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PROTECTIVE EFFECT OF CORIANDER (*CORINDRUM SATIVUM*) AGAINST LEAD TOXICITY IN RABBITS

Gehad Rashad Donia*

Toxins and Environmental Pollution Unit, Department of Animal Health, Animal and Poultry Production Division, DRC, Cairo, Egypt.

***Corresponding Author: Gehad Rashad Donia**
Toxins and Environmental Pollution Unit, Department of Animal Health, Animal and Poultry Production Division, DRC, Cairo, Egypt.

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ABSTRACT
Bioactive compounds from natural sources can act as oxygen free radical scavengers or metal chelators, which enables them to be used as natural antagonists to heavy metals toxicity. So in this study aqueous and ethanolic extract of *Coriandrum sativum* seeds were evaluated for their potential hepato & renal protective and antioxidant effects in lead intoxicated rabbits. Oxidative stress was induced by a daily dose of lead acetate (40 mg/kg body weight by oral gavage) for seven days. After that animals received an oral dose of coriander extracts (aqueous and ethanolic) daily to the end of the experiment. The effect of these treatments in influencing the lead induced changes on liver and kidney functions, oxidative stress, and histopathological alterations in liver and kidney were studied. The data showed elevation of ALT, AST, ALP, urea and creatinine in serum, increase in oxidative stress markers MDA levels in animals treated with lead acetate while the effect was attenuated by coriander seed extracts. Lead decreased the antioxidant enzymes activities and this effect was reversed in groups treated with coriander extracts. Also, extracts exhibited some improvement in the histological architecture of liver and kidney. From the findings of this study, the coriander is identified to possess antioxidant potential and hence it is worth to be considered as a natural chelating agent for lead intoxication.

KEYWORDS: *Coriandrum sativum, Lead, Oxidative stress, hepatotoxicity, nephrotoxicity, Rabbits.*

INTRODUCTION
The discharge of industrial wastewater containing toxic heavy metals in rivers and underground aquifers increasing environmental pollution and that are dangerous to animal and human health, the most common metals found in sewage lead, cadmium, chromium, zinc, copper and nickel (Tagharobiyan & Poozesh, 2015). Lead is a soft, bluish-gray heavy metal found ubiquitously and it is a common cause of poisoning of domestic animals throughout the world, it is known to induce a broad range of physiological, biochemical and behavioral dysfunctions in laboratory animals and humans (Kansal et al., 2012), including central and peripheral nervous systems (Flora et al., 2006 and Velaga et al., 2014), haemopoietic system, cardiovascular system, kidneys, hepatic (Al-Snafi, 2016) and male &female reproductive systems (Al-Rubaye, 2016). One of the major mechanisms behind heavy metal toxicity has been attributed to oxidative stress. Toxic metals increase production of free radicals and decrease availability of antioxidant reserves to respond to the resultant damage. A growing amount of data provide evidence that metals are capable of interacting with nuclear proteins and DNA causing oxidative deterioration of biological macromolecules (Bedi et al., 2016). Considering that lead toxicity is currently one of the serious problems worldwide, there is still no specific, reliable and safe treatment. Several metal chelators as EDTA (ethylenediaminetetraacetic), DTPA (diethylenetriaminepentaacetate) and DMSA (Dimercaptosuccinic acid) have been used to manage lead toxicity in the event of exposure but none are suitable in reducing lead body burden moreover, these chelators in turn are potentially toxic (Sears, 2013). The use of several plants with chelation properties is one of the principal research items in present days as garlic extract which alleviates Pb-induced neural, hepatic, renal and haematic toxicity in rats and prevents Cd-induced mitochondrial injury and apoptosis in tissue culture models (Sharma et al., 2010, Sadeghi et al., 2013 and Nicula et al., 2016). So in this study we used *Coraindrum sativum* Linn Umbeliferae, which is an annual herb, the fresh leaves and dried seeds are one of the most important spices in the world and a common component of Middle Eastern, Mediterranean, Indian, Latin American, African and Southeast Asian cuisines (Al-Rubaye., 2016). On the other hand, in addition to its culinary value coriander is known for its wide range of

healing properties, using in detox diet and helping in removeing toxic mineral residue such as mercury and lead and excrete them in the urine or faeces (Kansal et al., 2012, Velaga et al., 2014 and Tellez-lopez et al., 2017). Lead is reported to cause oxidative stress by generating the release of reactive oxygen species (ROS) such as superoxide radicals, hydrogen peroxide and hydroxyl radicals and lipid peroxides. Antioxidant enzymes as GPx, CAT, and SOD are potential targets for lead toxicity because they depend on various essential trace elements for proper molecular structure and activity (El-Nekeety et al., 2009 and Kansal et al., 2011). Some studies in mice and rats intoxicated with different concentrations of lead and treated with coriander show very encouraging results chelation and reduction poisoning in these animal models (Sharma et al., 2010; Velaga et al., 2014 and Tellez-lopez et al., 2017). The present study reports the effect of lead on liver and kidney function, oxidative stress, antioxidant activity and chelating property of coriander against lead induced toxicity in rabbits.

MATERIALS AND METHODS

This study was carried out at South Sinai Desert Research Station which is located in Ras Sudr City, South Sinai Governorate, belongs to Desert Research Center (DRC), Agriculture and Land Reclamation Ministry, Egypt.

Preparation of aqueous extract*:* Coriander seeds were collected from local market in Cairo. Seeds were dried and ground to a fine powder, which 100 g were added to 500 ml distilled water, after 24 h maceration at room temperature (34 ^{0}C) the mixture was then heated for 30 min in the water bath at 65 ^{0}C. The extract was filtered, concentrated by heating over the water bath (65 ^{0}C) and dried under vacuum (Gray & Flatt, 1999) with the yield of 5.9 % (w/ w). The extract was stored at 4 ^{0}C and used to treat animals as needed.

Preparation of ethanolic extract: Dried and powered seeds (200g) were extracted successively with ethanol (800ml) in a soxhlet extractor for 48 hours at 60^{0}C. After extraction the solvent was evaporated to dryness at 50-55^{0}C by using a rotary evaporator and the extract left behind (yield was 9.8 %) was stored at 4^{0}C. It was dissolved in distilled water whenever needed for Experiment.

Animals: Adult male New Zealand white rabbits weighing approximately 900-1000g were used for experimental purpose. All procedures were performed in accordance with the standards required by the Animal Ethics Committee of the Animal Health DRC. The rabbits were provided with a nutritionally adequate chow diet and drinking water ad libitum throughout the study.

Chemicals: Lead acetate was purchased from Sigma for chemicals company Cairo, Egypt. All other chemicals used in the study were of analytical reagent and obtained from Bio-Diagnostic Company, El-Dokki, Giza, Egypt.

Experimental design: Rabbits were divided into six groups of ten rabbit each and treated by oral gavage as follows:

Group I- Control (untreated) received distilled water.

Group II- Lead acetate treated group, received freshly dissolved lead acetate (Pb (CH3COO)2) in 1 ml distilled water at a dose of 40 mg/ kg body weight (b.w.) / day.

Group III and IV were administered with aqueous coriander extract at a dose of 300 and 600 mg/ kg b.w. respectively, by oral gavage once daily for 33 days from 8 day after beginning of lead exposure to the end of the experiment.

Group V and VI were administered with ethanolic coriander extract at a dose of 250 mg/ kg b.w. and 500 mg/ kg body weight, respectively, by oral gavage once daily for 33 days from 8 day after beginning of lead acetate exposure to the end of the experiment.

The dose for lead acetate was decided on the basis of experiments conducted in the laboratory and the concentration of lead acetate used in the experiment was 1/56 of LD_{50} (Plastunov & Zub, 2008). The plant doses were selected on the basis of earlier published reports (Kansal *et al.*, 2011). After the administration of last dose, the animals were given a one day rest and were slaughtered. Blood was clotted at room temperature for 20 min and centrifuged at 3000 rpm for 10 min, and clear, non hemolyzed serum samples were stored at -20°C until subsequent analysis. On the other hand, 2-cm portions from different areas of the hepatic and renal tissues were excised.

Biochemical and oxidative stress analysis

Activities of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were assayed by the method of Reitman and Frankel (1957), activity of alkaline phosphatase (ALP) was determined according to the protocol described in laboratory practical manual (Sadashivam & Manickam, 1996). Urea and creatinine were determined by colorimetric method according to Foster and Hocholzer, (1971) and Schirmeister et al., (1964) respectively. Meanwhile, serum MDA, SOD, GSH and CAT activities were measured by colorimetric techniques using commercially available kits (Bio-diagnostic, Egypt) by following kits instructions: malondialdehyde (MDA) is a product formed due to the peroxidation of lipids membrane, it was determined according to the method described by (Ohkawa, et al.,1979). Superoxide dismutase (SOD) activity according to the method described by Marklund and Marklund, (1974) and total reduced glutathione (GSH) was determined according to the method described by Beutler et al., (1963). On the other hand CAT activity was measured according to the method described by Aebi (1984).

Histological examination: Tissues (liver and kidneys) were removed, washed (in saline) and fixed in buffered 10 % formalin at room temperature for 72h. After fixing the tissue, it was thoroughly washed under running water and dehydrated in ascending grades of ethyl alcohol, cleared and then embedded in soft paraffin. Tissue sections of about 3-5µ were obtained using microtome (LEICA RM 2135) and stained by Haematoxylin and Eosin and examined under light microscope according to Bancroft and Gamble, (2008). Photos were taken using digital camera (LEICA DMLB Germany).

Statistical analysis: Data are expressed as the Mean ± SEM. Data were analyzed using General Linear Model Procedure (SAS, 2004). Statistical significance was considered at probability ($P< 0.05$).

RESULTS AND DISCUSSION

Biochemical and Oxidative stress changes: Liver is a large and vital organ that functions as a center of metabolism of nutrients, drugs and xenobiotics. Additionally, it is also responsible for elimination of waste products and toxic metabolites (Saleem et al., 2016). So to assess the effect of lead on liver and kidney the activities of serum ALT, AST &ALP and urea &creatinine and the correlations between them were illustrated in table 1&2. It is clear from the results that treatment with lead acetate showed a significant elevation ($p<0.05$) in some biochemical parameters which include AST, ALT and urea as compared to lead acetate group (GII), which recorded the highest values in these parameters. It is worth to mention that the levels of these measured enzymes, urea and creatinine were improved in the coriander extracts treated groups and they approached the normal levels in the aqueous and ethanolic extracts high doses (GV&G VI). Liver and kidney are considered as target organs affected by lead toxicity owing to its storage in them after lead exposure. In the current study, the significant elevation of serum ALT and AST activities enzymes might be due to increased cell membrane permeability or damage of hepatocytes caused by lead acetate and this is in agreement with the findings of Ibrahim, et al., (2012), Alwaleedi et al., (2015) and Obafemi et al., (2019). Generally, ALT&AST are widely used to evaluate the liver function, serum enzymes ordinarily found in the liver, but when there is damage to the liver they are found at high levels in the serum, their elevation may also be due to hepatic toxicities (Njidda et al., 2014& Donia et al., 2018). ALP is a marker enzyme for the plasma membrane. Damage to biological membrane may lead to any of the two abnormalities (increased or decrease in normal levels). This suggests possible damage to the plasma membrane of the tissues of experimental rabbits and this finding agree with Adeyemi et al., (2009). On the other hand elevation of serum urea and creatinine was observed in lead treated group (GII), this may be due to that lead might cause impairment of the brush border epithelial cells and making them impermeable to urea and creatinine thereby causing their elevated levels in the blood such increment indicated kidney dysfunction, this might be due to loss of kidney function and considered as functional evidence of lead induced nephrotoxicity, these results were agreed with Kansal et al., (2012), Alwaleedi et al., (2015) and Obafemi et al., (2019). Meanwhile the obtained data indicated significant improving effect of treatment with coriander extracts at different doses (G III &IV and V &VI) on the altered activities of serum ALT, AST and ALP induced by lead acetate intoxication. Herbal treatment of many diseases including hepatopathy is increasing in many countries. Various types of plants have been used for several centuries worldwide not only as dietary supplements but also as traditional treatments for many diseases (Attia et al., 2017). Coriander extracts preserves the structural integrity of liver against lead induced damage. Moreover, the kidney is another important target organ that has been affected by lead. In the current study, elevation of serum urea and creatinine was observed in lead acetate treated group. These results agreed with the results of Alwaleedi et al., (2015) and Obafemi et al., (2019) as they were illustrated, such increment indicated kidney dysfunction where the increase in creatinine concentration might be due to loss of kidney function and considered as functional evidence of lead induced nephrotoxicity. The presence of lead might cause impairment of the brush border epithelial cells and making them impermeable to urea and creatinine thereby causing their elevated levels in the blood (Adeyemi et al., 2009). To find new natural medication with biological activities we evaluate the antioxidant properties and chelating effects of coriander extracts on rabbits administrated with lead acetate. oxidative stress and antioxidant defense variables effect of lead acetate alone and ameliorating effect of aqueous and ethanolic coriander extracts individually during lead acetate exposure on MDA as oxidative stress marker and antioxidant related parameters and the correlation between them of various groups were assessed and are presented in Table 3&4. The obtained results revealed that exposure of male rabbits received lead at a dose of 40 mg/ kg b.w./ day for seven days induced significant increase ($P< 0.05$) of malondialdehyde (MDA) as oxidative stress markers associated with significant decrease ($P< 0.05$) in the values of antioxidant parameters (SOD, GSH, CAT) compared to group two in serum samples. The increase of MDA concentration in the sera of GII indicated high oxidative stress occurred due to lead toxicity, MDA is the main by-products formed by lipid peroxidation resulting from high oxidative stress which leads to excessive production of free radicals which are responsible for impaired cellular functions furthermore, lipid peroxidation causes irreversible damage of cell membrane, this is in agreement with (Naji and Zenad, 2015 and Tahoun et al., 2018). Meanwhile, Decreased concentrations of SOD, GSH and CAT activities may reflect oxidative stress in lead exposed group. On the other hand, administration of aqueous coriander extract at a dose of 300&600 mg/ kg body weight, respectively, to lead treated group as shown

in Table 3&4 there were significant increase in SOD, GSH, CAT associated with significant decrease in MDA in lead plus aqueous coriander extract and the lead plus ethanolic coriander extract at a dose of 250 and 500 mg/ kg body weight treated groups when compared with lead group. Taking into consideration, SOD is the first line of defense against ROS and is active in catalyzing detoxification of superoxide radical. Meanwhile, glutathione is considered the main antioxidant enzyme against heavy metals, It was suggested that the increase of glutathione occurs to offset the free radicals produced by lead toxicity and other heavy metals. In consistence, catalase is an enzymatic scavenger antioxidant, neutralizing reactive oxygen species and removes cellular superoxide and peroxides before their reaction with metal catalysts to form more reactive species, also it catalyzes the reduction of hydroperoxides thereby protects mammalian cells from oxidative damage (Gill et al., 2015, Naji and Zenad, 2015 and Tahoun et al., 2018). Attempts have been made to select protective agents and drugs which reduce overt toxicity to the exposed individuals. It is worth to mention that reverse correlation between oxidant/antioxidant markers was observed at table 4. The main cause of pathogenesis of liver injury is the involvement of a deadly agent or the bio-activation of free radicals that elicits an immune response or protein dysfunction, lipid peroxidation, DNA damage, oxidative stress and depletion of reduced glutathione (Qadir and Ahmad, 2017). Lead (Pb) is a ubiquitous environmental toxicant that induces a broad range of dysfunctions, although the exact mechanism of lead induced toxicity is not completely cleared but cumulative data showed that oxidative stress plays an essential role in its toxicity. Lead administration induces over production of reactive oxygen species (ROS) and depletes the cellular antioxidant capacity. The present study has investigated the efficacy of coriander which is considered both a traditional natural medicine and an edible vegetable, against the toxicological disorders induced by lead acetate using a rabbit model. It is evident from the results of the present investigation that supplementation of coriander aqueous and ethanolic extracts with lead acetate protected animals from toxic effects of lead in general and oxidative stress in particular. This study is in confirmation with the earlier report that suggests the preventive effects of coriander on localized lead deposition in male mice (Kansal et al. 2012, Sadeghi et al., 2013, Velaga et al., 2014 and Tellez-lopez et al., 2017). However, rabbits administered with coriander restored the altered levels to some extent suggest that the active ingredients in the coriander possess antioxidant properties and protects against lead induced oxidative stress. Such an extract can function as a primary or secondary chelator for mercury, as well as be used to prepare a primary chelator blend. Positive correlations were already found between total phenolic content in the extracts and antioxidant activity (Helle et al., 2004).

Table (1): Effect of administration of lead acetate alone or with coriander extracts on some liver and kidney parameters in control and experimental groups.

Groups	ALT (U/L)	AST (U/L)	ALP (U/L)	Urea (mg/dl)	Creat. (mg/dl)
GI	29.33^{b}±3.296	72.33^{b}±7.273	164.00^{b}±17.052	30.03^{b}±2.062	0.98^{b} ±0.073
GII	41.25^{a}±2.854	95.00^{a}±6.298	182.25^{b}±14.767	39.80^{a}±1.786	1.03^{b} ±0.063
GIII	20.67^{b}±3.296	76.00^{ab}±7.273	176.33^{b}±17.052	30.83^{b}±2.062	0.90^{b} ±0.073
G IV	28.33^{b}±3.296	59.67^{b}±7.273	165.00^{b}±17.052	30.43^{b}±2.062	1.00^{b} ±0.073
G V	26.50^{b}±2.854	74.75^{ab}±6.298	135.00^{b}±14.767	32.00^{b}±1.786	0.94^{b} ±0.063
G VI	23.50^{b}±2.854	70.00^{b}±6.298	161.75^{b}±14.767	28.58^{b}±1.786	0.90^{b} ±0.063

Values are expressed as mean± standard error. Means with different superscripts in the same column are significantly different at P<0.05.ALT: alanine aminotransferase, AST: aspartate aminotransferase, ALP: alkaline phosphatase, Creat.: creatinine.

Table (2): The correlation between some liver and kidney parameters.

	ALT	AST	ALP	Urea	Creat
ALT	1				
AST	0.56513	1			
	0.0076				
ALP	0.13372	-0.06229	1		
	0.5633	0.7885	0.1532		
Urea	0.62618	0.41876	0.19332	1	
	0.0024	0.0588	0.4011		
Creat	0.53885	0.05035	0.06951	0.44719	1
	0.0117	0.8284	0.7646	0.0421	

Table (3): Effect of administration of lead acetate alone or with coriander extracts on oxidant / antioxidant status in control and experimental groups.

Groups	MDA (nmol/L)	GSH (mg/dl)	CAT (U/L)	SOD (U /L)
GI	22.79^{b}±3.766	9.09^{a}±1.434	0.84^{a}±0.074	146.89^{a} ±8.831
GII	40.01^{a}±3.262	6.19^{a}±1.242	0.64^{b}±0.064	120.46^{b}±7.648
GIII	25.42^{b}±3.766	5.93^{a}±1.434	0.59^{ab}±0.074	132.74^{ab}±8.831
G IV	25.44^{b}±3.766	7.22^{a}±1.434	0.76^{ab} ±0.074	131.35^{a}±8.831
G V	22.97^{b}±3.262	8.08^{a}±1.242	0.73^{ab} ±0.064	135.86^{a}±7.648
G VI	18.67^{b}±3.262	9.68^{a}±1.242	0.77^{ab} ±0.064	134.97^{a}±7.648

Values are expressed as mean± standard error. Means with different superscripts in the same column are significantly different at P<0.05. MDA: malondialdehyde, GSH: Glutathione reduced, CAT: Catalase, SOD: Superoxide dismutase.

Table (2): The correlation between oxidant / antioxidant markers.

	MDA	GSH	CAT	SOD
MDA	1			
GSH	-0.33875	1		
	0.1331			
CAT	-0.38595	0.35181	1	
	0.084	0.1178		
SOD	-0.54811	-0.02687	0.52395	1
	0.0101	0.908	0.0148	

Histology of hepatic tissue: In consistent with these oxidative stress and antioxidant defense changes, the effect of lead acetate alone and ameliorating effect of coriander extracts individually during lead exposure on hepatic histologic images of experimental rabbits of various groups were examined (Figure 1-6). The histological examination of group I (untreated animals) showed normal architecture of liver (normal structure of the central vein and surrounding hepatocytes, normal hepatic parenchyma, blood sinusoids and no lesions were observed).

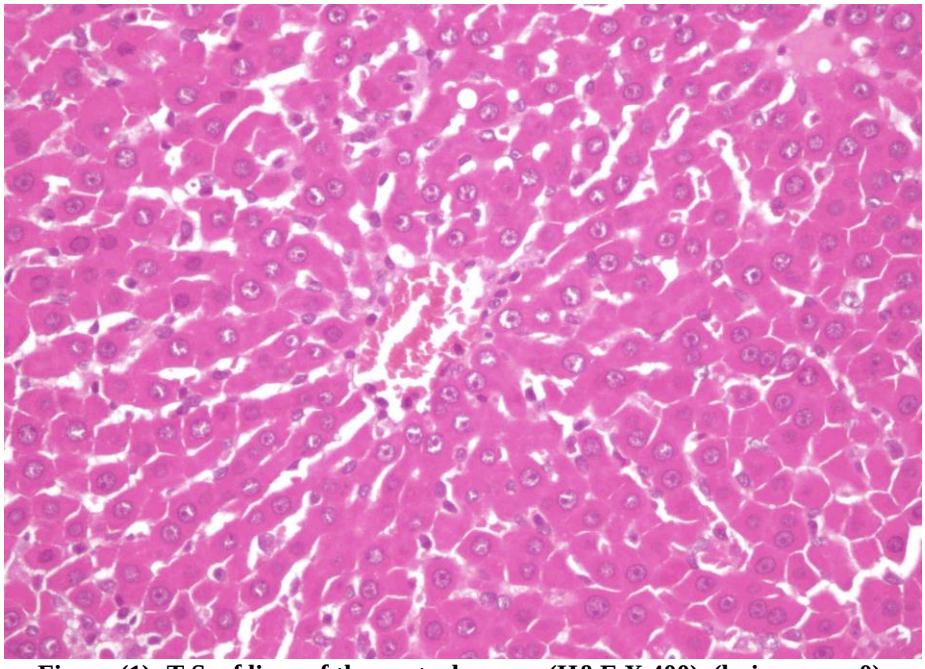

Figure (1): T.S. of liver of the control group. (H&E X 400), (lesion score 0).

Lead acetate exposed animals (G II)

While examination of group II, perilobular massive leucocyte cells infiltrations was observed, the normal structural organization of the hepatic lobules was impaired and the characteristic cord-like arrangement of the normal liver cells was lost. The central and portal veins were congested. Considerable number of hepatic cells were damaged and lost their characteristic appearance (Fig. 2), these findings are in support with Durgut et al., (2008) and Tellez-lopez et al., (2017). In

accordance with present finding Sharma, et al., 2010 and Kansal et al., 2011 showed that liver of lead treated rats revealed remarkable degenerative alterations. The last authors mentioned that in general, lead is well known to induce hepatic injury and the pathological changes may lead to impaired liver function, which interferes with the secretion of plasma proteins and this leads to decreased blood osmotic pressure with subsequent decreased drainage of tissue fluids, which explains the oedema and congestion which observed in the different tissues. Results also showed a remarkable cellular infiltration in the hepatic tissue, this was in accordance with the observations of Sharma et al., (2010), Jarrar and Taib, (2012) and Sharma et al., (2013) who found that mild necrosis of hepatocytes, with infiltration of inflammatory cells in between hepatocytes, bridging necrosis and portal triaditis and dilatations of central vein with eosinophilic degeneration in rats and rabbits exposed to high lead and nitrate ingestion.

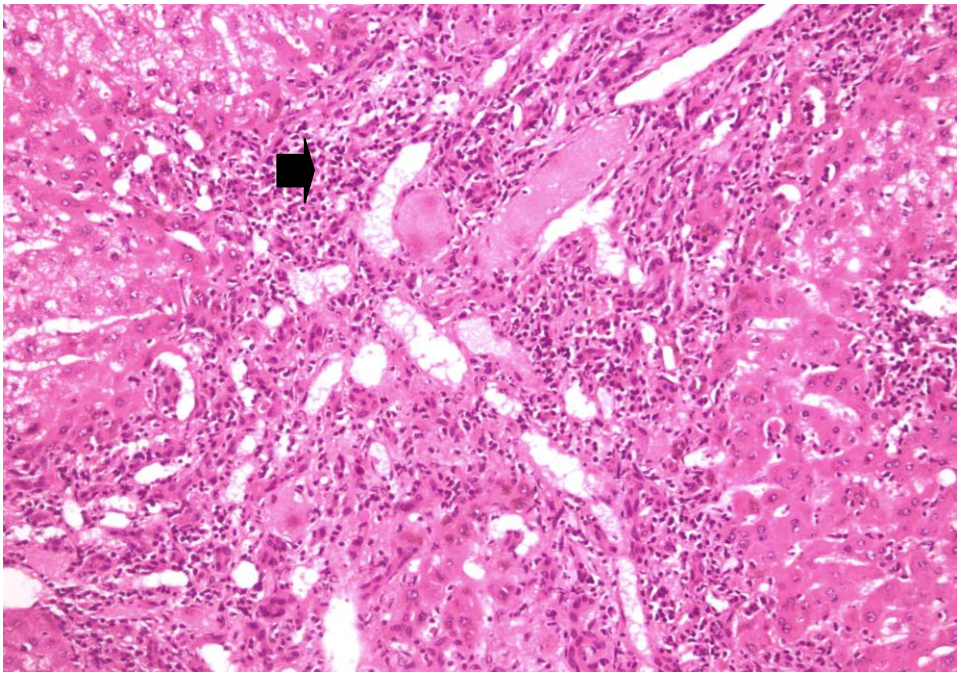

Figure (2): T. S. of liver of rabbit treated with lead acetate, (lesion score +++).

Group III, IV (lead acetate + aqueous extract of coriander) and group V and VI (lead acetate + ethanolic extract of coriander)

Animals treated with lead and coriander extracts showed that most of these histopathological changes were diminished, some vacuolated hepatocytes with faint granular cytoplasm and binucleation and blood sinusoids are compressed in low doses groups (Fig. 3 and 5). Meanwhile in high doses groups, the liver tissue restored most of its normal structure and showing marked regression in the perilobular leucocytic cells infiltrations. Also high doses were able to diminish the fibrosis, congestion, incidence of inflammatory cells infiltration, centrilobular hepatocytes swelling and hepatocytes vacuolization (Fig. 4 and 6). Our finding agree with Kansal et al., (2011), Kansal et al., (2012) and Tellez-lopez et al., (2017) who stated that the pathological changes were prevented to moderate extent in coriander extracts treated groups and this might be due to the presence of flavonoids and ascorbic acid which act as antioxidants by free radical scavenging. Others suggested that flavonoids are hepatoprotectives (Lal and Meena., 2018 and Obafemi et al., 2019).

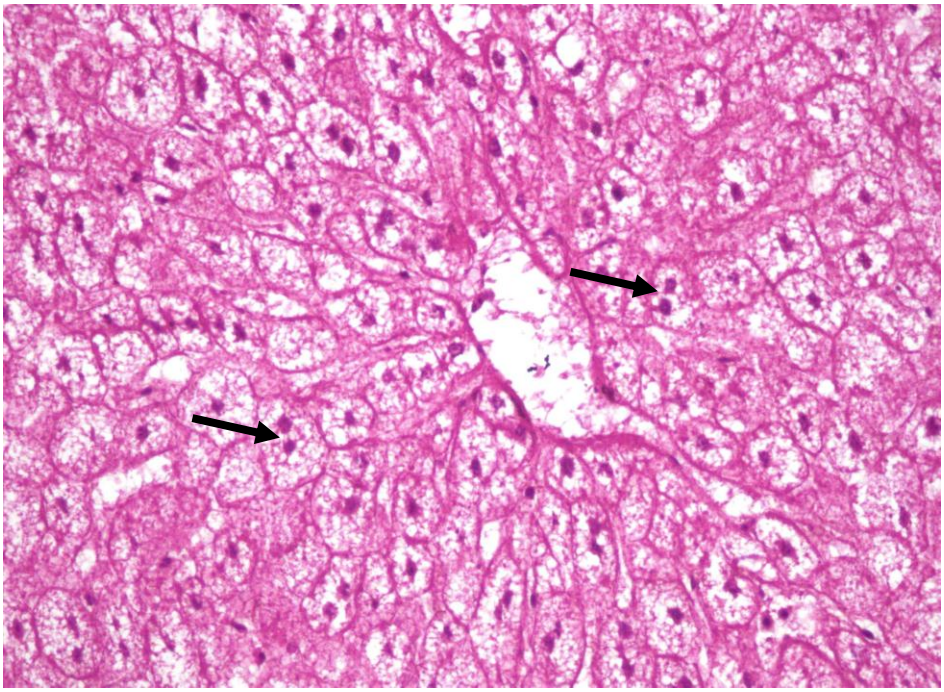

Figure (3): T. S. of liver of rabbit treated with lead acetate + aqueous extract of coriander at a dose of 300 mg/ kg body weight, (H&E X 400), (lesion score ++).

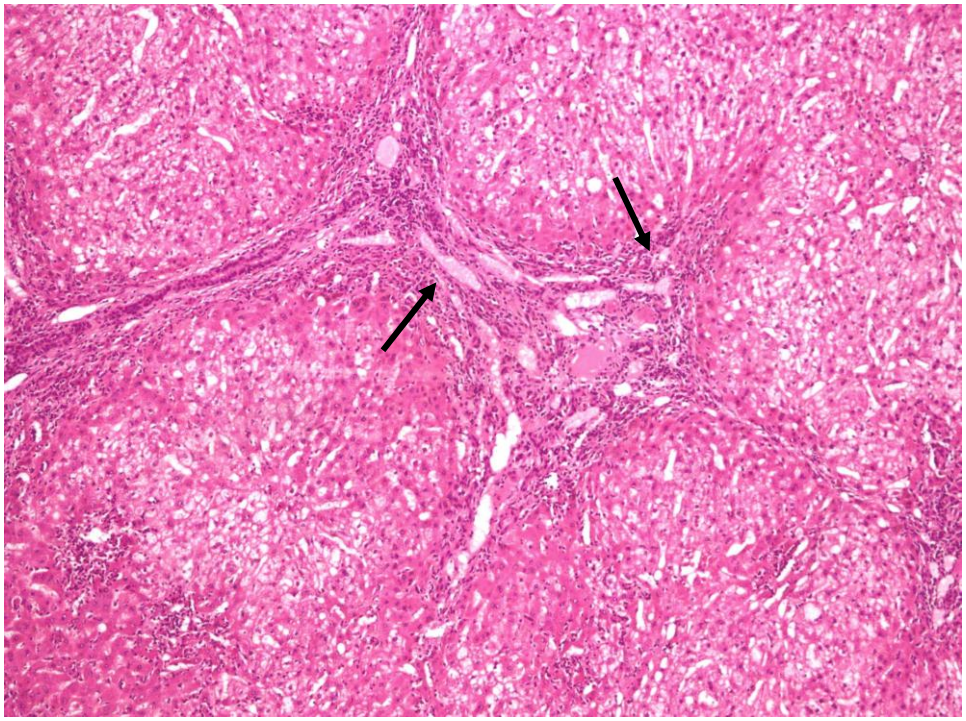

Figure (4): T. S. of liver of rabbit treated with lead acetate + aqueous extract of coriander at a dose of 600 mg/ kg body weight, (H&E X 200), (lesion score +).

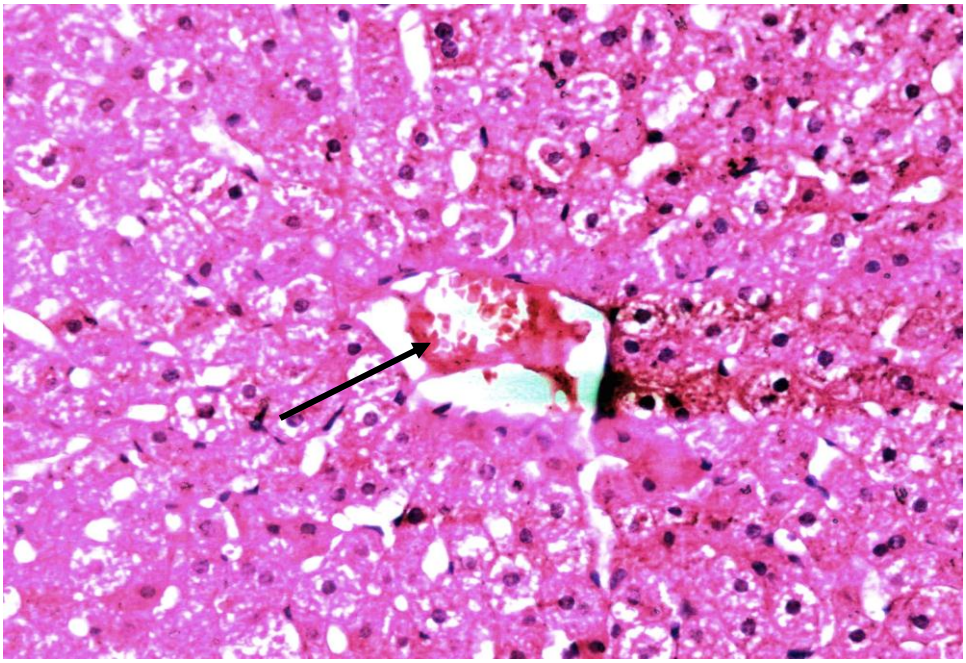

Figure (5): T. S. of liver of rabbit treated with lead acetate + ethanolic extract of coriander at a dose of 250 mg/ kg body weight, (H&E X 400), (lesion score ++).

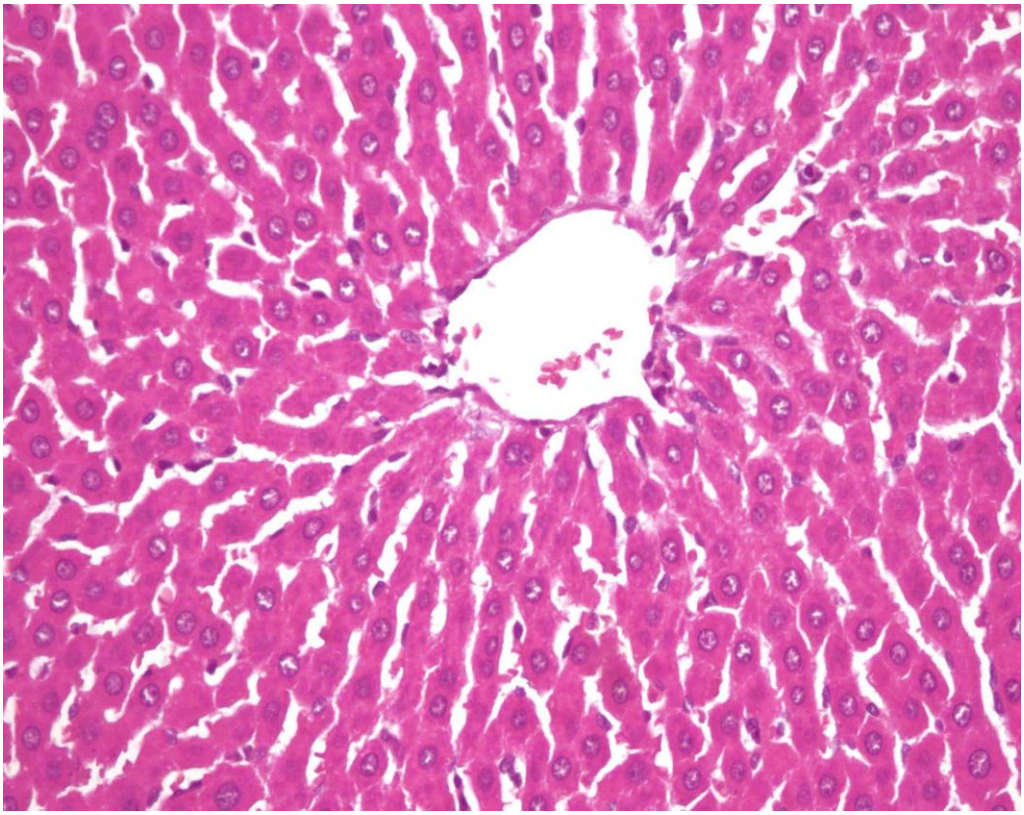

Figure (6): T. S. of liver of rabbit treated with lead acetate + ethanolic extract of coriander at a dose of 600 mg/ kg body weight, (H&E X 400), (lesion score 0).

Histology of renal tissues: Effect of lead acetate alone and ameliorating effect of coriander extracts individually during lead acetate exposure on renal histological images of experimental rabbits of various groups were examined (Fig. 7-12). According to group I, no pathological changes was seen in the kidney of the control rabbit, it showed normal renal parenchyma, glomeruli and renal tubules and they were well arranged and uniformly stained (Fig. 7).

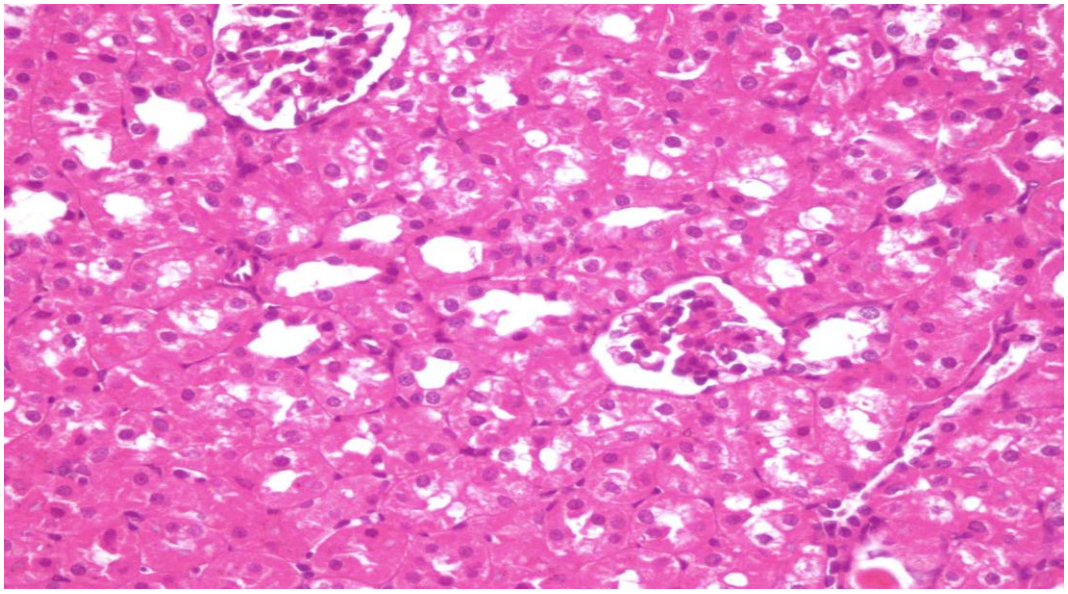

Figure (7): T.S. of kidney from control group (H&E X 400) lesion score 0.

Furthermore, lead acetate exposed animals (GII) as shown in figure 8, the kidney section of lead-induced group showed vacuolated glomerular taft epithelium and renal tubular epithelium together with congestion in the interstitial blood vessel. On the other hand, some blood sinusoids appeared to be filled with erythrocytes and glomeruli showed shrinkage. The toxic effects of lead on different body organs as kidney have been widely studied. The results of some previous investigation showed that subtoxic chronic lead exposure resulted in marked histological alternations in kidney include dilation of tubules; sloughing of epithelium indicates advanced disintegration of tubules (Kansal et al., 2011) progressive tubular, glomerular and interstitial alterations (Durgut et al., 2008). The report from Jabeen et al. (2010) showed that lead acetate decreased the renal cortical thickness and the diameter of corpuscles significantly and induced the moderate cortical tubular atrophy indicating the thickening of glomeruli basement membrane morphometric. Moreover, in a similar study which was done by Khalua, et al., (2015) it was found that lead even at low doses had adverse effects on renal tissue, proximal tubular damage degenerated epithelia and shrunken tubules. The report from Karimfar, et al., (2016) showed that lead exposure caused dilation in distal convoluted tubules, proximal convoluted tubules and collecting ducts. In addition, the thickness of epithelial cells of tubules decreased and the nuclei of epithelial cells were found to be more heterochromatic. On the other hand, Kansal et al., (2012) was explained that tubular alterations due to lead toxicity might be a result of a hydrolic changes in the renal tissue and suggest that lead intoxication yields to a partial failure in the ion pump transport of tubules cells which in turn produces tubular swelling and causes necrosis and vacuolization of the tubules. It worth mentioned that results of this study are in line with the above findings.

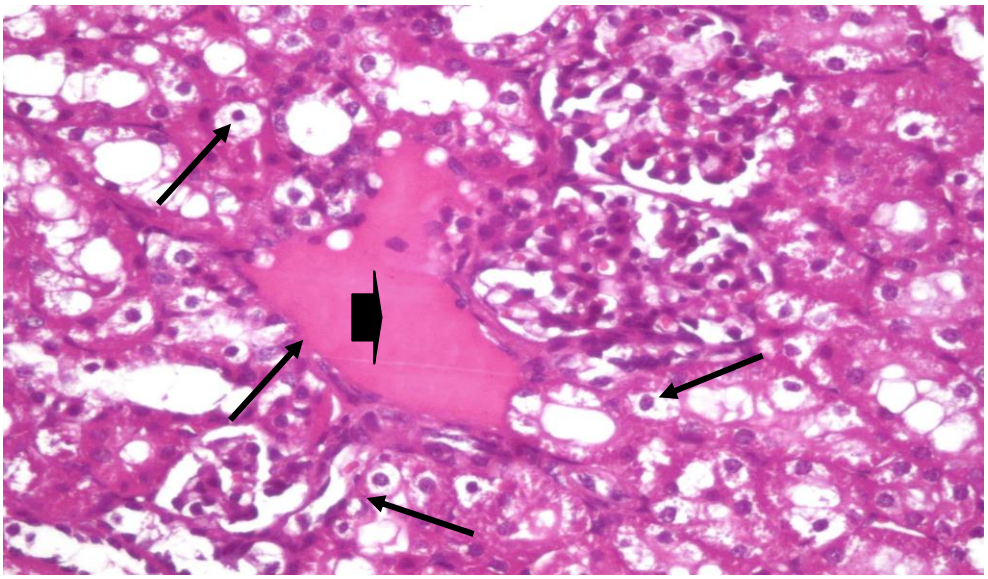

Figure (8): T. S. of kidney of rabbit treated with lead acetate (H&E X 400), lesion score +++.

Moreover, the remedial effect of coriander extracts was also confirmed by histological observations in group III, IV (lead acetate + aqueous extract of coriander) and group V,VI (lead acetate + ethanolic extract of coriander) which showing vacuolated glomerular taft epithelium and renal tubular epithelium (arrows) with absence of blood vessel congestion and congestion in the interstitial blood vessel (arrow) with regression in the glomerular and renal tubular epithelial vacolation (Fig. 9 & 11). in addition, showing vacuolated glomerular taft epithelium and renal tubular epithelium (arrows) with absence of blood vessel congestion and showing apparently normal renal parenchyma, note the normal glomeruli and renal tubules (Fig. 10 and 12).

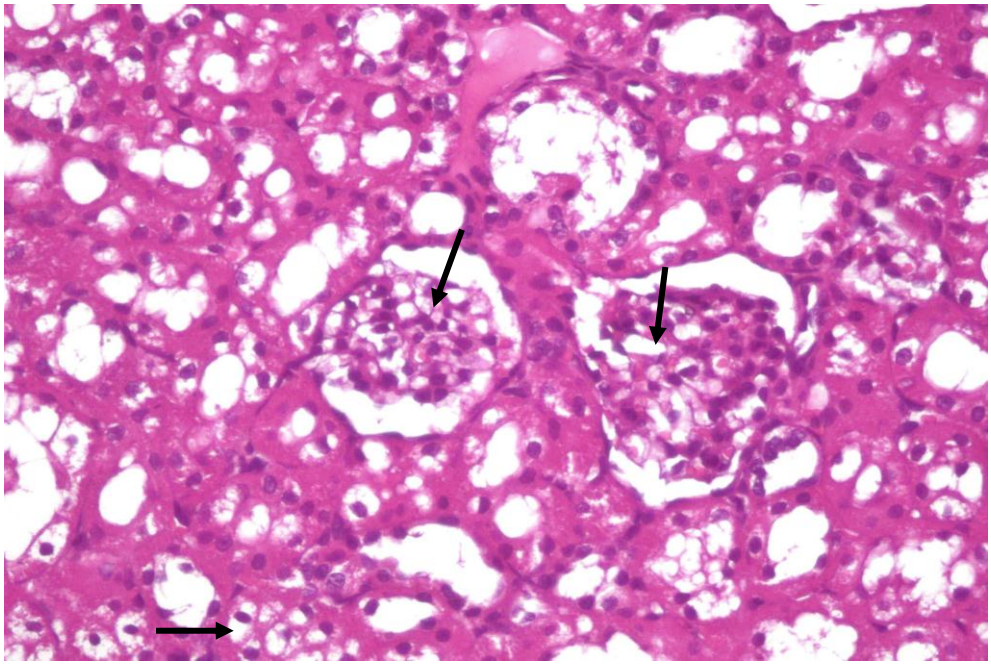

Figure (9): T.S. of kidney of rabbit treated with lead acetate + aqueous extract of coriander at a dose of 300 mg/ kg body weight (H&E X 400), lesion score ++.

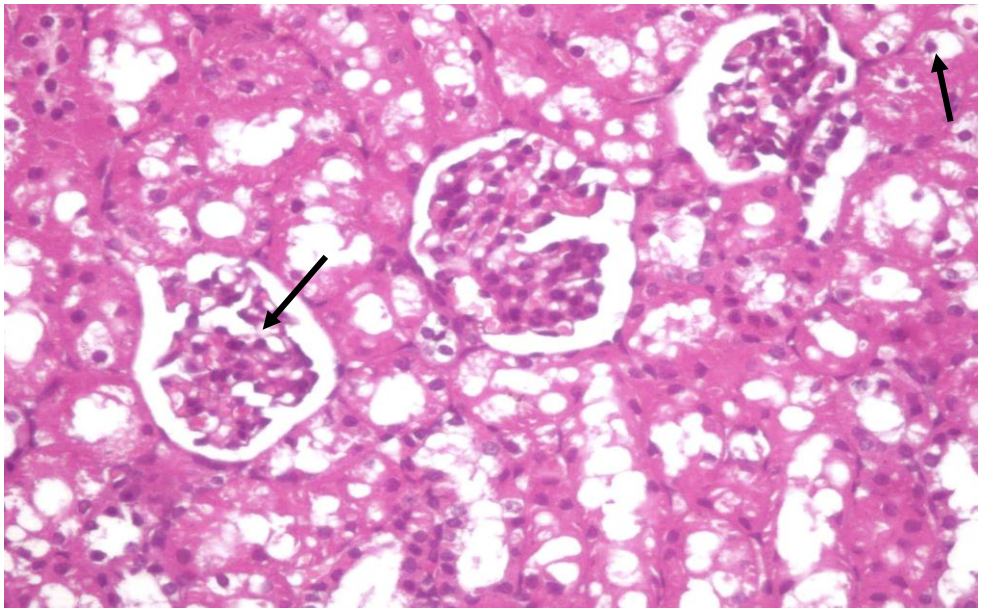

Figure (10): T.S. of kidney of rabbit treated with lead acetate + aqueous extract of coriander at a dose of 600 mg/ kg body weight (H&E X 400), lesion score +.

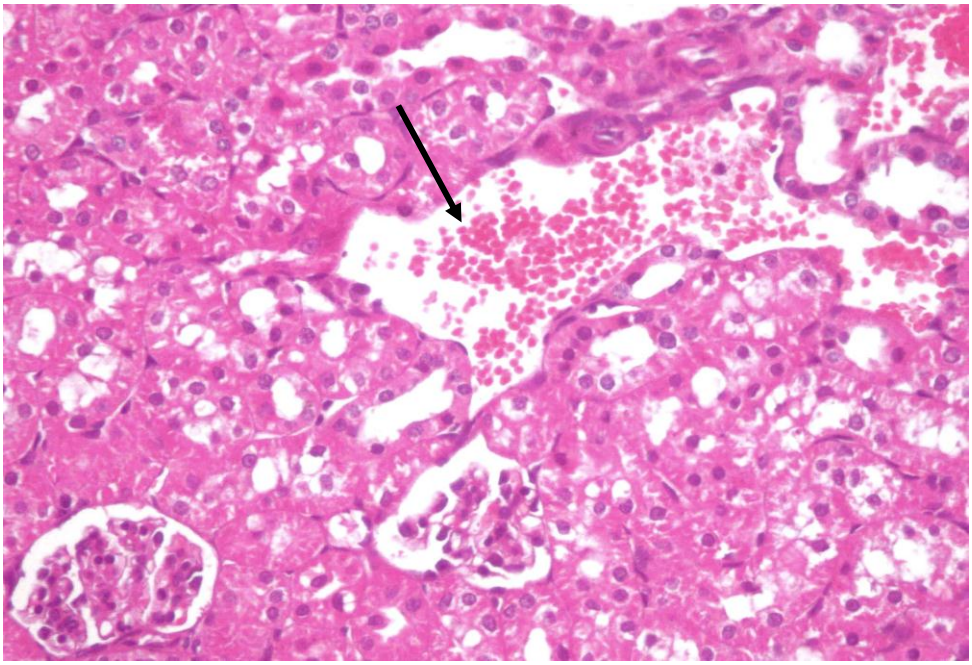

Figure (11): T.S. of kidney of rabbit treated with lead acetate + ethanolic extract of coriander at a dose of 250 mg/ kg body weight (H&E X 400), lesion score ++.

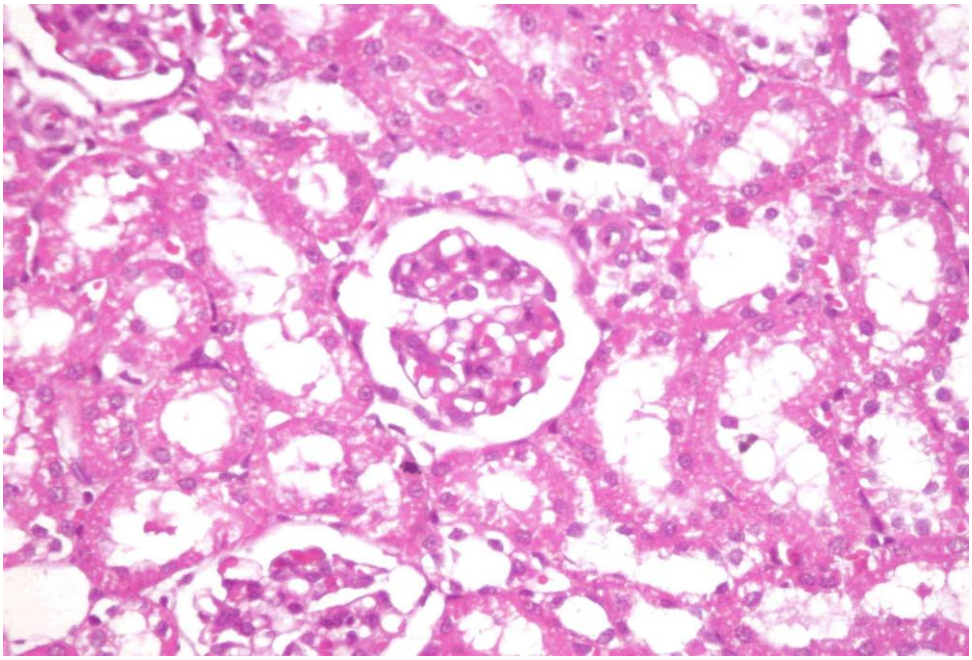

Figure (12): T.S. of kidney of rabbit treated with lead acetate + ethanolic extract of coriander at a dose of 500 mg/ kg body weight (H&E X 400), lesion score 0.

Lead can cause severe renal problems, kidney is one of targeted site of lead toxicity for being major route of excretion from body and facilitates kidney damage via oxidative stress and lipid peroxidation (Khalua et al., 2015 and Al-Snafi, 2016). It worth mentioned that, experimental evidences suggest that coriander extract have a wide application in treating pathological conditions of renal system, produce protective effects and is a good medication of drug induced renal ailments or heavy metal induced kidney toxicity attributable to its chelate, antioxidant and diuretic action (Kansal et al., 2011, Kansal et al., 2012 and Ghosh, et al., 2017). In the present study, we found that coriander aqueous and ethanolic extracts (especially high doses) used individually led to diverse results in relation to the histological alterations caused by lead toxicity. Thus coriander extract produced protective effects in renal tissue against lead toxicity.

CONCLUSION

The present data suggests that lead-induced haematotoxicity, hepatotoxicity and nepherotoxicity. Aqueous and ethanolic extracts of *Coriandrum sativum* can produced a good significant variation in most of the

evaluated tests (some biochemical parameters, oxidative stress marker, antioxidants enzymes and histological alternations) and prevent or slow down the oxidative damage induced by lead toxicity in rabbits. Further studies are needed to evaluate its pharmacokinetics and toxicity profile to determine its clinical dose.

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