Vol-7, Issue-5 PP. 116-134 ISSN: 2394-5788

GLOBAL JOURNAL OF ADVANCED RESEARCH
(Scholarly Peer Review Publishing System)

HEMATOBIOCHEMICAL CHANGES OF LEAD POISONING AND ITSIMPROVEMENT WITH CORIANDER(CORIANDRUM SATIVUM) EXTRACTS IN RABBITS.

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ABSTRACT

Rabbit is considered a very suitable animal model for lead intoxication with regard to haem synthesis, *Coriandrum sativum* is widely distributed and mainly cultivated for the seeds consequently, the current study planned to screen the protective effect of coriander aqueous and ethanolic seeds extracts on lead-induced body weight, hematobiochemical and heart & lung histopathological alternations in male rabbits. For this purpose, a daily dose of lead acetate(40 mg/kg body weight by oral gavage) for seven days was given to animals, however from day eight they received an oral dose of coriander extracts (300 and 600 mg kg^{-1} b.w. aqueous extract and 250 and 500 mg kg^{-1} b.w. ethanolic extract) along with lead acetate (Pb $(CH_3COO)_2$) daily for 33 days. The results showed that, weights of intoxicated rabbits has protected by coriander supplementation as compared to lead exposed animals. RBC count, WBC count, Hb level and serum Tp, Alb and Glb contents were significantly decreased in the lead treated animals while, total bilirubin levels were significantly increased after implication of lead metal. However, marked improvement in both hematological and serum biochemical changes was observed in lead treated rabbits which had oral administration of coriander extracts especially in high doses. Also the correlation between different parameters was shown. An extension of that, lead caused histopathological changes in heart and lung of male rabbites while coriander extracts administration to lead treated animals resulted in overall improvement in these organs damage, emphasizing its strong antioxidant properties. Oral administration of coriander extracts to lead acetate treated groups decline the deranged parameters to some extent. Results revealed that, treatment with coriander extracts significantly protect against lead induced toxicity and warrant the isolation and identification of the active compounds responsible for its antioxidant effect.

Keywords: Hematobiochemical, heart, lung, Lead, Coriandrum sativum, Rabbits.

1. INTRODUCTION

Contamination of the environment by heavy metals has increased, among these metals is lead which increased drastically along with the rapid development of modern industry which its levels have increased substantially during the last few years (Jesuorsemwen et al., 2016).Lead is a widespread natural element in the environment which is considered as one of the main persistent and common environmental pollutants, it can translocate through the food chain and cause harmful effects to human and other living organisms. It is poisonous and has deleterious impact on most organs of the human body (Duruibe et al., 2007). It is one of the main environmental contaminants that can threaten living organisms in many ways and its toxicity is associated with a number of physiological, biochemical and morphological alterations (Alwaleedi, 2016). Lead is a well-known multi-organ toxicant such as liver and kidneys(Kansal et al., 2011, Kumar et al., 2013 & Donia, 2019), cardiovascular(Navas-Acien et al., 2007), spleen and lung (Muselin et al., 2010and Kaczynska et al., 2013),testis (Hamadouche et al. 2009) and bone (Oliveira et al., 2002).Laboratory rabbit has some advantages in the study of physiological disorders and toxicology field. Recently, the rabbit become a favorite companion animal, it is often used as live model in scientific research where changes in blood count occur. In addition, a complete blood count is a good indicator of general health as stress and numerous illnesses, can modify haematological parameters especially with regard to erythrocyte and lymphocyte counts. Haematological diagnosis is becoming more immanent in veterinary medicine especially in the detection of health disorders in pet rabbits where being familiar with referent values is extremely important (Poljičak-Milas et al., 2009 and Šimek et al,2017).It worth mention that there has been an increase of interest in the therapeutic potential of medicinal plants as antioxidants in reducing free radical- induced tissue damage nervous, immune and hematopoietic systems. From these medicinal

plants, *Coriandrum sativum* which is a rich reservoir of micronutrients and nutritional elements which leads us to focus our study on this herb particularly it is widely distributed and mainly cultivated for the seeds and it has been reported to have a number of possible medicinal attributes including antispasmodic, carminative and stomachic properties. Additionally, it has been advocated as an anti-diabetic treatment (Aligita et al., 2018 and Kajal & Singh 2019). Moreover, it is very low in saturated fat however, contains good amount of linoleic acid which is a good source of α-tocopherol and vitamin K, leaves are rich source of vitamins while seeds are rich in polyphones and essential oils (Bhat et al., 2014).Also it can be used as a natural cleansing agent as it has potential to remove toxic metals from body because chemical compounds present in coriander attach to toxic metals and remove them from cells (Abidhusen, 2012). In this context, Aruna sagar et al. (2005) observed that coriander is very effective to remove inorganic (Hg^{2+}) and methyl mercury (CH_3Hg^+) from aqueous solutions and this was due to the binding effect of carboxylic group to mercury, the study clearly showed that sorbent can be used to remove inorganic and methyl mercury from contaminated water. On the other hand, Kansal et al., (2011) and Donia, (2019)were found that coriander seeds extracts led to marked decline in oxidative stress caused by lead. Otherwise, lead can penetrate the human or animal by inhalation, ingestion and by skin (El-Feki et al., 2000)and after absorption into the blood 95% of lead is bound to erythrocytes and the remaining percentage stay in plasma to be carried to other tissues. Erythrocytes have a high affinity for lead and contain the majority of the lead found in the blood stream which makes them more vulnerable to oxidative damage than many other cells. Moreover, erythrocytes can spread lead to different organs of the body(Sivaprasad et al., 2004).Furthermore, several reports have indicated that lead can cause neurological, hematological, gastrointestinal, reproductive, circulatory and immunological pathologies, all of them related to the dose and the duration of time of lead exposure (Park et al., 2006, Patrick, 2006 and Ademuyiwa et al., 2007).Human and animals are daily interact with their environment and exposed to broad spectrum of chemicals and heavy metals like aluminum, mercury, lead and cadmium which are belonging to the most important hazardous substances that can bioaccumulate in the body and collected in tissues with low execration (Jaishankar et al., 2014). In the light of aforementioned medical properties of coriander and to complete a previous study this study was carried out to investigate the possible protective properties of coriander extracts on lead-induced alternations in body weight, hematobiochemical and heart &lung histopathological of male rabbit.

2. MATERIAL AND METHOD

2.1 Animals

Male New Zealand white rabbits weighing approximately 800-900g were used throughout this study. Rabbits were provided with a nutritionally adequate chow diet and drinking water ad libitum throughout the study and all ethical points regarding the treatment of laboratory animals were observed in this research. 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, Agriculture and Land Reclamation Ministry, Egypt.

2.2 Preparation of aqueous and ethanolic extracts of *Coriandrum sativum*

Dried coriander seeds were collected from local market in Cairo and grounded to a fine powder. According to aqueous extract, 100g were added to 500ml distilled water, after 24h maceration was done at room temperature (34^0C), 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 (65^0C) and dried under vacuum (Gray & Flatt, 1999) with the yield of 5.9 % (w/ w). Also for ethanolic extract,200g were extracted successively with ethanol (800 ml) 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 %). The extracts were stored at 4^0C and used to treat animals as needed.

2.3 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.

2.4 Experimental design

Rabbits were divided into 6 groups of ten rabbit each and treated by oral gavage as follows:

Group 1- Control (untreated) received distilled water.

Group 2- Lead acetate treated group, received freshly dissolved lead acetate (Pb $(CH_3COO)_2$) in 1 ml distilled water at a dose of 40 mg/ kg body weight (b.w.) /day.

Group 3 and 4were 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 5 and 6were 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 (Sharma et al., 2011). After the administration of last dose, the animals were given a one day rest and were slaughtered.

2.5 Body weight

Nearest to gram the body weight of animals was recorded at the end of the experiment and the % change in body weight of animals in different groups was calculated by using the following formula:

$$\text{Change in body weight (\%)} = \frac{\text{Change in body weight}}{\text{Initial body weight}} \times 100$$

2.6 Haematology and Biochemistry

The animals were fasted for twelve hours prior to blood collection, for haematological and biochemical investigations blood was collected from each rabbit individually. Blood sample of each rabbit was then transferred to a sterile capped tube containing anticoagulant EDTA (ethylene diamine tetra acetic acid)for haematological estimation. Some of blood was transferred to other sterile anticoagulant-free tube and centrifuged at 3000 rpm for about 15 min to obtain the serum for biochemical examination. Blood cell counter URIT-2900 automated hematology analyzer (Dhanwantari Medical Systems, DMS, India) was used to determine haematological indices including red blood cell parameters { Red blood cells (RBC), hemoglobin (Hb), Hematocrit (Hct), packed cell volume (PCV), mean corpuscular volume (MCV), mean corpuscular hemoglobin(MCH), mean corpuscular hemoglobin concentration (MCHC) and platelet count (PLT)}and white blood cells (WBC) and white blood cells differentials (neutrophils, eosinophils, bosinophils, lymphocytes and monocytes). Meanwhile, serum biochemical parameters were contents of total protein (Tp.g/dl), albumin (Alb g/dl) and total bilirubin (T.bilir.)which were determined by colorimetric method using commercial kits supplied by Biodiagnostic-Egyptian Company. The concentration of globulin (Glb g/dl) and albumin to globulin (A/G) ratio were calculated.

2.7 Histological examination

Tissues (heart and lung) 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).

3. STATISTICAL ANALYSIS

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

4. RESULTS AND DISCUSSION

4.1 Effects on body weight

The present study describes the effects of coriander aqueous and ethanolic seeds extracts against lead induced alternations (body weight, hematobiochemical and histological) in rabbits. Table1 is tabulated for the change in body weight (%) of rabbits groups and it is observed that the decrease in body weight in lead group(G2)when compared to control group (G1).It is worth noting that G3,G4,G5&G6have retained some extent of body weight compared to G2 and shown some improvement. That may be linked to the protective effect of coriander extracts administrated to these groups. The changes in the body weight of animals were detected at the end of the experiment in different groups. Decrease in % body weight of lead group as compared to control group indicating a condition of weight loss at the ending of experiment. This observation is in agreement with several studies(Berrahal et al., 2007, Ibrahim et al., 2012, Phatak & Matule 2016 and Derouiche et al., 2017)which suggest that lead induces a reduction in body weight and food consumption by its effect on nerve centers which responsible for the regulation of satiety and hunger. In addition, may be caused by the toxic ions that could be associated with several factors, one of which is imbalance metabolism produced by impairing zinc status in zinc-dependent enzymes which are necessary for many metabolic processes. The reduction in body weight can also be explained by a reduction in muscle mass and cachexia due to lead-induced oxidative stress (Seddik et al., 2010, Reckziegel et al., 2016 and Derouiche et al., 2017). On the other hand it has been demonstrated that inorganic lead selectively bound to proteins in some tissues and that disrupts protein function and may cause to interfere with calcium absorption results in weight loss (Valle and Ulmer, 1972).However, it may be contradictory matter in a few studies like weight gain after lead exposure shown by Gajawat et al., (2006) and Sharma et al (2011). In addition, treatment with coriander extracts (G3, G4, G5& G6) along with lead acetate exhibited increase in body weight, compared to relevant lead acetate treated group. On the other hand, supplementation of antioxidant plant extracts which have therapeutic activities may help to recover the body weight loss, that documented by Sharma et al., (2011), Reckziegel et al., (2016), Derouiche et al., (2017) and Kajal & Singh (2019).

4.2 Effect on Hematology

Hematological study is the basic and an important diagnostic tool in medicine for disease diagnosis and has also been found valuable to monitor stress due to environmental toxicants (Sharma et al., 2010). From its contact with every body system, the blood will reflect many physiological changes of the organs andit is a readily accessible tissue to collect and analyze (Duncan et al., 2003). The effect of administration of lead acetate alone or with coriander extracts (aqueous and ethanolic) on red blood cell and white blood

cell parameters in control and experimental groups are illustrated in Table 2,3, 5&6. On the other hand, Table 4&7 showed the correlation between these parameters. A complete blood count is a good indicator of general health, stress and numerous illnesses can modify haematological parameters especially with regard to erythrocyte and lymphocyte counts (Hinton et al., 1982). The results indicated that alterations were observed in the experimental groups and revealed that there were significant differences (P>0.05) between the mean values of HB(haemoglobin), RBCs (red blood cells), Hct(hematocrit),MCH(mean corpuscular haemoglobin), MCHC(mean corpuscular hemoglobin concentration) and PLT (platelets count) and WBCs (white blood cells)but the mean corpuscular volume (MCV) differences were not significant when compared with the mean values of the lead group. The reduction in the RBCs might be due to the decreased life span of erythrocytes, increased fragility of erythrocytes and inhibitory effect of lead on erythrocyte enzymes (MuGahi et al. 2003,Jesuorsemwenet al., 2016, Ganim et al., 2017).Furthermore, the toxic action produced by lead might be attributed to its ability to generate reactive oxygen species which induce oxidative damage of the circulating blood cells leading to their breakdown and suppression of blood forming cells (Ivaicoli *et al*., 2003).Lowered RBCs count, decreased MCH and MCV are other concordant hematological change were found in the group which lead acetate was administrated. Meanwhile that may be due to that lead once absorbed into systemic blood flow, more than 95% of it is associated with erythrocytes mainly in cellular membrane or hemoglobin. Therefore, erythrocytes are considered as a prime target for Pb toxicity (Goyer et al., 2001). On the other hand, Pb denatures cellular protein and lipid components of erythrocytes and impairs the synthesis of hemoglobin. In addition, a variety of toxic responses can be induced in erythrocytes by Pb such as lipid peroxidation and oxidative stress. Our current findings were agreement with many previous studies (Helmy et al., 2000, Simsek et al., 2009,Abd El Kader et al., 2012 and Donia 2019). Moreover, the interaction of toxic substances with red blood cells may affect their Hb carrying capacity, consequently lowering Hb content(Abbas et al., 2017).Furthermore, Ancheva et al. (2003) illustrated that lead causes damage to the erythrocytes membrane resulting in hemolysis or decrease of blood iron level which maybe the cause of decreased concentration of Hb and PCV. Meanwhile, Othman *et al*., (2004)return the reason for lower count of RBCs and PCV in Pb acetate treated rats to lower level of erythropoietin -an essential hormone for red cells production and that has supported to our study.The platelet counts may decrease either due to bone marrow suppression or when they are trapped in the spleen (Abbas et al., 2017).RBCs reduction could be induced directly by the suppressive effect of lead on hematopoietic organ, which impairs erythropoiesis or could be attributed to binding of lead to RBCs that resulted in the increased erythrocyte membrane fragility, leading to accelerated erythrocyte destruction (Abdelhamid et al., 2020).Our observation dissimilar to Yagminas et al., (1990), Alwaleedi, (2016) who found that platelets count revealed a considerable increase in the intoxicated animals compared with the control one and explain that may be because of thrombocytopenia after lead intoxication followed by thrombocytosis. On the other hand, the highest total leukocyte count was recorded in control group and a significant (P<0.05) decline count in lead treated group and a significant improvement in coriander extracts groups. Alterations were observed between the experimental groups and there was significant difference (P<0.05) among the leukocyte differentials examined (neutrophils, eosinophils, bosinophils, lymphocytes and monocytes) when compared with the mean values of the lead group. Our finding were in accordance with previous studies(Suradkar et al., 2009, Abd El Kader et al., 2012& Ibrahim et al., 2012)who recorded decrease in WBCs following exposure of lead acetate in rats and they has been interpreted this either by directly related with their decreased production from the germinal center of lymphoid organs or increased lysis due to presence of lead in the body. It worth mentioned that, reduction in blood parameters could also be due to hemolysis and hemorrhages caused by lead toxicity and bone marrow suppression and stress in the treated animals. In the same context lead suppresses bone marrow hematopoiesis, probably through its interaction with the enteric iron absorption (Chmielnika and Nasiadek 1994). The lack of WBC impairs the body's ability to fight infections (Sharma, et al., 2010 and Abbas et al., 2017). Meanwhile, an opposite trend was observed by Yagminas et al., (1990),Alwaleedi, (2016), Jesuorsemwenet al., (2016) and Pagrut et al., (2018) for WBCs as noted by us. They have been reported that lead induced inflammation which lead to increasing in white blood cells.

4.3 Effects on biochemical parameters

To assess the effect of lead acetate alone or with coriander extracts on biochemical parameters, the activities of serum total protein, albumin, globulins, albumin/globulin ratio and total bilirubin were investigated and illustrated in Table7 and the correlation between these parameters illustrated in Table8. Oral administration of lead acetate (G2) showed significant decrease (P>0.05) in serum Tp, Alb and Glb but significant increase (P>0.05) in T.bilir. levels as compared to control group. On the other hand, the treatment with coriander extracts restored approximately normal levels of all the aforementioned parameters compared to lead group. This protective effect was more pronounced in rabbits supplemented with ethanolic extract of plant in group5 and 6. On the other hand, protective action of coriander against lead toxicity could be attributed to the antioxidant action of its component but the observed decrease in G2 Tp, Alb & Glb may be attributed to activation of anabolism of protein due to lead toxicity which affected on the enzyme of anabolism process (Karamala et al., 2011and Nabil et al., 2012& El Shater et al. 2019). In addition, this reduction may be attributed to reduced protein synthesis as a result of lead renal and hepatic toxicity which conduct to liver damage which responsible for protein synthesis in the body. Generally, this has been confirmed by Duncan1996 who stated that decreases of total protein occur in kidney or liver diseases. From another view, lead toxicity causing stress and destruction of muscles and that leading to decrease of proteins in tissue, the reduction in stress proteins can be affected by the inability to absorb food (Fatemeh et al., 2016, Alrawi et al., 2017).According to bilirubin, it is a reddish-yellow pigment which is produced during the normal breakdown of RBC. Total bilirubin includes both the conjugated and unconjugated (free) forms and if elevated that is usually indicative of liver damage or hemolysis. In addition, elevated of total bilirubin may be recognized by a visible yellow coloration of the plasma (Turcu-Stiolica & Sambandan, 2019).The findings of

this study also indicate a significant elevation (P<0.05) in serum bilirubin following with the administration of lead acetate (G2) may be because of induction of heme oxygenase that plays an important role in heme catabolism and can convert heme to bilirubin, this suggestion agrees with (Seddik et al.,2010, Alwaleedi, 2016, El Shater et al. 2019). It is worth noting that G3, G4, G5& G6 have shown some improvement of serum bilirubin compared to G2. That may be linked to the protective effect of coriander extracts administrated to these groups.

Table (1): Effect of lead acetate alone or with coriander extracts on body weight of control and experimental groups.

Group	Initial b.w.(g)	Final b.w.(g)	Body weight gain	% Change in b.w.
G1	834.38±6.716	1636.57^{a}±9.905	802.19^{a}±10.357	96.18^{a}±1.734
G2	834.37±6.716	1245.26^{e}±9.905	410.89^{e}±10.357	49.23^{d}±1.734
G3	833.29±6.716	1426.46^{d}±9.905	595.08^{d}±10.357	71.52^{c}±1.734
G4	821.38±6.716	1533.53^{c}±9.905	706.20^{c}±10.357	84.20^{b}±1.734
G5	833.10±6.716	1541.43^{bc}±9.905	708.33^{c}±10.357	85.05^{b}±1.734
G6	817.30±6.716	1564.54^{b}±9.905	747.24^{b}±10.357	91.47^{a}±1.734

Values are expressed as mean± standard error. Means with different superscripts in the same column are significantly different at P<0.05.b.w.(g):body weight (gram)

Table (2): Effect of lead acetate alone or with coriander extracts on red blood cell parameters of control and experimental groups.

Groups	HB (g/dl)	RBCs (mill/cu.mm)	HCT(%)	MCV (FL)
G1	13.24^{ab}±0.362	4.82^{a}±0.152	41.71^{b}±0.730	322.37^{a}±94.067
G2	10.72^{d}±0.314	4.15^{b}±0.131	31.85^{d}±0.632	70.65^{a} ±81.465
G3	11.66^{cd}±0.362	4.50^{ab}±0.152	33.77^{cd}±0.730	78.83^{a} ±94.067
G4	11.87^{c}±0.362	4.59^{ab}±0.152	33.69^{cd}±0.730	78.46^{a} ±94.067
G5	12.39^{bc}±0.362	4.82^{a}±0.152	34.83^{c}±0.730	87.46^{a} ±94.067
G6	13.91^{a}±0.362	4.72^{a}±0.152	45.53^{a}±0.730	87.77^{a} ±94.067

Values are expressed as mean± standard error. Means with different superscripts in the same column are significantly different at P<0.05. Hb: hemoglobin, RBCs: Red blood cells, Hct: Hematocrit, MCV, mean corpuscular volume.

Table (3): Effect of lead acetate alone or with coriander extracts on red blood cell parameters in control and experimental groups.

Groups	MCH (pg)	MCHC (g/dl)	PLT (/cmm)
G1	28.21^{b}±0.549	33.95^{a}±0.344	225.00^{ab}±19.618
G2	23.66^{d}±0.475	30.91^{b}±0.298	133.75^{c}±16.989
G3	26.31^{c}±0.549	33.82^{a}±0.344	181.67^{bc}±19.618
G4	26.25^{c}±0.549	34.05^{a}±0.344	191.67^{abc}±19.618
G5	29.29^{ab}±0.549	34.77^{a}±0.344	206.33^{ab}±19.618
G6	30.05^{a}±0.549	34.80^{a}±0.344	248.33^{a}±19.618

Values are expressed as mean± standard error, means with different superscripts in the same column are significantly different at P<0.05. MCH: mean corpuscular hemoglobin, MCHC: mean corpuscular hemoglobin concentration, PLT: Platelet Count.

Table (4): The correlation between red blood cell parameters

	Hb	RBCs	Hct	MCV	MCH	MCHC	PLT
Hb	1						
RBCs	0.81	1					
	<.0001						
Hct	0.87	0.51	1				
	<.0001	0.0249					
MCV	0.26	0.22	0.35	1			
	0.2849	0.3564	0.1362				
MCH	0.84	0.70	0.76	0.19	1		
	<.0001	0.0009	0.0002	0.4425			
MCHC	0.75	0.77	0.52	0.05	0.80	1	
	0.0002	0.0001	0.0219	0.8515	<.0001		
PLT	0.90	0.79	0.74	0.18	0.79	0.78	1
	<.0001	<.0001	0.0003	0.4548	<.0001	<.0001	

Table (5): Effect of lead acetate alone or with coriander extracts on white blood cell parameters in control and experimental groups.

Groups	WBCs (%)	Neut staff (%)	Neut_Segm (%)
G1	10.90^{cb}±0.717	1.09^{b}±0.531	65.19^{ab}±5.340
G2	6.71^{a}±0.717	0.59^{a}±0.531	42.81^{a}±5.340

G3	7.90^{b}±0.717	2.62^{ab}±0.531	50.10^{ab}±5.340
G4	10.00^{cb}±0.717	1.42^{b}±0.531	52.98^{b}±5.340
G5	9.70^{cb}±0.621	1.52^{b}±0.460	54.70^{b}±4.625
G6	10.70^{c}±0.621	2.32^{ab}±0.460	52.18^{b}±4.625

Values are expressed as mean± standard error. Means with different superscripts in the same column are significantly different at P<0.05. WBCs: white blood cells. Neut: neutrophils

Table (6): Effect of lead acetate alone or with coriander extracts on white blood cell parameters in control and experimental groups.

Groups	Eosinophils (%)	Bosinophils (%)	Lymphocytes (%)	Monocytes (%)
G1	2.46^{b}±0.432	0.40^{a}±0.247	17.47^{c}±2.251	3.33^{cb}±0.518
G2	1.01^{a}±0.432	0.20^{a}±0.247	11.39^{a}±2.251	1.40^{a}±0.518
G3	2.41^{b}±0.432	1.14^{ab}±0.247	26.99^{b}±2.251	4.50^{b}±0.518
G4	2.72^{b}±0.432	0.75^{ab}±0.247	21.50^{cb}±2.251	3.05^{cb}±0.518
G5	2.56^{b}±0.374	0.69^{ab}±0.214	21.73^{cb}±1.950	3.09^{cb}±0.449
G6	2.28^{b}±0.374	0.65^{ab}±0.214	18.69^{c}±1.950	2.15^{c}±0.449

Values are expressed as mean± standard error. Means with different superscripts in the same column are significantly different at P<0.05.

Table (7): The correlation between white blood cell parameters

	WBCs	Neut_staff	Neut_Segm	Eosinophils	Bosinophils	Lymphocytes	Monocytes
WBCs	1						
Neut_staff	0.79302	1					
	<.0001						
Neut_Segm	0.81784	0.68987	1				
	<.0001	0.0008					
Eosinophils	0.85565	0.69527	0.59726	1			
	<.0001	0.0007	0.0054				
Bosinophils	0.65475	0.77212	0.61159	0.45879	1		
	0.0017	<.0001	0.0042	0.0419			
Lymphocytes	0.8825	0.72371	0.72375	0.70025	0.71019	1	
	<.0001	0.0003	0.0003	0.0006	0.0005		
Monocytes	0.9706	0.73447	0.83643	0.81571	0.6188	0.90438	1
	<.0001	0.0002	<.0001	<.0001	0.0036	<.0001	

Table (8): Effect of administration of lead acetate alone or with coriander extracts on biochemical parameters.

Group	Alb. (mg/dl)	T.Pro. (mg/dl)	Glb. (mg/dl)	A/G ratio (%)	T.Bilir.((mg/dl)
G1	2.87^{a}±0.149	6.03^{a}±0.226	3.16^{a}±0.077	0.0316	0.95^{b}±0.061
G2	2.05^{b}±0.129	5.05^{b}±0.196	3.0 ^{b} ±0.067	0.0300	1.25^{a}±0.053
G3	2.57^{a}±0.139	5.60^{ab}±0.225	3.03^{a}±0.086	0.0303	0.96^{b}±0.061
G4	2.83^{a}±0.137	5.73^{a}±0.216	2.90^{a} ±.079	0.0290	0.91^{b}±0.061
G5	2.98^{a}±0.129	5.90^{a}±0.196	2.92 ^{a} ±.067	0.0292	0.86^{b}±0.053
G6	2.93^{a}±0.129	5.80^{a}±0.195	3.41 ^{a} ±.066	0.0341	0.94^{b}±0.053

Values are expressed as mean± standard error. Means with different superscripts in the same column are significantly different at P<0.05. Alb.: albumin, T. Pro. Total Protein, Glb.: Globulins , A/G ratio: Albumin/Globulin ratio and T.Bilir. (Total bilirubin)

Table (9): The correlation between biochemical parameters.

	Alb	T._Pro.	Bilir.
Alb	1		
T._Pro.	0.87082	1	
	<.0001		
Bilir.	-0.59702	-0.44524	1
	0.0043	0.0431	

4.4 Histology of heart tissue

4.4.1Control and lead acetate exposed animals (G1 and G2)

Several epidemiological and clinical studies have found a link between chronic lead exposure and elevated blood pressure& cardiovascular disorders (Navas-Acienet al., 2007). The effect of lead acetate alone and ameliorating effect of coriander extracts individually during lead exposure on heart histology images of experimental rabbits of various groups were examined (Figure 1-6). The histological examination of control group (G1) (untreated animals) showed normal architecture of heart (normal cardiac muscles, normal striations and normal nucleation) Figure1.While examination of group 2 reveals some variations relative to the control group,Figure2a&bshowing diffuse leucocytic cells infiltrations in between the myocardial muscle (arrow) and dilated and congested blood vessel with thickened wall (arrow), respectively. In accordance with Owolabi et al, 2017 who study the effect of lead poisoning on vital body tissues histology in Wistar rats and found that nuclei of several cardiac muscle cells are deformed and heterogeneous, a few cells appear unusually thin and elongated and there are unusual clusters of cells that appear to have unusual morphology as well. Furthermore, lead poising has been linked with cardiovascular disorders and produces cardiotoxic effects (Vaziri and Gonick 2008). Environmental toxicants including lead and other metals are potentially preventable exposures that may explain population variation in cardiovascular disease rates (Bhatnagar 2006). In this context Saad et al., (2018) mentioned that the heart of both sexes of aluminium chloride intoxicated rabbits showed congestion of blood vessels, interfibrillar edema, hemorrhage and necrosis of myocardium.

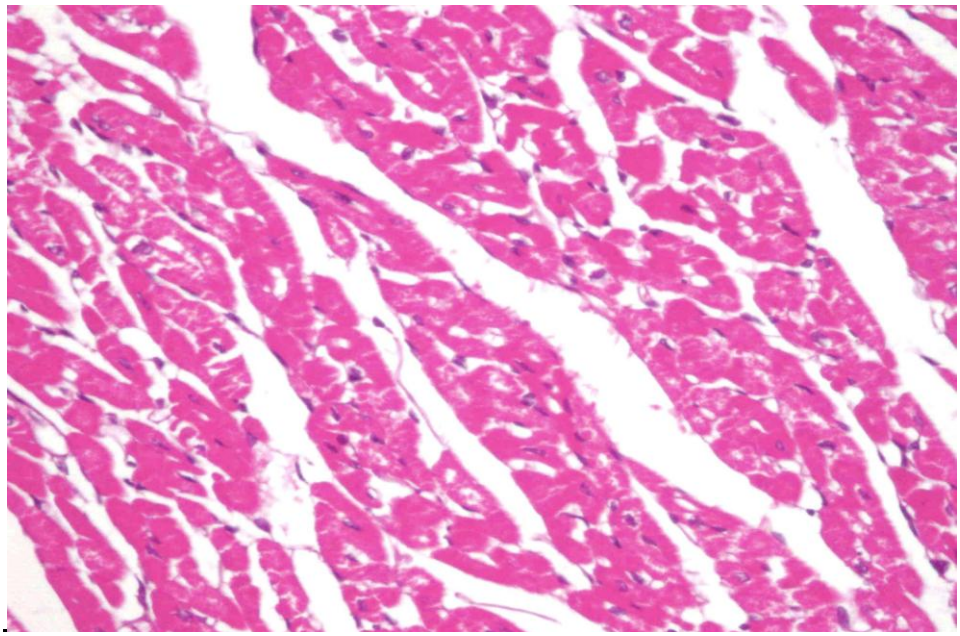

Figure (1): T. S. of heart of rabbit control group (H&E X 400). (lesion score 0).

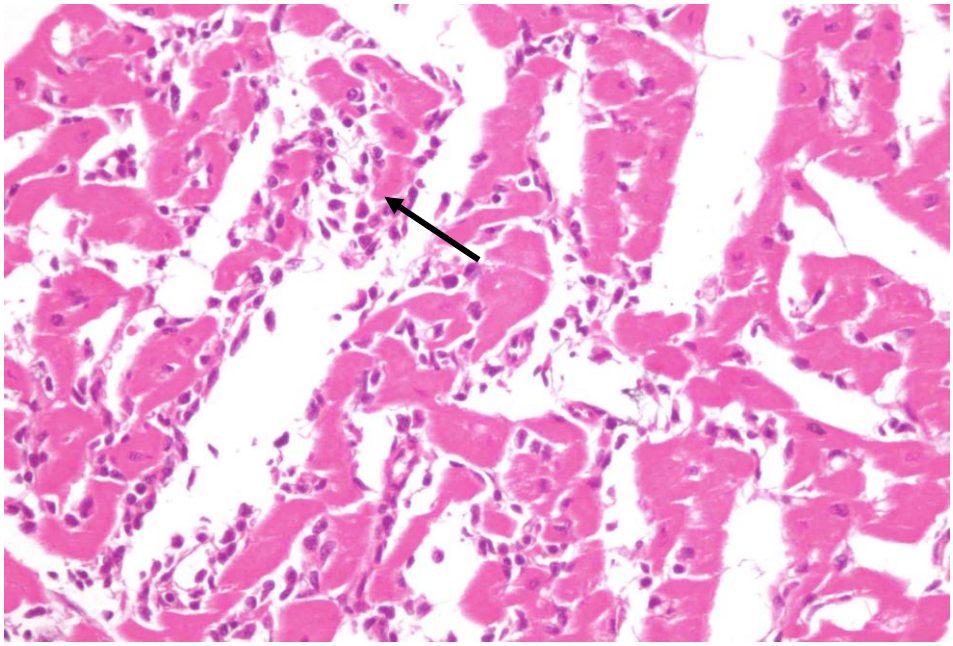

Figure (2 a): *T. S. of heart of rabbit treated with lead acetate. (lesion score +++)*

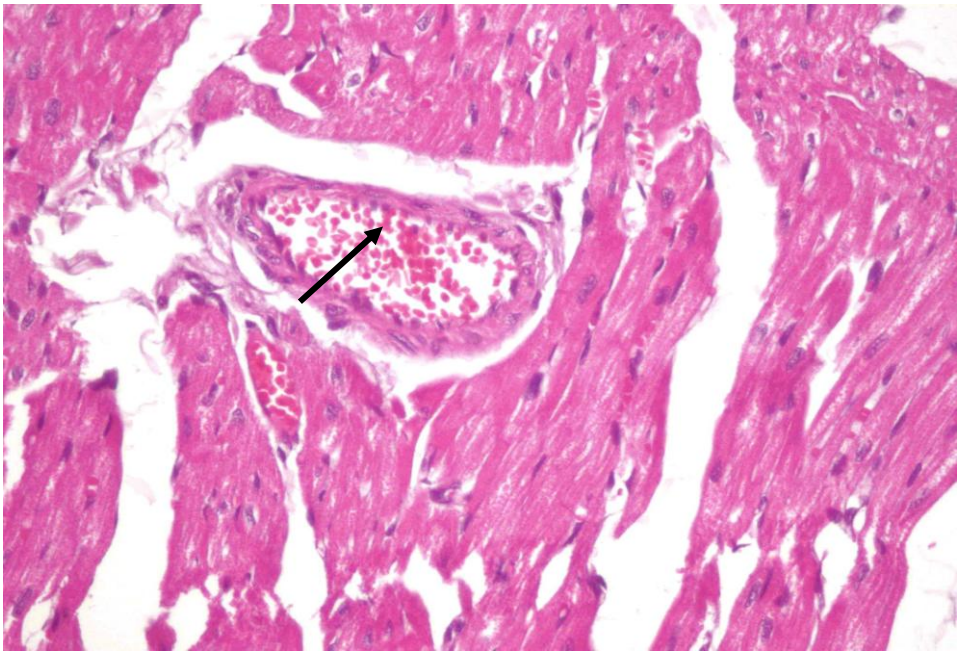

Figure (2b): T. S. of heart of rabbit treated with lead acetate, (H&E X 400). (lesion score +++)

4.4.2 Group 3, 4 (lead acetate + aqueous extract of coriander) and group 5 and 6 (lead acetate + ethanolic extract of coriander)

Animals treated with lead and coriander extracts showed that most of these histopathological changes were diminished, animals treated with lead and aqueous coriander extract at a dose of 300 mg/ kg b.w. showed cardiac muscles together with dilated and congested blood vessel with thickened wall (arrow) Figure3. Meanwhile, at a dose of 600 mg/ kg b.w. showed regression in the leucocytic cells infiltrations in between the myocardial muscle (arrow) Figure4. Furthermore, animals treated with lead and ethanol coriander extract at a dose of 250 mg/ kg b.w. showed focal hemorrhagic areas (arrow) in between the myocardial muscles Figure5. On the other hand animals treated with lead and ethanol coriander extract at a dose of 500 mg/ kg b.w. showed approximately normal cardiac muscles, note the normal striations and normal nucleationFigure6. In light of what was aforementioned in high doses groups, the heart tissue restored most of its normal structure. Various medicinal plants have extraordinary potential to treat cardiac diseases with better efficacy and safety (Rehman et al., 2016). It worth mention that many researchers have been interested in the protective effects of coriander extracts against various pathological changes as Patel et al., (2012) who found that isoproterenol induced cardiotoxicity in male Wistar rats and the coriander extract is potent in mitigating these myocardial necrosis and they concluded that hydro-methanolic coriander seeds extracts has cardioprotective potential, which is attributable to high polyphenol content in coriander seeds, Rehman et al., (2016) who investigate the anti-arrhythmic potential of coriander seeds against $BaCl_2$ induced tachycardia and KCl induced bradycardia and concluded that oral administration of coriander seeds can attenuate both type of cardiac arrhythmias. On the other hand, Quinones et al., (2013) and Zafar et al., (2015)mentioned that medicinal plants enriched with polyphenols, possessing free radical scavenging potential, may reduce the risk of heart diseases because of inverse relationship between cardiovascular diseases and intake of polyphenols. The later author found that histopathological examination of rabbit heart proved the safe cardioprotective potential of herbal combination. Moreover, the remedial effect of coriander extracts was also confirmed by Sharma et al., (2014) who concluded that the cardio protective effect of C. sativum seeds in high cholesterol diet induced atherosclerotic rabbits by preserving the membrane integrity. This might be due to the antioxidant effect of C. sativum which seem to be promising tools to explore as therapeutic agent in cardiovascular diseases. Our results of histopathological analysis are in line with the above finding.

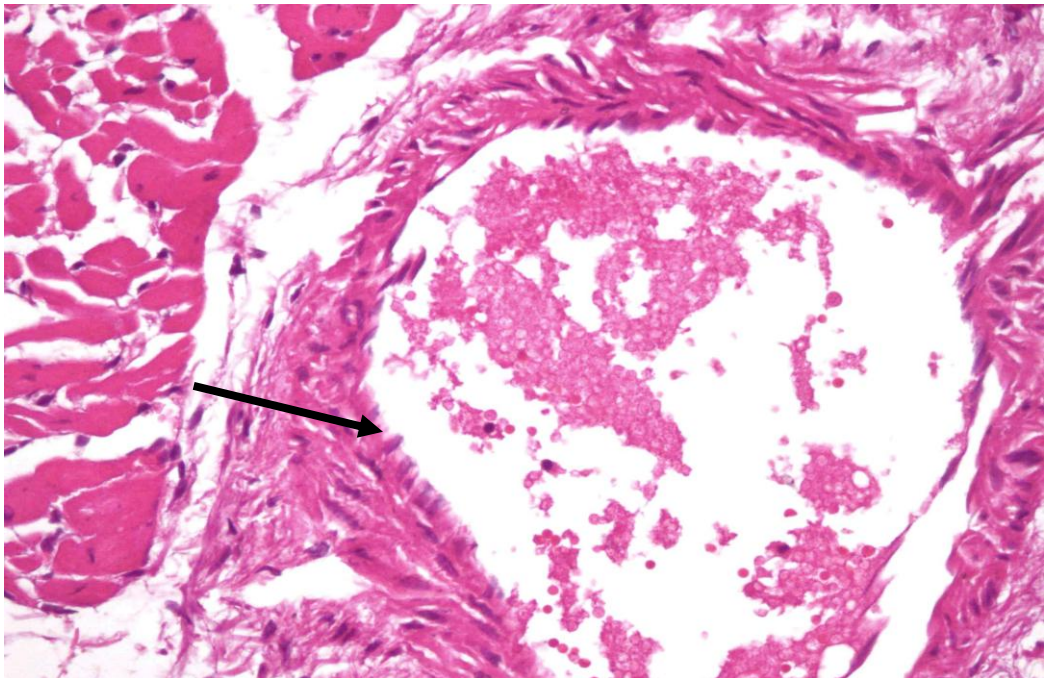

Figure (3): T. S. of heart of rabbit treated with lead acetate + aqueous extract of coriander at a dose of 300 mg/kg b.w., (H&E X 400), (lesion score ++).

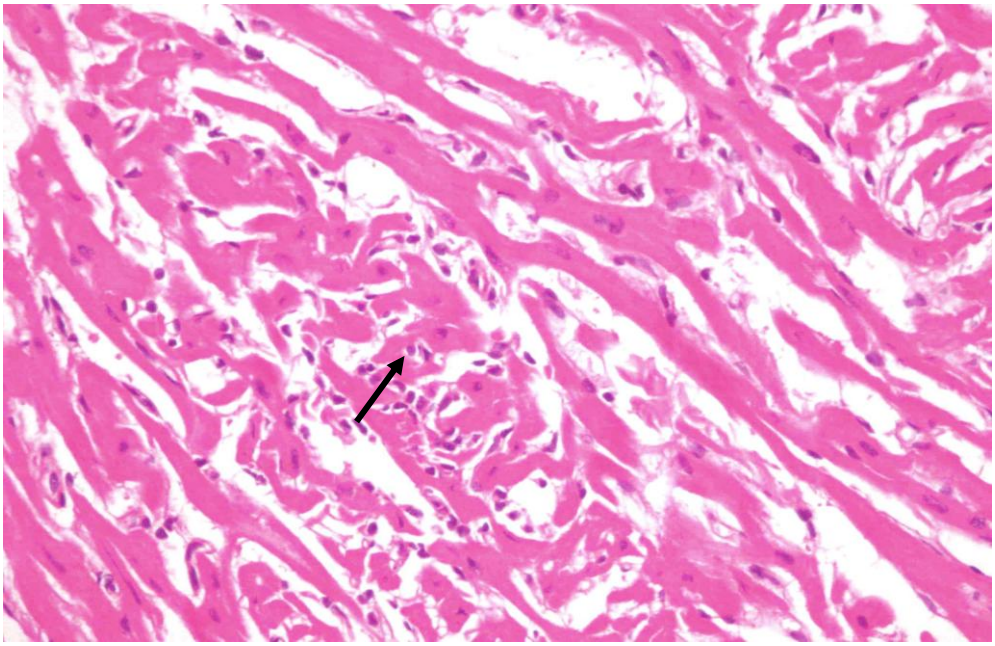

Figure (4): T. S. of heart of rabbit treated with lead acetate + aqueous extract of coriander at a dose of 600 mg/ kg b.w., ((H&E X 400), (lesion score +).

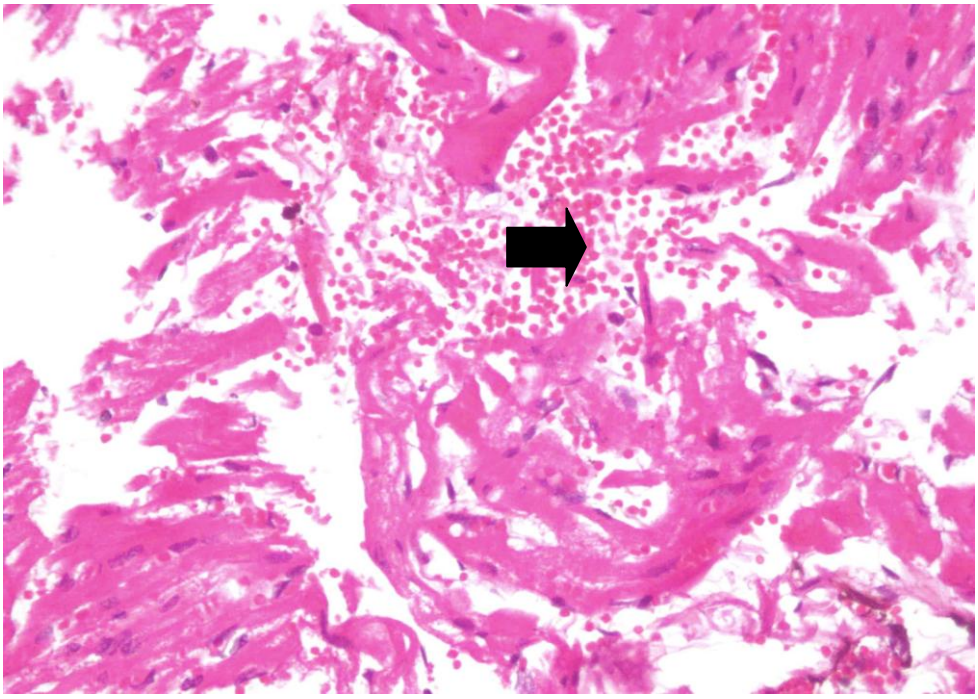

Figure (5): T. S. of heart of rabbit treated with lead acetate + ethanolic extract of coriander at a dose of 250 mg/ kg b.w., (, (H&E X 400), (lesion score +).

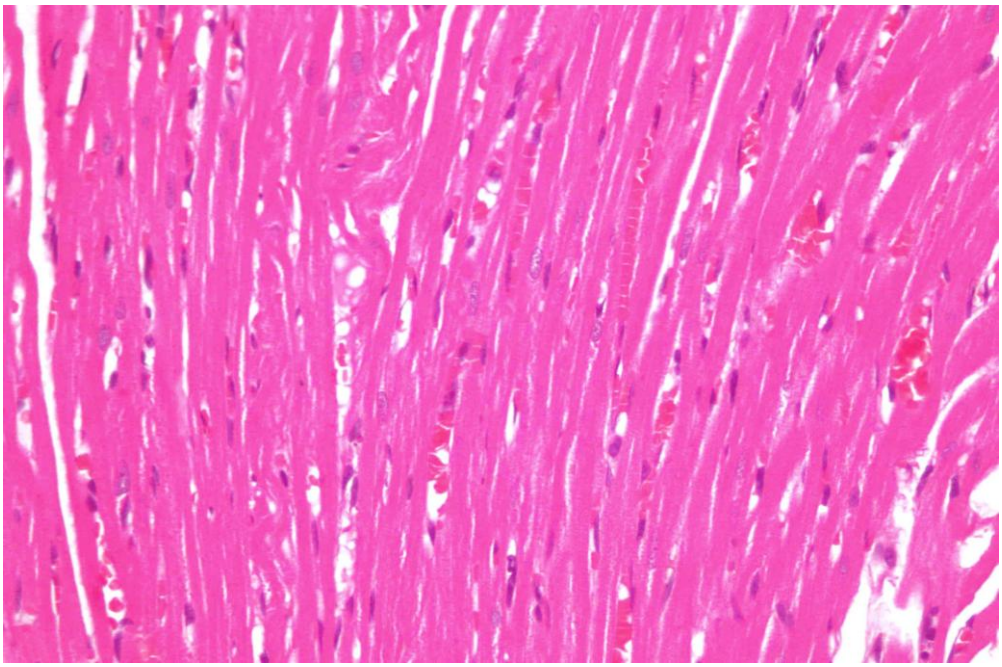

Figure (5): T. S. of heart of rabbit treated with lead acetate + ethanolic extract of coriander at a dose of 500 mg/ kg b.w., (H&E X 400), (lesion score 0).

4.5 Histology of lung tissue

4.5.1 Control and lead acetate exposed animals (G1 and G II).

Rabbits are often the species of choice as an experimental model for the study of pulmonary responses to long-term exposure to pollutants because there are multiple similarities between the rabbits and the human lungs in terms of anatomy, patterns of development, pulmonary function, and cellular composition (Alodeani and Makhlouf (2014). In consistent with the body weight,

heamatobiochemical and histology of heart tissue, the effect of lead acetate alone and ameliorating effect of coriander extracts individually during lead exposure on lung histologic images of experimental rabbits of various groups were examined (Figure 7-12). The histological examination of GI (untreated animals) showed normal architecture of lung (normal bronchi, bronchioles, and air alveoli and no lesions were observed) Fig.7.In contrast histopathology of lung tissue of lead acetate treated group showed considerable alterations, massive interstitial tissue reaction with thickening in the alveolar wall and mononuclear cells infiltrations (arrow head), together with thick walled blood vessel, hemorrhagic pneumonia in the form of filled alveoli with RBCs and lucocytic cells (arrow head) with formation of giant alveoli (arrows) (Fig.8a &b),respectively. Lead might reached to lung tissue through blood circulation and possibly caused pathological alteration in the lung. The present results are in line with the findings of Muselin et al., (2010) who showed that, in rats exposed to 1000, 2000, 3000 ppm of lead acetate for six months, lung histopathological evaluation showed compensatory alveolar emphysema, peribronchitis with septal proliferation and pulmonary edema. On the other hand, pulmonary toxicity of lead was studied in rats after an intraperitoneal administration of lead acetate at a dose of 25 mg/kg (Kaczyńska et al. 2011) who demonstrated that the effects of lead toxicity were observed in lung capillaries, interstitium, and alveolar lining layer. Accumulation of aggregated platelets, leucocytic elements and monocytes was found within capillaries.Furthermore, Kaczyńska et al., (2013) concluded that,long-term effects of Pb exposure to lung parenchyma induced fibrosis and elastosis of the tissue resulting in remodeling of the respiratory septa and essential changes in the structure of lamellar bodies of type II alveolar cells. Moreover, Alodeani and Makhlouf (2014) concluded that lead acetate has harmful effect on the lung alveoli of experimental male rabbits. Meanwhile, Jaiswal et al., (2017) studied the effect of lead intoxication on histopathology of lung broiler chicken and revealed degeneration, bronchopneumonia, pneumonia between the alveoli, hemorrhages, and hemosiderosis. Moreover, thickened alveoli wall due to accumulation of serofibrinous exudates inside the alveoli was also evident. In addition, rats treated with lead acetate 1, 100 and 1000 ppm in drinking water for 21 days revealed lesions in the lungs which were characterized by congestion, hemorrhage, emphysema and infiltration of mononuclear cells (Suradkar et al., 2010).

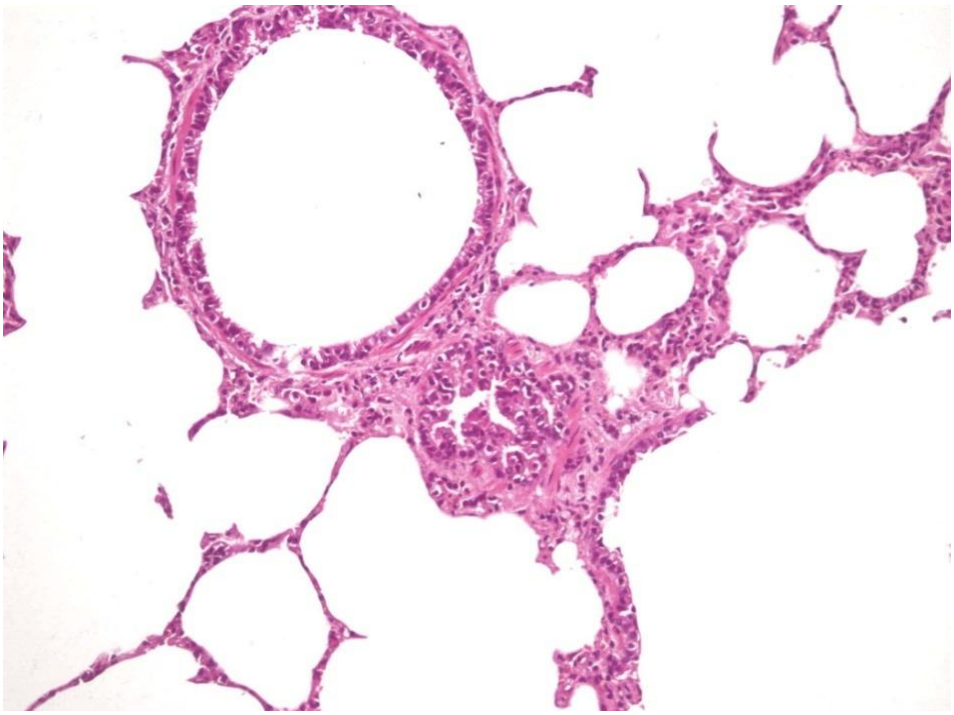

Figure (7): T. S. of lung of rabbit control group, (H&E X 400). (lesion score 0).

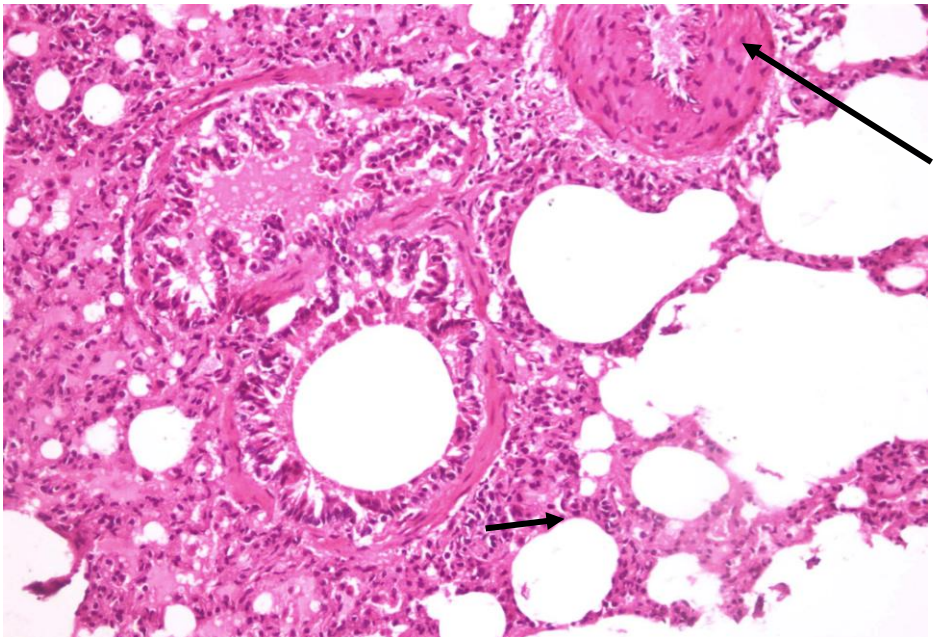

Figure (8 a): T. S. of Lung of rabbit treated with lead acetate (H&E X 200). (lesion score +++).

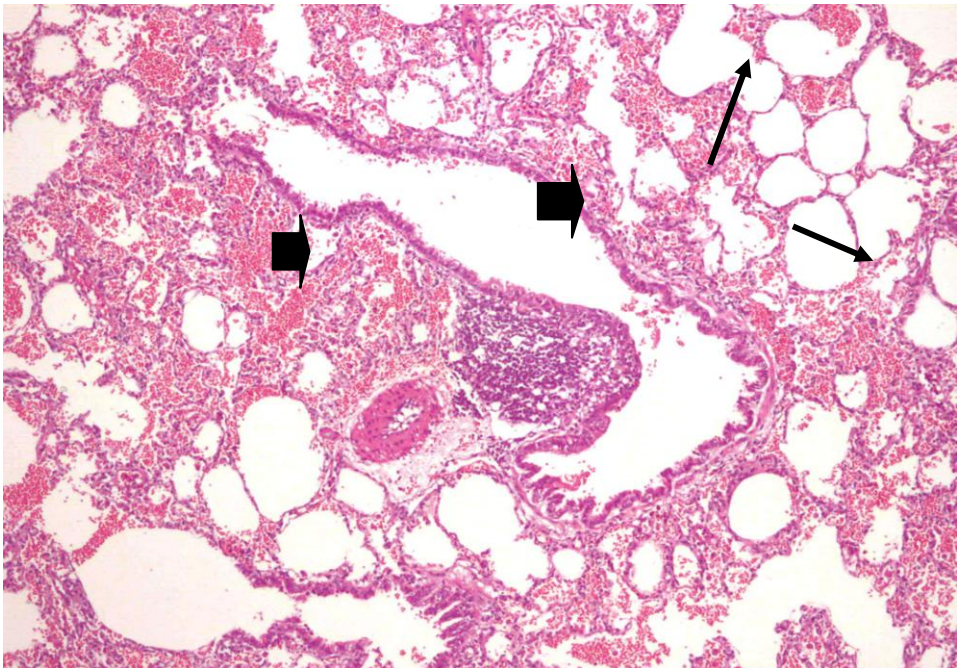

Figure (8b): T. S. of Lung of rabbit treated with lead acetate (H&E X 200). (lesion score +++).

4.5.2 Group 3& 4 (lead acetate + aqueous extract of coriander) and group 5 & 6 (lead acetate+ ethanolic extract of coriander).

We have tested the efficacy of the aqueous and ethanolic extracts of coriander against lead acetate-induced changes in the lung of rabbits. In the present study this treatment showed to some extent improvement and reduction in the histological of lung tissue changes (Fig. 9-12). Animals treated with lead and aqueous coriander extract at a dose of 300 mg/ kg b.w. showed diffuse edema in the form of pinkish fluid inside the lumen of most of the alveoli (arrows) Fig.9. Meanwhile, at a dose of 600 mg/ kg b.w. showed marked regression in the alveolar edema with slight peribronchial mild inflammatory reaction (arrows) Fig.10. Furthermore, animals treated with lead and ethanol coriander extract at a dose of 250 mg/ kg b.w. showed peribronchial inflammatory reaction in the form of massive leucocytic cells infiltrations (arrow) Fig.10. In addition, animals treated with lead and ethanol coriander extract at a dose of 500 mg/ kg b.w. showed nearly normal bronchi, bronchioles, and a considerable degree of preservation of air alveolar architecture Fig.10.Moreover, medicinal plants are used to treat various diseases, *Coriandrum sativum* is one of the most commonly plants that is used to treat several physiological disorders and its extracts have phenolic and flavonoids compounds, suggesting that these compounds contribute to the antioxidative activity and suppresses the deposition of lead by chelating the metal moreover, coriander

showed excretion of heavy metal (Aga et al., 2001, Velaga et al., 2014 and Tellez-lopez et al., 2017). This could explain the improvement in histological changes in the lung of animals treated with aqueous and ethanolic coriander extracts. Plant extracts have potential chelation effect on some metal, preventing or reversing the damage caused by lead in various tissues. Some studies in mice, rats and rabbits intoxicated with different concentrations of lead and treated with coriander show very encouraging results chelation and reduction poisoning in these animal models (Velaga et al., 2014 and Tellez-lopez et al., 2017 and Donia, 2019).In this same context, Alodeani and Makhlouf (2014)concluded that garlic can decreased the damage of lung alveoli from oxidative stress induced by lead acetate. It worth mention that, heart and lung histopathological findings of the present study suggested that co treatment with low doses of aqueous and ethanolic coriander extracts partially improved these alterations, while co treatment with high doses exhibited approximately full protection and more protective role and markedly reduced tissues damage induced by lead acetate.

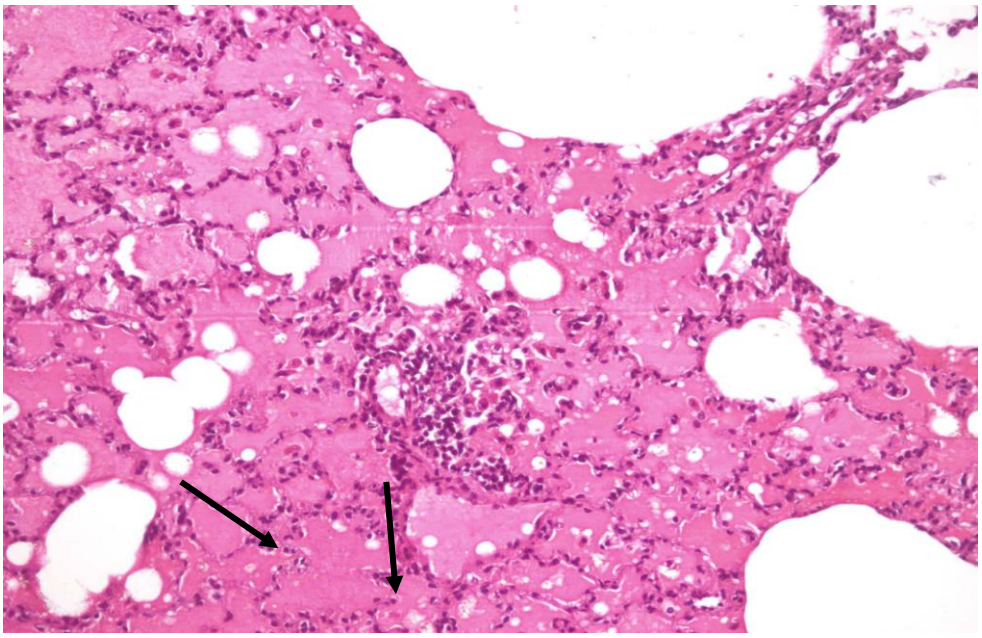

Figure (9): T. S. of Lung of rabbit treated with lead acetate + aqueous extract of coriander at a doseof 300 mg/ kg b.w., (H&E X 200). (lesion score ++)

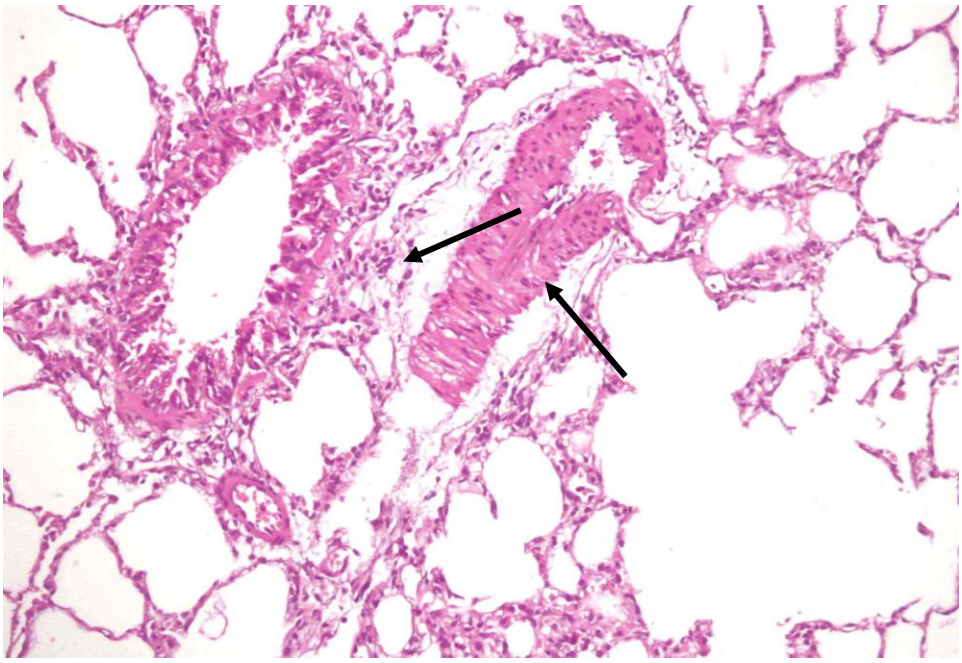

Figure (10): T. S. of Lung of rabbit treated with lead acetate + aqueous extract of coriander at a dose of 600 mg/ kg b.w., (H&E X 200). (lesion score +)

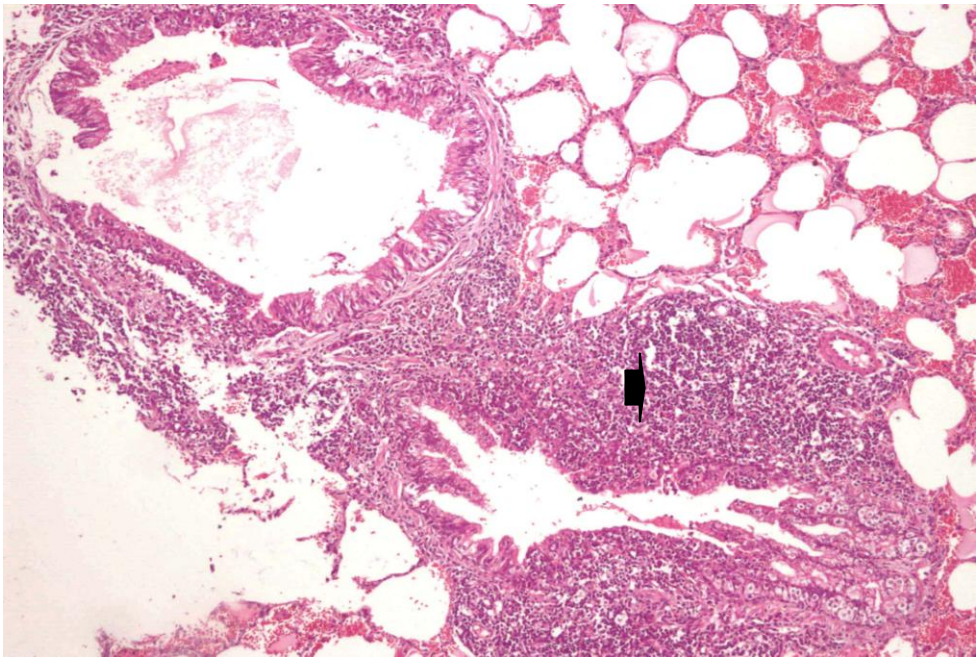

Figure (11): T. S. of Lung of rabbit treated with lead acetate + ethanolic extract of coriander at a dose of 250 mg/ kg b.w., (H&E X 200). (lesion score +)

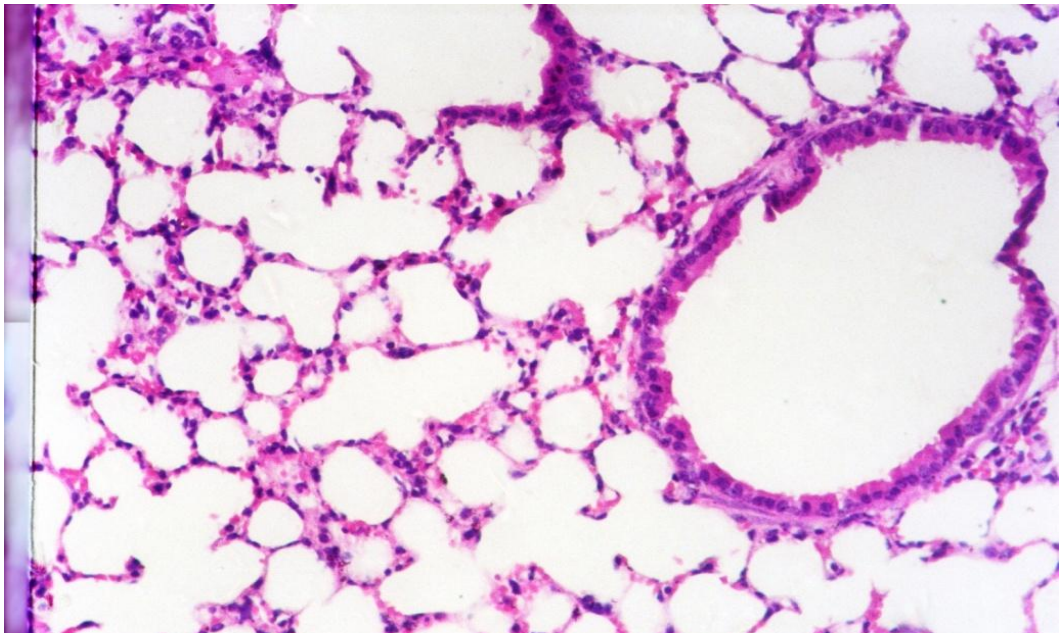

Figure (12): T. S. of Lung of rabbit treated with lead acetate + ethanolic extract of coriander at a dose of 500 mg/ kg b.w., (H&E X 200). (lesion score 0)

5. CONCLUSION

It can be concluded that lead is one of the main persistent and common environmental pollutants. It has harmful effect on experimental male rabbits and induced body weight, hematological and biochemical alterations. Lung and heart tissues also showed histopathological alterations. Coriander aqueous and ethanolic seeds extracts exhibited a significant ameliorative effect, especially at high doses against lead toxicity and can decreased the damage induced by lead. *Coriandrum sativum* possessed a significant protective and therapeutic values.

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