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EFFECT OF CADMIUM TOXICITY ON SOME BIOCHEMICAL BLOOD PARAMETERS AND THEIR MODULATION WITH CERTAIN NATURAL ANTIOXIDANTS IN RABBITS

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ABSTRACT

For the present study the harmful effects of cadmium toxicity on several biochemical blood parameters and evaluation of the possible protective effects of two natural antioxidants (vitamin C and vitamin E) in rabbits exposed to cadmium were investigated. Fourty two white male New-Zealand rabbits of 2-3 months old were used in this study. The rabbits were divided into six equal groups of seven rabbits each**. Group I: (**Control group) received no drugs. **Group II:** Administered with Vitamin C (46.67 mg/kg body weight orally and daily). **Group III:** Received Vitamin E (18.67 mg/kg body weight orally and daily). **Group IV:** Received cadmium chloride (0.5mg/kg. body weight orally and daily). **Group V:** Received cadmium chloride (0.5mg/kg. B.W) and treated daily with Vitamin C (46.67 mg/kg body weight). **Group VI:** Received cadmium chloride (0.5mg/kg. B.W) and treated daily with Vitamin E (46.67 mg/kg body weight). Heparinized blood samples were collected from all animal groups three times at one, two and three months from the onset of rabbits exposed to cadmium and administered with antioxidant compounds. Plasma was separated and processed directly for determination of AST, ALT and ALP activities. Total protein, Albumin, globulin, total cholesterol, triacylglycerols, Urea, creatinine, calcium, inorganic phosphorus, iron profiles (total iron, TIBC, UIBC, transferrin and transferrin saturation percent) and lipid peroxidation (L-MDA) concentrations as well as erythrocyte catalase enzyme activity were also determined. Liver and kidney cadmium residues were also determined. The obtained results revealed that, there was a significant increase in plasma ALT , AST, erythrocyte catatase activities, urea, creatinine and L-MDA concentrations, Liver and kidney cadmium residue in cadmium exposed rabbits. Vitamin C or E administrations in cadmium intoxicated rabbits exhibited significant decrease in all mentioned parameters. On the other hand, a significant decrease in plasma total cholesterol, triacylglycerols , calcium, inorganic phosphorus, iron, transferrin , TIBC, UIBC concentrations and transferrin saturation % were observed in cadmium intoxicated rabbits. Vitamin C or E administrations in cadmium intoxicated rabbits exhibited significant increase in all mentioned parameters. From the obtained results it could be concluded that, the potential of natural antioxidants (vitamin C and E) as a powerful agent against the toxic effect of cadmium, and these antioxidants also exerted modulators effect on heavy metals induced toxicity in white male New-Zealand rabbits.

INTRODUCTION

Cadmium, a divalent metal toxicant, is a widespread toxic environmental and industrial pollutant, Which induces severe alterations in the tissues of laboratory animals and in humans. Cadmium exposure may lead to carcinogenesis **(Waalkes et al., 1991).**

Cadmium (Cd^{2+}) is a highly toxic element found in food and water. Soluble cadmium salts accumulate in organisms and result in toxicity to liver, kidney, lung, bone **(Friedman and Gesek, 1994)**, testes **(Shen and Sangiah, 1995)**, brain, and nervous system **(Provias et al., 1994).**

Moreover, The molecular mechanisms of cadmium toxicity are not yet well defined. Recent studies on mammals have shown that cadmium stimulates formation of reactive oxygen species, including oxygen free anion radical **(Amoruso et al., 1982),** hydrogen peroxide **(Zhong et al., 1990)** and probably hydroxyl radical **(Ochi, et al., 1988)**. As a consequence, enhanced lipid peroxidation, DNA damage, altered calcium and sulfhydryl homeostasis, as well as marked disturbances of antioxidant defense system (AOS) occur **(Stohs and Bagchi, 1995).**

Furthermore, to prevent cadmium-induced peroxidative tissue damage, there are protective mechanisms in vivo, such as free-radical scavengers (antioxidants) and an enzymatic defense system **(Fariss, 1991).** Some vitamins play an efficacious protective role through direct or indirect mechanisms which interfere with the intestinal absorption of heavy metals by increasing urinary excretion or creating a synergic effect on the chelating element **Pace and Iannucci (1994)**.

Accordingly, the purpose of this study to elucidate the harmful effects of cadmium toxicity on several biochemical blood parameters in white male New-Zealand rabbits exposed to cadmium chloride. Also, evaluation of the possible protective effects of two antioxidant nutrients (vitamin C and vitamin E) administrations on some blood constituents and vital organs (liver and kidney) in male rabbits exposed to cadmium were also assessed to investigate whether Vitamin C or E administration would ameliorate these toxic effect of heavy metals induced biochemical abnormalities in male rabbits.

MATERIAL AND METHODS

Fourty two, white male New-Zealand rabbits, 2-3 months old and weighed 2-3kg were used in this work. Rabbits were housed in separate metal cages and kept at constant environmental and nutritional conditions throughout the periods of the experiment. Water was supplied ad- libitum.

Cadmium (Cadmium chloride) was the heavy metal of choice used in the present investigation. Also, two natural antioxidant agents such as Vitamin C (L-Ascorbic acid) 99.2 % and Vitamin E (DL- alpha-Tocopherol acetate) 100% were also used in this study.

Experimental Design:

The rabbits were randomly divided into six equal groups, each one consisting of seven animals placed in individual cages and classified as follows:

Group I: (Control group). Received no drugs. **Group II:** (Vitamin C treated group). Where Vitamin C was given orally and daily at a dose level of 46.67 mg/kg body weight. **Group III:** (vitamin E treated group). Where Vitamin E was given orally in a daily dose of 18.67 mg/kg body weight. **Group IV:** (Cadmium chloride exposed group). Received cadmium chloride (1/20 of $L.D._{50}$) orally and daily at a dose level of 0.5mg/kg. body weight. **Group V:** (Cadmium Chloride + Vitamin C). Exposed cadmium chloride orally and daily (0.5mg/kg. B.W) and treated daily with Vitamin C at a dose level of 46.67 mg/kg body weight. **Group VI:** ((Cadmium chloride + Vitamin E). Exposed to oral daily dose of Cadmium chloride (0.5mg/kg. B.W) and treated daily with vitamin E at a dose level of 18.67 mg/kg body weight.

Sampling:

Heparinized blood samples were collected by vein puncture of the marginal ear vein from all animal groups three times at one, two and three months from the onset of rabbits exposed to cadmium and administered with antioxidant compounds. Plasma were separated by centrifugation at 3000 r.p.m for 10 minutes. The clean, clear plasma was processed directly for determination of AST, ALT and ALP activities, then kept in a deep freeze at -20°C until used for subsequent biochemical analysis. Moreover, small portion of heparinized blood samples, were mixed gently and used directly for determination of erythrocyte catalase enzyme activity. Liver and kidney specimen were immediately removed, weighed and processed for determination of cadmium residues.

Biochemical analysis:

Plasma ALT, AST , ALP activities, Total protein, Albumin, globulin, total cholesterol, triacylglycerols, Urea, creatinine, calcium, inorganic phosphorus, iron profiles (total iron, total iron binding capacity, unsaturated iron binding capacity, transferrin and transferrin saturation percent) and lipid peroxidation (L-Malondialdhyde) concentrations as well as erythrocyte Catalase activity were assayed colorimeterically according to the methods discriped by **Reitman and Frankel (1957), Reitman and Frankel (1957), Kind and King (1954), Cannon et al. (1974), Bartholomew and Delaney,(1964), Meiattini et al., (1978), Bucolo and David(1973), Patton and Crouch, (1977), Henry, (1974), Gindler and King**

(1972), Kuttner and Lichtenstein (1930), Colenbrander and Vink, (1969), Kunish and Small,(1970), Orynich et al. (1976), Fairbanks and Klee (1994), Fairbanks and Klee, (1987), Esterbauer et al., (1982) and Sinha, (1972), respectively. Cadmium residue in liver and kidney specimen were determined by Atomic Absorption Spectrophotometer according to the method described by **Al Ghais (1995).**

Statistical analysis:

The obtained data were Statistically analyzed and the significant difference between groups was evaluated according to **Snedecor and Cochran (1969).**

RESULTS AND DISCUSSION

The obtained results demonstrated in (Table 1) revealed that, cadmium intoxicated rabbits showed significant decrease in plasma ALT activity after one month. Moreover, a significant increase in plasma AST and ALT activities were observed after one and three months, respectively. Similar results were recorded by **Hwang and Wang (2001)** who observed that, in male Wistar rats treated with cadmium the activities of AST and ALT in the plasma were increased with the increasing dose of cadmium. The observed significant elevation in plasma ALT and AST in cadmium exposed rabbits may be attributed to hepatic cell damage. This suggestion was supported by findings of **Aisha and Elham (2000)** who attributed such increases in serum ALT and AST activities to the degenerative changes and the destructive effects of Cd on skeletal muscles, liver and kidney tissues and consequently liberating their intracellular enzymes into the circulating blood stream. Furthermore, **Koizumi and Li (1996)** investigated the mechanism of cadmium-induced cytotoxicity in rat hepatocytes. Who demonstrated that, cadmium-induced active oxygen-related permeability changes of the plasma membrane and caused H_2O_2 accumulation and H^+, Cd and H_2O_2-related permeability changes of the plasma membrane. This early permeability changes may be linked to a subsequent extensive membrane damage occurring at near physiological cellular pH. On the other hand, the reported significant decrease in plasma ALT activity after one month may be indicate sever necrosis of the hepatocytes with an inability to produce enzymes and irreversible liver damage.

Vitamin C treatment to cadmium intoxicated male rabbits caused significant decrease in plasma ALT activity after three months. However, vitamin E treatment

caused significant decrease in plasma AST activity after two months when compared with cadmium exposed group (Tables 1). Ascorbic acid is known as a potential scavenger of reactive oxygen species (ROS) **(Mukhopadhyay et al., 1993)** and it may protect the lipids from detectable peroxidative damage induced by aqueous peroxyl radicals **(Frei et al., 1989).** Also, vitamin E has been found to have antioxidant and cytoprotective properties in cultured cells **Warren et al., (2000).** So the decreased in plasma ALT and AST activities in cadmium exposed rabbits treated with vitamin C or E could be attributed to decreased leakage of AST and ALT resulted from protective effect of vitamin C or E to liver against injury produced by cadmium toxicity. This suggestion was confirmed by the findings of **Shaikh et al., (1999)** who indicated that, free-radical scavengers and antioxidants are useful in protecting against cadmium toxicity. Also, dietary supplementation with antioxidants may be such as a new strategy to reduce the destructive effects caused by free radicals and ROS **(Frank and Biesalski, 1997).**

Cadmium exposed rabbits showed significant decrease in plasma ALP activity after two and three months of the experiment. Similarly, **Gur et al., (1995)** concluded that, cadmium probably exhibits an effect on the bone repair process (osteoblastic cells) as reflected by reduction in ALP activity and mineralization at the site of injury in the tibia of young rats. The observed decrease of plasma ALP activity in cadmium exposed rabbits may be attributed to decrease in plasma inorganic phosphorous concentration (hypophosphatemia) reported in the present study in cadmium exposed rabbits as a result from increased secretions of PTH, which may be related to cadmium-induced bone and renal tubular damage **Nogawa et al., (1984)**. Vitamin C and vitamin E treatment to cadmium exposed rabbits caused significant decrease in plasma ALP activity after one month (Table 1). The observed decrease of plasma ALP activity in cadmium exposed rabbits administered with vitamin C or E could be attributed to the possible hepato protective effect of antioxidant vitamins against free radical-related tissue injury mediated by heavy metals intoxications **(Rikans et al., 1991).**

Plasma total protein , albumin and globulin concentrations showed significant decrease in cadmium exposed animals allover the periods of experiment (Table 1). Similarly, **Moshtaghie et al., (1991)** recorded that, serum protein was decreased whereas urine proteins were elevated significantly after administration of 0.25 or 2 mg of cadmium as $CdCl_2$ i.p. to male Wister rats. The recorded significant decrease of

plasma total protein, albumin , globulins concentrations in cadmium exposed rabbits may be attributed to the toxic effect of cadmium on the renal tubules and glomeruli lead to renal damage and tubular dysfunction. This suggestion was confirmed by the finding of **Jun-Ichi et al., (1996)** who recorded that, cadmium induce renal damage and dysfunction manifested by elevation in blood urea nitrogen, serum creatinine and decrease in serum total protein. Also, **Brzoska et al., (2003**) recorded that, increased excretion of total protein were observed in rats exposed to cadmium.

Treatment of cadmium exposed rabbits with vitamin C and vitamin E exhibited significant increase in plasma albumin concentration after three months. On the other hand, vitamin C or E administrations exhibited significant decrease in plasma globulin concentration after three months as compared to cadmium intoxicated group (Tables 2). The increased in plasma albumin concentration in vitamin C or E treated cadmium exposed rabbits may be due to the protective role of vitamin E on cadmium induced thyroid dysfunction with special reference to type-I iodothyronine -'5monodeiodinase (5'D-I) activity in liver. Such increase in plasma albumin level could be attributed to increase of plasma thyroxine concentration **Habeeb et al., (1989)** who indicated that, the increase of thyroxine stimulated the protein synthesis. On the other hand, the observed significant decrease in plasma globulins concentration in vitamin C or E treated cadmium intoxicated rabbits could be attributed to increased plasma albumin level.

A significant decrease in plasma triacylglycerols concentration observed in cadmium intoxicated rabbits after one month followed by a significant increase after three months when compared with control (Table 2). Similarly, **Grabowska-Maslanka and Janik (1994)** reported that, blood serum level of triglycerides was increased under the influence of chronic cadmium poisoning. This suggest the hypothesis of the possible development of atherosclerotic changes resulting from chronic cadmium poisoning. Also, **Fujita, (1992)** indicated that, cadmium may inhibit lipogenesis by binding with the thiol group (SH) of coenzyme A, thereby reducing the serum levels of free fatty acids and lipid peroxides. Also interesting is that cadmium by interfering with the action of the thiol group may be interfering with the metabolism of vitamin D and possibly the conversion of cholesterol into the steroid (sex) hormones.

The obtained results demonstrated in (Table 2) revealed that, vitamin C and vitamin E treatment in cadmium exposed rabbits exhibited significant increase in

plasma total cholesterol and triacylglycerols concentration allover the period of experiment. However, treatment with vitamin E exhibit significant decrease in triacylglycerols concentration after three months as compared to cadmium exposed group (Tables 2). The decrease in plasma triacylglycerols in vitamin E treated cadmium exposed rabbits may be attributed to lowering of the hepatic triglycerides synthesis and secretion of VLDL- and also by increasing the activity of lipoprotein lipase, which in turn promotes the catabolism of the triglycerids-rich lipoproteins, VLDL- and LDL **(Grundy and Vega 1987)**. The dramatic increase in plasma total cholesterol and triacylglycerols concentrations observed in vitamin C or E treated cadmium exposed rabbits may be due to reduced rates of clearance of LDL from circulation due to defective LDL receptors and is associated with increased plasma total cholesterol concentration **(Zulet et al., 1999).** Moreover, the increased serum triacylglycerols concentration might be attributed to increased hepatic triacylglycerol synthesis and very low density lipoprotein (VLDL) secretion **(Hussein and Azab 1998)**. Furthermore, marked hypertriglyceridemia observed might be a consequence of either over production of VLDL by the liver or defective removal of triglyceride rich lipoproteins from the circulation, or both**(Yost et al., 1995).** Another suggestion for dramatic increase in plasma total cholesterol level in cadmium exposed male rabbits treated with vitamin C may be due to the reduced catabolic rate of serum cholesterol or reduced activity of hepatic cholesterol 7 alpha- hydroxylase, the rate limiting enzyme in bile acid synthesis from cholesterol **(Szymanski et al.,1981).** This suggestion was confirmed by the findings of **Peterson et al., (1983)** who reported that, the 7 alpha-hydroxylation of cholesterol was depressed by both inadequate and excessive vitamin C intake, demonstrating the unique sensitivity of cholesterol 7 alpha-hydroxylase to dietary ascorbate.

A significant increase in plasma urea concentration observed in cadmium exposed rabbits after one and three months. Also, cadmium intoxicated rabbits showed significant increase in plasma creatinine concentration allover the periods of the experiment (Table 2). The increase of plasma urea and creatinine concentrations in cadmium exposed rabbits may be attributed to the toxic effect of cadmium on the renal tubules and glomeruli lead to nephrotoxicity and renal tubular damage **Aisha and Elham (2000)**.This suggestion was supported by **Lall et al., (1997)** who mentioned that, rise in creatinine value is an indication of renal tubular damage due to cadmium-induced naphrotoxicity**.** As confirmed by **(Skoczynskaand and Smolik**

1994) who reported that, cadmium intake increased lipoperoxide concentration. This indicated that, the renal toxicity induced by cadmium involved superoxide radicals. Who concluded that, the toxicity of cadmium involves oxidative reactions such as cadmium-induced lipid peroxidation. Superoxide radical is an important toxic intermediate in the development of renal damage induced by cadmium.

Vitamin C and Vitamin E treatment in cadmium exposed rabbits caused significant increase in plasma urea and creatinine concentrations after two months. However, a significant decrease in creatinine concentration observed in vitamin C treated rabbits after one month as compared with cadmium exposed group (Tables 2). The obtained results were in agreement with that recorded by **Shiraishi et al., (1993)** who indicated that, the antioxidant L-ascorbic acid pretreatment had no effect on cadmium-induced testicular lesions nor on cadmium content in testes, liver, kidney and urine. These results indicate that ascorbic acid pretreatment decreases the toxicity of cadmium in the rat without markedly modifying its toxicokinetics. The decreased in plasma creatinine concentration observed in vitamin C treated cadmium intoxicated rabbits could be attributed to the protective effect of vitamin C to kidney against damage produced by cadmium toxicity. This suggestion was supported by **Nagyova et al., (1994)** Who demonstrated that, high vitamin C (AA) intake apparently reduced the extent of renal damage in Cd-intoxicated guinea pigs. The recorded significant increase of plasma urea and creatinine concentrations observed in vitamin E treated cadmium exposed rabbits after two months may be attributed to sever renal dysfunction due to the toxic effect of cadmium on the kidney.

The obtained results (Table 2) revealed that, a significant decrease in plasma calcium and inorganic phosphorous concentrations observed in cadmium intoxicated rabbits allover the periods of the experiment. These results are nearly similar to those reported by **Karagl et al., (2000)** who observed that, with the increasing dietary Cd, the reduction in serum P concentrations may result from either increased P excretion due to tubular damage in kidney or suppressed absorption of this element or both. Moreover, **Pilat-Marcinkiewicz et al., (2002)** observed that, chronic oral cadmium administration (5 or 50 mg Cd/dm3) to rats showed a decrease in serum Ca concentration. The marked decrease in plasma calcium concentrations observed in cadmium intoxicated rabbits could be attributable to increased urinary excretion of calcium due to the direct interaction of cadmium with the calcium reabsorption

process or to the toxic actions of cadmium against the renal tubules **(Wang and Bhattacharyya 1993)**.

Because cadmium can affect $Ca2^{+}$ uptake by tubular cells, with decreased renal $Ca2^{+}$ reabsorption, calciuria may reflect tubular cell damage caused by cadmium. Urinary calcium can therefore be used as a biomarker of renal dysfunction induced by cadmium **Wu et al., (2001).** The marked decrease in plasma inorganic phosphorous concentration observed in cadmium intoxicated rabbits may be attributed to increased secretions of parathyroid hormone **Nogawa et al., (1984)**. Who recorded that, the negative correlations between serum parathyroid hormone (PTH) concentration and percentage of tubular renal phosphorus reabsorption (% TRP) was significant in the cadmium (Cd)-exposed group. Moreover, chronic cadmium intoxication could cause increased secretions of PTH, which may be related to cadmium-induced bone damage. PTH modulates tubular transport of calcium, phosphate, and other ions and stimulates production of 1,25 (OH_2)D. PTH decreases the reabsorption of phosphate by the proximal tubule, resulting in phosphaturia. Moreover, the kidneys regulate phosphate homeostasis. Therefore, any cause of excessive PTH secretion may result in hypophosphatemia (primary and secondary hyperparathyroidism) **(Hussein, 2003).** Furthermore, **Karagl et al., (2000)** observed that, with the increasing dietary Cd, the reduction in serum P concentrations may result from either increased P excretion due to tubular damage in kidney or suppressed absorption of this element or both.

Treatment of vitamin C or E in cadmium intoxicated rabbits caused significant increase in plasma calcium and inorganic phosphorous concentrations after two and three months of the experiment when compared with cadmium exposed rabbits (Tables 2). The marked significant increase of plasma calcium and inorganic phosphorous concentrations in cadmium intoxicated rabbits treated with vitamin C or E could be attributed to the decreased glomerular filtration rate and the diminished tubular reabsorption with unchanged phosphate excretion. Moreover, elevated serum phosphorus levels are also present in renal disease. The hyperphosphatemia is due, in part, to renal phosphate retention from the reduced filtered load of phosphate.

Cadmium intoxication caused significant increase in plasma iron concentration after two months and in plasma TIBC and transferrin after three months. On the other hand, a significant decrease in plasma UIBC and transferrin observed after one month. The value of transferrin saturation % showed significant increase after two months

followed by significant decrease after three months when compared with the control group (Table 3). One of the symptoms associated with cadmium intoxication is the development of anemia in the exposed individual, a result of the inhibitory effect of cadmium on iron metabolism and absorption. Rats receiving a diet with 100 mg cadmium/kg for several weeks have shown reduced liver and kidney concentrations of iron **(Stonard and Webb 1976).** This could be attributable to the interference of cadmium with iron absorption at the intestinal level. Cadmium binds to liver ferritin, which is also present in the intestinal mucosa and involved in the mucosal uptake and transfer of iron. It has been suggested that higher gastrointestinal absorption of cadmium is due to lower body iron stores as measured by the concentrations of serum ferritin **(Vahter et al., 1996)**. The protein transferrin, which donates iron to the heme moiety in hemoglobin synthesis, binds to a variety of metals in addition to iron. Ferritin or transferrin could be involved in the cadmium-iron interaction observed during cadmium intoxication. The marked increase of plasma iron concentration in cadmium exposed rabbits could be attributed to increased red blood cell destruction (hemolytic anemia). This suggestion was confirmed by the findings of **Shaikh et al., (1999)** who observed that, cadmium caused damage of the erythrocyte membrane resulting in hemolysis. On the other hand, the increase in plasma TIBC in cadmium exposed rabbits was due to the observed increase in the plasma transferrin concentration in cadmium exposed rabbits. An increase in the plasma concentration of transferrin elevates the TIBC. This may occur in iron deficiency anemia and after destruction of liver cells. The TIBC is an indirect measurement of the amount of transferrin. It is a measure of the iron-binding capacity of transferrin when fully saturated with iron. During iron deficiency anemia due to causes other than chronic infections, transferrin levels increase as a result of increased synthesis of the protein in an attempt to transport more iron to the depleted tissues. Because of the increased transferrin hut depleted iron stores, the % saturation of transferrin decreases **(Hussein, 2003).** Furthermore, the observed increase in % saturation is due to hemolytic anemia.

Vitamin C and Vitamin E treatment to cadmium exposed rabbits caused significant increase in plasma TIBC and transferrin concentrations after one month. Furthermore, vitamin C treatment induced significant decrease in transferrin saturation % after two months followed by significant increase after three months, while vitamin E treatment caused significant increase in plasma UIBC concentration after two months as compared to cadmium exposed group (Tables 3). **Fox and Fry**

(1970) showed that, ascorbic acid does not have a direct effect on cadmium, but improves iron absorption in the gastrointestinal tract. On the other hand, **Hill, (1980)** recorded that, the effect of ascorbic acid in alleviating cadmium toxicity has been attributed to the effect of the vitamin on iron metabolism, since ferrous iron will also improve cadmium toxicity in the Japanese quail.

The obtained results (Tables 3) revealed that, cadmium exposed rabbits showed a significant increase in plasma L-MDA concentration allover the periods of experiment as compared to normal control group. These results are nearly similar to those reported by **Manca et al., (1991)** who reported that, administration of Cd at a lower level (500 µg/kg body weight) significantly increased lipid peroxidation concentration in the kidney and other organs of rats. The recorded significant increase in plasma L-MDA in cadmium intoxicated rabbits may be due to cadmium induced production of reactive oxygen species may contribute to the tissue damaging effects of this metal ion **(Stohs and Bagchi 1996)**. This suggestion was confirmed by the findings of **Sumathi et al., (1994)** who reported that, cadmium may induced oxidative damage in different tissues by enhancing peroxidation of membrane lipids in tissues and by inhibiting the enzymes involved in the utilization of some of the activated oxygen species**.** Treatment of cadmium intoxicated rabbits with vitamin C or E caused significant decrease in plasma L-MDA concentration allover the periods of the experiment. Similarly, **Fariss, (1991)** reported that, the exogenous administration of alpha-tocopheryl succinate completely protected rat hepatocytes from Cd-induced injury and lipid peroxidation. Furthermore, **Hudecova and Ginter (1992)** recorded that, high intake of ascorbic acid (100 mg/animal/day) decreased lipid peroxidation in the kidney, liver and serum of Cd-treated guinea pigs. The recorded significant decrease in plasma L-MDA concentration in cadmium intoxicated rabbits treated with vitamin C or E may be due to vitamin C has been shown to scavenge aqueous superoxide and hydroxyl radicals and act as a chain-breaking antioxidant in lipid peroxidations. Ascorbic acid may also act indirectly in protecting lipid membranes by regenerating the active form of membrane-bound vitamin E. Evidence suggests that there is an ascorbate-vitamin E interaction **(Thomas et al 1995).**

A significant increase in erythrocyte catalase activity observed in cadmium exposed rabbits allover the periods of the experiment (Tables 4). These results are nearly similar to those reported by **Ognjanovic et al., (2003)** who recorded that, erythrocyte catalase activity was significantly increased in cadmium intoxicated male

Wistar albino rats. Who added that, the pretreatment with Vit E prior to Cd intoxication caused significant decreased in the activity of erythrocyte CAT as compared with animals given Cd alone. Cadmium induced an increase in CAT activity which may be explained by their influence on hydrogen peroxide as substrate which is formed in the process of dismutation of superoxide anion radicals **(Shaikh et al. 1999).**

The obtained results demonstrated in (Table 4) revealed that, treatment with vitamin E to cadmium intoxicated rabbits caused significant decrease in erythrocyte catalase activity after one month when compared with cadmium intoxicated group (Tables 4). These obtained results are in accordance with the results of **Ognjanovic et al., (2003)** who recorded that, the pretreatment with Vit E prior to Cd intoxication in male Wistar albino rats caused significant decreased in the activity of erythrocyte CAT as compared with animals given Cd alone. It is known that antioxidants, such as Vit E, coenzyme Q, vitamin C , glutathione (GSH) and selenium may act synergically, preventing lipid peroxidation and cell destruction **(Navarro et al. 1999, Lass and Sohal 2000).** Furthemore, the pretreatment with Vit E prior to Cd administration in male rats decreased erythrocyte CuZn SOD and GR activities indicating that Vit E eliminates the toxic effects of Cd on the activity of these enzymes **Ognjanovic et al., (2003)**.

Liver and kidney cadmium concentrations in cadmium exposed rabbits were significantly increased along the periods of the experiment (Table 4). Treatment of vitamin C or E to cadmium exposed rabbits induced a significant decrease in liver and kidney cadmium concentrations in cadmium treated rabbits. These results are in accordance with the results of **Katsuta et al., (1993** recorded that, the hepatic and renal Cd concentrations increased in female rats after intravenous administration of cadmium chloride. Cadmium administered by parenteral injection was rapidly accumulated in the liver **(Mennear, 1979).** In addition to, cadmium provided orally to rats induces the synthesis of a cadmium-binding protein, metallothionein, in liver **(Sabbioni and Girardi 1977).** Hepatic metallothionein also binds zinc **(Webb, 1972).** Possibly, in cadmium supplemented rats, hepatic concentration of cadmium and zinc increased because these elements bound to an induced metallothionein **(Meyer et al., 1982).** This suggestion was confirmed by **Chan et al., (1992)** indicated that, the liver was the primary organ for accumulation of Cd salts while kidney for Cd-metallothionein (Cd-MT). The recorded decrease in liver and kidney cadmium

concentrations in vitamin C or E treated intoxicated rabbits are nearly similar to those reported by **Fox et al., (1980)** observed reduced accumulation of cadmium under the influence of vitamin C in the kidney of Japanese quail fed a very low level of cadmium. Furthermore, **Tandon et al., (1992)** reported that, accumulation of Cd in blood, liver and kidney decreased significantly upon co-exposure to vitamin E.

From the obtained results it could be concluded that, the potential of natural antioxidants (vitamin C and E), as a powerful agent against the toxic effect of cadmium in white male New-Zealand rabbits. Also, these antioxidants exerted modulators effect on cadmium induced toxicity as revealed by marked improvements and distinct decreases of cadmium residues in liver and kidney. Because, vitamin C or E may have a protective antioxidant effect and could be also applicable as a cytoprotective against any tissue damage mediated by heavy metals intoxication. Consequently, people eating a diet deficient in micronutrients will be predisposed to toxicity. Therefore, we recommended that, vitamin C or E administration are very essential and should be used with save and therapeutic dose level which may attenuate the undesirable and dangerous effects during hazardous exposure to heavy metals intoxication.

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Table (1) Effect of cadmium treatment alone and in combination with vitamin C or vitamin E on Plasma ALT, AST, ALP activities, Total protein, Albumin, and Globulin concentrations of male rabbits.

Parameters \ Animal groups		Control	Vitamin C	Vitamin E	Cadmium	Cadmium + Vit.C	Cadmium + Vit. E
ALT (U/L)	One month	51.48 ± 0.64^{a}	40.72 ± 0.99^{b}	52.07 ± 0.64^{a}	31.55 ± 0.55^{c}	33.21 ± 0.59^{c}	31.98 ± 0.68^{c}
	Two months	47.67 ± 4.17^{a}	54.00 ± 6.09^{a}	55.83 ± 4.22^{a}	51.16 ± 3.13^{ab}	55.33 ± 3.05^{ab}	64.16 ± 4.44^{a}
	Three months	42.33 ± 2.67^{c}	46.67 ± 0.88^{bc}	62.67 ± 1.33^{a}	62.66 ± 1.33^{a}	47.33 ± 2.33^{b}	57.33 ± 3.52^{a}
AST (U/L)	One month	29.66 ± 2.63^{c}	27.00 ± 1.84^{c}	25.33 ± 1.23^{c}	49.25 ± 3.71^{b}	66.50 ± 4.14^{a}	48.00 ± 3.16^{b}
	Two months	48.33 ± 4.09^{a}	29.16 ± 3.40^{b}	52.00 ± 1.73^{a}	47.66 ± 3.17^{a}	46.00 ± 2.74^{a}	30.50 ± 1.58^{b}
	Three months	30.66 ± 3.93^{b}	48.33 ± 2.90^{a}	43.00 ± 4.04^{a}	40.66 ± 2.33^{ab}	32.33 ± 4.70^{b}	36.33 ± 6.66^{ab}
ALP (U/L)	One months	18.18 ± 0.78^{bc}	20.68 ± 0.87^{ab}	21.33 ± 1.64^{ab}	16.08 ± 0.70^{c}	11.41 ± 0.98^{d}	13.11 ± 0.44^{a}
	Two months	16.45 ± 1.34^{a}	11.63 ± 0.64^{b}	13.13 ± 0.81^{b}	5.46 ± 0.29^{d}	6.98 ± 0.95^{cd}	8.13 ± 0.13^{c}
	Three months	9.00 ± 0.26^{a}	7.83 ± 1.02^{ab}	7.86 ± 0.49^{ab}	5.80 ± 0.20^{c}	6.90 ± 0.25^{bc}	5.96 ± 0.46^{c}
T.P. (gm/dL)	One month	6.71 ± 0.12^{a}	6.86 ± 0.12^{a}	6.94 ± 0.31^{a}	5.17 ± 0.17^{b}	5.19 ± 0.17^{b}	5.48 ± 0.12^{b}
	Two months	6.82 ± 0.12^{a}	6.67 ± 0.12^{a}	6.50 ± 0.20a	4.77 ± 0.10^{b}	5.00 ± 0.19^{b}	5.09 ± 0.12^{b}
	Three months	6.86 ± 0.20^{a}	6.67 ± 0.20^{a}	6.86 ± 0.20^{a}	4.90 ± 0.19^{b}	4.90 ± 0.19^{b}	4.90 ± 0.19^{b}
Alb. (gm/dL)	One month	3.00 ± 0.07^{a}	2.57 ± 0.15^{b}	2.37 ± 0.09^{b}	1.50 ± 0.07^{c}	1.64 ± 0.07^{c}	1.64 ± 0.08^{c}
	Two months	3.00 ± 0.05^{a}	2.99 ± 0.11^{a}	2.47 ± 0.09b	1.46 ± 0.06^{d}	1.40 ± 0.03^{d}	1.68 ± 0.06^{c}
	Three months	2.86 ± 0.07^{a}	2.93 ± 0.07^{a}	2.86 ± 0.07^{a}	1.64 ± 0.07^{b}	2.71 ± 0.07^{a}	2.79 ± 0.00^{a}
Globulin (mg/dL)	One months	3.67 ± 0.11^{abc}	4.29 ± 0.17^{ab}	4.38 ± 0.30^{a}	3.53 ± 0.25^{c}	3.55 ± 0.22^{c}	4.01±0.21^{abc}
	Two months	4.02 ± 0.17^{a}	3.67 ± 0.17^{a}	4.06 ± 0.20^{ab}	3.14 ± 0.14^{b}	3.19 ± 0.18^{b}	3.41 ± 0.14^{b}
	Three months	4.00 ± 0.27^{a}	3.74 ± 0.27^{ab}	4.00 ± 0.17^{a}	3.25 ±0.07^{b}	2.32 ± 0.10^{c}	2.11 ± 0.19^{c}

Data are presented as Mean ± S.E S. E = Standard error

Mean with different superscript letters in the same row are significantly different at ($P \leq 0.05$).

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Table (2) Effect of cadmium treatment alone and in combination with vitamin C or vitamin E on plasmaTotal Chlesterol, Triacylglycerols, Urea, Createnine, Calcium and inorganic Phosphorus concentrations of male rabbits.

Parameters / Animal groups		Control	Vitamin C	Vitamin E	Cadmium	Cadmium + Vit. C	Cadmium + Vit. E
Total Cholest. (mg/dL)	One month	107.33 ± 2.03^{b}	148.00 ± 16.46^{a}	115.67 ± 6.06^{ab}	86.33 ± 4.48^{b}	97.00 ± 9.53^{b}	88.66 ± 8.25^{b}
	Two months	84.33 ± 1.67^{bc}	85.00 ± 0.58^{bc}	103.00 ± 2.08^{a}	78.00 ± 3.05^{c}	83.00 ± 4.27^{c}	92.33 ± 6.33^{b}
	Three months	72.00 ± 2.08^{d}	94.33 ± 2.33^{a}	75.67 ± 5.48^{cd}	73.33 ± 3.38^{b}	98.33 ± 7.79^{a}	85.00 ± 1.73^{ab}
Triacyl. (mg/dL)	One month	83.00 ± 5.20^{b}	102.00 ± 5.78^{a}	75.00 ± 2.00^{bc}	49.66 ± 7.83^{c}	85.66 ± 2.60^{b}	73.66 ± 3.75^{b}
	Two months	62.33 ± 1.86^{b}	60.33 ± 2.03^{b}	83.67 ± 2.33^{a}	71.66 ± 4.40^{abc}	72.66 ± 6.48^{abc}	73.33 ± 3.38^{ab}
	Three months	51.00 ± 3.46^{c}	78.00 ± 1.15^{ab}	61.00 ± 0.88^{b}	66.00 ± 4.58^{bc}	72.33 ± 0.33^{ab}	58.00 ± 1.15^{de}
Urea (mg/dL)	One months	27.90 ± 1.99^{b}	27.55 ± 1.95^{b}	32.51 ± 1.20^{ab}	34.78 ± 1.29^{b}	51.71 ± 3.55^{a}	40.76 ± 1.06^{b}
	Two months	34.19 ± 1.54^{b}	39.64 ± 1.40^{ab}	27.77 ± 2.77^{c}	37.77 ± 1.82^{b}	47.17 ± 2.57^{a}	46.16 ± 1.38^{a}
	Three months	32.06 ± 1.48^{b}	33.76 ± 2.26^{b}	33.98 ± 0.65^{b}	38.43 ± 0.66^{ab}	37.49 ± 1.96^{ab}	40.64 ± 0.90^{a}
Creat. (mg/dL)	One months	1.33 ± 0.03^{c}	1.33 ± 0.03^{b}	1.33 ± 0.06^{b}	3.86 ± 0.16^{a}	3.11 ± 0.13^{b}	4.22 ± 0.28^{a}
	Two months	1.00 ± 0.15^{de}	0.67 ± 0.01^{e}	1.31 ± 0.03^{cd}	3.59 ± 0.21^{c}	4.67 ± 0.05^{a}	4.22 ± 0.15^{b}
	Three months	1.33 ± 0.05^{b}	1.33 ± 0.03^{c}	1.33 ± 0.06^{c}	3.11 ± 0.22^{ab}	2.89 ± 0.22^{b}	3.55 ± 0.22^{a}
Calc. (mg/dL)	One month	11.50 ± 0.50^{a}	10.08 ± 0.23^{a}	11.25 ± 0.47^{a}	10.41 ± 0.49^{ab}	11.55 ± 0.45^{a}	11.45 ± 0.26^{a}
	Two months	11.33 ± 0.47^{ab}	10.08 ± 0.20^{abc}	11.55 ± 0.57^{ab}	8.76 ± 0.10^{c}	10.61 ± 0.39^{ab}	11.13 ± 0.49^{ab}
	Three months	12.30 ± 0.11^{a}	11.33 ± 0.72^{ab}	11.10 ± 0.73^{ab}	7.53 ± 0.14^{b}	11.33 ± 0.72^{a}	10.50 ± 0.50^{a}
Phos.. (mg/dL)	One month	5.82 ± 0.30^{a}	6.00 ± 0.29^{a}	4.32 ± 0.31^{b}	2.89 ± 0.13^{c}	3.25 ± 0.04^{c}	3.07 ± 0.07^{c}
	Two months	4.53 ± 0.20^{ab}	3.86 ± 0.25^{b}	4.27 ± 0.30^{b}	3.28 ± 0.31^{c}	5.14 ± 0.11^{a}	5.17 ± 0.10^{a}
	Three months	5.82 ± 0.30^{a}	6.00 ± 0.29^{a}	4.32 ± 0.31^{b}	3.16 ± 0.30^{b}	3.11 ± 0.15^{b}	4.12 ± 0.17^{a}

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Table (3) Effect of cadmium treatment alone and in combination with vitamin C or vitamin E on Plasma Iron, TIBC, UIBC, transferrin , transferrin saturation percent and L-MDA concentrations of male rabbits.

Parameters \ Animal groups		Control	Vitamin C	Vitamin E	Cadmium	Cadmium + Vit. C	Cadmium + Vit. E
Iron (µg/dL)	One month	190.48 ± 3.40^{c}	210.79 ± 2.67^{bc}	195.97 ± 7.74^{bc}	177.49 ± 4.38^{b}	193.13 ± 10.57^{ab}	178.20 ± 8.61^{b}
	Two months	153.91 ± 5.79^{bc}	171.38 ± 4.11^{ab}	168.84 ± 1.24^{ab}	193.99 ± 7.02^{a}	184.79 ± 6.24^{ab}	179.33 ± 0.71^{ab}
	Three months	198.00 ± 12.35^{a}	170.61 ± 8.45^{ab}	168.25 ± 8.52^{ab}	193.25 ± 12.56^{a}	185.78 ± 6.33^{a}	186.14 ± 8.52^{a}
TIBC (µg/dL)	One months	458.01 ± 5.23^{ab}	439.88 ± 13.86^{b}	481.29 ± 7.60^{a}	430.10 ± 5.91^{c}	464.55 ± 8.96^{ab}	466.63 ± 7.69^{ab}
	Two months	491.60 ± 8.28^{ab}	497.47 ± 5.84^{a}	473.47 ± 19.35^{ab}	484.85 ± 13.56^{b}	537.08 ± 12.09$^{a\ c}$	487.56 ±4.85^{b}
	Three months	422.27 ± 17.23^{bc}	524.46 ± 14.77^{a}	524.46 ± 11.42^{a}	493.02 ± 7.83^{ab}	446.10 ± 26.29^{bc}	495.86 ± 8.46^{ab}
UIBC (µg/dL)	One month	300.41 ± 30.95^{a}	262.74 ± 2.90^{ab}	285.31 ± 7.91^{ab}	252.69 ± 3.69^{b}	277.44 ± 7.24^{ab}	289.81 ± 8.68^{ab}
	Two months	329.69 ± 7.93^{a}	326.08 ± 5.85^{a}	296.80 ± 5.45^{b}	282.32 ± 3.97^{d}	366.12 ± 12.10^{a}	312.23 ± 2.68^{bc}
	Three months	268.69 ± 5.18^{bc}	354.18 ± 7.60^{a}	353.20 ± 5.22^{a}	312.09 ± 8.03^{ab}	312.41 ±39.89^{ab}	311.06 ± 3.00^{ab}
Transferrin (gm/L)	One month	3.31 ± 0.11^{a}	3.33 ± 0.04^{a}	3.36 ± 0.05^{a}	3.01 ± 0.04^{b}	3.11 ± 0.13^{b}	3.28 ± 0.05^{a}
	Two months	3.38 ± 0.01^{a}	3.48 ± 0.04^{a}	3.31 ± 0.13^{a}	3.31 ± 0.04^{b}	3.76 ± 0.08^{a}	3.39 ± 0.02^{b}
	Three months	3.14 ± 0.04^{b}	3.65 ± 0.11^{a}	3.65 ± 0.09^{a}	3.45 ± 0.05^{ab}	3.30 ± 0.05^{bc}	3.53 ± 0.02^{a}
Ttransferrin saturation percent	One month	40.36 ± 1.06^{bc}	45.01 ± 3.79^{ab}	37.71 ± 1.69^{c}	41.26 ± 0.66^{ab}	37.83 ± 1.10^{b}	37.11 ± 2.69^{b}
	Two months	34.66 ± 2.55^{a}	34.35 ± 1.05^{a}	34.37 ± 0.21^{a}	39.10 ± 1.21^{a}	31.86 ± 0.75^{c}	36.81 ± 0.42^{ab}
	Three months	40.06 ± 0.45^{a}	30.68 ± 0.86^{c}	30.86 ± 0.86^{c}	37.75 ± 0.42^{b}	41.54 ± 0.70^{a}	37.50 ±1.12^{b}
L-MDA (nmol/mL)	One months	4.35 ± 0.09^{bc}	3.06 ± 0.22^{c}	5.20 ± 0.93^{b}	9.76 ± 0.53^{a}	5.22 ± 0.14^{b}	5.66± 0.40^{b}
	Two months	4.72 ± 0.20^{bc}	5.15 ± 0.17^{bc}	4.45 ± 0.31^{c}	16.59 ± 0.83^{a}	4.23 ± 0.43^{c}	11.39 ± 0.75^{b}
	Three months	4.34 ± 0.22^{b}	4.78 ± 0.21^{b}	4.88 ± 0.19^{b}	15.62 ± 0.65^{a}	3.68 ± 0.78^{b}	4.73 ± 0.41^{b}

Data are presented as Mean ± S.E S. E = Standard error

Mean with different superscript letters in the same row are significantly different at ($P \leq 0.05$).

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Table (4) Effect of cadmium treatment alone and in combination with vitamin C or vitamin E on Erythrocyte catalase activity , liver and kidney cadmium concentrations of male rabbits.

Parameters / Animal groups		Control	Vitamin C	Vitamin E	Cadmium	Cadmium + Vit. C	Cadmium + Vit. E
Erythrocyte catalase activity unit/gm Hb	One month	34.03 ± 0.83^{b}	36.04 ± 0.97^{b}	34.76 ± 1.04^{b}	47.04 ± 2.28^{a}	46.08 ± 1.67^{ab}	41.76 ± 2.23^{b}
	Two months	28.61 ± 0.12^{d}	33.14 ± 0.76^{bc}	30.76 ± 2.20^{cd}	39.85 ± 1.99^{a}	39.93 ± 0.83^{a}	39.81 ± 0.21^{a}
	Three months	29.19 ± 0.30^{c}	33.59 ± 0.29^{c}	31.98 ± 0.31^{c}	41.43 ± 1.53^{a}	41.06 ± 1.82^{a}	40.04 ± 1.48^{a}
liver cadmium (ppm/gm wet tissue)	Two month	0.26 ± 0.03^{b}	0.30 ± 0.05^{b}	0.26 ± 0.03^{b}	0.96 ± 0.08^{a}	0.50 ± 0.15^{b}	0.46 ± 0.16^{b}
	Three months	0.26 ± 0.03^{b}	0.30 ± 0.05^{b}	0.26 ± 0.03^{b}	1.30 ± 0.15^{a}	0.53 ± 0.13^{b}	0.53 ± 0.03^{b}
kidney cadmium (ppm/gm wet tissue)	Two months	0.23 ± 0.03^{c}	0.25 ± 0.02^{c}	0.26 ± 0.03^{c}	2.46 ± 0.03^{a}	0.70 ± 0.05^{b}	0.60 ± 0.01^{b}
	Three months	0.26 ± 0.03^{b}	0.23 ± 0.03^{b}	0.30 ± 0.05^{b}	5.83 ± 1.41^{a}	1.03 ± 0.12^{b}	0.60 ± 0.05^{b}

Data are presented as Mean ± S.E S. E = Standard error
Mean with different superscript letters in the same row are significantly different at ($P \leq 0.05$).

تأثير التسمم بالكاديميوم على بعض قياسات الدم البيوكيميائية وتحسينها ببعض مضادات الأكسدة الطبيعية في الأرانب

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الملخص العربي

يعتبر التلوث بالعناصر الثقيلة من اخطر أنواع التلوث التي يتعرض لها الإنسان والحيوان على حد سواء لما يحدثه من تدمير خلايا وأنسجة وأعضاء الجسم الحيوية ذلك لما تنتجة داخل الخلايا من الشوارد الحرة. وحيث أن مضادات الأكسدة تلعب دورا هاماً في السيطرة والتقليل من خطور ة الشوارد الحرة على الأنسجة والأعضاء المختلفة فقد جاءت فكرة هذا البحث لدارسة الآثار الضارة للتسمم بعنصر الكاديميوم وأستخدام بعض مضادات الأكسدة مثل فيتاميني ج وفيتامين هـــ. أجريت الدراسة على عدد إثنين وأربعون من ذكور الأرانب النيوزيلاندية البيضاء قسمت إلى ستة مجموعات متساوية كلآتي: المجموعة الأولى (المجموعة الضابطة) لم تتلقى أى علاجات . والمجموعة الثانية تم تجريعها فيتامين ج يوميا عن طريق الفم بجرعة 46.67 ملى جرام لكل كيلو جرام من وزن الجسم. والمجموعة الثالثة تم تجريعها فيتامين هـــ يوميا بجرعة مقدارها 18.67 ملى جرام. والمجموعة الرابعة أعطيت كلوريد الكاديميوم بجرعة مقدارها 0.5 ملى جرام لكل كيلو جرام من وزن الجسم. والمجموعة الخامسة أعطيت إلى جانب كلوريد الكاديميوم جرهة يومة من فيتامين ج مقدارها 46.67 ملى جرام لكل كيلو جرام. والمجموعة السادسة اعطيت إلى جانب كلوريد الكاديميوم جرعة يومية من فيتامين هـــ مقدارها 18.76 ملى جرام لكل كيلو جرام.. تم تجميع عينات الدم على هيبارين على ثلاث فترات كلا منها شهر من بداية تجريع الأرانب بالكادويوم ومضادات الأكسدة واستخدم مباشرةً لقياس نشاط أنزيم الكتاليز في كرات الدم الحمراء. وتم فصل البلازما وأستخدمت لأجراء بعض القياسات البيوكيميائية مثل نشاط إنزيم أسبرتيت أمينوترانسفيريز، وألآنين أمينو ترانسفيريز،

والفوسفاتيز القاعدى، البروتين الكلى، والزلال، والجلوبيولين، والكوليسترول الكلى، والدهون الثلاثية، واليوريا، والكرياتينين، والكالسيوم، والفسفور غير العضوى، صورة الحديد (الحديد الكلى، والأرتباط الكلى للحديد، والإرتباط الحديد غير المشبع، وترانسفيرين البلازما، والنسبة المئوية لتشبع ترانسفيرين البلازما)، والأكسدة الفوقية للدهون. كما جمعت عينات من أنسجة الكبد والكلى عند نهاية الشهرين الثانى والثالث من كل مجموعة وذلك لتقدير نسبة عنصر الكادميوم المتبقي في أنسجتهما. وقد خلصت النتائج في نهاية هذه الدراسة إلى حدوث زيادة معنوية في نشاط أنزيم ألآنين أمينوترانسفيريز، وأسبرتيت أمينوترانسفيريز، والفوسفاتيز القاعدى، الأكسدة الفوقية للدهون و أنزيم الكتاليز في كرات الدم الحمراء في المجموعة التى تعرضت للكادميوم. وقد أحدث إعطاء فيتامين ج أو هـــ مع الكادميوم نقص معنوى في نشاط هذه الإنزيمات والأكسدة الفوقية للدهون والتقليل من الزيادة التي حدثت في مستوى تركيز اليوريا، والكرياتين. كما حدث انخفاض معنوى في تركيز البروتين الكلى، والزلال، والجلوبيولين، وتركيز الكالسيوم، والفسفور غير العضوي تركيز الكوليسترول الكلى والدهون الثلاثية وتركيز الحديد الكلى والسعة الارتباطية للحديد الكلى، و السعة الأرتباطية للحديد غير المشبع، وترانسفرين البلازما، ونسبة تشبع ترانسفيريين البلازما أما الأرانب التى تعرضت للكاديميوم مع فيتامين ج أو هـــ، فقد لوحظ حدوث زيادة معنوية في مستوى هذه القياسات. كما أحدث تعرض الارانب للكادميوم إلى حدوث زيادة معنوية في مستوى تركيز بقايا عنصر الكادميوم في أنسجة الكبد والكلى مع إنخفاض في تركيز بقايا هذا العنصر مع إعطاء بفيتامين ج أوهـــ . ولذلك ننصح بأعطاء فيتامين ج وفيتامين هـــ بالجرعة العلاجية الآمنة وذلك للتقليل من الأثار الضارة غير الرغوب فيها التي يحدثها التعرض للتسمم بالعناصر الثقيلة.