

Effect of Cadmium Toxicity on Some Biochemical Blood Parameters and Their Modulation with Certain Natural Antioxidants in Rabbits

Hussein, S. A. ^{*} Abd El-Maksoud, H. A. ^{*} Agag B. I. ^{**}
El-Nile, M. B. ^{***}

^{*} Bioch. Depat., Fac. Vet. Med., Moshtohor, Benha University.
Animal Health Research Institute, Dokki^{**} and Zagazig Provincial Laboratory^{***}.

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. Forty 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 catalase 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 (69).

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 (17), testes (57), brain, and nervous system (52).

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 (3), hydrogen peroxide (75) and probably hydroxyl radical (46). As a consequence, enhanced lipid peroxidation, DNA damage, altered calcium and sulfhydryl homeostasis, as well as marked disturbances of antioxidant defense system (AOS) occur (62).

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 (12). 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 (49).

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

Forty 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 was separated by centrifugation at 3000 r.p.m for 10 minutes. The clean, clear plasma was processed directly

*Third Inter. Sci. Conf., 29 Jan.- 1 Feb./ 2009, Benha & Ras Sudr, Egypt
Fac. Vet. Med. (Moshtohor), Benha Univ*

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-Malondialdehyde) concentrations as well as erythrocyte Catalase activity were assayed colorimetrically according to the methods described by (53, 32, 7, 4, 38, 6, 19, 9, 34, 48, 17, 10 and 59), respectively. Cadmium residue in liver and kidney specimen were determined by Atomic Absorption Spectrophotometer according to the method described by (2).

Statistical analysis:

The obtained data were statistically analyzed and the significant difference between groups was evaluated according to (61).

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 (28) 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 (1) 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, (33) 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 H₂O₂ accumulation and H⁺, Cd and H₂O₂-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 (Table, 1). Ascorbic acid is known as a potential scavenger of reactive oxygen species (ROS) (42) and it may protect the lipids from detectable peroxidative damage induced by aqueous peroxy radicals (16). Also, vitamin E has been found to have antioxidant and cytoprotective properties in cultured cells (71). 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 (56) 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 (15).

Cadmium exposed rabbits showed significant decrease in plasma ALP activity after two and three months of the experiment. Similarly, (22) 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 (45). 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 (54).

Plasma total protein, albumin and globulin concentrations showed significant decrease in cadmium exposed animals allover the periods of experiment (Table, 1). Similarly, (41) recorded that, serum protein was decreased whereas urine proteins were elevated significantly after administration of 0.25 or 2 mg of cadmium as CdCl₂ i.p. to male Wister rats. The recorded significant decrease of plasma total protein, albumin, and 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 (29), 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, (5) recorded that, increased excretion of total protein was observed in rats exposed to cadmium.

Treatment of cadmium exposed rabbits with vitamin C and vitamin E exhibited significant increase in plasma albumin concentration afte. 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 (Table, 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 -¹⁴C monodeiodinase (5'D-I) activity in liver. Such increase in plasma albumin level could be attributed to increase of plasma thyroxine concentration (23) 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, (20) reported that, blood serum level of triglycerides was increased under the influence of chronic cadmium poisoning. This suggests the hypothesis of the possible development of atherosclerotic changes resulting from chronic cadmium poisoning. Also, (18) 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 all over the period of experiment. However, treatment with vitamin E exhibit significant decrease in triacylglycerols concentration after three months as compared to cadmium exposed group (Table, 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 (21). 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 (76). Moreover, the increased serum triacylglycerols concentration might be attributed to increased hepatic triacylglycerol synthesis and very low density lipoprotein (VLDL) secretion (27). 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 (74). 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 (65). This suggestion was

*Third Inter. Sci. Conf., 29 Jan.- 1 Feb./ 2009, Benha & Ras Sudr, Egypt
Fac. Vet. Med. (Moshtohor), Benha Univ*

confirmed by the findings of (50) 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 (1). This suggestion was supported by (35) who mentioned that; rise in creatinine value is an indication of renal tubular damage due to cadmium-induced nephrotoxicity. As confirmed by (60) 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 (Table, 2). The obtained results were in agreement with that recorded by (58) 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 (43) 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 all over the periods of the experiment. These results are nearly similar to those reported by (30) 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, (51) observed that, chronic oral cadmium administration (5 or 10 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 (70).

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 (73). The marked decrease in plasma inorganic phosphorous concentration observed in cadmium intoxicated rabbits may be attributed to increased secretions of parathyroid hormone (45). 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) (26). Furthermore, (30) 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 (Table, 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 (63). 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 (68). 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 (56) 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 but depleted iron stores, the % saturation of transferrin decreases (26). Furthermore, the observed increase in % saturation is due to hemolytic anemia (11).

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 (Table, 3). (13) showed that, ascorbic acid does not have a direct effect on cadmium, but improves iron absorption in the gastrointestinal tract. On the other hand, (24) 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 (Table, 3) revealed that, cadmium exposed rabbits showed a significant increase in plasma L-MDA concentration all over the periods of experiment as compared to normal control group. These results are nearly similar to those reported by (37) 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 (62). This suggestion was confirmed by the findings of (64) who reported that, cadmium may induce 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, (12) reported that, the exogenous administration of alpha-tocopheryl succinate completely protected rat hépatocytes from Cd-induced injury and lipid peroxidation. Furthermore, (25) 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 rēgenerating the active form of membrane-bound vitamin E. Evidence suggests that there is an ascorbate-vitamin E interaction (67).

A significant increase in erythrocyte catalase activity observed in cadmium exposed rabbits allover the periods of the experiment (Table, 4). These results are nearly similar to those reported by (47) 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 (56).

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 (Table, 4). These obtained results are in accordance with the results of (47) 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 (44 and 36). Furthermore, 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 (47).

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 (31) 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 (39). In addition to, cadmium provided orally to rats induces the synthesis of a cadmium-binding protein, metallothionein, in liver (55). Hepatic metallothionein also binds zinc (72). Possibly, in cadmium supplemented rats, hepatic concentration of cadmium and zinc increased because these elements bound to an induced metallothionein (40). This suggestion was confirmed by (8) 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 (14) 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, (66) 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.

References

1. Aisha M. Fahim and Elham A. Mohamed (2000): Interaction of iron, zinc and calcium with cadmium toxicity in rats and goats. *J. Egypt Vet. Med. Ass.*, 60(6): 203-218.
2. Al-Ghais, S. M. (1995): Heavy metal concentration in the tissues of Sparus Serba (Forkal, 1975) from the United Arab Emirates. *Bull. Environ. Contam. Toxicol.*, 55: 581.
3. Amoroso, M. A.; Witz, C. and Stein, B. D. (1982): Enhancement of rat and human phagocyte superoxide anion radical production by cadmium in vitro. *Toxicology Letters*, 10, 133-138.
4. Bartholomew, R. J. and Delaney, A. M. (1966): *Proceedings of the Australian Association of Clinical Biochemists*, 1: 214.
5. Brzoska, M. M.; Kaminski, M.; Supernak-Bobko, D.; Zwierz, K. and Moniuszko-Jakoniuk, N. (2003): Changes in the structure and function of the kidney of rats chronically exposed to cadmium. I. Biochemical and histopathological studies. *Arch Toxicol.*, 77(6): 344-52.
6. Bucolo, G. and David, H. (1973): Quantitative determination of serum triglycerides by use of enzymes. *Clin. Chem.*, 19: 475-482.
7. Cannon, D.C. (1974): In *clinical chemistry-principales and Techniques*, 2nd Ed. R. J. Henry et al.: Eds. Harper and Row, Hagerstown, M. D., pp 411-421.
8. Chan, H. M.; Satoh, M.; Zalups, R. K. and Chenan, M. G. (1992): Exogenous metallothionein and renal toxicity of cadmium and mercury in rats. *Toxicology*, 76: 15-26.
9. Colenbrander, H. J. and Vink, C. L. (1969): *Clin. Chem. Acta.*, 28, 175-184.
10. Esterbauer, H.; Cheeseman, K. H.; Danzani, M. U.; Poli, G. and Slater, T. F. (1982): Separation and characterization of the aldehyde products of ADP/Fe²⁺+C stimulated lipid peroxidation in rate liver microsomes. *Biochem. J.*, 208: 129-140.
11. Fairbanks, V. F. (1982): Hemoglobin, Hemoglobin derivatives and myoglobin in: *Fundamentals of Clinical Chemistry*. Ed by NW Tietz, pp 411-414, Saunders Company Philadelphia.
12. Fariss, M. W. (1991): Cadmium toxicity: unique cytoprotective properties of alpha tocopheryl succinate in hepatocytes. *Toxicology*, 69(1): 63-77.
13. Fox, M. R. S. and Fry, B. E. Jr. (1970): Cadmium toxicity decreased by dietary ascorbic acid supplements. *Science*, 169:989.
14. Fox, M. R. S.; Jacobs, R. M.; Jones, A. O. L.; Fry, B. E. Jr. and Stone, C. L. (1980): Effects of vitamin C and iron on cadmium metabolism. *Ann. New York, Acad. Sci.*, 355, 249.
15. Frank, J. and Biesalski, H. K. (1997): Involvement of reactive oxygen species in the progression o renal disease and the significance of antioxidants in the therapy. *Nieremud Hochdruckk Rannkhei Ten*, 26 (8): 342-346.
16. Frei, B.; England, L. and Ames, B. N. (1989): Ascorbate is an outstanding antioxidant in human blood plasma. *Proc. Natl. Acad. Sci. USA*, 86, 6377-6381.
17. Friedman, P.A., and Gesek, F.A. (1994): Cadmium uptake by distal convolute tubule cells. *Toxicol, Apoppl. Pharmacol.* 128, 257-263.

18. Fujita, D. (1992): Effect of cadmium on lipid components: relation of cadmium to thyroid hormone and growth hormone *Nippon Eiseigaku Zasshi*, 47(3): 704-14.
19. Gindler, E. M. and King, J. D. (1972): Rapid colorimetric determination of calcium in biologic fluids. With methyle thymol blue. *Am. J. Clin. Pathol.*, 58, 777.
20. Grabowska-Maslanka, H. and Janik, A. (1994): Evaluation of the toxic effects of cadmium on the body in light of research on the behavior of lipid compounds in aortic walls of animals. *Folia. Med. Cracov.*; 35(1-4): 39-44.
21. Grundy, S. M. and Vega, G. L. (1987): Fibric acids: effects on lipids and lipoprotein metabolism. *Am. J. Med.* 83, 513, 9.
22. Gur, E.; Waner, T.; Barushka-Eizik, O. and Oron, U. (1995): Effect of cadmium on bone repair in young rats. *J. Toxicol. Environ. Hlth.*, 45(3): 249-60.
23. Habeeb, A. A.; Ayyat, M. S. and Basiuny, S. M. (1989): Thyroid function, some blood constituents and fattening performance of rabbits as affected by thyroxine treatments. 3rd Egyptian-British Conf. Animal, Fish and Poultry Production, Alex., Egypt.2: 1017.
24. Hill, C. H. (1980): Interactions of vitamin C with lead and mercury. *Ann. NY Acad. Sci.*, 355: 262-6.
25. Hudecava, A. and Ginter, E. (1992): The influence of ascorbic acid on lipid peroxidation in Guinea pigs intoxicated with cadmium. *Food and Chemical Toxicology*, 30(12): 1011-1013.
26. Hussein, S. A. (2003): *Clinical Biochemistry, Interpretation and Applications* (First Edition, Volume II, Fac. Vet. Med. Zagazig University, Benha Branch, Egypt.
27. Hussein, S. A. and Azab, M. E. (1998): Plasma concentrations of lipids and lipoproteins in newborn kids and female baladi goats during late pregnancy and onset of lactation. *Dtsch. Tierärztl. Wschr.*, 105, 6-9.
28. Hwang, D. F. and Wang, L. C. (2001): Effect of taurine on toxicity of cadmium in rats. *Toxicology*, 167(3): 173-80.
29. Jun-Ichi, S. T.; Shin-Ichi, K.; Kakuno, K.; Terui, J.; Takashima, K. and Soyama, M. (1996): Mechanism of nephrotoxicity induced by repeated administration of cadmium chloride in rats. *J. Toxicol. Environ. Hlth.*, 48: 333-348.
30. Karagl, H.; Altintas, A.; Fidanci, U. R. and Sel, T. (2000): *Klinik Biyokimya. Medisan Yayi nevi.* Ankara.
31. Katsuta, O.; Hiratsuka, H.; Matsumoto, J.; Tsuchitani, M.; Umemura, T. and Marumo, F. (1993): Ovariectomy enhances cadmium-induced nephrotoxicity and hepatotoxicity in rats. *Toxicol. Appl. Pharmacol.*, 119(2): 267-74.
32. Kind P.R.N. and king E.J. (1954): Estimation of plasma phosphatase by determination of hydrolyzed phenol with-amino-antipyrine. *J. Cln. Pathol.*; 7: 322-326.
33. Koizumi, T. and Li, Z. (1996): Role of oxidative stress in single-dose. Cadmium-induced testicular cancer. *J. Toxicol. Environ. Health*, 37, 25-36.
34. Kunish, J. P. and Small, L. L. (1970): *Clin. Chem.*, 16, 148-150.
35. Lall, S. B.; Das, N.; Rama, R.; Peshin, S. S.; Khatter, S.; Gulati, K. and Seth, S. D. (1997): Cadmium induced nephrotoxicity in rats. *Indian. J. Exp. Biol.* 35, 151-154.

36. Lass, A.; Sohal, R. S. (2000): Effect of coenzyme Q10 and alpha-tocopherol content of mitochondria on production of superoxide anion radicals. *FASEB. J.*, 14: 87-94.
37. Mancu, D.; Icard, A. C.; Trottier, B. and Chevalier, G. (1991): Studies on lipid peroxidation in rat tissues following administration of low and moderate doses of cadmium chloride. *Toxicology*, 67, 303-323.
38. Meattini, F.; Prencipe, L.; Bardelli, F.; Giannini, G. and Tarli, P. (1978): The 4-hydroxybenzoate/ 4-aminophenazone chromogenic system used in the enzymic determination of serum cholesterol. *Clin. Chem.*; 24: 2161-2165.
39. Mennear, J. H. (1979): *Cadmium Toxicity*, Marcel Dekker, New York, pp. 61-158.
40. Meyer, S. A.; House, W. A. and Welch, R. M. (1982): Some metabolic interrelationships between toxic levels of admium and nontoxic levels of selenium fed to rats. *J. Nutr.*, 112(5) 954-61.
41. Moshtaghie, A. A.; RAISI, A. and Goodarzi, H. (1991): A study of the effect of Cadmium toxicity on serum Proteins and it's relation to proteinuria in male rats. *J. Islamic Academy of Sciences* 4(3): 192-195.
42. Mukhopadhyay, M.; Mukhopadhyay, C. K. and Chat-terjee, I. B. (1993): Protective effect of ascorbic acid against lipid per oxidation and oxidative damage in cardiac microsomes. *Mol. Cell. Biochem.*, 126, 69-75.
43. Nagyova, A. and Ginter, E. (1994): Interactions between hepatic ascorbic acid, cytochrome P-450 and lipids in female guinea pigs with different ascorbic acid intake. *Physiol. Res.*; 43(5):307-12.
44. Navarro, F.; Arroyo, A.; Martin, S. F.; Bello, R. L.; DE Cabo, R.; Burgess, J. R.; Navas, P. and Villalba, J. M. (1999): Protective role of ubiquinone in vitamin E and selenium-deficient plasma membranes. *BioFactors* 9: 163-170.
45. Nogawa, K.; Kobayashi, E.; Yamada, Y.; Honda, R.; Kido, T.; Tsuritani, I. and Ishizaki, M. (1984): Parathyroid hormone concentration in the serum of people with cadmium-induced renal damage. *Int. Arch. Occup. Environ. Health.*, 54(3): 187-93..
46. Ochi, T.; Otsuka, F.; Takahashi, K. and Oshawa, M. (1988): Glutathione and metallothioneins as cellular defense against cadmim toxicity in culture Chinese hamster cells. *Chem. Biol. Interactions* 65: 1-14.
47. Ognjanovic, b. I.; Pavlovic, S. Z.; Maletic, S. D.; Zikic, R. V.; Stajn, S. A. Radojicic, R. M.; Saicic, Z. S. and Petrovic, V. M. (2003): Protective Influence of Vitamin E on Antioxidant DefenseSystem in the Blood of Rats Treated with Cadmium. *Physiol. Res.* 52: 563-570.
48. Orynich, R. E.; Tietz, N. W. and Fireck, E. A. (1976): *Infundamentals of clinical chemistry*, Ed. By N. W. Tietz. Philadelphia, W. B. Saunders, P. 926.
49. Pace, V. and Iannucci, E. (1994): The importance of vitamins in relation to the presence of heavy metals in food. *Panminerva Med.* 36(2): 80-2.
50. Peterson, F. J.; Holloway, D. E.; Duquette, P. II. and Rivers, J. M. (1983): Dietary ascorbic acid and hepatic mixed function oxidase activity in the guinea pig. *Biochem. Pharmacol.* 32(1): 91-6.

51. Pilat-Marcinkiewicz, B.; Sawicki, B.; Brzoska, M. M. and Moniuszko-Jakoniuk, J. (2002): Effect of chronic administration of cadmium on the rat thyroid: radioimmunological and immunohistochemical studies. *Folia. Histochem. Cytobiol.* 40(2): 189-90.
52. Provias, J. P.; Ackerley, C. A.; Smith, C. and Becker, L. E. (1994): Cadmium encephalopathy: a report with elemental analysis and pathological findings. *Acta Neuropathol.* (88): 583-586.
53. Reitman, S. and Frankel, S. (1957): A colorimetric method for the determination of serum glutamic oxaloacetic and glutamic pyruvic transaminase. *Am. J. Clin. Path.*, 26, 56.
54. Rikans, L. E.; Moore, D. R. and Snowden, C. D. (1991): Sex-dependent differences in the effects of aging on antioxidant defense mechanisms of rat liver. *Biochimica. et Biophysica. Acta.*, 1074: 195-200.
55. Sabbioni, E. and Girardi, F. (1977): Metallobiochemistry of heavy metal pollution: nuclear and radiochemical techniques for long term-low level exposure (LLE) experiments. *Sci. Total Environ.*, 7, 145-179.
56. Shaikh, Z. A.; Vu, T. T. and Zaman, K. (1999): Oxidative stress as a mechanism of chronic cadmium-induced hepatotoxicity and renal toxicity and protection by antioxidants. *Toxicol. Appl. Pharmacol.*, 154: 256-263.
57. Shen, H. M. and Sangiah, S. (1995): Na^+ , K^+ -ATPase, glutathione and hydroxyl free radicals in cadmium chloride-induced testicular toxicity in mice. *Arch. Environ. Contain. Toxicol.*, 29, 174-177.
58. Shiraiishi, N.; Uno, H. and Waalkes, M. P. (1993): Effect of L-ascorbic acid pretreatment on cadmium toxicity in the male Fischer (F344/NCr) rat. *Toxicology*, 85(2-3): 85-100.
59. Sinha, A. K. (1972): Colorimetric assay of catalase. *Analytical biochemistry*, 47, 389.
60. Skoczynska, A. and Smolik, R. (1994): The effect of combined exposure to lead and cadmium on serum lipids and lipid peroxides level in rats. *Int. J. Occup. Med. Environ. Health.* 7(3): 263-71.
61. Snedecor, G. W. and Cochran W. G. (1969): *Statistical Methods*. 6th Ed. The Iowa State Univ. Press, Iowa, USA.
62. Stohs, S. J. and Bagchi, D. (1996): Oxidative mechanisms in the toxicity of metal ions. *Free Rad. Biol. Med.*, (18): 321-336.
63. Stonard, M. D. and Webb M. (1976): Influence of dietary cadmium on the distribution of the essential metals copper, zinc and iron in tissues of the rat. *Chem. Biol. Interact. Toxicol.*, 15: 349-363.
64. Sumathi, A.; Basharan, G. and Varalakshmi, P. (1996): Relationship between glutathione and DL-alpha lipoic acid against cadmium induced hepatotoxicity. *J. Med. Sci. Bio.*, 49, 39-48.
65. Szymanski, E. S.; Little, N. A. and Kritchevsky, D. (1981) Phospholipid metabolism in livers of young and old fischer 344 and sprague-Dawley rats. *Exp. Geront.*, 163-169.
66. Tandon, S. K.; Singh, S. and Dhawan, M. (1992): Preventive effect of vitamin E. in cadmium intoxication. *Biomed. Environm. Sci. Mar.*, 5(1): 39-45.

Third Inter. Sci. Conf., 29 Jan.- 1 Feb./ 2009, Benha & Ras Sudr, Egypt
Fac. Vet. Med. (Moshtohor), Benha Univ

67. Thomas, S.; Neuzil, J. and Mohr, D. (1995): Coantioxidants make-tocopherol an efficient antioxidant for low-density lipoprotein. *Am. J. Clin. Nutr.*, 62, 1357 S-1346S.
68. Vahter, M.; Berglund, M.; Nermell, B. and Akesson, A. (1996): Bioavailability of cadmium from shellfish and mixed diet in women. *Toxicol. Appl. Pharmacol.*, 136: 332-341.
69. Waalkes, M. P.; Rehm S.; Sass, B.; Konishi, N. and Ward, J. M. (1991): Chronic carcinogenic and toxic effects of a single subcutaneous dose of cadmium in the male Fischer rat. *Environmental Research*, 55, 40-50.
70. Wang, C. and Bhattacharyya, M. H. (1993): Effect of cadmium on bone calcium and ⁴⁵Ca in non pregnant mice on a calcium-deficient diet: evidence of direct effect of cadmium on bone. *Toxicol. Appl. Pharmacol.*, 120: 228-239.
71. Warren, S.; Patel, S. and Kapron, C. M. (2000): The effect of vitamin E exposure on cadmium toxicity in mouse embryo cells in vitro. *Toxicology*, 142(2): 119-26.
72. Webb, M. (1972): Binding of cadmium ions by rat liver and kidney. *Biochem. Pharmacol.* 21. 2751-2765.
73. Wu, X.; Jin, T.; Wang, Z. Ye, T.; Kong, Q. and Nordberg, G. (2001): Urinary calcium as a biomarker of renal dysfunction in a general population exposed to cadmium. *J. Occup. Environ. Med.*, 43(10):898-904.
74. Yost, T. J.; Froyd, K. K.; Jenson, D. R.; and Eckel, R. H. (1995): Changes in skeletal lipoprotein lipase activity in response to insulin/ glucose in non-insulin dependent diabetes mellitus. *Metabolism*, 44(6): 786-790.
75. Zhog, Z.; Troll, W.; Koenig, K.L. and Frenkel, K. (1990): Carcinogenic sulfide salts of nickel and cadmium induce H₂O₂ formation by human polymorphonuclear leukocytes. *Cancer Res.*, 20: 7564-7570.

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.

Animal groups Parameters		Control	Vitamin C	Vitamin E	Cadmium	Cadmium + Vit.C	Cadmium + Vit. E
ALT (U/L)	One month	102.67 ± 5.50 ^a	81.33 ± 6.73 ^{bc}	106.50 ± 6.35 ^a	52.66 ± 3.90 ^c	60.50 ± 2.27 ^c	66.33 ± 1.20 ^c
	Two months	47.67 ± 4.17 ^a	54.00 ± 6.09 ^a	55.83 ± 4.22 ^a	51.16 ± 3.13 ^{ab}	64.16 ± 4.44 ^a	55.33 ± 3.05 ^{ab}
	Three months	42.33 ± 2.67 ^c	46.67 ± 0.88 ^{bc}	62.67 ± 1.33 ^a	62.66 ± 1.33 ^a	57.33 ± 3.52 ^a	47.33 ± 2.33 ^b
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	48.00 ± 3.16 ^b	66.50 ± 4.14 ^a
	Two months	48.33 ± 4.09 ^a	29.16 ± 3.40 ^b	52.00 ± 1.73 ^a	47.66 ± 3.17 ^a	30.50 ± 1.58 ^b	46.00 ± 2.74 ^a
	Three months	30.66 ± 3.93 ^b	48.33 ± 2.90 ^a	43.00 ± 4.04 ^a	40.66 ± 2.33 ^{ab}	36.33 ± 6.66 ^{ab}	32.33 ± 4.70 ^b
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	13.11 ± 0.44 ^d	11.41 ± 0.98 ^d
	Two months	16.45 ± 1.34 ^a	11.63 ± 0.64 ^b	13.13 ± 0.81 ^b	5.46 ± 0.29 ^d	8.13 ± 0.13 ^c	6.98 ± 0.95 ^{cd}
	Three months	9.00 ± 0.26 ^a	7.83 ± 1.02 ^{ab}	7.86 ± 0.49 ^{ab}	5.80 ± 0.20 ^c	5.96 ± 0.46 ^c	6.90 ± 0.25 ^{bc}
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	5.48 ± 0.12 ^l	5.19 ± 0.17 ^b
	Two months	6.82 ± 0.12 ^a	6.67 ± 0.12 ^a	6.50 ± 0.20 ^a	4.77 ± 0.10 ^b	5.09 ± 0.12 ^b	5.00 ± 0.19 ^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 ± 0.09 ^b	1.46 ± 0.06 ^d	1.68 ± 0.06 ^c	1.40 ± 0.03 ^d
	Three months	2.86 ± 0.07 ^a	2.93 ± 0.07 ^a	2.86 ± 0.07 ^a	1.64 ± 0.07 ^b	2.79 ± 0.00 ^a	2.71 ± 0.07 ^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	4.01 ± 0.21 ^{abc}	3.55 ± 0.22 ^c
	Two months	4.02 ± 0.17 ^a	3.67 ± 0.17 ^a	4.06 ± 0.20 ^{ab}	3.14 ± 0.14 ^b	3.41 ± 0.14 ^b	3.19 ± 0.18 ^b
	Three months	4.00 ± 0.27 ^a	.74 ± 0.27 ^{ab}	4.00 ± 0.17 ^a	3.25 ± 0.07 ^b	2.11 ± 0.19 ^c	2.32 ± 0.10 ^c

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

Third Inter. Sci. Conf., 29 Jan.- 1 Feb./ 2009, Benha % Ras Sudr, Egypt
Fac. Vet. Med. (Moshtohr), Benha Univ

Table (2): Effect of cadmium treatment alone and in combination with vitamin C or vitamin E on plasma Total Cholesterol, Triacylglycerols, Urea, Creatinine, Calcium and inorganic Phosphorus concentrations of male rabbits.

Animal groups Parameters		Control	Vitamin C	Vitamin E	Cadmium	Cadmium + Vit. C	Cadmium + Vit. E
Total Cholest. (mg/dL)	One month	107.33± 2.03b	148.00± 16.46a	115.67± 6.06ab	86.33± 4.48b	88.66± 8.25b	97.00± 9.53b
	Two months	84.33± 1.67bc	85.00± 0.58bc	103.00± 2.08a	78.00± 3.05c	92.33± 6.33b	83.00± 4.27c
	Three months	72.00± 2.08d	94.33± 2.33a	75.67± 5.48cd	73.33± 3.38b	85.00± 1.73ab	98.33± 7.79a
Triacyl. (mg/dL)	One month	83.00± 5.20b	102.00± 5.78a	75.00± 2.00bc	49.66± 7.83c	73.66± 3.75b	85.66± 2.60b
	Two months	62.33± 1.86b	60.33± 2.03b	83.67± 2.33a	71.66± 4.40abc	73.33± 3.38ab	72.66± 6.48abc
	Three months	51.00± 3.46c	78.00± 1.15ab	61.00± 0.88b	66.00± 4.58bc	58.00± 1.15de	72.33± 0.33ab
Urea (mg/dL)	One months	27.90± 1.99b	27.55± 1.95b	32.51± 1.20ab	34.78± 1.29b	40.76± 1.06b	51.71± 3.55a
	Two months	34.19± 1.54b	39.64± 1.40ab	27.77± 2.77c	37.77± 1.82b	46.16± 1.38a	47.17± 2.57a
	Three months	32.06± 1.48b	33.76± 2.26b	33.98± 0.65b	38.43± 0.66ab	40.64± 0.90a	37.49± 1.96ab
Creat. (mg/dL)	One months	1.33± 0.03c	1.32± 0.03b	1.33± 0.06b	3.86± 0.16a	4.22± 0.28a	3.11± 0.13b
	Two months	1.00± 0.15de	0.67± 0.01e	1.31± 0.03cd	3.59± 0.21c	4.22± 0.15b	4.67± 0.05a
	Three months	1.33± 0.05b	1.33± 0.03c	1.33± 0.06c	3.11± 0.22ab	3.55± 0.22a	2.89± 0.22b
Calc. (mg/dL)	One month	11.50± 0.50a	10.08± 0.23a	11.25± 0.47a	10.41± 0.49ab	11.45 ± 0.26a	11.55± 0.45a
	Two months	11.33± 0.47ab	10.08± 0.20abc	11.55± 0.57ab	8.76± 0.10c	11.13 ± 0.49ab	10.61± 0.39ab
	Three months	12.30± 0.11a	11.33± 0.72ab	11.10± 0.73ab	7.53± 0.14b	10.50 ± 0.50a	11.33± 0.72a
Phos.. (mg/dL)	One month	5.82± 0.30a	6.00± 0.29a	4.32± 0.31b	2.89± 0.13c	3.07 ± 0.07c	3.25± 0.04c
	Two months	4.53± 0.20ab	3.86± 0.25b	4.27± 0.30b	3.28± 0.31c	5.17 ± 0.10a	5.14± 0.11a
	Three months	5.82± 0.30a	6.00± 0.29a	4.32± 0.31b	3.16± 0.30b	4.12 ± 0.17a	3.11± 0.15b

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

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.

Animal groups Parameters		Control	Vitamin C	Vitamin E	Cad-mium	Cadmium + Vit. C	Cadmium + Vit. E
Iron (µg/dL)	One month	190.48 ± 3.40c	210.79 ± 2.67bc	195.97 ± 7.74bc	177.49 ± 4.38b	97.00 ± 9.53b	193.13 ± 10.57ab
	Two months	153.91 ± 5.79bc	171.38 ± 4.11ab	168.84 ± 1.24ab	193.99 ± 7.02a	83.00 ± 4.27c	184.79 ± 6.24ab
	Three months	198.00 ± 12.35a	170.61 ± 8.45ab	168.25 ± 8.52ab	193.25 ± 12.56a	98.33 ± 7.79a	185.78 ± 6.33a
TIBC (µg/dL)	One months	458.01 ± 5.23ab	439.88 ± 13.86b	481.29 ± 7.60a	430.10 ± 5.91c	85.66 ± 2.60b	464.55 ± 8.96ab
	Two months	491.60 ± 8.28ab	497.47 ± 5.84a	473.47 ± 19.35ab	484.85 ± 13.56b	72.66 ± 6.48abc	537.08 ± 12.09a
	Three months	422.27 ± 17.23bc	524.46 ± 14.77a	524.46 ± 11.42a	493.02 ± 7.83ab	72.33 ± 0.33ab	446.10 ± 26.29bc
UIBC (µg/dL)	One month	300.41 ± 30.95a	262.74 ± 2.90ab	285.31 ± 7.91ab	252.69 ± 3.69b	51.71 ± 3.55a	277.44 ± 7.24ab
	Two months	329.69 ± 7.93a	326.98 ± 5.85a	296.80 ± 5.45b	282.32 ± 3.97d	47.17 ± 2.57a	366.12 ± 12.10a
	Three months	268.69 ± 5.18bc	354.18 ± 7.60a	353.20 ± 5.22a	312.09 ± 8.03ab	37.49 ± 1.96ab	312.41 ± 39.89ab
Trans-ferrin (gm/L)	One month	3.31 ± 0.11a	3.33 ± 0.04a	3.36 ± 0.05a	3.01 ± 0.04b	3.11 ± 0.13b	3.23 ± 0.05a
	Two months	3.38 ± 0.01a	3.48 ± 0.04a	3.31 ± 0.13a	3.31 ± 0.04b	4.67 ± 0.05a	3.76 ± 0.08a
	Three months	3.14 ± 0.04b	3.65 ± 0.11a	3.65 ± 0.09a	3.45 ± 0.05ab	2.89 ± 0.22b	3.30 ± 0.05bc
Ttrans-ferrin saturati on percent	One month	40.36 ± 1.06bc	45.01 ± 3.79ab	37.71 ± 1.69c	41.26 ± 0.66ab	11.55 ± 0.45a	37.83 ± 1.10b
	Two months	34.66 ± 2.55a	34.35 ± 1.05a	34.37 ± 0.21a	39.10 ± 1.21a	10.61 ± 0.39ab	31.86 ± 0.75c
	Three months	40.06 ± 0.45a	30.68 ± 0.86c	30.86 ± 0.86c	37.75 ± 0.42b	11.33 ± 0.72a	41.54 ± 0.70a
L-MDA (nmol/m)	One months	4.35 ± 0.09bc	3.06 ± 0.22c	5.20 ± 0.93b	9.76 ± 0.53a	3.25 ± 0.04c	5.22 ± 0.14b
	Two months	4.72 ± 0.20bc	5.15 ± 0.17bc	4.45 ± 0.31c	16.59 ± 0.83a	5.14 ± 0.11a	4.23 ± 0.43c
	Three months	4.34 ± 0.22b	4.78 ± 0.21b	4.88 ± 0.19b	15.62 ± 0.65a	3.11 ± 0.15b	3.68 ± 0.78b

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

Third Inter. Sci. Conf., 29 Jan.- 1 Feb./ 2009, Benha & Ras Sudr, Egypt
 Fac. Vet. Med. (Moshtohor), Benha Univ

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.

Animal groups		Control	Vitamin C	Vitamin E	Cadmium	Cadmium + Vit. C	Cadmium + Vit. E
Parameters							
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	41.76 ± 2.23 ^b	46.08 ± 1.67 ^{ab}
	Two months	28.61 ± 0.12 ^d	33.14 ± 0.76 ^{bc}	30.76 ± 2.20 ^{cd}	39.85 ± 1.99 ^a	39.81 ± 0.21 ^a	39.93 ± 0.83 ^a
	Three months	29.19 ± 0.30 ^c	33.59 ± 0.29 ^c	31.98 ± 0.31 ^c	41.43 ± 1.53 ^a	40.04 ± 1.48 ^a	41.06 ± 1.82 ^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	0.46 ± 0.16 ^b	0.50 ± 0.15 ^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 ± 0.03 ^b	0.53 ± 0.13 ^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	0.60 ± 0.01 ^b	0.70 ± 0.05 ^b
	Three months	0.26 ± 0.03 ^b	0.23 ± 0.03 ^b	0.30 ± 0.05 ^b	5.83 ± 1.41 ^a	0.60 ± 0.05 ^b	1.03 ± 0.12 ^b

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

Mean with different superscript letters in the same column are significantly different at (P ≤ 0.05).

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

سامي علي حسين* وبدير إبراهيم عجاج** وحسين عبد القصود علي* ومحمد بدر النيل***
قسم الكيمياء الحيوية- كلية الطب البيطري بمشتهر- جامعة بنها* و معهد بحوث صحة الحيوان
الدقى** ومعمل فرعي الزفازيق***.

الملخص العربي

يعتبر التلوث بالعناصر الثقيلة من أخطر أنواع التلوث التي يتعرض لها الإنسان والحيوان على حد سواء لما يحدثه من تدمير خلايا وأنسجة وأعضاء الجسم الحيوية ذلك لما تنتج داخل الخلايا من الشوارد الحرة. وحيث أن مضادات الأكسدة تلعب دوراً هاماً في السيطرة والتقليل من خطورة الشوارد الحرة على الأنسجة والأعضاء المختلفة فقد جاءت فكرة هذا البحث لدراسة الآثار الضارة للتسمم بعنصر الكاديميوم واستخدام بعض مضادات الأكسدة مثل فيتاميني ج وفيتامين هـ. أجريت الدراسة على عدد إثنتين وأربعين من ذكور الأرانب النيوزيلندية البيضاء قسمت إلى ستة مجموعات متساوية كالتالي: المجموعة الأولى (المجموعة الضابطة) لم تتلقى أي علاجات. والمجموعة الثانية تم تجريعها فيتامين ج يومياً عن طريق الفم بجرعة ٤٦,٦٧ ملغ جرام لكل كيلو جرام من وزن الجسم. والمجموعة الثالثة تم تجريعها فيتامين هـ يومياً بجرعة مقدارها ١٨,٦٧ ملغ جرام. والمجموعة الرابعة أعطيت كلوريد الكاديميوم بجرعة مقدارها ٥ . ملغ جرام لكل كيلو جرام من وزن الجسم. والمجموعة الخامسة أعطيت إلى جانب كلوريد الكاديميوم جرعة يومية من فيتامين ج مقدارها ٤٦,٦٧ ملغ جرام لكل كيلو جرام. والمجموعة السادسة أعطيت إلى جانب كلوريد الكاديميوم جرعة يومية من فيتامين هـ مقدارها ١٨,٧٦ ملغ جرام لكل كيلو جرام.. تم تجميع عينات الدم على هيبارين على ثلاث فترات كلا منها شهر من بداية تجريع الأرانب بالكاديوم ومضادات الأكسدة واستخدم مباشرة لقياس نشاط أنزيم الكاتاليز في كرات الدم الحمراء. وتم فصل البلازما واستخدمت لأجراء بعض القياسات البيوكيميائية مثل نشاط أنزيم أسبرتيت أمينوترانسفيريز، والأنين أمينو ترانسفيريز، والفوسفاتيز القاعدي، البروتين الكلي، والزال، والجلوبيولين، والكوليسترول الكلي، والدهون الثلاثية، واليوريا، والكرياتينين، والكالسيوم، والفسفور غير العضوي، صورة الحديد (الحديد الكلي، والأرتباط الكلي للحديد، والأرتباط الحديد غير المشبع، وترانسفيرين البلازما، والنسبة المنوية لتشبع ترانسفيرين البلازما)، والأكسدة الفوقية للدهون. كما جمعت عينات من أنسجة الكبد والكلى عند نهاية الشهرين الثاني والثالث من كل مجموعة وذلك لتقدير نسبة عنصر الكاديميوم المتبقي في أنسجتهما. وقد خلصت النتائج في نهاية هذه الدراسة إلى حدوث زيادة معنوية في نشاط أنزيم الأنين أمينوترانسفيريز، وأسبرتيت أمينوترانسفيريز، والفوسفاتيز القاعدي، الأكسدة الفوقية للدهون وأنزيم الكاتاليز في كرات الدم الحمراء في المجموعة التي تعرضت للكاديميوم. وقد أحدث إعطاء فيتامين ج أو هـ مع الكاديميوم نقص منوي في نشاط هذه الإنزيمات والأكسدة الفوقية

للدّهون والتقليل من الزيادة التي حدثت في مستوى تركيز اليوريا، والكرياتينين. كما حدث انخفاض معنوي في تركيز البروتين الكلي، والزلال، والجلوبيولين، وتركيز الكالسيوم، والفسفور غير العضوي تركيز الكوليسترول الكلي والدهون الثلاثية وتركيز الحديد الكلي والسعة الارتباطية للحديد الكلي، و السعة الارتباطية للحديد غير المشبع، وترانسفيرين البلازما، ونسبة تشبع ترانسفيرين البلازما أما الأرانب التي تعرضت للكاديميوم مع فيتامين ج أو هـ، فقد لوحظ حدوث زيادة معنوية في مستوى هذه القياسات. كما أحدث تعرض الأرانب للكاديميوم إلى حدوث زيادة معنوية في مستوى تركيز بقايا عنصر الكاديميوم في أنسجة الكبد والكلى مع إنخفاض في تركيز بقايا هذا العنصر مع إعطاء بفيتامين ج أو هـ. ولذلك ننصح بإعطاء فيتامين ج وفيتامين هـ بالجرعة العلاجية الآمنة وذلك للتقليل من الآثار الضارة غير الرغوب فيها التي يحدثها التعرض للتسمم بالعناصر الثقيلة.