruments used in physics and medicine [16-18]. Mercury is a volatile heavy metal, being found in atmosphere especially in volcanic areas [18]. The use of various fertilizers in agriculture with the aim of an adequate N, P, and K providing for crop growth, usually adds contaminants such as Hg, Pb, and Cd which are potentially toxic to the soil, plants, and animals and humans which consume the obtained vegetables [19-21].

Nickel (Ni) is naturally found in various forms, such as nickeline (NiAs), millerite (NiS), pentlandite [(Ni, Fe)S]. It is a heavy metal (8.9 g/cm³) that contaminates the environment as a result of mining process, volcanic eruptions, or from the melting of stainless steel (at whose manufacture Ni is used). Nickel-cadmium batteries are one of the most important sources of pollution in their wastes sites [22].

Copper (Cu) is usually found in natural combinations, especially as sulfides [chalcopyrite (CuFeS₂), chalcocite (Cu₅S₄)] or in carbonates (Cu₅CO₃₂(OH)₆, Cu₅(OH)₆(CO₃)₂). It is a heavy metal (9 g/cm³) used in electronics, metallic industry, agriculture (fertilizers, pesticides containing Cu), animal husbandry (as a feed additive) or in food industry (containers, pipes) [23].

Zinc (Zn) is a heavy metal (7.14 g/cm³) naturally occurring as sphalerite (ZnS) and smithsonite (ZnCO₃) [12]. The environmental Zn pollution is related to mining activities, coal combustion, steel processing. Water and foods are usually Zn enriched if they are stored in metal (Zn containing) tanks [19].

Mechanisms of Pb, Cd, Hg, Ni, Cu, and Zn toxicity in humans and animals

The effects of heavy metal residues on human and animal organisms involve specific mechanisms for each of them. Some of xenobiotics (Cd, Pb and Hg) disrupt the functional mechanisms by replacing physiological metals (Cu, Zn and Fe) [29]. Due to their affinity in special for sulfhydryl groups (-SH) found in proteins and enzymes, it is well-known the heavy metals ability to bind these kind of molecules and to alter their activity [24, 30]. However, there are various mechanisms of action for reviewed xenobiotics related to well-known clinical symptoms. Lead ions (Pb⁺) for example, are capable to interfere with Ca²⁺ ions due to some of their similarities. As a result, the access of calcium at the synaptic levels is limited, reducing the signal transduction [31]. Lead is also shown to inhibit the synthesis of hemoglobin, inactivating the delta-Aminolevulinic Acid Dehydratase (ALAD or porphobilinogen synthase), an enzyme which catalyses the conversion of two molecules of delta-Aminolevulinic Acid (ALA) in one molecule of porphobilinogen. As a result, the ALA concentration in blood will increase, and also of Fe²⁺ due to the lead inhibition of ferrochelatase enzyme responsible for protoporphyrin IX and Fe³⁺ joining for hem synthesis. This affecting of hem synthesis lead to anemia; the same effect is obtained due to lead induced changes in the composition of proteins and lipids located in the membrane of red blood cells, increasing their fragility and decreasing their average life span [32]. As a primary toxic effect, cadmium ions (Cd²⁺) inhibit the Ca²⁺ transporting enzymes, disturbing cellular Ca²⁺ metabolism [32]. However, Cd is a well-known thiol reagent, its main mechanism of toxicity being represented by essential thiol groups (-SH) binding in the cysteine-containing enzymes with mercaptide complexes formation. Another mechanism of Cd enzymes inhibition is that of essential metal cofactors (such as Zn) replacing. There are various studies on different enzymes inactivated by Cd, some of them referring to superoxide dismutase, catalase, succinate dehydrogenase, glutathione related enzymes,
delta-ALA dehydrase [33-35]. The inhibitory effect of Cd on delta-ALA dehydrase is not singular, the same effect being already mentioned for Pb, and also reported for Hg, Zn and Cu [35, 36]. Considering the role of sulfhydryl groups of membrane proteins in electrical conduction and chemical transmission processes, the electrical excitability and synaptic transmission are affected by heavy metals binding at these groups [37]. Proteins participating in the DNA repair systems are also targets of Cd toxicity. Therefore, Cd is considered one of the main heavy metals with carcinogenic potential due to its inhibitory effects on DNA repair activities [38, 39]. Besides sulfhydryl, phosphoryl, carboxyl, amide and amine groups binding, and toxic effects by protein precipitation and enzyme inhibition [40], the inorganic Hg$^{2+}$ is able to be converted to its organic form, methyl mercury (by the action of microorganisms), the resulted compound being very stable, with cumulative effect, especially in aquatic organisms. It represents a dietary risk for the consumers, having a well-known neurotoxic effect. The phenomenon of biological methylation is also known for Pb and As [41, 42]. Neurotoxic and carcinogenic properties were also reported for Ni ions. They are usually bound to sulfhydryl groups of proteins and, as other reviewed heavy metals (Pb, Cd, Hg and Cu), are oxidative stress inductors, with metabolic damages (lipoxygenation, proteins dysfunction) and at the DNA level [43, 44]. As previously mentioned, the mechanism of Cu toxicity is related to sulfhydryl groups binding and subsequent enzymes inactivation (glucose-6-phosphate dehydrogenase, glutathione reductase). Hemolysis was reported as an important effect of Cu intoxication, being caused either by a direct red cell membrane damage (the cell membrane integrity is affected by protein sulfhydryl groups binding and oxidative degradation of constituents lipids) or as a result of enzymes inactivation (with functions of protection against oxidative stress). The methemoglobin formation is of a particular significance in Cu intoxications, the oxidation of hem iron leading to the reduction of blood oxygen carrying capacity [45]. Comparing to other reviewed heavy metals, Zn is considered relatively harmless. At high doses and for a long time of exposure, there was reported to interfering with Cu uptake, which lead to effects associated with Cu deficiency: hypocupremia, impaired iron immobilization, anemia, leukopenia, neutropenia, decreased amounts of copper dependent enzymes, such as superoxide dismutase, ceruloplasmin, cytochrome-c oxidase, increased levels of plasma cholesterol and LDL, HDL cholesterol, and abnormal cardiac function. Soluble zinc salts, such as zinc chloride, are generally caustic [46].

**Heavy metals in different elements of the ecosystem and bioremediation pathways**

The importance of heavy metals pollution comes from the fact that it affects all the components of the ecosystem: air, soil, water, and the health of living organisms. Their circuit in nature, and subsequently, the possibility of their maintaining at risk levels for many generations, is due to the connections among soil, plants, animals and humans. However, various studies reported ways of phyto-remediation for contaminated soils, limiting the presence of heavy metals residues in superior organisms. This limitation is important taking into account that the contamination of animals with heavy metals is significant in high polluted areas. For example, Cd was found in liver at 10 fold higher concentrations than the Maximum Residue Limits (MRL)* and up to 30 fold higher in kidneys. Milk samples collected from the same areas and analyzed for Pb, Cd, and Zn contents showed contamination of 66% of samples for Pb, 100% for Cd, and 22% for Zn, at levels that exceeded 15-20 fold the MRL* [47]. In a previous study were reported concentrations of 0.56 ppm for Pb, 0.09 ppm for Cd, and 28.16 ppm for Zn, well above the MRL* of 0.2 ppm, 0.01 ppm, and 5 ppm, respectively [48]. Other authors reported that the average Zn concentration in liver and kidney samples collected from cattle raised within a range of 2 up to 6 km around a chemical plant, exceeding the MRL* about two times. In kidney and liver samples collected from sheep raised in the same areas, and also in sheep and cattle spleen samples, Zn did not exceeded the MRL* at any of the control sites [49].

The mobility of heavy metals in soil depends mainly on pH and the amount of organic matter. As the binding of heavy metal is stronger to the organic matter of the soil, the more immobile in the soil it will become but with the possibility of being picked up easier by the plants. This is a reported behavior for Cd [50], Cu [51], Pb [52], and Zn [53]. Generally, the presence of heavy metals in soil affects the plants growing and the content of plants dry matter, decreasing it [54, 55]. The order of toxicity of some of the reviewed heavy metals was reported for plants by [54] as the following one: Cd > Hg > Pb. Considering the effect of heavy metals uptake by plants through contaminated soils on dry matter yields decreasing, Wang et al (2002) [54] established the following order; field pea, wheat, fodder vetch, rapeseed, and maize. The accumulation of heavy metals in plant tissues depends on various factors, such as: plant species, the vegetative organ, the plant age, the pH of soil. Wang et al (2002) [54] reported that field pea, fodder vetch, and wheat were more susceptible to soil metals accumulation (Cd, Zn, Pb and Cu) than were rapeseed and maize. Among the crops, maize was the highest accumulator for Zn, and Cd, fodder vetch for Cu, and wheat for Pb. In an experiment performed in contaminated soil due to a former waste incineration plant, Kacálková et al. (2014) [55] reported that Ni and Pb accumulated in highest amounts in plant roots, higher in herbs (maize, sunflower) than in trees (willow, poplar). Cd showed a different pattern of accumulation, highest in roots of willow, followed by the leaves of willow. Wang et al (2002) [54] reported a more Cd and Cu accumulation in the grain of wheat than of maize, suggesting safer the growing of maize as a phytoremediation of lightly contaminated soils due to its tendency to accumulate less heavy metal residues than other plants. The idea of maize using as phytoremediation is also supported by [56, 57]. On sites with multiple metal contamination, Wang et al (2002) [54] consider safer the growing of maize and rapeseed than wheat or legumes. Lu et al (2015) [57] reported that Pb and Ni mainly accumulated in maize roots, but Zn in the maize seeds. The same tendency of Pb accumulation in higher amounts in maize roots, and smaller in seeds was also reported by [58, 59]. Considering the reviewed heavy metals, their concentration in maize increased in the following order: Zn > Ni > Pb [58]. Considering the age of plants, it seems that roots of young ones display greater ability to absorb ions than old plants when they are with similar size [60]. Hough et al (2003) [60] reported for Cd uptake a greater dependence on soil pH in the case of wheat, comparing to maize. The aforementioned authors suggested that limiting the soil pH to 7.0, it will reduce the Cd concentrations in wheat grain.

Lately, a number of studies which involve the process of biosorption become increasingly significant [61-66]. This
process is an alternative to the more expensive electrochemical, chemical precipitation, coagulation or flocculation methods for heavy metal ions removal from aqueous media [64-66]. Utilization of various biological materials, such as different types of algae (Ulva sp., for example), agricultural waste and by-products (rape or grain straw, rice or soy husks, sawdust, mustard waste), in an eco-friendly and cost-effective alternative for Zn(II), Hg(II), Pb(II) and Cd(II) ions absorption from aqueous media was tried [20, 21, 63-66]. Furthermore, the essential microelements, such as Zn, which was retained by ion-exchange interactions, could be released in tested soils up to a saturation level is obtained [65]. An interesting process of phytoremediation was described in a microbe-plant symbiosis relationship (plant-growth-promoting rhizobacteria on radish plants for Ni phytoextraction enhancement) [62].

Conclusions

Copper and zinc are important microelements for human and animal organism, considering the role of copper in hematopoiesis and those of zinc as a component of various metalloenzymes involved in the synthesis of proteins and nucleic acids. The other heavy metals reviewed in this study are important as toxic xenobiotics, their presence in the organisms being a consequence of ecological pollution.

The presence of heavy metals in nature and their risks to organisms are constantly monitored by competent institutions. Based on toxicological studies, the Joint FAO/WHO Expert Committee on Food Additives establishes safety indicators of residue levels to which the consumer may be exposed (for example, Provisional Tolerable Weekly Intake, Acceptable Daily Intake). Moreover, various countries use normative acts in which Maximum Residue Limits are provided for some heavy metals in different foodstuffs, the others which are not set being considered with zero tolerance. However, such efforts must always be supported by people's concern for the protection of the environment.

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