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The Effect of Cadmium Nanoparticles on Hepatic Enzymes Variation in Blood of Rattus

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***Abstract* — Nanoparticles can be used in disease detection, Medical imaging, Pharmaceutical Drug, cancer treatment, gene therapy, Cosmetics and textile productions. These materials accumulate in cells that create Oxidative stress because of reviving oxygen production. Cadmium is a toxic pollutant that has no constructive role in the body and is partially harmful. This metal can create oxidative stress in the body with an increase of free radicals and a decrease of antioxidant capacity that can be lead to the destructive effects in liver and kidneys. At first, nanoparticles of cadmium oxide was synthesized by chemical method in the library. The evaluation of these nanoparticles by X-Ray diffraction (XRD) confirmed that synthesized nanoparticles were cadmium oxide and an absorption was indicated in the 380nm area by Uv – vis spectrum of cadmium oxide's nanoparticles. Then, three concentrations of synthesized nanoparticles of cadmium oxide including 100, 200 and 300 ppm were used. Wister male rats were fed during 10 days through the mouth. After these periods, blood samples were taken from rats and creatine phosphate kinase, Alanine aminotransferase and AAspartate transaminase enzymes were measured. The results indicated that the enzymes concentration was increase in blood with increasing concentrations of treated nanoparticles and this increase was considerable and higher in groups that received the highest concentration. Also, it was significance in group with intermediate level of nanoparticles.**

Keywords* — *Cadmium Oxide nanoparticles; Alanine Aminotransferase; AAspartate Amino Transferase enzymes; enzyme Creatine Phosphate Kinase.

I. INTRODUCTION

Nanoscience and nanotechnology had a considerable effect on all science fields, including physics, chemistry, biology and etc., after Richard Feynman lecture in 1959. International investment in nanotechnology has been increased and an impressive number of nanotechnology products have been supplied in the modern era [1]. In recent decade, nanoparticles are used in a large part of industries. The structure of thiol groups of proteins and enzymes can be changed by a reaction with most metal nanoparticles. Then, proteins known as foreign antigen, which create an autoimmune reactions against them [2]. Nanoparticles also had a role in inflammatory reactions, oxidative shock or distribute of mitochondria after endocytosis by phagocytic cells. Mitochondria is the most sensitive cell member against metal nanoparticles and it was identified that nanoparticles have the highest toxic effect on mitochondria, which lead to death of mitochondria by increase secretion and necrosis [3]. There are some results about the nanoparticles presence in mouse brain because of inhalation of metal nanoparticles, while their toxic effect on neurotic cells has not been proven, yet [4]. Some Experience of spermatozoa infertility has been recorded as a result of silver nanoparticles in spermatozoa cells in in vitro state [5]. Therefore, studies about their effect on cancer cells to be continued. Now, many studies have begun about a variety of nanoparticles, their different sizes and shapes on biological systems in invitro and invivo.

Cadmium is a toxic pollutant that has no constructive role in the body and is partially harmful. This metal can create oxidative stress in the body with an increase of free radicals and a decrease of antioxidant capacity that can be lead to destructive effects in liver and kidneys. Nanoparticles of Cadmium Oxide be used in most industries including medical equipment, plastic containers and household appliances because of important and special

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characteristics of these particles. Some of the special properties of nanoparticles such as very small size, large surface area and reactivity have created new dangers for human, potentially.

Food and Drug Administration (FAD) has warned about the use of solutions containing cadmium oxide nanoparticles and expressed that these substances can have side effects including poisoning, skin discoloration and Kidney damage. Increased production of free radicals and reduce the antioxidant power is the main cause of complications due to cadmium poisoning [6].The study of Vljevic et al (2011) in relation to oxidative stress caused by ethanol and cadmium indicated that ethanol with cadmium causes the synergistic mode in induction of lipid peroxidation which lead to superoxide enzyme decrease in in the mitochondria.

Cadmium can be effective on the activity of protein kinases, phosphatases and transcription factors bound to DNA. Also, this metal can decrease survival time of calcium channels located in the cell membrane of neurons, decrease the flow of calcium entry and restrict neurotransmitter release. Cadmium can be placed on the proteins and enzymes instead of zinc. Therefore, zinc shortage can increase risk of cadmium poisoning. High doses of cadmium in acute conditions cause necrosis and apoptosis through mitochondrial and cell death receptor. Some symptoms, including focal necrosis, Accumulation of inflammatory cells and sinusoidal obstruction were reported under microscopic examination of rat liver with cadmium poisoning [7]. The Liver is the biggest tubers in a body that was located under diaphragm. This tuber is involved in the most of body's metabolic actions such as protein synthesis and detoxification. Liver was divided into four lobes. Each lobe was covered by a thin layer of connective tissue. This layer infiltrated into the lobe and liver lump divided into small units called lobules. The blood was arrived to liver through two resources. Approximately 75% of blood was entered to the liver by the portal vein, which is rich in nutrients and be evacuated of the alimentary canal. The remaining 25% was arrived through the hepatic artery that is rich in oxygen. The trailing branches of these blood supply sources joined to each other as capillary substrates and formed liver sinusoid. Finally, a combination of blood arteries and veins provide blood for liver cells. Sinusoids will be evacuated into veins in center of each lobe, then these veins were joined to each other and form hepatic vein. In the final phase, the blood was evacuated to venae cavae near to diaphragm. In addition hepatocyte cells in the liver, there are other cells which called Kupffer. These cells are phagocytosis and were belonged to Reticuloendothelial system. The main task of these cells is trapping of special substances such as bacteria that was entered to the liver through central vein of the liver. This organism can have an effective role about create, store, change and release of large amount of metabolic substances in the body.

The Liver receives nutrient-rich blood of Gostro Intestinal, after storage or chemical transformation of materials, these materials will be used in other part of body for metabolic needs. Also, the liver is important in regulation of glucose and protein metabolism. The liver makes and increase Bile that have a major role in the digestion and absorption of fat. As well as, liver takes a waste product of blood and releases them into bile. Bile produced by liver will be stored temporarily in the Gallbladder. 80% of liver cells composed of Hepatocytes cells. These cells store fat and sugar and produce Albumin, prothrombin and fibrinogen [8].

II. Material and Methods

A. *Equipment*

Scanning electron micrographs have been taken by microscope model DSM 960A and CEM 902A of President Company. X-ray diffraction (XRD) was studied by Siemens of Germany and X-ray wavelength (CuKα). UV- Vis spectroscopy devices was obtained by Spectrophotometer Shimadzu UV 160 and UV- Vis spectrum. Cadmium oxide nanoparticles were prepared by a horizontal furnace with fixed bed and a ceramic boot (Length, width, height: 8×1× 1.5). Enzymes were measured by centrifuges (Rotofix 32A, Siemens, German) and biochemistry devices (model 902, Hitachi, Spain).

B. *Requirements*

Graduated cylinders, Gavage, Protective mask, Gloves, Beaker, Test tube.

C. *Materials*

Required Material to prepare cadmium oxide nanoparticles, including Cetyltrimethyl Ammonium Bromide (CTAB) as Surfactant, Cadmium sulfate 0.03 M ($CdSO_4$), Sodium Hydroxide 0.09 M (NaOH), Acetic Acid 0.06 M (CH_3COOH), Toluene, Ethanol 70% (C_2H_6O), Phosphate buffer (PBS) containing Sodium Phosphate solution (NaH_2PO_4 and Na_2HPO_4), NaCl (sodium chloride), $Na_2HPO_4.2H_2O$ (disodium hydrogen phosphate

dihydrate). All of the material and solution were purchased of Sigma and Aldrich companies. All of the solution were made by deionized distilled water. Finally, laboratory kits were prepared of Pars Azmon Company with Reference laboratory confirmation.

1. The synthesis method of Cadmium oxide nanoparticles

The co-precipitation method by (CTAB) as surfactant was selected for the synthesis of cadmium oxide nanoparticles. The first solution sample was prepared by acetic acid (0.06 molar), Cadmium sulfate (0.03 molar), and 40 mg of Cetyltrimethylammonium bromide as surfactants in a one dm cube of twice distilled water. Then, the second solution was prepared with NaOH particles (0.09 molar) and 25 ml of ethanol 70% in a one dm cube of twice distilled water. Two solution were combined along with continuous mixing. The obtained sediment was filtered by using whatman filter paper and was dried in 80°C temperature in hot air furnace for one hour. Dried sediment was moved to silica crucible and was burned in 400°C temperature during 2 hours. Obtained powder was washed three to four times by ethanol to eliminate impurities of particles. Finally, they were determined through x-ray diffraction and absorption spectrometry of visible-ultraviolet spectrums. Obtained nanoparticles were tested by Brucke D/MAX 2500 with The X-ray diffraction, radiation (λ=1/540 56 Å) Cu Kα, flow 250 mA and operating voltage 40 kV. Samples were measured and identified after being dispersed in a solution of toluene by using two throw UV-visible spectrometer.

2. Laboratory animals, diet and conditions for maintenance

The experiment was done on adult male rats of Wistar breed. Totally, 32 rats with the age of 8 weeks and weighing 250-35 0 g were purchased of the Pasteur Institute of Iran. The rats were classified in four groups with 8 abundance, one group as a control group and three as the experimental groups. Then were kept in polypropylene cages which were present in an animal nest of biotechnology department. The floor of the cages was covered with sawdust and had some conditions such as suitable water dish under controlled temperature about 22 ± 1 C˚ and humidity of 60 ± 10%, 12 hours of daylight and 12 hours of darkness and full access to water and food (concentrate). All rats were placed in animal nests in equal environmental conditions for 2 weeks before the start of the experiment to adaptation with environment in terms of consistency, familiarity and diet. All animal experiments were performed in accordance with the ethics committee. The rats were determined in each experimental group with some signs and were fed by oral gavage for 10 days.

3. The method of blood preparation and Supplying serum

To blood chemical tests, blood was taken of rats 10 days after gavage. Serum was isolated by Centrifuges RPM 3000 during 10 minutes. The concentration of ALT, AST and CPK enzymes were measured by Autoanalyser. These devices have high efficiency for biochemical and enzyme tests and can do 200 tests per hour.

4. The method of data extraction

The obtained data by Autoanalyser were saved in SPSS software and were moved to Excel. Some parameters such as enzyme activity (by injection method) was extracted. The obtained data were analyzed by ANOVA and the final results were indicated as mean and standard error.

III. RESULTS

A. The properties of synthesized cadmium oxide nanoparticles

1. X-ray diffraction samples for cadmium oxide nanoparticles

The X-ray diffraction for cadmium oxide nanoparticles were shown in figure 1. The results indicated that diffraction peaks were absorbed in the amount of 2θ. Prominent peaks were used to estimate the grain size of samples by using Scherrer equation D=Kλ/ (βcosθ). In this equation K is constant (0.9), λ is the wavelength and (Cu Kα) ((λ= 1.5418 A°) ,β is width of line half-maximum and θ is the angle of the diffraction. The size of the pattern grain was estimated by the ratio of peak intensity (100). The size of cadmium oxide particle was 47.8. An increase in steepness peaks of XRD indicated that particles were in crystalline nature. The clearly reflections clearly were corresponded to reference model of cadmium oxide (Figure 1).

2. UV-Vis absorption spectra of cadmium oxide nanoparticles

UV-Vis absorption spectra of cadmium oxide nanoparticles were indicated in figure 2. Although spectrometer wavelength was limited to a light source, but absorption band of nanoparticles showed a blue change location due to present restriction value in sample in

comparison with particles of CdO. This phenomenon reveals lights that these nanoparticles show amount of Quantum effects. The formation of nanoparticles depends on surfactants and organic solvents, because CTAB surfactant helps to attach the surface of synthesized nanoparticles (Figure 2).

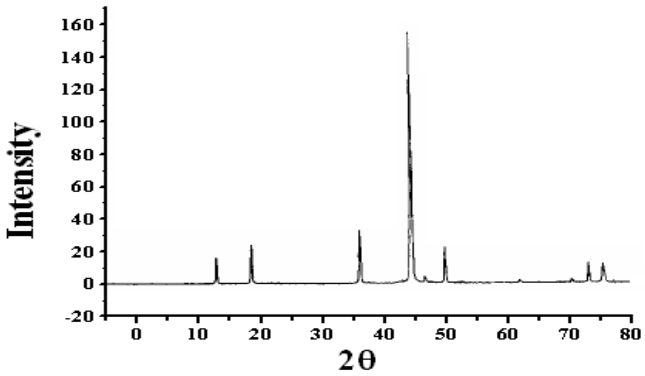

FIGURE 1. X-RAY DIFFRACTION PATTERNS OF CADMIUM OXIDE NANOPARTICLES

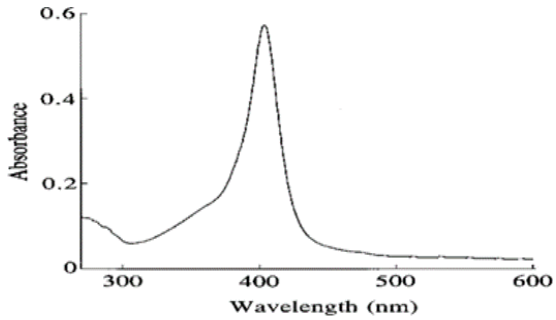

FIGURE 2. UV-VISIBLE ABSORPTION SPECTRUM OF CDO NANOPARTICLES

3. Evaluation of cadmium oxide nanoparticles by using scanning electron microscopy (SEM)

The image of cadmium oxide nanoparticles by Scanning Electron Microscope were shown in figure 3. Also, figure 5 indicates an image of cadmium oxide nanoparticles with different magnification that was prepared by Scanning electron microscope. Smaller nanoparticles are able to play an important role during the consolidation process because of increased surface to volume ratio with reduced the size of nanoparticles. Synthesized nanoparticles have spherical shape in terms of morphological characteristics. Scanning electron microscope image of cadmium oxide nanoparticles indicated that the size of these particles was 40- 45nm that had a suitable coordination with Debye – Scherrer formula (Figure 3-4).

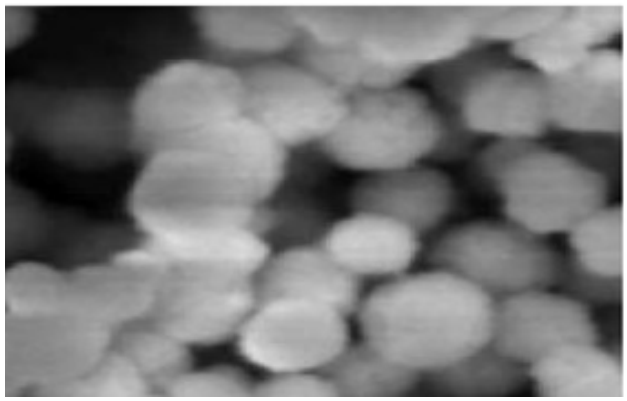

FIGURE 3. SEM IMAGE OF PREPARED CADMIUM OXIDE NANOPARTICLES

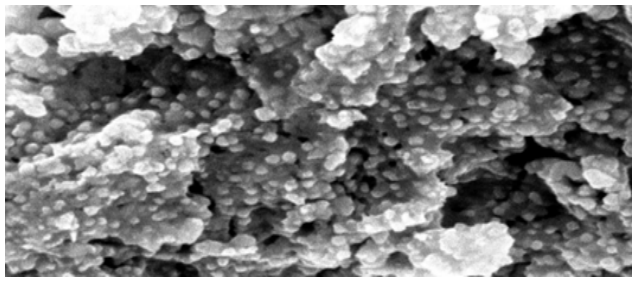

FIGURE 4. THE SEM IMAGE OF SYNTHESIZED CADMIUM OXIDE NANOPARTICLES WITH A MAGNIFICATION OF 1500

B. The measurement of activity level of Alanine aminotransferase enzyme (ALT)

The results indicated that the level of Alanine Aminotransferase enzyme was increased with increasing concentrations of cadmium oxide in in each of the experimental groups (Table 1 and Figure 5). The results of One-way analysis of variance (one-way ANOVA) in relation to alanine aminotransferase enzyme in control and experimental groups were shown in Table 2. According to these results different concentrations of cadmium oxide had a significant effect on Alanine Aminotransferase enzyme activity in control and experimental groups. Also, there was a significant difference of Alanine Aminotransferase enzyme activity between control and experimental groups ($p \leq 0.01$, $F(3, 28) = 4276/733$) (Table 2).

The results indicated that there was a significant difference between Alanine Aminotransferase enzyme activity levels in the control group. Also, different

concentration, such as 100, 200 and 400 ppm had significant differences in experimental groups (P≤0.01) (Table 3).

TABLE 1. THE MEAN, STANDARD DEVIATION, MINIMUM AND MAXIMUM LEVELS OF THE LIVER ENZYME ALANINE AMINOTRANSFERASE

Groups	Mean	Standard deviation	Minimum	Maximum
Control	36.697	0.944	35.250	37.675
Cadmium Oxide (100 ppm)	43.003	1.000	42.000	44.575
Cadmium Oxide (200 ppm)	52.813	0.577	52.000	53.625
Cadmium Oxide (400 ppm)	79.388	0.652	78.425	80.125

TABLE 2. ONE-WAY ANALYSIS OF VARIANCE (ANOVA) OF ALANINE AMINOTRANSFERASE ENZYME ACTIVITY IN CONTROL AND EXPERIMENTAL GROUPS

	SS	df	MS	F	*P*
Between groups	8496.498	3	2832.166	4276.733	0.000
Within groups	18.542	28	0.622		
Total	8515.040	31			

TABLE 3. LSD TEST TO EVALUATE SIGNIFICANT DIFFERENCES OF ALANINE AMINOTRANSFERASE ENZYME ACTIVITY BETWEEN CONTROL AND EXPERIMENTAL GROUPS

variables	**mean differences between two groups**	**standard error**	**p- value**	**confidence interval**		
				upper limit	**lower limit**	
Experiment	100 ppm	-6.30	0.40	0.000	-7.13	-5.47
	200ppm	-16.11	0.40	0.000	-16.94	-15.28
	400 ppm	-42.69	0.40	0.000	-43.50	-41.85
100 ppm	Experiment	6.30	0.40	0.000	5.47	7.13
	200ppm	-9.80	0.40	0.000	-10.64	-8.97
	400 ppm	-36.38	0.40	0.000	-37.21	-35.55
200 ppm	Experiment	16.11	0.40	0.000	15.28	16.94
	100 ppm	9.80	0.40	0.000	8.97	10.64
	400 ppm	-26.57	0.40	0.000	-27.40	-25.74
400 ppm	Experiment	42.69	0.40	0.000	41.85	43.52
	100 ppm	36.38	0.40	0.000	35.55	37.21
	200 ppm	26.57	0.40	0.000	25.74	27.40

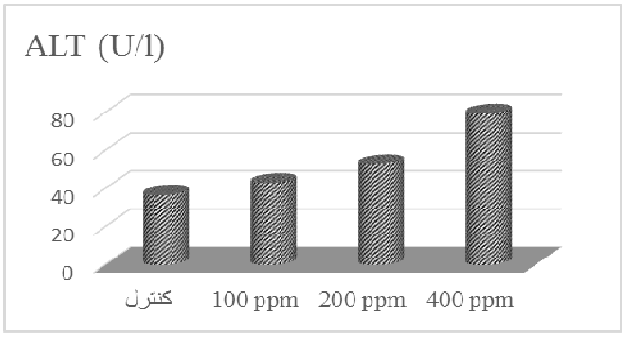

FIGURE 5. AVERAGE OF ALANINE AMINOTRANSFERASE ENZYME ACTIVITY IN DIFFERENT CONCENTRATIONS OF SAVAGED CADMIUM OXIDE OF WISTAR RATS

C. The measurement of activity level of Creatine Phosphate Kinase enzyme (CPK)

The results indicated that the level of Creatine Phosphate Kinase enzyme increased with increasing concentrations of cadmium oxide in in each of the experimental groups (Table 4 and Figure 6). The results of One-way analysis of variance (one-way Anova) in relation to Creatine Phosphate Kinase enzyme in control and experimental groups were shown in Table 5. Results showed that different concentrations of cadmium oxide had a significant effect on Creatine Phosphate Kinase enzyme activity in control and experimental groups. Also, there was a significant difference of Creatine Phosphate Kinase enzyme activity between control and experimental groups (p≤ 0.01, F (3, 28) =636952/247).

The results of table 6 showed that there was a significant difference Creatine Phosphate Kinase enzyme activity levels in the control group. Also, different concentration, such as 100, 200 and 400 ppm had significant differences in experimental groups (P≤0. 01) (Table 6).

TABLE 4. MEAN, STANDARD DEVIATION, MINIMUM AND MAXIMUM LEVEL OF OF CREATINE PHOSPHATE KINASE

Group	Mean	Standard Deviation	Minimum	Maximum
Control	1271.18	6.067	1258.92	1277.15
100 ppm cadmium oxide	1601.84	3.152	1597.97	1606.72
200 ppm cadmium oxide	1682.063	2.34	1678.77	1685.45
400 ppm cadmium oxide	3828.91	4.050	3823.500	3834.97

TABLE 5. ONE-WAY ANALYSIS OF VARIANCE (ANOVA) OF CREATINE PHOSPHATE KINASE ENZYME ACTIVITY IN CONTROL AND EXPERIMENTAL GROUPS

	SS	df	MS	F	*P*
Between groups	32790770.85	3	10930256.95	636952.247	0.000
Within groups	480.487	28	17.160		
Total	32791251.34	31			

TABLE 6. LSD TEST TO EVALUATE SIGNIFICANT DIFFERENCES OF CREATINE PHOSPHATE KINASE ENZYME ACTIVITY BETWEEN CONTROL AND EXPERIMENTAL GROUPS

Variables		Mean Differences Between Two Groups	Standard Error	P- Value	Confidence Interval	
					Upper Limit	Lower Limit
Experiment	100 ppm	-330.90	2.071	0.000	-334.90	-326.41
	200ppm	-410.88	2.071	0.000	-415.12	-406.63
	400 ppm	-2557.73	2.071	0.000	-2561.9	-2553.4
100 ppm	Experiment	330.662	2.071	0.000	326.419	334.90
	200ppm	-80.21	2.071	0.000	-84.46	-75.97
	400 ppm	-2227.06	2.071	0.000	-2231.3	-2222.8
200 ppm	Experiment	410.88	2.071	0.000	406.63	415.124
	100 ppm	80.21	2.071	0.000	75.97	84.46
	400 ppm	-2146.85	2.071	0.000	-2151.0	-2142.6
400 ppm	Experiment	2557.73	2.071	0.000	2553.48	2561.97
	100 ppm	2227.06	2.071	0.000	2222.82	2231.31
	200 ppm	2446.85	2.071	0.000	2142.60	2142.60

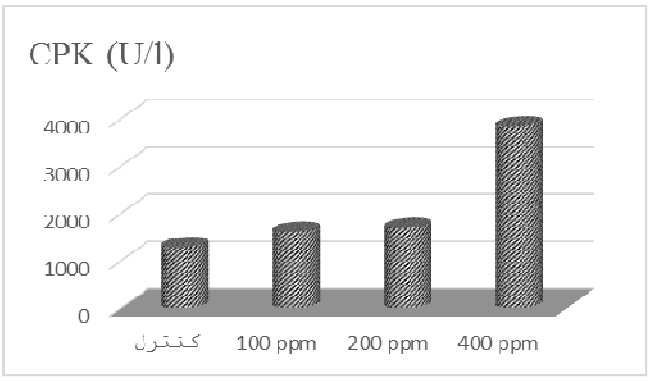

FIGURE 6. AVERAGE OF CREATINE PHOSPHATE KINASE ENZYME ACTIVITY IN DIFFERENT CONCENTRATIONS OF SAVAGED CADMIUM OXIDE OF WISTAR RATS.

D. The measurement of activity level of Aspartate Aminotransferase (AST)

The results indicated that the level of Aspartate Aminotransferase enzyme increased with increasing concentrations of cadmium oxide in in each of the experimental groups (Table 7-8 and Figure 7). Also, the results of One-way analysis of variance (one-way Anova) in relation to Aspartate Aminotransferase enzyme in control and experimental groups were shown in Table 8. Results indicated that different concentrations of cadmium oxide had a significant effect on Aspartate Aminotransferase enzyme activity in control and experimental groups and there were a significant difference of Aspartate

Aminotransferase enzyme activity between control and experimental groups ($p \leq 0.01$, $F(3, 28) = 3981/754$).

TABLE 7. THE MEAN, STANDARD DEVIATION, MINIMUM AND MAXIMUM LEVELS OF THE LIVER ENZYME ASPARTATE AMINOTRANSFERASE

Groups	Mean	standard deviation	minimum	Maximum
Control	37.034	1.12	35.25	38.3
Cadmium Oxide (100 ppm)	43.65	0.699	42.72	44.57
Cadmium Oxide (200 ppm)	53.13	0.613	52.55	54.12
Cadmium Oxide (400 ppm)	78.96	0.777	77.87	79.87

TABLE 8. ONE-WAY ANALYSIS OF VARIANCE (ANOVA) OF ASPARTATE AMINOTRANSFERASE ENZYME ACTIVITY IN CONTROL AND EXPERIMENTAL GROUPS

	SS	df	MS	F	*P*
Between groups	8131.54	3	2710.51	3981.75	0.000
Within groups	19.061	28	0.681		
Total	8150.60	31			

TABLE 9. LSD TEST TO EVALUATE SIGNIFICANT DIFFERENCES OF ASPARTATE AMINOTRANSFERASE ENZYME ACTIVITY BETWEEN CONTROL AND EXPERIMENTAL GROUPS

Variables		**Mean Differences Between Two Groups**	**Standard Error**	**P- Value**	**Confidence Interval**	
					Upper Limit	**Lower Limit**
Experiment	100 ppm	-6.62	0.412	0.000	-7.46	-5.77
	200ppm	-16.10	0.412	0.000	-16.94	-15.25
	400 ppm	-41.93	0.412	0.000	-42.77	-41.089
100 ppm	Experiment	6.62	0.412	0.000	5.77	7.46
	200ppm	-9.48	0.412	0.000	-10.32	-8.63
	400 ppm	-35.31	0.412	0.000	-36.15	-34.46
200 ppm	Experiment	16.10	0.412	0.000	15.25	16.94
	100 ppm	9.48	0.412	0.000	8.63	10.32
	400 ppm	-25.83	0.412	0.000	-26.67	-24.98
400 ppm	Experiment	41.93	0.412	0.000	41.08	42.77
	100 ppm	35.31	0.412	0.000	34.46	34.15
	200 ppm	25.83	0.412	0.000	24.98	26.67

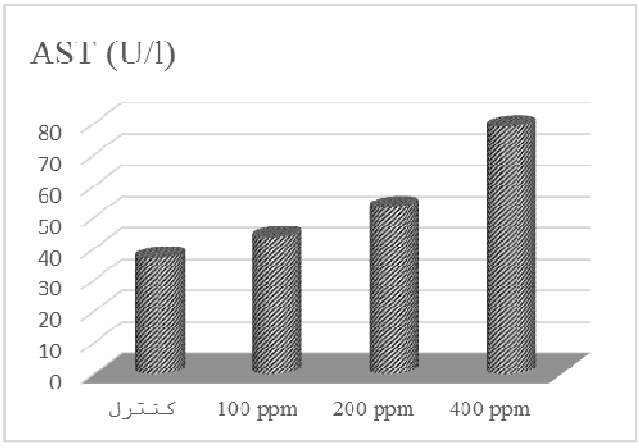

FIGURE 7. AVERAGE OF ASPARTATE AMINOTRANSFERASE ENZYME ACTIVITY IN DIFFERENT CONCENTRATIONS OF SAVAGED CADMIUM OXIDE OF WISTAR RATS.

The results showed that there was a significant differences Aspartate Aminotransferase enzyme activity levels in the control group. Also, different concentration, such as 100, 200 and 400 ppm had significant differences in experimental groups ($P \leq 0.01$) (Table 9).

IV. DISCUSSION AND CONCLUSION

Nanoparticles can enter to body directly through water, food, cosmetics and drugs. Metal oxides of nanoparticles be used on a vast scale of industry, medicine and household consumption [9]. The growing use of nanoparticles in human communities can lead to the release of these materials in the environment and ecosystems [10]. However, little research was done about environmental behavior, release rate and potential risks of nanoparticles [11]. Understanding about nanoparticle toxicity and biological effects of that is an emergency and urgent need in chemical

and pharmaceutical sciences [12]. Exposure to very small particles can have important effects on health. In Alveolar ducts, Macrophages surround insoluble particles by phagocytosis mechanisms and digest them by their slow mixing with mucositis moderator. This is a relatively slow process with a half-life of about 700 days in humans [13]. The toxic effect of Ferric oxide (Fe2O3) on rats was studied by researchers; the rats received 5.8 mg/kg of Ferric oxide. The amount of ALP was measured 36 hours after injection. The results indicated that ALP were increased compared to control group, significantly [14]. The toxic and biochemical effect of Selenium nanoparticles was studied in male mouse with concentrations of 2.5, 5, 10, 20. Results showed that Alkaline Phosphatase (ALP) and Creatine Phosphate Kinase (CPK) enzymes were significantly decreased in a concentration of 20 and changes in enzyme activity were dependent on used concentration. In our study, The nanoparticles were lead to enzyme elevations in blood [15]. Yang (2012) studied the effect of Zinc oxide (100, 300 and 000 mg/ kg) in rats. Their results indicated that only a concentration of 1000 mg/kg lead to Kidney damage [16]. A study conducted on the toxicity of silver nanoparticles and mitochondria was considered as the primary objective of Silver nanoparticles in liver cells of rats [17]. Silver nanoparticles act in rat liver by ROS production and glutathione reduction. Hansen and Nagli (2003) indicated that Free radicals of the catalytic mechanism of Silver nanoparticles damage to unsaturated fatty acids in membrane phospholipids in the process of lipid peroxidation that cause apoptosis in cells [18]. Researchers (2008) showed that environmental toxicity of silver nanoparticles depends on various factors such as shape, size and their mechanism [19]. Nanoparticles can be harmful for health by two main resources, these particles can cross very fast of biological membranes. Also, they were not completely identified because of their toxicity. On the other hand, the toxicity of nanoparticles depends on their shape and diameter [20]. Nanoparticles of Magnesium oxide with a diameter of 100 and 500 nm were tested on cells growth and showed that lower concentrations of nanoparticles had fewer toxic effects [21].

In this study three levels of cadmium oxide nanoparticles were used (100, 200 and 400 ppm). Nanoparticles were given to male rats of the Wistar breed during the days through the mouth. After these periods, blood samples were taken of rats. Then, Creatine Phosphate Kinase and Alanine Aminotransferase and AAspartate Aminotransferase enzymes were measured. Results indicated that the enzymes' concentration in blood was increased with increasing the concentration of gavaged nanoparticles. Whereas, this increasing was more intense and significant in groups with highest concentration. Also, the changes were significant in some groups with moderate amount of nanoparticles.

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