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Original Research Article

SELENIUM MODULATES HEPATORENAL DAMAGE AND GENOTOXICITY INDUCED BY POTASSIUM DICHROMATE IN ADULT ALBINO RATS

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ABSTRACT

Background: Potassium dichromate (K2Cr2O7) is a major environmental pollutant and is known for its wide toxic manifestations. The present study shows the protective role of selenium (Na2SeO3) against chromium induced hepatorenal toxicity.

Materials and Methods: Sixty adult albino rats were divided into four groups of fifteen each. Group I is control group which received standard diet; group II received K2Cr2O7 (67mg/kg B.W) in drinking water; group III received selenium only (0.5 ìg/kg B.W) and group IV received both K2Cr2O7 (67mg/kg B.W) and selenium (0.5 ìg/kg B.W) for 6 weeks.

Results: Selenium supplementation to the group IV improved all the kidney and liver chemical function parameters. In addition, it down-regulates endoplasmic reticulum stress genes.

Conclusion: The biochemical results confirmed the improvement of histopathological findings. Therefore, our study revealed that selenium was effective in preventing K2Cr2O7-induced hepatorenal toxicity.

KEY WORDS: Selenium, hepatorenal, Potassium dichromate, PCR, Rats.

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INTRODUCTION

Chromium (Cr), a naturally occurring heavy metal which exists in dust and earth crust. It also present in high ratios in water, air soil, plants and rocks [1]. Chromium exists in many forms, the most stable forms of chromium in the environment are hexavalent chromium [2]. Water contaminated with hexavalent chromium is a worldwide problem as it is a major route of exposure to chromium. The wide distribution of chromium in the environment is the result of its extensive use to produce stainless steel, wood treatment products, tanning of leather or pigments[3]. Occupational exposure to chromium is found among approximately several million industrial workers worldwide[4]. Experimental animals exposed to K2Cr2O7 exhibit acute tissue damage, including testicular lesions, kidney tubular necrosis and liver toxicity [5].

The liver is at great risk of injury and induced hepatotoxicity as demonstrated by [6].Also, K2Cr2O7 promotes expression of specific markers of nephrotoxicity [7].

It can cause genotoxicity, mutagenicity and carcinogenicity [8]. K2Cr2O7 can cross cellular membranes and undergoes an intracellular reduction, resulting in the generation of toxic strong oxidants. Reactive oxygen species (ROS) generated in excess by these reactions can cause injury to cellular proteins, lipids and DNA leading to oxidative stress [9]. Since free radical generation is implicated in the pathogenesis of chromium toxicity, supplementation of antioxidants can be considered as the alternative method for chelation therapy. Selenium is an essential nutrient for animals and humans which plays an important role in antioxidant defense systems through protection of the cells against damages induced by free radicals[10]. It enters in the structure of selenoproteins and participates in antioxidant defense, thyroid hormone production, and immune responses[11]. Selenium can play role in the cellular oxidative defense and can protect liver and kidney from injury induced by chromium toxic effects [12].Endoplasmic reticulum (ER) is an organelle involved in the intrinsic pathway of apoptosis[13]. It participates in folding of secretory and membrane proteins[14]. Various conditions can disturb the functions of the ER and result in ER stress resulting in an up-regulation of ER chaperones such as glucose regulated proteins 78 (GRP78) [13]. Excessive and prolonged ER stress can induce apoptosis by activation of caspase-12 [15].

However, the molecular mechanisms of chromium-induced hepatorenal injury and the protective effect of selenium on liver and kidney are not yet completely understood.

This study aimed to investigate the possible toxic oxidative effect of chromium, as an environmental pollutant, on the liver and kidney of adult albino rats and evaluate the possible antioxidant protective effect of selenium on chromium induced hepatorenal toxicity. This was done by histological study by using (H&E) stain and biochemical and molecular assessment in the liver and kidney tissues of all groups.

MATERIALS AND METHODS

Chemicals: Potassium dichromate obtained from (EL- Gomhouria Pharm. Chem. Co., Egypt) Selenium obtained from (Sigma St. Louis, MO, USA).

Experimental Design: Sixty albino rats of both sexes with average weight 150-200 grams. They were obtained from the Laboratory Animal Unit, Faculty of Medicine, Zagazig University. They have kept in fan ventilated wide polypropylene animal cages, under the prevailing environmental conditions at the room temperature under pathogen-free conditions. Their food was a balanced diet in the form of barely, lettuce, milk, carrots, bread and water. Before the experiment, rats were acclimatized to the experimental conditions for a period of one week. All rats were handled accordance to the standard guide for the care and use of laboratory animals. One week after acclimatization rats were randomly divided into four experimental groups (Fifteen animals each). Group I (control group) recieved 1 ml distilled deionized water orally via metal gastric tube for 6 weeks. Group II received Potassium dichromate orally in a dose of 67 mg/kg B.W dissolved in 0.5 ml distilled water for 6 weeks[12]. Group III received selenium in a dose of 0,5 µg/kg body weight dissolved in distilled water (0.5 ml/rat/day) orally for 6 weeks [12]. Group IV received 67 mg/kg B.W Potassium dichromate + selenium daily in a dose of (0.5µg/kg) for 6 weeks orally via gastric tube.

Methods

Histological study: At the end of the administration, rats will be sacrificed then the livers and kidneys were taken out and bisected, and fixed in 10% buffered formalin 6 hours. Specimens from the livers and kidneys were processed to prepare 5ìm paraffin sections stained with haematoxylin and eosin stain for the histological study by light microscopic examination [16]. All experiments were carried out following recommendations of the Institute Review Board of Faculty of Medicine, Zagazig University.

Biochemical study

Blood samples collection: 1.5 ml venous blood samples were collected from rats centrifuged at 3000 rpm for 10 min and serum was separated. Superoxide dismutase (SOD), catalase, alanine transaminase (ALT) and aspartate transaminase (AST), urea, creatinine and uric acid levels were assayed by using commercial kits (Biodiagnostic Co., Giza, Egypt) spectrophotometrically according to the manufacturer

instructions.

RNA-extraction and Real time-PCR analysis: Samples of liver tissues was homogenized with a power homogenizer. Total RNA was isolated using RNA-spin™ Total RNA Extraction Kit (iNtRON Biotechnology, Seongnam, Korea) according to the manufacturer instructions. One ug of RNA was reverse transcribed using Power cDNA synthesis Kit (iNtRON Biotechnology Seongnam, Korea) according to the instructions of the manufacturer. Quantitative Real-time PCR was performed using Mx3005P™ (Stratagene, La Jolla, CA, USA) according to the following protocol: 15 min at 95 ºC, followed by 40 cycles for 15 sec at 94 ºC; 30 sec at 55 ºC; and 30 sec at 70 ºC. Twenty uL volume reactions were performed with 5 uL of the cDNA, 100 pmol/uL of each primer (0.5 uL each) (Biolegio, Netherlands), 10 uL of PCR EvaGreen Master Mix (Jena Bioscience GmbH, Jena, Germany) and 4 uL distilled water. The sequence of the primers utilized in the study was listed in Table1[17]. To ensure accurate gene quantification, the expression levels of the studied genes were normalized to the mean of an internal control glyceraldehyde-3-phosphate dehydrogenase (GADPH). The cycle threshold (Ct) values were calculated. The expression level of the studied genes was normalized by calculating the ÄCt value. The amplitude of change of the expression (fold change) in different groups relative to the control group was analyzed by the $2^{-ÄÄCt}$ equation.

Table 1: primer sequence of the studied genes.

Gene	Forward	Reverse
Regulated protein78 (Grp78)	AACCCAGATGAGGCTGTAGCA	ACATCAAGCAGAACCAGGTCAC
Caspase 12	CACTGCTGATACAGATGAGG	CCACTCTTGCCTACCTTCC
GAPDH	GTCGGTGTCAACGGATTTG	ACAAACATGGGGGCA TCAG

Statistical Analysis: Statistical analysis of all data were performed using SPSS for Windows (version 14; SPSS Inc., Chicago, IL, USA). Data were expressed as the mean ± standard deviation. P values <0.05 were considered statistically significant. Differences between means were assessed using ANOVA. LSD test was used for post hoc multiple comparisons.

RESULTS

Histological results: Examination of the liver sections of the control (group I) revealed normal architecture of hepatic lobule which was formed of tightly packed cords of polygonal hepatocytes with rounded vesicular nuclei and acidophilic cytoplasm radiating from the central vein. Blood sinusoids with their endothelial lining were noticed between the hepatic cords (Fig.1a). Portal triad is composed of a portal vein which has a large lumen and thin vessel wall, hepatic artery, which has a small lumen and a wall of smooth muscle and a bile duct which is lined by single cuboidal cells with dark rounded nuclei (Fig.1b). Examination of the liver sections of the potassium dichromate (group II) showed a marked loss of the normal liver architecture with variable hepatocellular changes. Some hepatocytes are with ill defined borders and condensed nuclei, while others had vacuolated cytoplasm due to liver degeneration. There was monocellular infilteration around the portal area (Fig.1c). Hepatic peliosis characterized by sinusoidal dilatation and the presence of multiple blood filled lacunar spaces within the liver tissue leads to pressure atrophy of hepatic cords. There was hepatocyte anisonucleosis, a morphological manifestation of nuclear injury, in the form of variation in the size of the cell nuclei (Fig.1d). The portal area showed congested dilated portal veins and hepatic artery with edema and mononuclear cell infiltration around the vessels and the bile ducts were also observed. There was portal endotheliosis characterized by proliferation of the endothelium lining the portal vein (Fig.1e). Bile duct proliferation characterized by proliferation of the biliary epithelium forming bile ductules surrounded the necrotic degenerated hepatic tissue. There was spindle shaped fibroblasts surrounded the necrotic hepatic foci (Fig.1f). No histological differences were noticed between the liver sections of the animals (group III) treated with selenium alone and the liver sections of the control animals (group I). Examination of the liver section of group IV (potassium dichromate + selenium) revealed variable degrees of improvement. Some hepatocytes showed vacuolated cytoplasm and condensed nuclei. While others revealed normal lobular architecture, as hepatocytes have vesicular nuclei and acidophilic cytoplasm. There was no monocellular infilteration around the portal area. The portal area showed a portal vein, hepatic

artery and a bile duct which is lined by a single layer of cuboidal epithelial cells with dark rounded nuclei (Fig.1g).

Kidney sections of the control (group I) showed the kidney consisted of renal cortex and renal medulla. The renal cortex formed of tubules and corpuscles. The renal corpuscles are formed of Bowman's space which surrounds a tuft of capillaries (glomerulus). The Bowman's space of the renal corpuscles exhibited two layers, the visceral layer surrounded the glomerular capillary endothelium and the parietal layer which lined with flat cells resting on the basement membrane. The renal convoluted tubules formed of proximal tubules which had narrow lumina and the distal tubules had wide lumina, both tubules are lined by cuboidal epithelium. The proximal tubules were packed and appeared oval and circular in histological sections & were mostly confined to the cortex. The cells of the tubules appeared cuboidal with fine and granular cytoplasm and they were arranged on an intact basement membrane in a regular arrangement (Fig.2a). Examination of the kidney sections of the potassium dichromate treated (group II) showed a marked loss of the normal kidney architecture with different renal injuries including both the tubules and the glomeruli. Acute cell injury and degenerative changes of the tubular epithelium occurred. The renal interstitial tissue invaded with monocellular inflammatory cells (Fig.2b). The tubular epithelium had degenerated vacuolated cytoplasm with pyknotic nuclei. There was focal replacement of the renal parenchyma with fibrous tissue invaded with mononuclear inflammatory cells (Fig.2c).

In some sections there were areas of tubular necrosis surrounded with the spindle shaped fibroblasts (Fig.2d). The renal corpuscles showed narrow irregular obliteratedb Bowman's space due to glomerular mesengial proliferation (Fig.2e).Vacuolations of the glomerular tuft and irregular discontinous parietal layer of the Bowman's space lined with flat cells resting on ruptured basement membrane which continued with ruptured renal tubule. The renal tubules ruptured and continous with each other forming elongated tubular sacs in between the vacuolated glomeruli (Fig.2f). No histological differences were noticed between the kidney sections of the animals (group III) treated with selenium alone and the kidney sections of the control animals (group I). Examination of the kidney section of group IV (Potassium dichromate + selenium) revealed improvement of the renal parynchema according to the severity of changes observed in potassium dichromate treated group. There was reversible recovery of the histological structure of the cuboidal tubular epithelium with regular arranged nuclei inside the granular cytoplasm and they were arranged on an intact normal basement membrane with little mononuclear inflammatory cells in the renal interstial tissue (Fig.2g).

Fig.1a: Photomicrograph of a section in the liver of control group showing a part of hepatic lobule with tightly packed cords of hepatocytes with rounded vesicular nuclei and acidophilic cytoplasm (arrow heads) radiating from the central vein (CV). Normal blood sinusoids with their endothelial lining (arrows) in between the liver cords. (H&E; ×400. Scale bar = 20 µm).

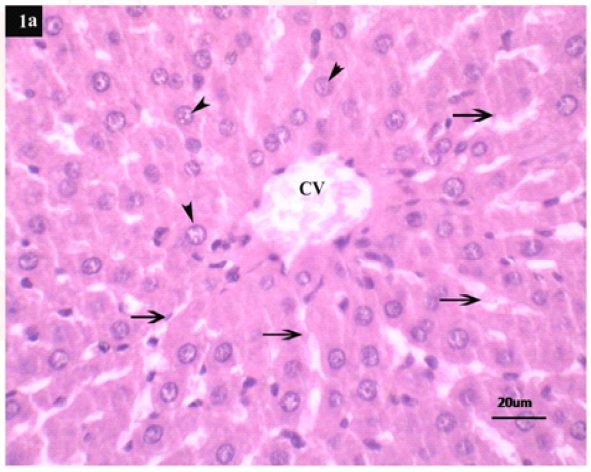


Fig.1b: Photomicrograph of a section in the liver of control group showing a portal area containing portal vein (PV), hepatic artery (A) and bile duct(B). (H&E; ×400. Scale bar = 20 µm).

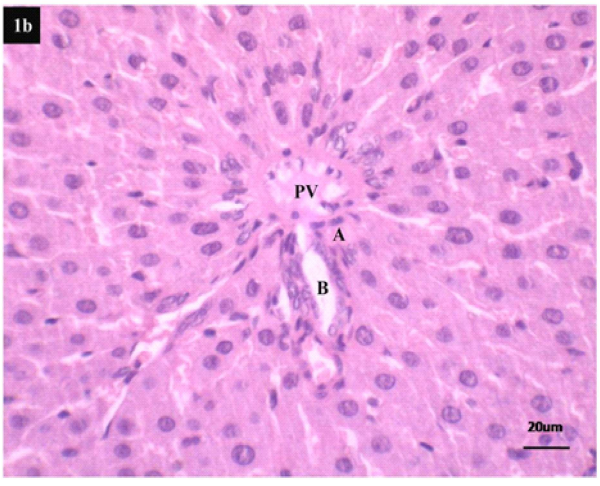


Fig.1c: Photomicrograph of a section in the liver of potassium dichromate treated (group II) showed monocellular infilteration around the portal area (arrows) and degenerated hepatocytes with ill defined borders and condensed nuclei and vacuolated cytoplasm (arrow heads). (H&E; ×400. Scale bar= 20 µm).

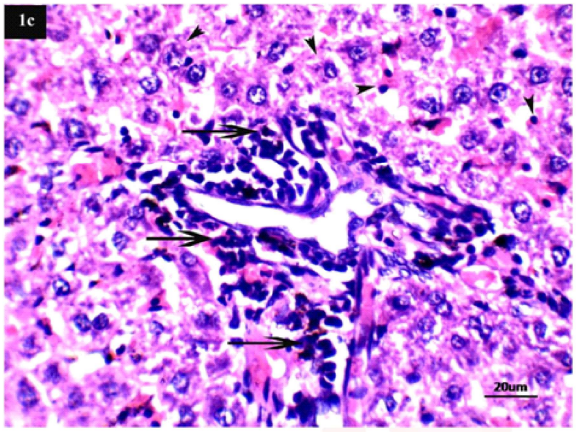


Fig.1d: Photomicrograph of a section in the liver of potassium dichromate treated (group II) showed hepatic peliosis which is a congested dilated sinusoids (arrows). Hepatic cords atrophy and size variation in the hepatocytes nuclei (anisonucleosis) (arrowheads). (H&E; ×400. Scale bar = 20 µm).

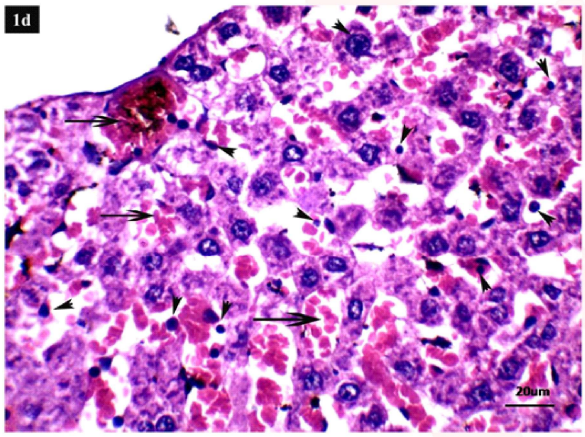


Fig.1e: Photomicrograph of a section in the liver of potassium dichromate treated (group II) showed congested dilated portal vein (PV) and hepatic artery (A), bile duct (B). The vessels and bile duct surrounded with edema and mononuclear inflammatory cells (arrows).There was portal endotheliosis (arrow heads). (H&E; ×400.Scale bar = 20µm).

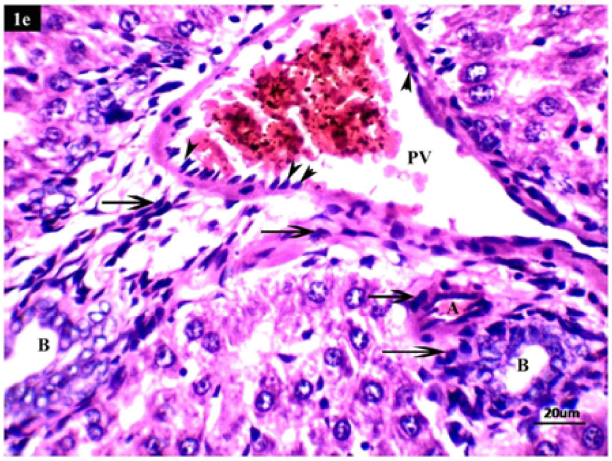


Fig.1f: Photomicrograph of a section in the liver of potassium dichromate treated (group II) showed bile duct epithelial proliferation (arrows) surrounded the necrotic hepatic tissue (N). The spindle shaped fibroblasts (arrow heads).(H&E; ×400. Scale bar = 20 µm).

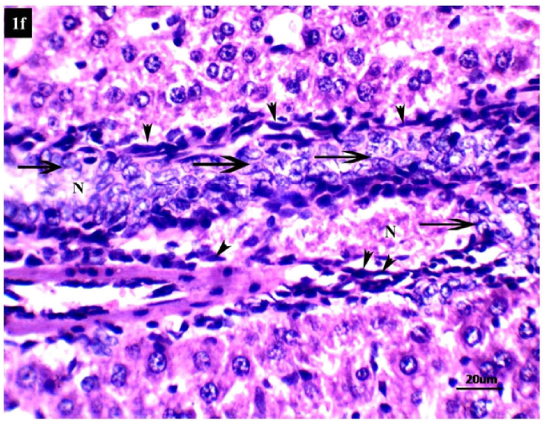


Fig.1g: Photomicrograph of a section in the liver of potassium dichromate and selenium treated (group IV) showed the normal lobular architecture with binucleated hepatocytes with acidophilic cytoplasm and condensed vesicular nuclei (arrows). The portal area containing portal vein (PV), hepatic artery (A) and bile duct (B) lined with single layer of cuboidal epithelium (arrow heads). (H&E; ×400. Scale bar = 20 µm).

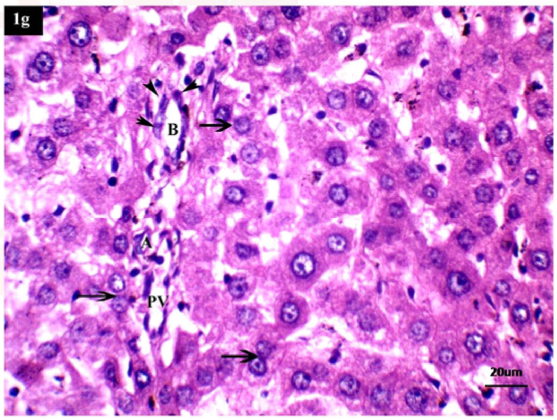


Fig.2a: Photomicrograph of a section in the renal cortex of control group showing the glomerulus (G). The Bowman's capsule (B). The renal proximal tubules (P) with narrow lumina and the distal tubules (D) with wide lumina, both tubules are lined by cuboidal epithelium (arrows).(H&E; ×400. Scale bar = 20 µm).

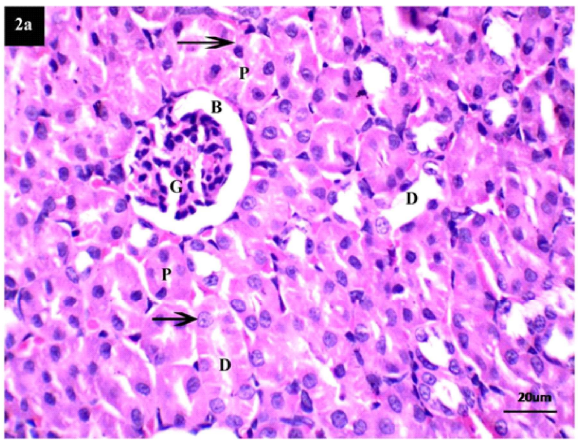


Fig.2b: Photomicrograph of a section in the renal cortex of potassium dichromate treated (group II) showed a marked loss of the normal kidney architecture .The renal interstitial tissue invaded with monocellular inflammatory cells (arrows).(H&E; ×400. Scale bar = 20 µm).

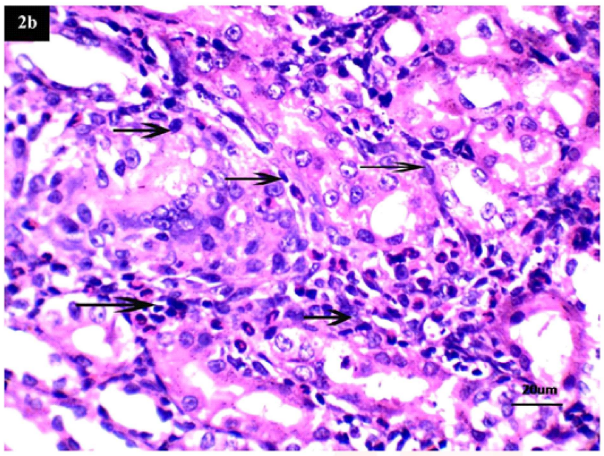


Fig.2c: Photomicrograph of a section in the renal cortex of the potassium dichromate treated (group II) showed the tubular epithelium had degenerated vacuolated cytoplasm with pyknotic nuclei (arrow heads). There is fibrous tissue invaded with mononuclear inflammatory cells in the renal parenchyma (arrows).(H&E; ×400. Scale bar = 20 µm).

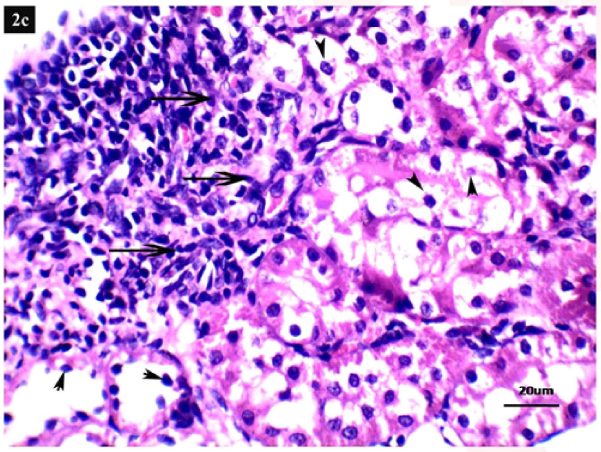


Fig.2d: Photomicrograph of a section in the renal cortex of potassium dichromate treated (group II) showed areas of tubular necrosis (N) surrounded with the spindle shaped fibroblasts (arrows). (H&E; ×400. Scale bar = 20 µm).

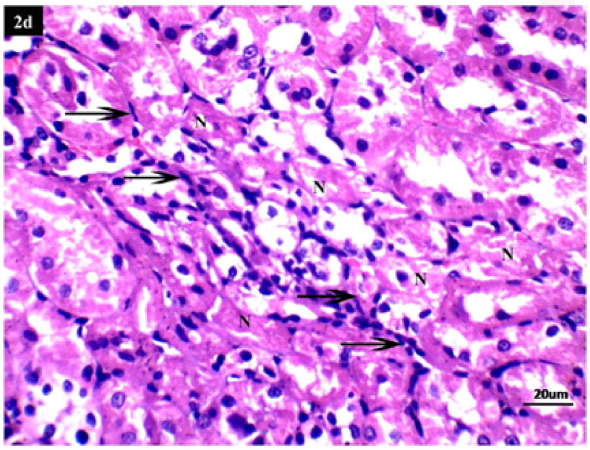


Fig.2e: Photomicrograph of a section in the renal cortex of potassium dichromate treated (group II) showed renal corpuscles with narrow irregular obliterated Bowman's space (B) and glomerular mesengial proliferation (arrows).(H&E; ×400. Scale bar = 20 µm).

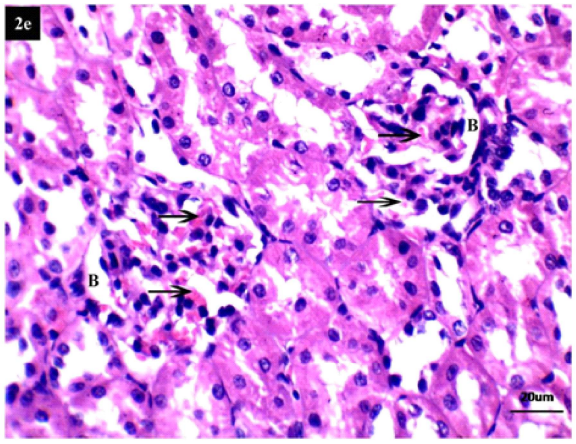


Fig.2f: Photomicrograph of a section in the renal cortex of the potassium dichromate treated (group II) showed glomerular tuft (G) vacuolations (arrow heads).The parietal layer of the Bowman's space (B) lined with flat cells resting on ruptured basement membrane(arrows). The renal tubules ruptured and continous with each other forming elongated tubular sacs(stars).(H&E; ×400. Scale bar = 20 µm)

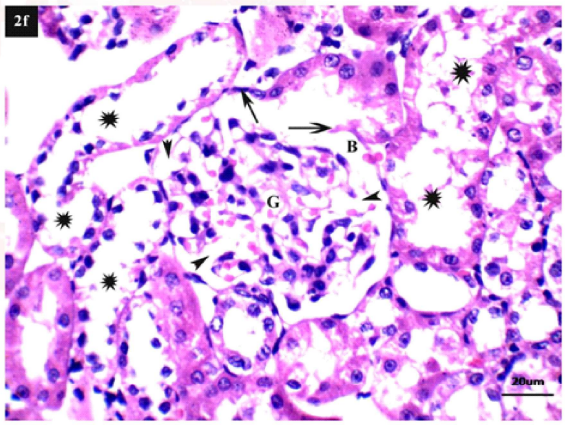
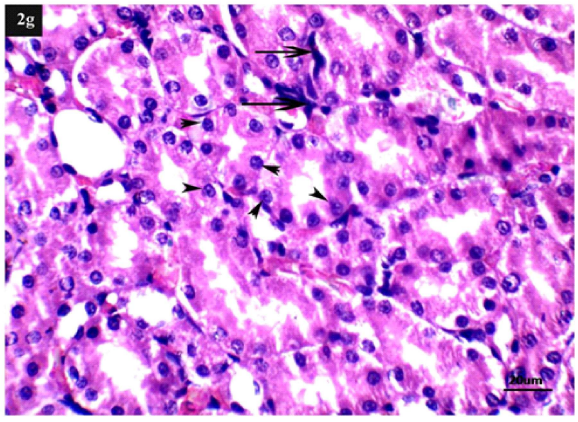


Fig.2g: Photomicrograph of a section in the kidney of the potassium dichromate and selenium treated (group IV) showed the normal renal parynchema and recovery of the cuboidal tubular epithelium with regular arranged nuclei inside the granular cytoplasm (arrow heads) with little mononuclear inflammatory cells (arrows) in the renal interstial tissue.(H&E; ×400. Scale bar = 20 µm).



Biochemical results: Potassium dichromate treated group (II) showed a highly significant increase in liver enzymes (ALT and AST) and kidney biomarkers (serum urea, creatinine and uric acid) compared to control group (p<0.001). On the other hand, selenium received rats (groups III and IV) showed no significant difference in liver and kidney biomarkers, compared to control group (p >0.05). (Table 2&3). Concerning oxidative stress, both serum catalase and SOD showed a highly significant reduction after chromium administration in group II compared to normal control (p< 0.001). However, selenium recipient rats (groups III and IV) showed no significant difference with normal control rats (group I) (p >0.05) (Table4).

Gene expression results: Grp78 showed a highly significant up-regulation after chromium administration in group II when compared to normal control (group I) (p< 0.001). Selenium recipient rat (Group III and IV) showed a significant down-regulation of Grp78 compared to group II with no significant difference between both groups and group I (p>0.05) (Table5).

Selenium recipient rats (groups III and IV) showed no significant difference with normal control rats (group I) (p >0.05).

Table 2: Serum levels of liver biomarkers in all groups.The liver biomarkers is highly significant (** p<0.001) in group II compared to groups I,III ,IV.

Parameter	Group I	Group II	Group III	Group IV
Serum ALT	39.97±2.53	59.3*±3.25*	39.9± 2.97	40±3.11
Serum AST	59.02±2.67	73.5*±3.14*	58.95±3.54	58.99±2.77

Table 3: Serum levels of kidney biomarkers in all groups. The kidney biomarkers is highly significant (** p<0.001) in group II compared to groups I,III ,IV

Parameter	Group I	Group II	Group III	Group IV
Serum urea(mg/dl)	15.6±3.1	40.4±3.6**	16.03±3.3	15.4±2.4
serum creatinine (mg/dl)	0.61 ± 0.07	1.6±0.03**	0.66 ± 0.06	0.6 ± 0.07
serum uric acid (mg/dl)	0.94± 0.08	1.7±0.19**	0.96±0.2	0.93±0.07

Table 4: Serum level of antioxidant and oxidative stress markers in all groups. Catalase (CAT) and Superoxide dismutase (SOD) are highly significant (** p< 0.001) in group II compared to groups I,III ,IV. Selenium recipient rats (groups III and IV) showed no significant difference with normal control rats (group I) (p >0.05).

Parameter	Group I	Group II	Group III	Group IV
Catalase (CAT) U/ml	30.1±0.7	18.4± 1.1**	30.12±0.9	30.07±0.6
Superoxide dismutase (SOD) U/ml	2.6± 0.2	1.8± 0.1**	2.79± 0.15	2.5 ± 0.2

Table 5: Gene expression of ER stress markers in the studied groups. Caspase 12 and regulated protein78 (Grp78) are highly significant (** p< 0.001) in group II compared to groups I,III ,IV.

Gene	Group I	Group II	Group III	Group IV
Caspase 12	1±0.01	1.22± 0.03**	0.93±0.04	1.1± 0.1
Regulated protein78 (Grp78)	1±0.01	1.4±0.05**	0.98±0.02	1.23±0.06

DISCUSSION

We have selected liver and kidney in this study because these are major target organs of toxicity and are susceptible to the effects of oxidative stress. The liver is the primary organ of biotransformation of compounds. It contains metabolizing enzymes that change most toxicants to less toxic substances. Kidneys on the other hand detoxify, filter and bioactivate materials[18].Chromium is a toxic metal and enhances the formation of different pathological conditions because of its retention in the body tissues[19-20].

Chromium induces a broad spectrum of biochemical dysfunctions constituting serious hazards to health. However, the molecular mechanism by

which Cr(VI) induces biological responses is unclear[21]. Chromium exposure results in oxidative stress with significant impairments of redox homeostasis and essential element status in the liver and kidneys [22]. In the current study, the light microscopic examination of chromium treated group exhibited different histopathological changes in the liver and kidney as sever inflammatory cell infiltration, hepatocytes degenerative changes with pyknotic nuclei, hepatic necrosis, peliosis and congested dilated portal veins and hepatic arteries.The proliferation of the biliary epithelium occured forming new bile ductules and the spindle shaped fibroblasts appeared surrounded the necrotic degenerated hepatic tissue. The kidney sections revealed destructed tubular epithelium with vacuolated cytoplasm, necrosis, injuried glomeruli and replacement of the renal parenchyma with fibrous tissue invaded with mononuclear inflammatory cells.

Some findings like hepatorenal degenerative changes, cytoplasmic vacuolization and inflammatory leucocyte cells in the liver and kidney sections in agreement with [12-23] who observed these pathological changes occured after chromium exposure for 3 weeks. Some authors found necrotic regions in the liver with collapsed nuclei[5-24]. In the current study, the light microscopic examination of albino rats receiving both selenium and chromium, (group IV) selenium attenuated the development of the changes observed in the liver and kidneys after exposure to chromium. There were no marked histological changes observed in the liver and kidney tissues. These observations confirmed by[12-23].

The power of selenium to restore the hepatorenal tissues integrity explained by [25]who said that selenium lowering oxidative stress, as the administration of selenium causes a significant increase in hepatic antioxidant activities; reduces glutathione, glutathione reductase, and glutathione-S-transferase levels; and depletes the malondialdehyde level. Concerning hepatic enzymes, hepatotoxic rats showed a significant increase in liver enzymes (ALT and AST) compared to control. On the other hand, selenium received rats showed no significant difference in liver biomarkers, compared to control. These results demonstrate the protective effect of selenium in chromium toxicity in agreement with previous studies[23].Concerning oxidative stress, both catalase and SOD showed a significant reduction after chromium administration in hepatotoxic rats compared to normal control. However, selenium recipient rats showed no significant difference with normal control rats. These results were similar to previous observation by[23].

Regarding ER stress, Grp78 and the pro-apoptotic gene caspase 12 in the rat liver showed a significant up-regulation after chromium administration when compared to normal control. This result is similar to that found by[26].However, dietary selenium significantly decreased the expression of the ER stress-related genes GRP78 and apoptotic caspase 12 with no significant difference between both groups and normal control rats. These findings can be explained by that selenium significantly inhibits oxidative stress and oxidative stress-induced ER stress, resulting in decreased apoptosis[27].Oxidative stress is caused by an imbalance between the generation of ROS and the defense mechanism of antioxidants, such as SOD and catalase, which are important in the elimination of free radicals [28]. Oxidative stress causes cellular apoptosis by both the mitochondria-dependent and mitochondria-independent pathways and is involved in apoptosis [29].The ER is a eukaryotic organelle that synthesizes, folds, and transports native proteins. When the protein folding exceeds the processing capacity of the ER, unfolded proteins accumulate inducing ER stress and triggering the unfolded protein response (UPR), a cytoprotective signaling pathway that can overcome ER stress and maintain cellular homeostasis [30].

Various cell toxins can stimulate the cell to trigger ER stress and consequently the UPR. The UPR induces increased expression of ER-resident chaperones, such as glucose-regulated proteins GRP 78[31]. Upregulated expression ofGRP78 suggested that Cr exposure may cause ER stress in the liver and kidney. Different pathways in the ER participate in UPR to increase the capacity of the ER to manage newly synthesized and misfolded proteins[32].

But, if the protein load in the ER is excessive

and then causes ER stress to persist, the UPR could induce the apoptosis pathways [33]. In this study, we found that chromium significantly decreased the levels of SOD and catalase. These results indicated that chromium exposure in rats inhibited the body antioxidant defense system and led to oxidative stress, which may be responsible for chromium-induced apoptosis.

CONCLUSION

Our results demonstrated that chromium can induce oxidative stress, ER stress and apoptosis in the liver and kidney of the rat. However, selenium prevents chromium induced oxidative stress and ER stress in the hepatorenal tissue of rats at histopathological, biochemical and molecular levels.

ABBREVIATIONS

ALT: Alanine transaminase
AST: Aspartate transaminase
CAT: Catalase
Cr: Chromium
ROS: reactive oxygen species
ER: endoplasmic reticulum
Grp78: Glucose regulated protein 78
GADPH: glyceraldehyde-3-phosphate dehydrogenase
PCR: Polymerase chain reaction
RNA: Ribonucleic acid
SOD: Superoxide dismutase
UPR: Unfolded protein response

Ethical statement: The study has been approved by faculty of medicine, Zagazig University Institutional 11 Review Board (ZU- IRB) and performed in accordance with the ethical standards for experimental animal rights.

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Conflicts of Interest: None

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