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The Ameliorative Effect of Vitamin C Against Hematological, Biochemical, Oxidative and Immunosuppressive Effect of Cadmium Chloride in Rats

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THIS current investigation's objective was to ascertain whether vitamin C has a safe-guarding impact in opposition to the harmful effects of cadmium, a heavy metal with a high toxicity and a substantial environmental pollutant. The experimental group consisted of 20 rats divided into 4 groups. The current study was carried out for 30 days. A (Control) , B (Cadmium group, 15 mg\kg $CdCl_2$) , Vitamin C group (150 mg\kg vitamin C) , D ($CdCl_2$ 15 mg/kg +150 mg/kg b.wt) orally. After 4 weeks blood samples were taken and liver tissues. Findings revealed a substantial drop in RBC count, Hb concentration, and PCV ($P > 0.05$) and a substantial rise in WBC count ($P < 0.05$). On another hand, findings also revealed a substantial drop in total protein, albumin and an increase concentration of globulin, total and direct bilirubin. Also increase concentrations of ALP , AST and ALT . In addition to antioxidants GST, GSH, CAT, SOD, rise in MDA of cadmium group in comparison to A group but, when vitamin C combined by cadmium chloride, the results indicated a noticeable improvement in the parameters under study, indicating the therapeutic effect of vitamin C against cadmium chlorides toxicity in rats.

Keywords: Cadmium, Vitamin C, Antioxidant enzymes, Antioxidants parameters, Amelioration potential.

Introduction

Earth frequently contains heavy metals, which are also referred to as metalloids and metals in the periodic Table[1]. Heavy metals (such as lead, cadmium, nickel, arsenic, chromium, and mercury) have a negative impact on human and animal health [2] "A soft, silvery-white metal with an atomic weight of 113.41 and an atomic number of 48", cadmium (Cd) found in the earth's crust in combination with zinc also consists in the industries as an inevitable by-product of zinc, lead and copper . present in food, water, and cigarette smoke accumulates in the liver and causes a number of hepatic dysfunctions, toxic, and carcinogenic. It belongs to chemical element group XII on the periodic Table [3] The mechanisms and routes of Cd›s toxicity at the tissue level in biological systems are still poorly understood. Reactive oxygen species (ROS) are produced more readily and oxidative stress is induced in several tissues as a result of Cd toxicity, according to a number of studies [4,5] .Furthermore, exposure to Cd promotes tissue damage brought on by lipid peroxidation [6]. Presently, numerous research have demonstrated that cadmium causes, hematological, biochemical effects, histopathological, immunosuppressive, and alterations in the gene expression pathway-

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induced damage to the antioxidant enzyme system [7,8] . It has been noted that Cd causes cell death, most likely via targeting mitochondria. Caspase-3 activity is a dynamic shape of cellular necrosis induced via the release of cytochrome C, and it was raised with mitochondrion-dependent apoptosis. Intracellular homeostasis and the redox system are affected by Cd. Apoptosis happens when the calcium equilibrium is disturbed [9], in addition a key biological sign in the severe hepatic tissue injury is tumor necrosis factor alpha (TNF-α) [10].

Natural antioxidants are substances that prevent the chemical process of oxidation, which can result in the production of free radicals and trigger a cascade that may harm living organisms give a multitude of biological benefits of natural antioxidants, including the ability to fight cancer, ageing, inflammation, and atherosclerosis [11]. Ascorbate, C is a water-soluble vitamin. with potent antioxidant, chain-breaking, and hydrogen peroxide and superoxide scavenger properties, is found both within and outside of cells [12] **.** Given that humans lack a necessary enzyme in the biosynthetic route, which prevents them from synthesizing vitamin C**,** there has been a lot of interest in its application in the prevention and/or treatment of infections. The proper operation of the immune system depends on vitamin C [13] By repairing or neutralizing free radicals by donating one electron, followed by a proton, to produce dehydroascorbic acid, Vitamin C functions as a potential antioxidant utilized to lessen the liver and kidney toxicity brought on via certain medications [14].

Vitamin C demonstrated excellent therapeutic benefits against the rat toxicity-related problems and brought back these abnormalities to nearly normal levels. In the end, it was determined that cadmium has extreme destruction effects on liver cells, liver enzymes, and oxidative status of the liver. The current investigation›s objective was to determine the vitamin C›s protective effects against Cadmium chloride on hematological, biochemical, and immune-histopathological parameters as well as to track its potential to mitigate Cd-induced oxidative damage and hepatotoxicity in rats.

Material and Methods

Cadmium chloride ($Cdcl_2$) (powder dissolved in distilled water immediately before use) and purchased vitamin C (powder) from the Egyptian business Sigma. Catalase, GST, GSH, SOD, and MDA kits of the Bio-diagnostic, Egypt, human company kits for total protein, albumin, AST and ALT, ALP measured using kites from ELITech company (Paris, France). Diamond company (Cairo, Egypt) for Bilirubin total and direct. Recombinant of TNF-alpha and Caspase 3 from Scy Tek company.

Experimental animal handling

Twenty rats weighing between (150-200g) were bought from Tanta University's. They were housed in clean, well-ventilated plastic cages at a room temperature of 25 °C, with a relative humidity of 55 to 65%, and were exposed to light and darkness every 12 hours. Fourteen days before treatment, given fresh tap water and standard regular rodent diets to eat, ration used to feed rats composed of (yellow corn, soyabeans, vegetables oil, calcium carbonate salt and vitamins). According to the Mansoura University of Veterinary Medicine's recommendations, every experiment was approved and carried out.

Experiment, tissue processing

After the period of acclimation, the rats divided into 4groups of five animals. Rats' LD50 value for cadmium determined by the oral route was 2696.54mg/kg for 90 days by Bliss method [15], via intraperitoneal injection was 5.98 and 3.9 mg/kg/ b.w for 24 h exposure and 48h exposure respectively [16].

Group A (control): rats received normal diet and fresh water without cadmium chloride.

Group B (rats were only given cadmium chloride) in dose of 15mg/kg b.wt for 4 weeks orally.

Group C (rats received vitamin C only in dose 150 mg/kg b.wt over a period of 4 weeks orally.

Group D (vitamin C 150mg/kg/ b.wt and cadmium chloride 15mg/kg b.wt).

Sample preparation

Blood samples collected individually from each rat in all group from the eye canthus with capillary tubes after anesthesia with i.p injection of ketamine & xylazine at a dose of 50-10mg/kg, respectively, in two different tubes for each sample tube with EDTA (50 µl/ml blood), complete blood picture (CBC). The other blood sample was collected without anticoagulant, placed until complete clotting in room temperature then

centrifugated (3000 rpm/ 10 minutes) "separated serum in Eppendorf and kept at -20 °C till biochemical testing.

Tissue homogenate, "Rats dissected after cervical dislocation, liver was then removed, Phosphate-buffered saline (PBS) was used to clean the item before it between two filter sheets, where it dried. Half gram of liver grinded with 4.5 ml of phosphate buffer saline to create hepatic tissue homogenates centrifuged (4000 rpm/15 min) at 4 °C. The clear fluid aspirated and freezed at 20 °C. Another part of liver preserved in 10% formalin for conduction of histological and immunohistochemical analyses.

Hematological estimation

Numerated number of erythrocytes (RBCs) counts , hemoglobin (Hb) content , packed cell volume (PCV) % , leukocytes (TLC) counts . Calculations were made to determine the blood indices , mean corpuscular volume (MCV) , mean corpuscular haemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC) [17] .

Biochemical estimation

The collected frozen serum samples were analyzed for alanine transaminase (ALT) , aspartate transaminase (AST) , alkaline phosphatase (ALP) , total bilirubin (TB) , direct bilirubin, total protein , and albumin using a sinostic automatic suction analyser , China . Globulin was calculated by subtracting albumin from total protein ; also calculate A/G ratio , [18] . The manufacturer's instructions were followed while measuring the levels of MDA , SOD , Catalase , GSH and GST in the liver homogenates using commercially available kits (Bio-diagnostic, Egypt) [19].

Histopathological estimation

Hematoxylin and eosin (H&E) stain was applied to the formalin-fixed liver material, which was then embedded in paraffin, tissue section is cut by micrometer into 5-mm-thick sections, and viewed under a microscope. according to Bancroft and Gamble [20].

Immunohistochemistry of TNF-α and Caspase-3 expression

Formalin-fixed, paraffin-embedded liver tissue slices were used for immunohistochemistry. is significantly enhanced by treatment with citrate plus (Scy Tek catalog CPL500) were carried out as describe by[21]. Following deparaffinization, tissue sections were incubated with monoclonal rabbit anti-mouse primary antibody (1:100) against caspase-3 (Biocare Medical, Pacheco, CA) and TNF-α overnight at 4 °C, then washed with TBS (tris buffer saline treated with goat anti-rabbit antibody for an hour at room temperature. (1:1000) and anti-mouse antibodies, developed for 1.5 minutes with 3, 3′-diaminobenzidine tetrahydrochloride (DAB), counterstained with hematoxylin, and covered. Using a light microscope (Nikon Eclipse TE2000-U, NIKON, Japan), Semi-quantitative research was done on the immuno-positive cells' distribution pattern within the hepatic lobule. The number of immuno-positive cells per 1000 cells was also counted and analyzed using Image-J analysis software (Image J, 1.46a, NIH, USA).

The analysis of cadmium residue in liver

Using atomic absorption spectrophotometry (Perkin-Elmer A.A. Model 800) with the Zeeman-effect for background correction. In brief, 1:3 ultra-pure concentrated nitric acid and chlorine perchlorate employed to assimilate 0.5g at ratio (6:1). then complete dehydrated by a hot plate. Dilution with distilled water before being subjected to an atomic absorption spectrophotometry test for cadmium [22].

Analytical Statistics

Data presented as Mean ± SEM for 5 rats in each group for the tables and figures. All data was analyzed using the SPSS application for (Windows, version 20 USA). ANOVA comparing the sets, Duncan employed to evaluate whether there was a significant difference ($P < 0.05$) [23].

Results

The experimental period in the current investigation was set at 30 days, and the nine rat batches were kept as such. No fatalities were noted during the experimental times.

Cadmium concentration in liver of experimental rat

According to (Table 1) , cadmium in the hepatic cadmium-toxicated tissues were substantially higher than the control group, whereas with co-treatment with vitamin C, the concentration of cadmium was significantly decline than cadmium intoxicated rats. The amount of cadmium residue in the liver of vitamin C-treated group and the control rats were the same.

TABLE 1. the residues of cadmium in liver at 4th week post treatment with vitamin C in rats (Mean± SE).

Group	Cadmium residues in liver ug/L (mean ±SD)
Cont.	0.00013 ±0.000042[b]
Cd	0.024496±0.0036 [a]
Vit C	0.00033 ±0.00992 [b]
Cd+Vit C	0.027 ±0.007 [a]

Cont. (Control) ,**Cd** (Cadmium chloride), Vit C (Vitamin C), Cd+**VitC** (rats treated with Cadmium Chloride and vitamin C). Values with different superscript letters consider significance at ($p< 0.05$).

Hematological result

According to the hematological results shown in **(Figure 1 A, B, C),** the cadmium-intoxicated group had a significantly lower in (RBCs$\times 10^6$) counts, (Hb g/dl) concentration, and (PCV%) value than the control group. Meanwhile WBCs ($\times 10^3\mu L$) counts showed significant increase in cadmium intoxicated group compared with control one (Mean ± SE). Our study showed prominent ameliorative effect of co-treatment of vitamin C with cadmium, via significantly up-regulate in RBCs counts, Hb conc, and PCV %, beside the significantly decreased in WBC counts (**Figure-1G)** (Mean ± SE). At the same study blood indices not changed significantly in different groups (**Figure 1 D, E, and F)** (Mean ± SE). from the previous data we found that cadmium chloride caused normocytic normochromic anemia with evidence of leukocytosis which correlated via vitamin C administration.

Biochemical result

Liver function Tests

Cadmium induced hepatocellular inflammation that manifested by clear rise in serum liver enzymes than control rats **(Figure 2 A, B and C).** Meanwhile the cadmium intoxicated treated with vitamin C showed a significant down-regulation in serum liver enzymes compared with cadmium intoxicated group, but not return to the normal value. Total bilirubin (TB) in Cd-intoxicated rats substantially superior to control rats. When compared to Cd-intoxicated rats, the level of bilirubin was dramatically reduced by vitamin C administration together with Cd. although they still vary from control levels. In rats exposed to Cd, there was a notable increase in the direct bilirubin. Co-treatment with vitamin C and Cd dramatically reduced the level of direct bilirubin, but it did not approach the normal level. **(Figure 2 D, E, F)**. Cadmium exposure led to a considerable decrease in total protein and albumin. Groups co-treated with vitamin C had significantly increase in total protein and albumin than groups exposed to cadmium only **(Figure 3 A, B).** Otherwise, globulin value in cadmium toxicated group rats were slightly decreased than control one, also with treatment with vitamin C, globulin significantly up-regulated but still less than normal level **(Figure 3, C)** In the group that had consumed cadmium, the A/G ratio had drastically decreased.

Hepatic antioxidant and oxidative damage markers

A considerable rise in liver MDA and considerable decrease in (Catalase, SOD, GSH, and GST) indicate that cadmium toxicity causes hepatic oxidative stress **(Table 2**). In comparison to cadmium-intoxicated rats, co-treatment with vitamin C brought about a considerable drop in liver MDA and prominent increase in (GSH, CAT, SOD and GST).

Histopathological investigation of liver

There were hepatic cords extending toward the peripheral normal portal area around each hepatic lobule's thin-walled core vein., divided by relatively little barriers as shown by H&E in control group (A) (liver portal vein, artery, and bile ductile) in (**Figure 4).** Hepatocytes hydropic degeneration, the hepatic sections of the cadmium group show localized zones of clot death infiltrated with inflammatory cells, occluded sinusoids, and congested veins in middle with inflammatory cell infiltration (B) **(Figure 5).** These histological abnormalities were lessened in rats given vitamin C along with these treatments, as evidenced by hepatocyte patterns that were noticeably normal, decreased portal inflammation, and a reduction in hepatocyte hydropic degeneration (**Figure6)**

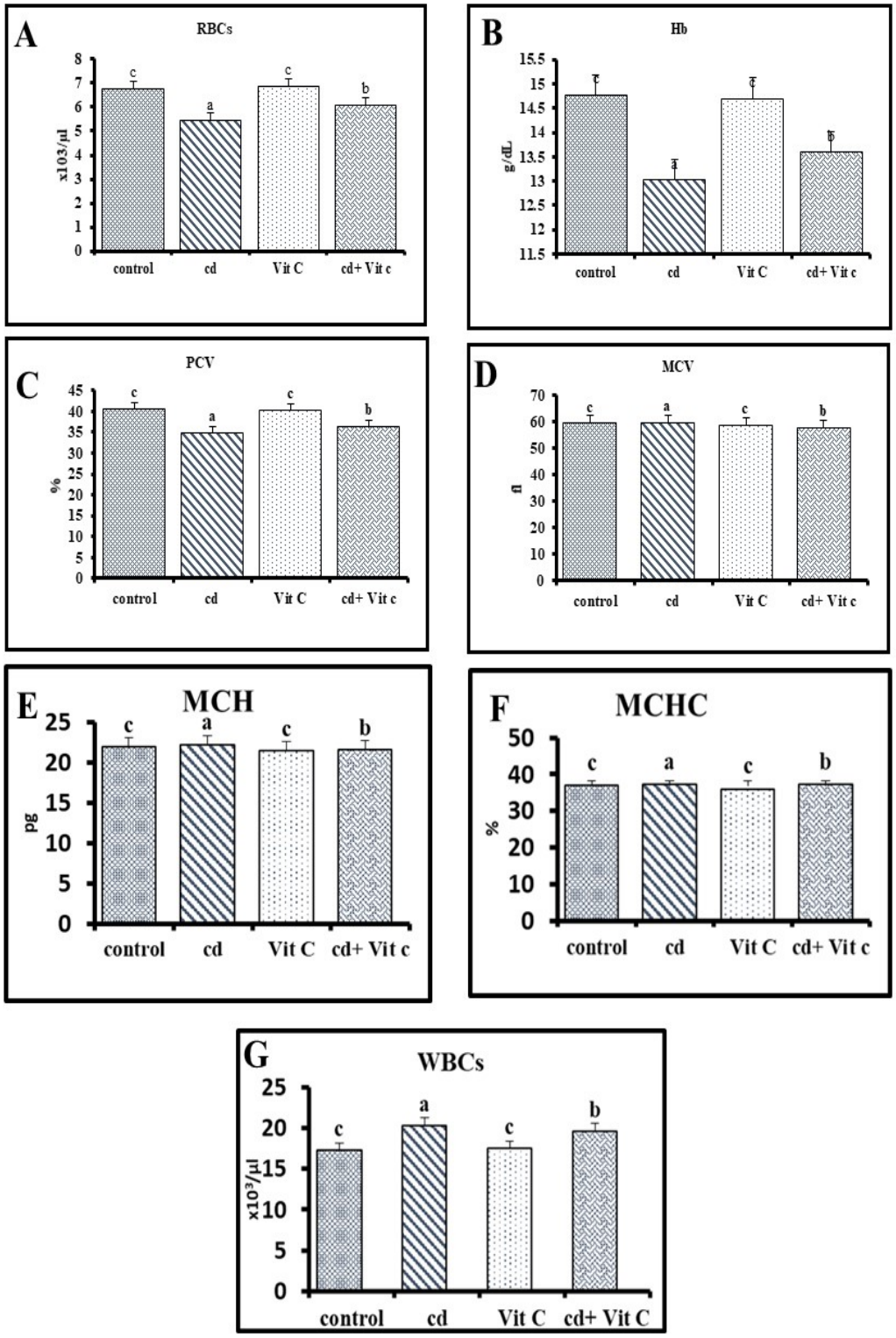


Fig. 1. Hematological result at the end of 4th weeks post treatment of vitamin C and in cadmium intoxicated rats (Mean ± SE). (A) RBCs count, (B) Hb concentration, (C) PCV % (Packed cell volume), (D) MCV (Mean corpuscular volume), (E) MCH (Mean corpuscular hemoglobin, and (F) MCHC (Mean corpuscular hemoglobin concentration), (G) WBCs (White blood cells) count. Values with different superscript letters consider significance at ($p<0.05$).

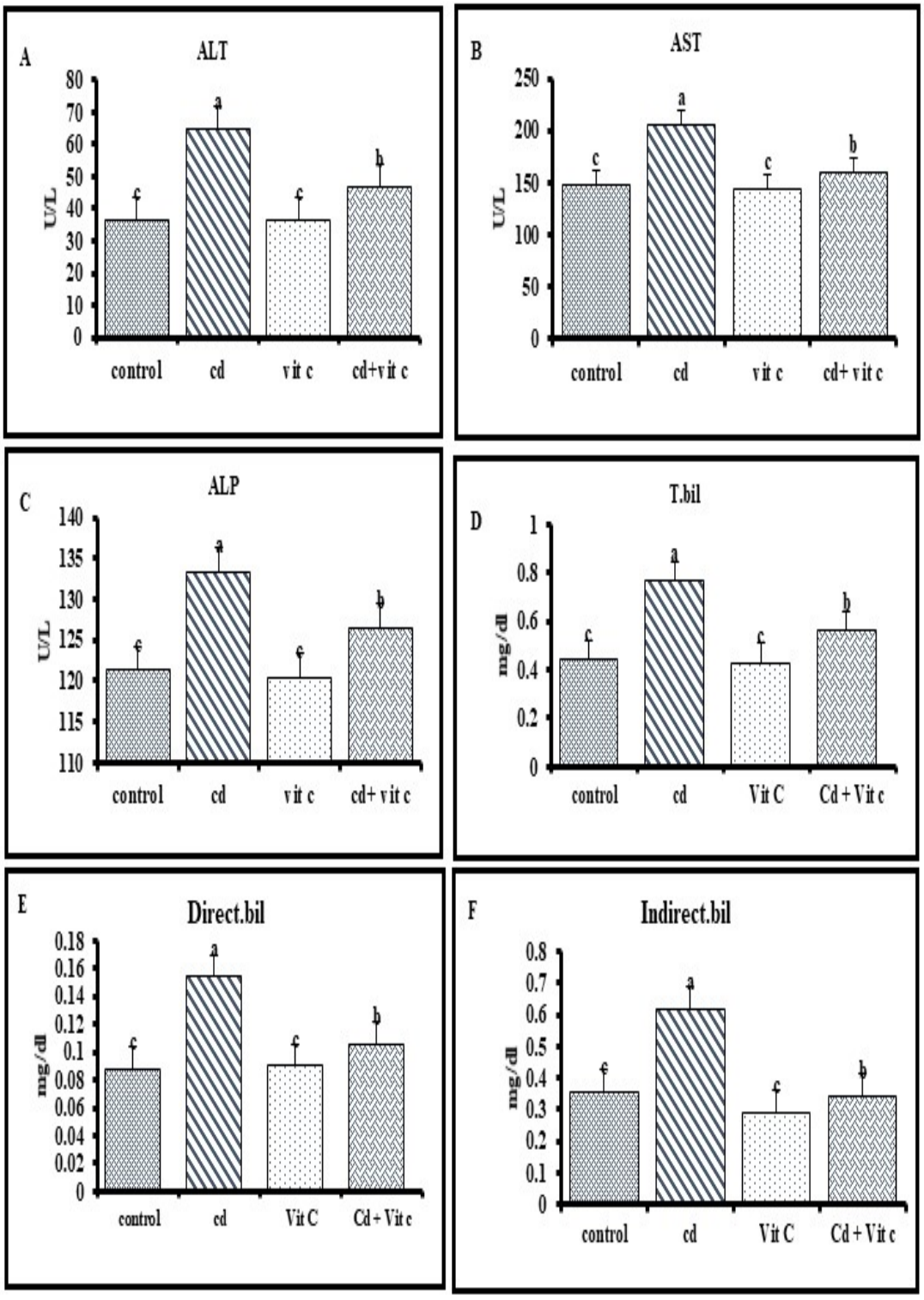


Fig. 2. Liver function tests at the end of 4th weeks post treatment of vitamin C in cadmium intoxicated rats (Mean ± SE). (A) Alanine aminotransferase (ALT), (B) Aspartate aminotransferase (AST), (C) Alkaline phosphatase (ALP), (D) Total. bil (total bilirubin), (E) Direct. bil (direct bilirubin) and (F) and Indirect. bil (indirect bilirubin). Values with different superscript letters consider significance at ($p<0.05$).

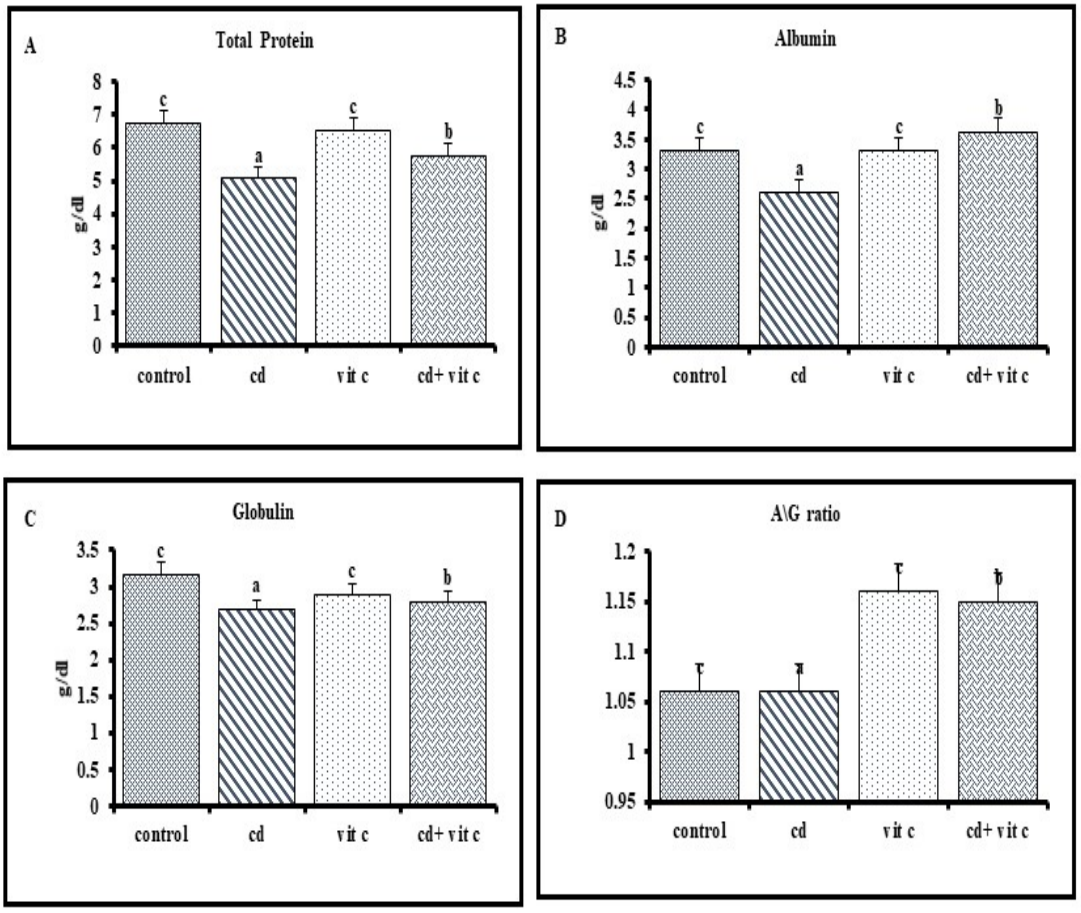


Fig. 1. Protein profile at the end of 4th week post treatment of vitamin C in cadmium intoxicated rats (Mean ± SE). (A)Total protein, (B) Albumin, (C) Globulin and (D) A/G ratio. Values with different superscript letters consider significance at ($p<0.05$).

TABLE 2. Oxidative stress and antioxidant biomarkers in hepatic homogenate at 4th week post treatment of vitamin C in cadmium toxicated rats (Mean ± SE).

Group	MDA (n mol/g)	SOD (U/tissue)	CAT (U/tissue)	GSH (mg/g.tissue)	GST (mg/g tissue)
Cont.	24.54±2.87^{c}	611.60±0.92^{a}	1.93±0.07^{a}	19.54±1.42^{a}	24.49±0.59b
Cd	72.93±6.19^{a}	320.24±44.09^{c}	1.07±0.16^{c}	9.68±0.55^{c}	18.67 ± 0.56d
Vit C	24.00±0.8^{c}	610.20.00±1.49^{a}	1.97 ± 0.007^{a}	19.68±2.32^{a}	26.24 ± 0.54^{a}
Cd+Vit C	40.23±2.82^{b}	505.4± 14.96^{b}	1.74 ±0.02^{b}	14.94±0.86^{b}	20.41± 0.29^{c}

Cont. (control), Cd (cadmium chloride), Vit C (vitamin C), Cd +Vit C (Cadmium & vitamin C). MDA (Malondialdehyde), SOD (Superoxide dismutase), CAT (Catalase), GSH (Reduced glutathione), GST (Glutathione-S-transferase). Values with different superscript letters consider significance at ($p< 0.05$).

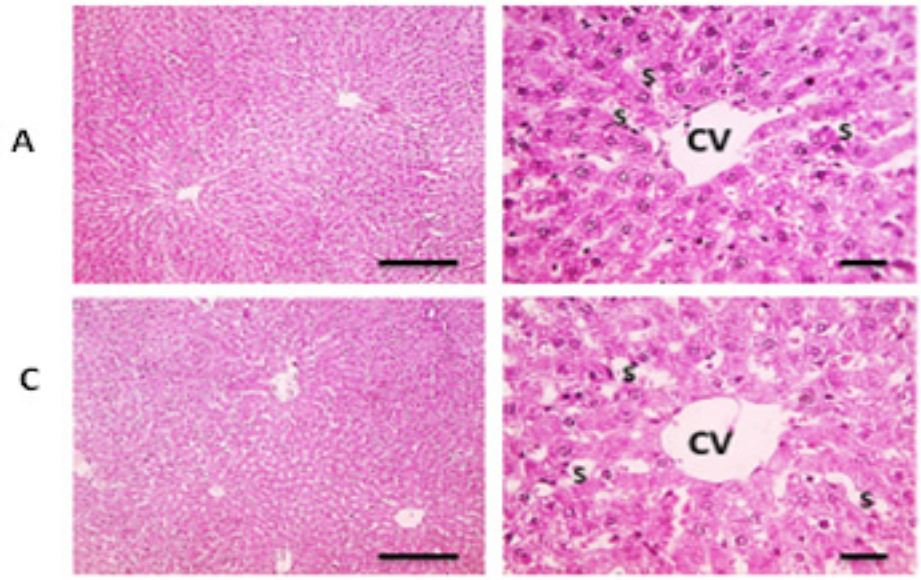


Fig. 4. . Microscopic pictures of H&E-stained hepatic sections showing normal radially arranged hepatic cords around central veins (CV) with normal portal areas and sinusoids (S) in control group (A) and groups (C) (group of vitamin C only Low magnification X: 100 bar 100 and high magnification X: 400 bar 50

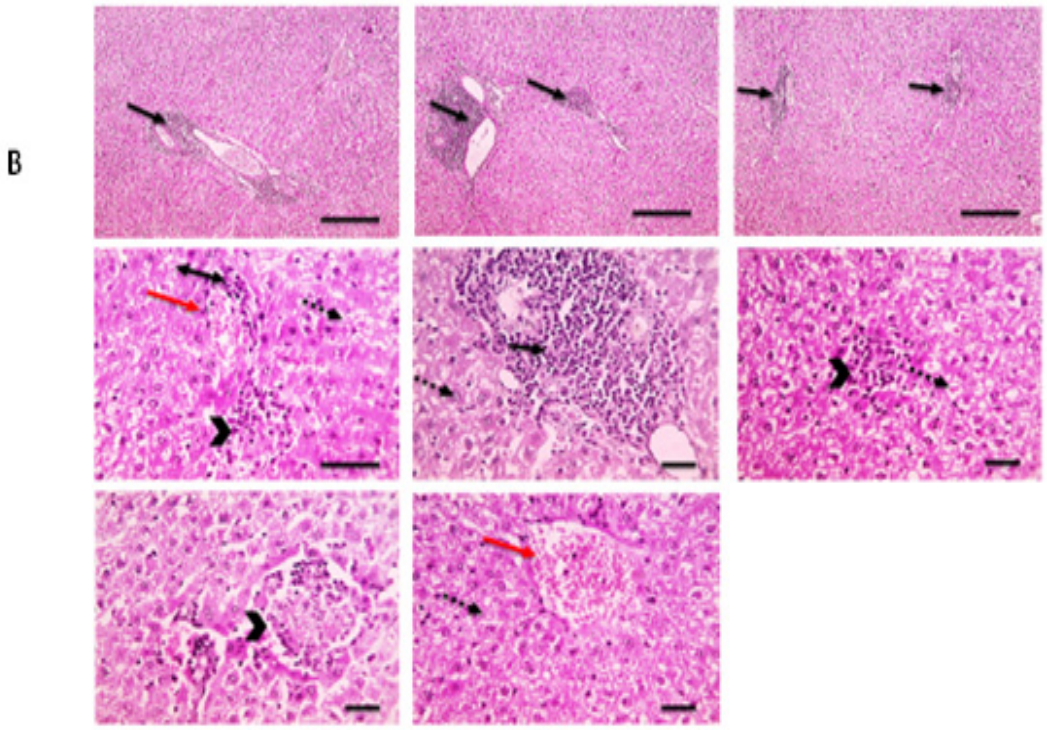


Fig. 5. Microscopic pictures of H & E stained hepatic sections showing marked portal inflammation (black arrows) , hepatocytes hydropic degeneration (dashed black arrows) and focal areas of coagulative necrosis (black arrowheads) infiltrated with leukocytic cells, occluded sinusoids, congested central veins (CV) (red arrows) with leukocytic cells infiltration around CV (double headed black arrows) in group (B) (group intoxicated with cadmium) Low magnification X: 100 bar 100 and high magnification X: 400 bar.

Immunohistochemistry result

According to immunohistochemistry of caspase-3 &TNF-α proteins of hepatic slices of all rat sets increased with toxicity (**Figures 7 and 8)** compared to the control group. The expression of them were considerably decreased when vitamin C and cadmium were coupled (**Table 3).**

Discussion

Scientists and physicians have long been interested in how natural anti-oxidants can reverse the oxidative damage brought on by xenobiotic intoxication. The primary factor in acute cadmium toxicity was a shift in cellular redox balance, which led to oxidative stress, hepatocellular damage, and cadmium buildup in the liver **[24] .** The route, dose, length of exposure, and species sensitivity all have an impact on how quickly metals are absorbed, distributed, and accumulated in tissues and organs **[25]**. Liver is first organ affected by toxicity of cadmium, and it sustains substantial damage and accumulation **[26].** In present study found sets intoxicated with cadmium showed clear accumulation of cadmium of hepatic cells. Numerous researches looked at health advantages of vitamin C to lessen the toxicity caused by cadmium. The current study discovered that supplementing with vitamin C lessen accumulation in hepatic tissue due to its antioxidant effect **[27] .**The current study demonstrated that cadmium-intoxicated rats displayed prominent anemia with a decrease in PCV, RBCs and hemoglobin (Hb). This anemia was explained by hemolysis, increased permeability, and decreased erythropoietin hormone synthesis **[28-30].** Although blood indices (MCV, MCH, and MCHC) show no change (normocytic normochromic anemia) and this agreed with some authors**[8] .**As opposed to that, systemic inflammation was evident in the cd intoxicated rats, where leukocytes significantly increased and that agreed with many investigators**[31,32].**

Co-treatment (vitamin C+ cadmium) ameliorated the level of PCV %, RBCs counts and Hb conc. due to reduction of oxidative damage to vascular walls, and renal cells which produced

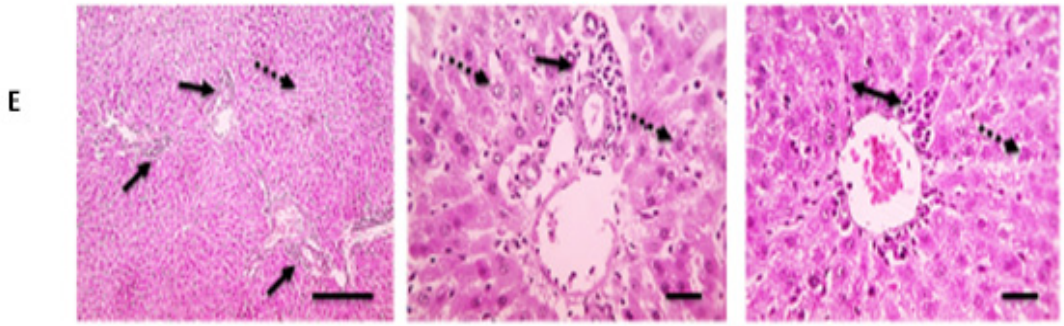


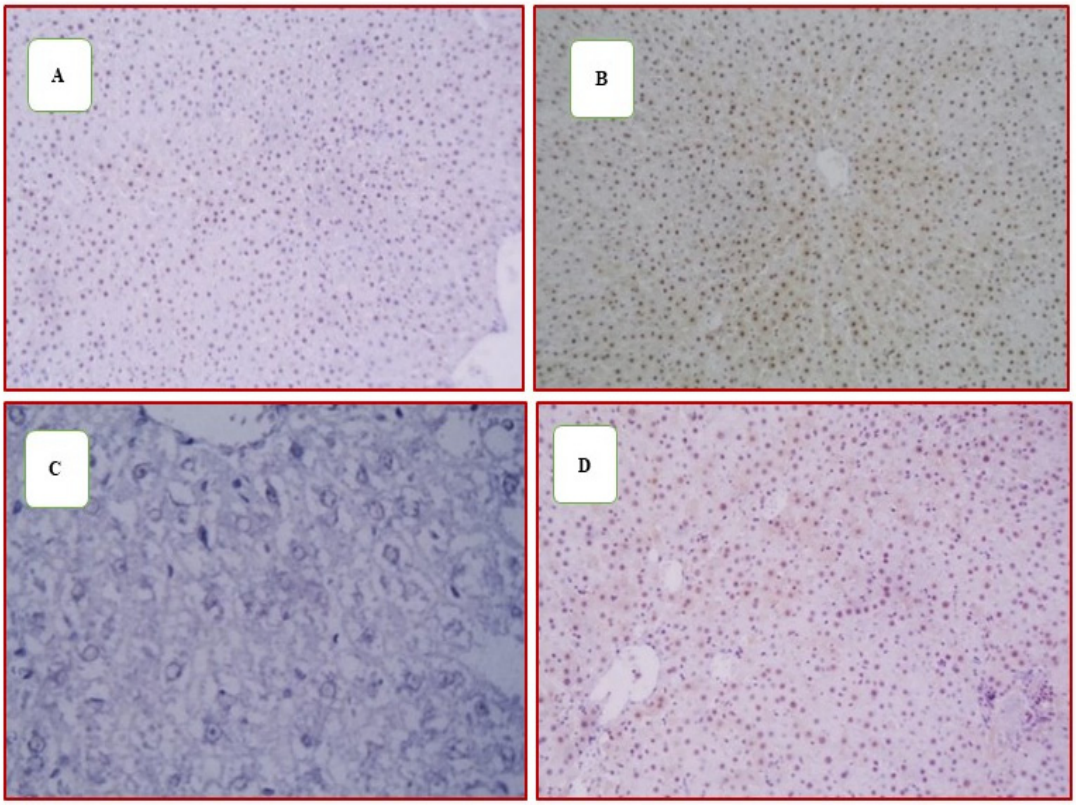
Fig. 6. Microscopic pictures of H&E-stained hepatic sections showing markedly decreased portal inflammation (black arrows) and hepatocytes hydropic degeneration (dashed black arrows) few leukocytic cells infiltration around CV (double headed black arrows) in group (E) groups co treated with vitamin C). Low magnification X: 100 bar 100 and high magnification X: 400 bar 50

TABLE 3. Immunohistochemistry result:

Group	Caspase 3	TNF-α
Cont.	0.25 ± 0.049^{c}	0.25 ± 0.05^{a}
Cd	91.13 ± 2.07^{a}	79.41 ± 4.49^{c}
Vit C	0.21 ± 0.04^{c}	$0.06^{a} \pm 0.25$
Cd + Vit C	42.17 ± 3.96^{b}	19.13 ± 1.48^{b}

Cont. (control), Cd (cadmium chloride) Cd.
Values with different superscript letters consider significance at ($p< 0.05$).

1-Caspase



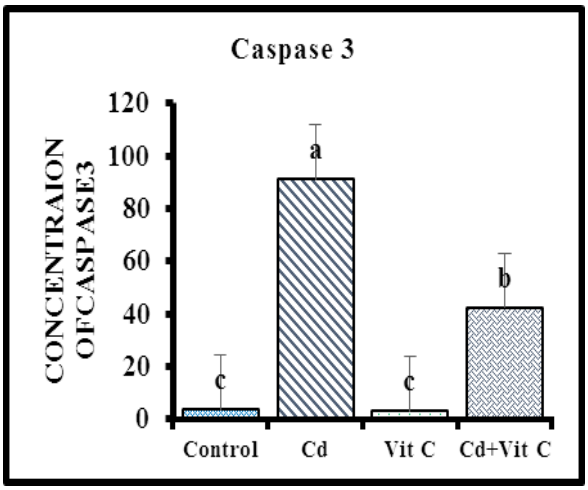


Fig.7.

A - Control: Liver displayed negative immunostaining against Caspase 3. (IHC, DAB immunostaining, hematoxylin as a counter stain) .

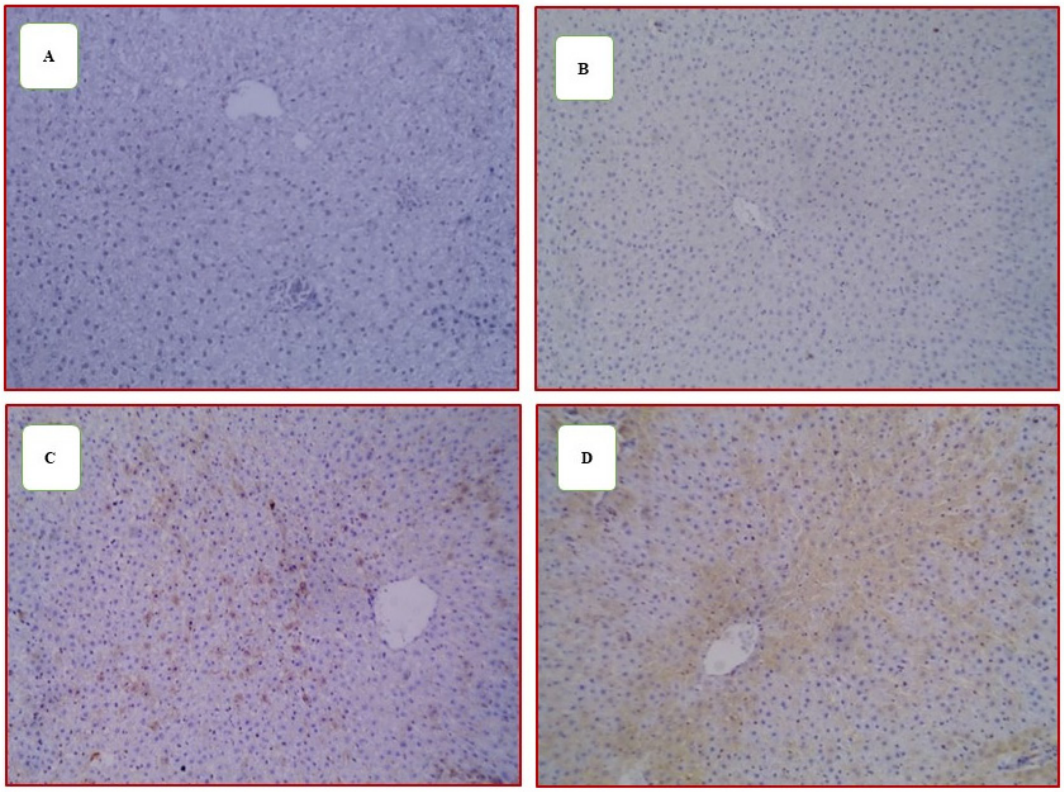
B - Cadmium group: Liver displayed strong immunostaining against Caspase 3. (IHC, DAB immunostain, hematoxylin as a counter stain, 100x) .

C – vitamin C group: Liver displayed negative immunostaining against Caspase 3. (IHC, DAB immunostaining, hematoxylin as a counter stain) .

D - Cadmium group with vitamin C: Liver displayed moderate immunostaining against Caspase 3. (IHC, DAB immunostaining, hematoxylin as a counter stain, 100x)

E - Immunohistopathological result of rats liver at the end of 4th week post treatment of vitamin C in cadmium intoxicated rats Caspase 3 (Mean ± SE) Values with different superscript letters consider significance at ($p<0.05$) .

2-TNF-α:



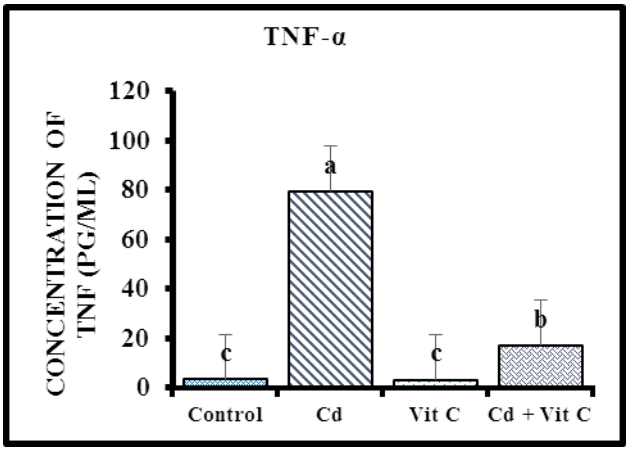


Fig. 8.

A - Control: Liver displayed negative immunostaining against TNFα. (IHC, DAB immunostaining, hematoxylin as a counter stain, 100x).

B - Cadmium group: Liver displayed strong immunostaining against TNFα. (IHC, DAB immunostaining, hematoxylin as a counter stain, 100x) .

C - Vitamin C group: Liver displayed negative immunostaining against TNFα. (IHC, DAB immunostaining, hematoxylin as a counter stain).

D - Cadmium group with vitamin C: Liver displayed moderate immunostaining against TNFα. (IHC, DAB immunostaining, hematoxylin as a counter stain, 100x).

E - Immunohistopathological result of rat's liver at the end of 4th week post treatment of vitamin C in cadmium intoxicated rats TNF-α (Mean ± SE). Values with different superscript letters consider significance at ($p<0.05$).

erythropoietin hormone, maintains physiological homeostasis, and encourages the small intestine to absorb more iron **[33] .**The anti-inflammatory properties of vitamin C, on the other hand, prevented leukocytes from increasing **[34] .** Liver is important location to biotransformation &cadmium metabolism **[35] .**This indicated by Changes in levels of (ALT, AST, and ALP), which are markers to hepatitis and other conditions **[36].** The rate of metabolic protein degradation reflects the impact of cadmium on ALT and AST activity **[37]** due to enhanced plasma membrane permeability or cellular necrosis lead to enter the bloodstream from the cytosol, as well as the use of amino acids for oxidation or gluneogenesis as a result of toxicity **[38],** and all results confirmed with histopathological findings in liver tissue**.** As founded degeneration and necrosis in hepatic cells. Our results showed that vitamin C reduces the hepatotoxicity brought on by cd, likely by lowering oxidative damage and lipid peroxidation while maintaining the antioxidant defense system and that agreed with some researchers **[39] .** Liver which is body's only location for protein synthesis, was impacted by oxidative stress, which may be the main cause of the drastic decrease in albumin & total protein of cadmium-toxicated groups as clarified on our study and this may be due to damage of the endoplasmic reticulum, DNA& mitochondria by excessive ROS production, which has an impact on how proteins are formed **[40]**. So, cadmium toxicity changed the liver's ability to synthesize, which may have an impact on how much fluid is retained in the tissue space. On other hand the current study revealed increase in globulin level in cadmium group than control one as defense mechanism against toxicity which led to decrease of A/G ratio **[4] .** Significantly raised by vitamin C due to the ability to decrease damage of oxidation **[41].**Due to an increase in oxidant substances, a decrease in glutathione, stimulation of the heme oxygenase enzyme, and an increase in red blood cell lysis, direct & total bilirubin of cadmium-intoxicated rats is higher than in normal control groups **[42] .** With the co-treatment of vitamin C led to significant decrease in total and direct bilirubin because red blood cells' ability to counteract oxidative stress is reduced, which can enhance red cell lysis **[43] .** In the current investigation, cadmium chloride markedly decreased CAT , SOD, and GST as well as amount of GSH , showing that oxidative stress exists. Endogenous antioxidant enzymes SOD and CAT are considered the initial band of resistance because their potent capacity to neutralize ROS **[44] .** CAT facilitates the transformation of H2O2 into H2O & oxygen by avoiding creation to OH **[45].** SOD was produced as a by-product of oxidative stress into H2O2 **[46] .** GST plays a crucial part in the detoxification process in the hepatic tissues by facilitating binding of any toxic substance with GSH **[47].** According to research, exposure to Cd causes the production of ROS, which causes the lipids to oxidize either by decreasing the GSH concentration or by depleting antioxidant enzymes **[48] .** Due to lipid peroxidation, Cd increased the amount of MDA **[49].** The delivery of vitamin C successfully increased GSH, CAT, GST, and SOD as Due to its reducing properties, vitamin C can diminish ROS like H2O2 and neutralize them**.** MDA and ROS levels, however, were reduced **[50].** This study demonstrated a considerable rise in TNF- α expression of cadmium intoxicated groups **[51].** Increased reactive oxidative species brought on by decreased anti-oxidant enzyme activity and more oxidation of lipids in Cd toxicity may result in significant alterations to membrane functions, damage to cellular integrity, DNA fragmentation, and caspase-3 activation. The prevention of cell death is connected to vitamin C's impact on oxidative stress **,** and decrease level of caspase3 **[52] .**

Conclusion

The findings of our study demonstrated vitamin C's value in lowering the toxicity of cadmium chloride on hematological, biochemical, antioxidant, immunosuppressive, and histopathological effects.

Funding statement:

There was no external support for this study.

Conflict of Interest:

The writers say they have no competing of concern.

Acknowledgement:

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التأثير التحسيني لفيتامين سي ضد التأثير المثبط للمناعة والمتغيرات في الكيميائية الحيوية والدموية والأكسدة لكلوريد الكاديوم على الجرزان

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كان الهدف الاساسي من هذا البحث هو التأكد مما إذا كان لفيتامين سي تأثيراً وقائياً آمناً في مواجهة الآثار الضارة للكاديوم الذي يعتبر من المعادن الثقيلة ذات السمية العالية والتلوث البيئي الكبير , تكونت المجموعة التجريبية من ٢٠ فأر مقسمة إلى ٤ مجموعات , أجريت الدراسة عليها لمدة ٣٠ يوم , قسمت على النحو التالي : مجموعة أساسية لم تعطى شيء , (مجموعة كلوريد الكاديوم) تم تجريعها بـ ١٥ مجم / كجم من كلوريد الكاديوم , (مجموعة فيتامين سي) تم تجريعها بـ ١٥٠ مجم / كجم من فيتامين سي , (مجموعة كلوريد الكاديوم مع فيتامين سي) تم تجريعها بـ ١٥ مجم/كجم من كلوريد الكاديوم و ١٥٠ مجم / كجم من فيتامين سي , وكانت جميع الجرعات عن طريق الفم , وبعد انقضاء ٤ أسابيع من التجريع تم أخذ عينات مختلفة من الدم وأنسجة الكبد لإجراء الفحوصات المختلفة , حيث كشفت النتائج عن انخفاض في عدد كريات الدم الحمراء , وتركيز الهيموجلوبين , وحجم الخلايا المكدسة بما يعادل (P ٠,٠٥ >), وارتفاع عدد كريات الدم البيضاء بما يعادل (P ٠,٠٥ >)من ناحية أخرى , كما كشفت النتائج عن انخفاض كبير في البروتين الكلي والألبيومين وزيادة تركيز الجلوبيولين والبيليروبين الكلي والمباشر , وزيادة تركيز إنزيمات الكبد (ALT,AST,ALP) بالإضافة لمضادة الأكسدة (GST,GSH,CAT,SOD) , وارتفاع MAD لمجموعة كلوريد الكاديوم مقارنة بالمجموعة الأساسية التي لم يتم اعطاءها شيء , ولكن عند دمج فيتامين سي مع كلوريد الكاديوم أشارت النتائج إلى تحسن ملحوظ في المعلمات قيد الدراسة , مما يشير إلى التأثير العلاجي لفيتامين سي ضد التسمم بكلوريد الكاديوم في الفئران .

الكلمات الدالة : كاديوم – فيتامين سي – انزيمات مضادة للأكسدة – دلالات مضادات الاكسدة – امكانية التحسين .