The Accumulative Effect of Heavy Metals on Liver and Kidney Functions

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Abstract

Some of the heavy metals exist in the outer layer of the earth, which is utilized for different economic and manufacturing objectives. As some of these minerals impact humans in several ways, which are direct and indirect, others like Cadmium and Zinc are needed for several body activities, such as organ functions and biological chemical processes. Within these tests, we employed analysis of liver enzyme, urea, and creatinine, to discover the damaged tissue causing after exposure to heavy metals. Results of liver function enzymes, Aspartate aminotransferase (AST), Alanine transaminase (ALT), and Alkaline phosphatase (ALP), were registered a significantly increasing (P≤0.05) for control, Cadmium treatment and zinc treatment groups, with (32.1, 39.3, and 30.5) IU/ml, (9.6, 16.0, and 8.4) IU/ml, and (1.6, 2.5 and 2.12) IU/ml, respectively. Cadmium administration was significantly reduced (P≤0.05) in serum creatinine concentration (1.26) IU/ml, compared to the control group (2.02) IU/ml. While the average serum creatinine concentration increased to (4.99) IU/ml after giving rat group Zinc solution. Moreover, the urea concentration was significantly decreased to (18.85) IU/ml in the Cadmium treatment group than values of control and Zinc group (30.61, and 35.97) IU/ml, respectively.

Keywords: *Liver enzymes, creatinine, urea, heavy metals.*

Introduction

The effect of heavy metals on biochemical enzymes in living systems has been studied. The changes refer to the action of enzymes and/or embryonic tissues to determine the developmental processes, which are distinguished by the growth and formation of new tissues in viviparous animals, as embryonic nutrition.

Heavy metals stimulate enzyme activity via the transformation process of maternal or embryonic tissues and display in the form of natural growth variations. The metabolic levels of the embryo foreseeable to be various from the maternal, which is reflected in the enzymatic activity. Dosing of Cadmium chloride with concentration from (50 to 200) ppm to the male of Sprague Dawley rats increased aspartate aminotransferase (AST or AAT) and alanine aminotransferase (ALT or ALAT) enzymes in the kidney, liver, and brain tissues [26]. Exposure *katelysia opima* to the Mercuric chloride (0.07 and 0.14) mg/l has raised the activity of AST and reducing the activity of Na+-K+ ATPase[17].

Rainbow trout *Oncorhynchus mykiss* were significantly influenced by a sub-lethal concentration of Cadmium (Cd) and responses on growth and biochemical parameters, while chronic exposure was developing early elevation or depression, this pattern is showing adaptation to the toxicant over time. So, exposing of *Oreochromis mossambicus* to the concentration of Cadmium chloride, caused necrosis, rising the activity of AST and ALT in tissues, and increasing cell membrane permeability, resulting in damage of tissues after 1 and 2 weeks.

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Heavy metals cause damage and malfunction in tissues of organisms [33]. Persistent exposure to Cd concentrations raised the enzyme›s activity of AST and ALT in *Oreochromis niloticus*, which are accomplish an important role in the metabolisms of amino acid and protein and maybe releasing into plasma, then destruction and dysfunction tissue. It has become clear that a decrease in the activity of ALP enzymes is an outcome of disruption in the membrane of the transport system, while the increase in the activity probably associated with damaged tissue, which is affected by various factors, such as water quality, lifetime history, Cd concentration and exposure period [10].

One of the major health in the recent world was prolonged exposure to environmental pollution with heavy metals, which diffusion by industrial operation, volcanic explosion, bacterial activity, spring waters, anthropogenic activities including fossil fuel combustion, erosion, agricultural activities like feeding, and bioaccumulation. Environmental health hazards of these metals are easily distinguishable from the top 10 in the list of Dangerous Materials of the Agency for Toxic Substances and Disease Registry [8] [2]. Heavy metals have a cumulative toxic affection causes chronic degradation, particularly in the neural system, renal, and liver, besides some cases affect teratogen and carcinogenic [12] [13].

The high toxicity of Cd is due to its long biological half-life (10-30) years in person tissues, which makes him attack numerous organs and systems, mainly the liver, kidney, and neural system, also. Acute and chronic Cd exposure causes hepatocyte swelling and massive necrosis as a result of elevation in enzymatic biomarkers [4] [23]. Human tissue is exposed to Cd by smoking cigarettes, agricultural uses, electroplating Cd-Nickel batteries as industrial sources, and paint pigment manufacturing units [39].

Although numerous researches on Cd toxicity performed, the molecular technique dependent on Cd toxicity has not been defining so far. The presence of Reactive Oxygen Species (ROS) resulting from the destruction of macromolecules indicates to pathogenicity caused by Cd-toxicity [22]. Anyway, it is not recognized if Cd was producing ROS directly by interacting with molecular oxygen or after represses the antioxidant protection system.

Cellular regulatory proteins are the target of free radicals generated from carcinogenic heavy metals, although they are involved in apoptosis, DNA repair, cell cycle regulation, cell growth, DNA methylation, and differentiation [15].

Cd was utilized in the production of paint, pigment alloys, coating, electrode components in producing alkaline batteries, and plastic. Cd is discharged from smelters and released into sewage sludge, fertilizers, and groundwater than is used up by plants, and reached to humans by ingestion contaminated food like cereals, vegetable, grains, and fruits [7] [34] [16].

This research aimed to study the influences of chronic oxidative tension in the liver, kidney, and liver function parameters in mice, as an outcome of exposure to environmental doses of heavy metals.

Materials and Method

This research was achieved at the Ministry of Science and Technology laboratories, three groups of mice (male and female), (C57BL), (50) mice for each group were subjected them to the same conditions of experience, such as accommodation, nutrition, and attention. The experiments were started at the beginning of April and ended after 90 days later. The first group of mice was given drinking water with a concentration of Cd salts (0.685) mg/l.

Whereas, the second group was given concentration of Zinc salts (0.572) mg/l with drinking water, while the third group was considered as a control group, which was given only distilled water throughout this period. Finally, blood was collected after drawn directly from the heart to obtain the blood serum, and then biochemical examinations of liver and kidney functions were performed. The diagnostic examination kit was of AFCO type.

Results

The difference in liver function enzyme concentrations is an indirect indication in diagnosing liver damage, as high concentrations of these enzymes in the blood cause an imbalance in liver cells. Table (1) shows that the level of AST in the Cd treatment group significantly increasing ($P \leq 0.05$) was (39.3) IU/ml compared to a control group (32.1) IU/ml. Whereas, the average significantly decreased to (30.5) IU/ml in the Zinc treatment group compared to a Cd treatment group and control group. While, ALT was significantly

increasing to (16) IU/ml in the Cd treatment group compared to the control group and Zinc treatment group with (9.6, and 8.4) IU/ml, respectively. At low concentrations of liver function enzymes, we note the presence of mathematical differences compared to the control group and significant differences when using the Cd treatment group. However, ALP concentration significantly increased (P≤0.05) in the Cd treatment group reaching to (2.57) IU/ml compared to the control, and Zinc treatment groups with (1.61, and 2.12) IU/ml, respectively.

Table (1): Effect of cadmium and zinc administration on liver enzymes

ALP	ALT	AST	Treatment
Control group	32.10±5.60^{b}	9.60±1.50^{b}	1.61±0.18^{b}
Cadmium group	39.30±9.26^{a}	16.00±3.65^{a}	2.57±0.29^{a}
Zinc group	30.50±5.64^{b}	8.40±2.31^{b}	2.12±0.29^{ab}
LSD	7.2	6.2	0.96

Besides, table (2) showed that the concentration of serum creatinine was significantly decreased (P≤0.05) in the Cd treatment group with (1.26) IU/ml compared to the control group (2.02) IU/ml. While the average serum creatinine concentration significantly increased to (4.99) IU/ml when gave Zinc treatment group. Moreover, the concentration of urea was significantly decreasing to (18.85) IU/ml in the Cd treatment group compared to control, and Zinc treatment groups with (30.61, and 35.97) IU/ml, respectively.

Table (2): Effect of cadmium and zinc administration on kidney functions

Urea	Creatinine	Treatment
Control group	2.02±0.41^{c}	30.61±9.40^{a}
Cadmium group	1.26±0.65^{b}	18.85±8.18^{b}
Zinc group	4.99±0.79^{a}	35.97±6.93^{a}
LSD	0.76	11.76

Statistical Analysis: Statistical analysis achieving by extracting the mean ± standard error and significant differences were tested between the mathematical rate using the Duncan test [6]. Analysis by using a T-test accomplish to study differences between rates of various samples [30].

Discussion

In this research, determined the toxic influences of Cd and Zinc on liver and kidney tissues. Oxidative stress was the harmful effect of heavy metals on human health. Cd metal can generate several ROS, increase lipid peroxidation, and decrease the antioxidant supply. Increasing oxidative stress markers may refer to elevate the generation of ROS, which causes damage to large molecules through an occurrence of diseases related to aging, like heart disease, Parkinson's disease, diabetes, and mitochondrial diseases[19] [4] [37].

Existence high concentration of heavy metals in the environment like Zinc and/or Cd causing food fracturing to molecules, and throw away free radicals which killing some friendly bacteria, as well as, damage to vitamins, enzymes, and yields chemicals like pesticides can form new chemicals called unique radiolysis products-URLs or toxins[5]. Some of these chemicals the long-term effect on our food was unknown, so we cannot be safe, while the immune system was affected and inhibited its functions by forming the oxidizers[38].

On the contrary, Zinc exhibit increases the efficacy of liver enzymes due to its antioxidant activity, which gives rise to a decrease in oxidative pressures, oxidation and damages the cell as a result of the interaction between hydroxyl root (unstable free root) and some life molecules. Researchers, Stohs and Bagchi [31] and Sies [28] indicated that hydroxyl produced from hydrogen peroxide by lipid peroxidation or oxidizing the DNA or protein gave an improvement to the texture of liver tissue.

DNA damage causes mutations and maybe cancer if the repair mechanisms for DNA do not work, whereas protein damage causes inhibition of enzymes and teratogen proteins [29] [35] [21]. A system of antioxidant

metabolites and enzymes prevents damage of nucleic acids, proteins, and lipids, from occurring or removed before they cause damage, and the amount of protection depends on the concentration of antioxidant and reaction conditions [28] [36].

Oxidative stress is an essential causative of several chronic diseases, such as cardiac disorders, immunologic disorder, cancer, atherosclerosis, and neurodegeneration[25]. In eukaryotic cells, the sources of ROS such as O_2, H_2O_2, and OH, were a mitochondrial respiratory chain, microsomal cytochrome P450 enzymes, flavoprotein oxidases, and peroxisomal fatty acid metabolism [3]. Zinc is an inhibitor of nicotinamide adenine dinucleotide phosphate (NADPH) oxidase, decreased production a cofactor of superoxide dismutase (SOD) (enzyme catalyzes the transfer of H_2O_2 to O_2), like ROS, and stimulate the generation of metallothionein, which is very rich in cysteine (an excellent scavenger of OH). Supplementation of Zinc to healthy human (20-50) years decreasing the concentration of malondialdehyde (MDA), 4hydroxy alkenes (HAE), and 8-hydroxy deoxyguanine in the plasma[24].

The period of exposure was the main cause of Cd accumulation in all tissues, for example, the concentration of Cd in mice was much higher in the blood, liver, and kidneys exposing for only one-day per/week for 5 weeks than exposed through 5 weeks [18]. Several tests in mice were done and discovered that the concentration of Cd in blood plasma was more than red cells after injection, and the first symptom of Cd toxicity remarked in the epithelium of blood vessels, and damage of hepatocytes due to oxygen deficiency [9] [11] [14].

The accumulation of Cd in kidneys has several reasons, transmitted from other tissues, and release from hemoglobin during hemolysis, or liberating metallothionein from red cells [9]. The molecular analysis of Cd toxicity in kidneys is still unknown, and propose that Cd encourage the lipid peroxidation and inhibits enzymes implicated in removing of activated oxygen species from various tissues [27].

Large numbers of macromolecules and more than 300 enzymatic reactions in which Zinc performs as a necessary element responsible for its structure and functions [32]. Whereas, Cd is a toxicity element causes structural distortions to proteins due to its association with sulfhydryl groups [35].

Liver destruction is determined by estimating the concentration of liver transaminase enzymes. After liver parenchymal cells damage or membrane permeability, enzymes like glutamate pyruvate transaminase (GPT), glutamate oxaloacetate transaminase (GOT), lactate dehydrogenase, arginase, and gamma-glutamyl transaminase, discharged out of the cell, and the result is an increase in the level of enzymes in the blood than normal [1] [20].

Conclusion

The research determined a new path to the study of biological impacts associated with environmental susceptibility to heavy metals. The aim is to distinguish antioxidant defense disorders and the oxidative processes in organs, like the kidney and liver, as a result of continuous exposure to lower doses of Cd and Zinc, and establish the effects of these metals on oxidation processes in the liver and kidney function indicator.

Source of Funding: This study is self-funded

Conflict of Interest: Disclosure the authors declare no conflict of interest.

Ethical Clearance: Ethical clearance from the institutional ethical committee obtained for the study.

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