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Impact of toxic heavy metals in food systems: A systemic review

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Abstract : Heavy metal pollution has shown great threat to the environment and public health worldwide. Heavy metals are among the most problematic pollutants as they are non-biodegradable and can accumulate in ecological systems. In case of food chain systems, they will eventually result in food chemical contamination which can lead to various diseases, threatening public health. For instance, cadmium (Cd) accumulates in kidney and liver for over10 years and affects physiological functions of a human body. Prolonged exposure to heavy metals such as cadmium, copper, lead, nickel, and zinc can cause deleterious health effects in humans. Therefore, this review was written to provide a deep understanding of the mechanisms involved in eliciting their toxicity in order to highlight the necessity for development of strategies to decrease exposure to these metals, as well as to identify substances that contribute significantly to overcome their hazardous effects within the body of living organisms.

Key words: Heavy metal, Health, Toxic, Food Additives.

1. Introduction

Heavy metal contamination in natural environments is an urgent problem due to the increasing industrial activities. Generally, metal ions can be classified into essential and nonessential lions. Nonessential heavy metals, such as cadmium (Cd), mercury (Hg), arsenic (As) and lead (Pb), even at trace amount exposure, are highly toxic and carcinogenic[1,2]. Although essential metals like copper (Cu) and zinc (Zn) are required to support biological activities, these essential metals are toxic when in excess[3,4]. Furthermore, both of them can pose a severe threat to human health and environment due to their non-biodegradable nature and accumulation in the food chain. Therefore, it is essential to quantify these metals at trace level in the environment food and drinking water. Traditional quantitative methods, such as atomic absorption/emission spectroscopy[5], inductively coupled plasma/atomic emission spectrometry[6], and cold vaporatomic fluorescence spectrometry (CVAFS)[7,8], have been extensively applied to monitor metal ions. Although these techniques are highly selective and sensitive, they require sophisticated and expensive instrumentations, especially, complicated chemical processes for extracting metal ions from the as-sampled water, in which the speciation of metal ions might be changed[9,10].

Moreover, several studies have reported that the uptake of heavy metals by organisms depends on the free metal ion concentration rather than the total metal concentration in solution. In fact, free metal ion concentration ultimately determines the bioavailability and toxicity of heavy metal, owing to better correlations between metal uptake and the concentration of free metal ion or labile metal[11,12]. Besides, traditional methods cannot be used as portable devices for on-site/in-site quantification, and meanwhile large-scale determination of heavy metals can be time consuming, labor intensive and costly. In contrast, sensors have great potential for on-site/in-site detection of multiple heavy metals. Rapid development of nanotechnology has provided new opportunity for improving the performance of sensors such as sensitivity, selectivity and reproducibility.

These heavy metal ions are considered as the “Environmental health hazards” as they are ranked in the top 10 in the listings from “Agency for Toxic Substances and Disease Registry Priority List of Hazardous Substances”, based on toxicity of substance and potential exposure to contaminated air, water and soil. In order to evaluate this heavy metal ion toxicity, several international agencies like World Health Organization (WHO)[13,14], Centre for Disease Control (CDC)[15], Joint Food and Agricultural Organization (FAO)/WHO Expert Committee on Food Additives (JECFA), and International Agency for Research on Cancer (IARC)[16] are working on it. Among various heavy metals, lead (Pb), cadmium (Cd), mercury (Hg), arsenic (As) and chromium (Cr) are the most probable causes for most of the heavy metal-related diseases[17,18,19]. In most cases, trace levels of metals are important in the biological functioning of cells such as transportation and cell signalling[20]. If these metal ions move out of the mechanistic pathway, then they interact with other regular protein sites instead of natural binding sites and thereby lead to toxicity in humans, animals[21] and plants[22,23]. The toxicity mechanism of heavy metal ions is through enzyme inhibition, oxidative stress and impaired antioxidant metabolism. These mechanisms show adverse health effects through free radical generation that leads to lipid peroxidation and depletion of protein sulfhydryl[20,24]. This review highlights the few toxicity mechanisms of heavy metal ions that inhibit the enzymes and induce oxidative stress thereby affecting human health.

2. Effects of toxic chemicals on human health

The term heavy metal refers to any metallic chemical element that has a relatively high density and is toxic at low concentrations. Metals are widely distributed throughout nature and occur freely in soil and water. Heavy metals in herbal preparations may not be a result of accidental contamination but may be introduced for supposed therapeutic properties; for example, mercury was used to treat syphilis until the introduction of penicillin, while arsenic-derived compounds are still used for treatment of some forms of malignancy. Among the heavy metals mercury, lead, arsenic and cadmium are toxic metals and have mutagenic effects even at very low concentration. Several cases of human disease, malfunction and malformation of organs due to metal toxicity have been reported. Along with human beings, animals and plants are also affected by toxic levels of heavy metals[25].

The effects of toxicity vary between metals; for example, while lead poisoning typically may cause abdominal pain, vomiting, severe anemia, hemoglobulinuria and the stools have dark color owing to the presence of lead sulfide, mercury poisoning may cause peripheral neuropathy, psychological disturbances and arrhythmias may develop due to the toxic effect of mercury on the myocardium. Late, marked renal impairment occurs due to its nephrotoxic action leading to death. The specific identification of metals is required for accurate diagnosis due to considerable overlap between the clinical syndromes associated with heavy metal poisoning[26] (Table 1).

Table 1. Common uses, principal toxic effects and permissible limits of some heavy metals[27].

Toxic metals	Toxic metals	Principal toxic effects	Permissible limits (mg/l)
Arsenic	Pesticides, herbicides	Lung cancer and skin diseases	0.02
Cadmium	Batteries, plastics, pigments, plating	Kidney damage, lung cancer and bone disorder	0.06
Chromium	Dyes , alloys, tanning	Respiratory effects, allergic dermatitis, kidney and liver damage	0.05
Lead	Batteries, wire and cable, alloys	Neurological effects, hematopoietic system damage and reproductive effects	0.1
Mercury	Chloro alkali industry, pesticides, thermometers, Batteries	Neurological effects and kidney damage	0.01
Manganese	Pesticides , batteries	Central nervous system effects	0.26
Zinc	Pharmaceuticals, dyes, Batteries	Gastrointestinal disturbances and anemia	15

Soil heavy metal studies which include plant available indices, total concentrations, and fraction distributions have also been conducted on many agricultural systems, including rice (Oryza sativa) production. Rice has a high water requirement compared to other crops and during the growing season, Eh can reach roughly 300–200 mV[28]. Soil samples, including from rice paddies under submerged conditions, are routinely air-dried prior to heavy metal analysis[29,30]. Zheng and Zhang[31] studied the effect of moisture regimes on paddy soil heavy metals and found that soil moisture did not affect the direction or pathways of fractionation distribution (from active to stable fractions), but did affect the transformation rate. Zheng and Zhang[31] dried rice paddy soil samples after collection and then reconstituted three moisture regimes under controlled conditions in the lab. It does not appear that sample preparation was conducted in an anaerobic environment, therefore this result does not represent in situ soil moisture regime that controls the distribution of heavy metals.

Redox conditions are known to have a significant effect on heavy metal speciation in sediments[32]. As indicated by Calmano et al. (1993), if anoxic sediments are exposed to atmosphere, redox condition change and redistribution and transformation of heavy metal fractions in the sediments takes place[33]. A few studies show the effect of redox conditions on heavy metal availability[34,35]. Paddy soil has the anoxic condition during rice growing season similar to the river sediment.

3. Cytotoxic Mechanisms of Heavy Metals

Heavy metal induced toxicity has been studied extensively and reported by various workers. Having the potential to produce highly reactive chemical entities such as free radicals, heavy metals are known to cause oxidation of sulfhydryl groups of proteins, depletion of protein, DNA damage, lipid peroxidation, and several other effects. The underlying factors making the greatest contribution to toxicity for different metals involves generation of reactive oxygen (ROS) and nitrogen (RNS) species that disturb cell redox systems. ROS that are distinguished by their high chemical reactivity, include free radicals such as superoxide ($O_2^{\cdot -}$), hydroxyl ($OH^{\cdot}$), peroxyl ($RO_2^{\cdot}$) and alkoxyl ($RO^{\cdot}$), as well as certain non-radicals such as peroxynitrite ($ONOO^-$) and H2O2, which are either oxidizing agents or get easily converted to radicals (Figure 1).

Intracellular generation of superoxide anion ($O_2^{\cdot -}$) primarily occurs non-enzymatically through the intervention of redox components such as semi-ubiquinone (a component of the mitochondrial electron transport chain)[36,37], or via the intervention of enzymes such as NADPH-oxidase (NOX)[38], xanthine-oxidase or auto-oxidation reactions[39,40]. Superoxide anion ($O_2^{\cdot -}$) acts as a mild reactant under physiological conditions, with poor ability to cross the biological membranes. Upon interaction with nitric oxide (NO), production of peroxynitrite ($ONOO^-$) transforms superoxide into very reactive intermediates such as hydroxyl radical ($^{\cdot}OH$), which have a very short half-life[41].

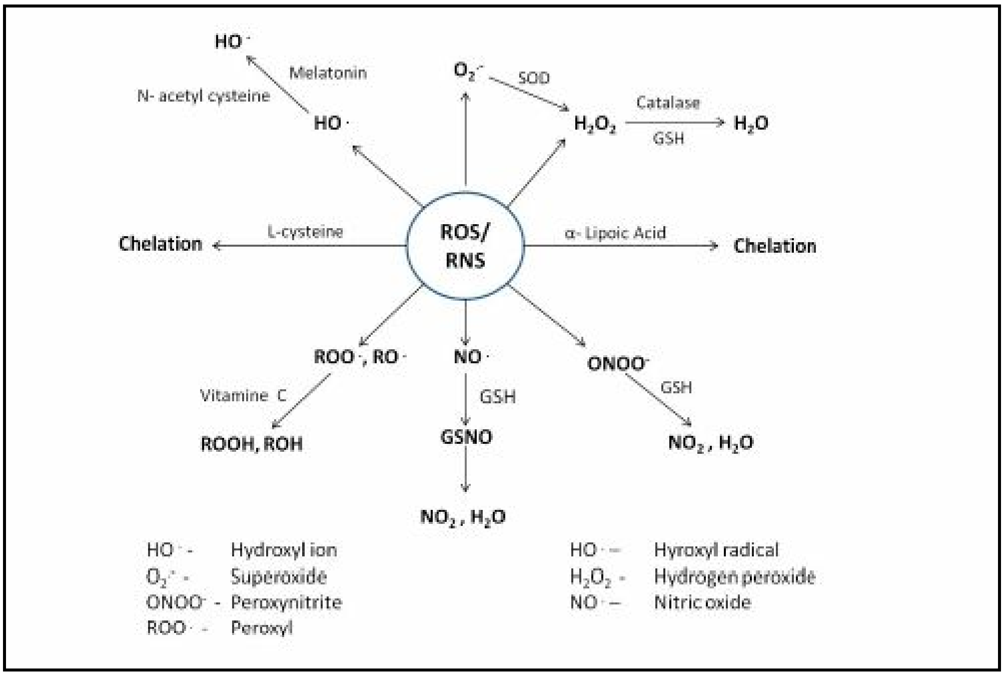

Figure 1. Modes of action of different antioxidants in mitigating the toxic effects imposed by metals.

Through the involvement of nitric oxide synthase isozymes like endothelial nitric oxide synthase and (eNOS) mitochondrial nitric oxide synthase (mtNOS), generation of nitric oxide occurs via conversion of L-arginine to citrulline. $NO^{\cdot}$ has been shown to have greater stability in oxygen deprived environments. Because of its amphipathic nature, $NO^{\cdot}$ easily diffuses through the cytoplasm and plasma membranes. Upon interacting with superoxide anion, NO generates peroxynitrite ($ONOO^{-}$)[42]. An increase in ROS/RNS production or decrease in ROS-scavenging activity that arises as a result of exogenous stimuli has been found to alter cellular functions through direct modifications of biomolecules and/or by aberrant stimulation/suppression of certain signalling pathways affecting growth factor receptors.

Previously, there were many studies have been done regarding the heavy metal contamination and determination in rice worldwide[43]. However, the studies were using total heavy metal concentrations rather than bioavailability heavy metal concentrations in rice[43]. Thus, the main objective of the present study was to determine the bioavailability of heavy metal (Cd, Cu, Cr, Co, Al, Fe, Pb, As and Zn) concentrations in 22 varieties of cooked rice samples. Based on Malaysian Food Regulation (1985)[44], maximum permitted levels of heavy metal from Fourteenth Schedule (Regulation 38) were used to protect the consumer. Food and Agriculture Organization (FAO) of the United Nations (1989)[45] stated that the food standards such as FAO/WHO Codex Alimentarius Commission (CAC) 1984[46] and FAO/WHO Codex Alimentarius Commission (CAC) 1989[45] aim at protecting consumers' health and ensuring fair practices in the food trade. Thus, the bioavailability of heavy metals concentrations were compared with the permissible levels of heavy metal stated in Malaysian Food Regulation (1985)[44], FAO/WHO CAC 1984[46] and FAO/WHO CAC 1989[45].

4. Significance of heavy metal detection

Hazard and Operability Analysis (HAZOP) is a structured and organized technique for risk management [47, 48,49]. Heavy metals are often defined in literature as the metals with densities exceeding ($5 g/cm^3$)[50]. However, this definition is arguable as it neglects all chemical properties of the substances. Cadmium is commonly used in industrial manufacturing and can be applied in electroplating[51], nuclear fission[52]. For instance, the so-called "itai-itai" disease in Japan was caused by cadmium[53,54,55]. Nickel is another heavy metal that is of high importance for industrial applications. It is widely used in the production of alloys[56], batteries[57], and plating[58]. But nickel has been classified as carcinogen by various agencies and institutions worldwide[59]. Additionally, mercury has also been used in diverse applications in the past, including barometers[60], switches[61], and fluorescent lamps[62,63,64,64,65]. This element can cause severe problems to our ecosystem. Therefore, the usage of mercury has been significantly restricted in the past decade. Overall, to mitigate and prevent heavy metal pollution, detection and monitoring of heavy metals is an essential step.

4.1. Current detection methods

One of the most reliable and versatile methods of detection of heavy metals is ICP-MS. It has been developed since the1980s. For instance, Tokalıoğlu (2012) successfully determined different heavy metal elements (e.g., Fe, Sr, Mn, Zn, and Pb) in thirty medicinal herb samples after microwave digestion[66]. Fatema et al. (2015) applied AAS to quantify the concentrations of Pb, Cd, As, Cr, and Hg in shrimps[67].

Overall, current techniques have advantages in the detection of heavy metals as they are adequately sensitive, specific and accurate for the determination at tracelevels[68,69,70]. However, all of them require expensive and bulky equipment, trained personnel, and laborious operation. Therefore, researchers have been striving to develop cheap, simple, sensitive, specific, accurate, user-friendly, and environmental-friendly detection devices, and μPAD is one of the most promising solutions.

5. Conclusion

Agents responsible for multiple human complications vary grossly in their physiochemical properties, and metals are no exception. After entering an ecosystem, metals induce a broad range of physiological, biochemical, and behavioural dysfunctions via induction of oxidative stress in humans. Oxidative and nitrative stress developed in response to toxicants plays an important role in damaging biomolecules, as well as disrupting signalling pathways, which in turn leads to pathogenesis of multiple human diseases. Despite the protection afforded by the cellular redox environment in biological systems, its disruption due to exogenous stimuli or endogenous metabolic alteration leads to increased intracellular ROS/RNS levels. Buffering and muffling reactions between ROS/RNS generation and elimination to redress the deleterious effects caused by oxidative stress are maintained by complex antioxidant (enzymatic and non-enzymatic) systems. In terms of a reactivity standpoint, the enzymatic antioxidant system constitutes the first line of defence, followed by reduced thiols and low molecular weight antioxidants and then by a broad range of products from dietary sources. Defense systems for overcoming the deleterious effects of oxidative and nitrative stress generated by production of reactive oxygen species (ROS) and reactive nitrogen species (RNS) are essential to maintenance of cellular homeostasis.

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