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Original article

Toxic Effect of Deltamethrin on Some Hematological and Biochemical Parameter of Male Rats

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ABSTRACT

Background and aims*. Deltamethrin (Dm) is a synthetic pyrethroid insecticide used worldwide in agriculture, home pest control, protection of foodstuff and disease vector control. The aim of this study was to investigate the propensity of deltamethrin to induce oxidative stress and changes in hematology, biochemical parameters and teratogenic effect in male rats.* ***Methods****. Fifteen adult male albino Wistar rats were divided into three groups Group 1 served as control and received distilled water orally. Group 2 received DM 1/10 LD 50 (0.6 mg/kg BW) orally for 30 days, and Group 3 received DM 1/20 LD 50 (0.3 mg/kg BW) orally for 30 days.* ***Results****. Deltamethrin caused significant changes of some hematological parameters (red blood cells (RBC), hemoglobin (Hb), hematocrit (PCV), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC) and white blood cells (WBC)) in treated rats compared to controls. Significant increases in the levels of hepatic markers enzymes (alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP). Furthermore, renal markers such as urea and creatinine were increased in deltamethrin treated rats.* ***Conclusion****. deltamethrin is harmful on animal and human health.*

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INTRODUCTION

Deltamethrin (De) is a synthetic pyrethroid insecticide widely used in crop production, forestry, and household activities [1]. Technical grade deltamethrin consists of eight stereoisomeric esters (four cis and four trans isomers) of 2,2-dimethyl-3-cyclopropanecarboxylic acid, a dibromo analog of chrysanthemum acid. It is widely used in agriculture and forestry because of its high activity against many types of insects [2]. It is also used as an alternative pesticide in malaria control programs in India and other developing countries [3].

Deltamethrin is known to be toxic to fish and some aquatic animals [2]. Adverse effects on the nervous, hematological, and respiratory systems of De have been reported [4], and biochemical and histopathological effects at low and high concentrations have also been documented [5]. Biochemical and histopathological effects in several organs after single LD50 dose levels in rats have also been reported [6].

Humans and animals are simultaneously exposed to multiple chemicals in the environment from a variety of sources. However, relatively few studies have evaluated the degree of hazard posed by simultaneous exposure to toxic chemicals, especially at low doses [7]. Therefore, in this study, we determined the median oral lethal dose of deltamethrin dissolved in distilled water and investigated the subacute toxicity (30 days) of deltamethrin in distilled water using rats.

METHODS

Chemical Substance

Deltamitrin, a synthetic pyrethroid insecticide (C22H19Br2NO3), purchased from Al-feda, Amman-Jordan, CAS chemical name (a-cyano-3-phenoxybenzyl(1R,3R)-3-(2,2-dibromovinyl)-2,2- dimethylcyclopropanecarboxylate) was administered to male Wistar rats.

Animals

Fifteen (150-160 g) adult male albino Wistar rats were obtained from a barn. Animals were handled under standard experimental conditions of a 12-hour light/dark cycle in a temperature- and humidity-controlled room. Water and feed were provided.

Rats were randomly divided into three groups of five animals each (n=5). Group 1 served as control and received distilled water orally. Group 2 received DM 1/10 LD 50 (0.6 mg/kg BW) orally for 30 days, and Group 3 received DM 1/20 LD 50 (0.3 mg/kg BW) orally for 30 days.

Blood samples

Blood samples were collected 30 days after administration. One sample was collected in an Eppendorf tube and mixed with dipotassium salt of EDTA as anticoagulant (0.5 mg/ml blood) for hematological examination; the second blood sample was collected in a clean centrifuge tube. Samples were allowed to incline at room temperature for 20 minutes and then placed in a refrigerator to avoid glycolysis and to contract clots. The samples were then centrifuged at 3000 rpm for 10 minutes, and clear serum samples were carefully separated and collected and stored at -20°C in Eppendorf tubes until serum biochemistry was estimated. In addition, liver and kidney tissue samples were collected for histopathological studies.

Hematological studies

Red blood cell count, hemoglobin concentration, filled cell volume, mean volume, mean body hemoglobin, mean body hemoglobin concentration, platelet count, white blood cell count and differential white blood cell count were detected by manual methods according to previous study [8].

Serum Biochemical Analysis

Serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were detected spectrophotometrically (BM Co.) using a ready-made kit (Randox, Co. UK) according to previous study [9]. Alkaline phosphatase (ALP) was measured according to [10] (ELTech kits, Co. France).

Urea, total protein, albumin, globulin, and creatinine were measured according to methods described in previous studies [11-15] using ready-made kits (Diamond Co. Egypt, Stanbio laboratory USA.) using spectrophotometry.

Histopathological studies

Liver and kidney specimens were fixed in 10% neutral buffered formalin. Five-micron thick sections were prepared from all specimens, stained with hematoxylin and eosin (H and E), and examined microscopically according to earlier report [16].

Statistical Analysis:

All data were statistically analyzed using statistical software program (SPSS for Windows, version 20, USA). Means and standard error for each variable were estimated. Differences between means of different groups were carried out using one way ANOVA with Duncan multiple comparison tests, dissimilar superscript letters in the same column show a significance difference if P value was statistically lower than ($P<0.05$).

RESULTS

Hematological results

The red blood cells, Packed cell volume (pcv), hemoglobin concentration (Hb%), Mean Corpuscular Hemoglobin Concentration (MCHC) and mean corpuscular volume (MCV), were significantly decreased($P<0.05$) in treated 1/10 LD50 and 1/20 LD50 doses deltamethrin as compared to control group.

Also, the total leucocytic count (TLC) was significantly decreased ($P<0.05$) in treated groups compared with control one (table 1) figures from (1) to (6) respectively.

Table 1. Hematological result of deferent groups.

Parameter	Control	1/10LD50 deltamethrin	1/20LD50 deltamethrin
RBCs 10^6 µl	7.41± 0.04[a]	7.21 ± 0.05[b]	6.12 ± 0.08[c]
PCV %	51 + 1.3[a]	35.3 ± 0.33[b]	31.8 ± 0.46[c]
Hb g/dl	17.68 ± 0.38[a]	11.05± 0.16[b]	10.48 ± 0.17[b]
mcv pg	70.76 ± 1.73[a]	47.60 ± 0.79[c]	52.0 ± 0.61[b]
mchc %	34.67 ± 0.16[a]	31.33 ± 0.38[c]	32.95 ± 0.38[b]
TLC 10^3 µl	8.050 ± 0.23[b]	16.125 ± 0.76[a]	18.65 ± 0.83[a]

Means with different superscripts are significantly different (P<0.05), while with the same superscripts indicate non-significant changes

Biochemical analysis

As displayed in a table (2) Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), ALP (Alkaline phosphatase), creatinine and urea (blood urea) were significantly increased in treated groups compared with control group as shown in the following figures 7,8,9,13 and 14 respectively.

In contrast the total protein, albumin and globulin showed significant decrease in 1/10 LD50 and 1/20 LD50 treated groups compared with control group as shown in the following figures 10,11and 12 respectively.

Table 2. Biochemical result of deferent groups.

Parameters	Control	1/10LD50 deltamethrin	1/20LD50 deltamethrin
ALT U/L	24.98 ± 0.19[c]	42.75 ± 2.06[b]	57.5 ± 2.5 [a]
AST U/L	36.67 ± 0.25 [b]	81± 2.27[a]	84.5± 1.04[a]
Alp U/L	65.5± 0.22 [c]	90 ± 7.15[b]	116 ± 8.38[a]
Total protein g/dl	6.31± 0.016[a]	5± 0.0001[b]	4.58± 0.25[b]
Albumin g/dl	3.92±0.02[a]	3.4± 0.08[b]	3.37± 0.21[b]
Globulin g/dl	2.39 ±0.004[a]	1.59 ± 0.08[b]	1.66 ±0.46[b]
Creatinine mg/dl	0.62± 0.006[b]	0.85 ± 0.023[a]	0.85 ± 0.029 [b]
Urea mg/dl	25.76 ± 0.22[b]	33.5 ± 1.7[a]	34.75 ± 0.48[a]

Means with different superscripts are significantly different (P<0.05), while with the same superscripts indicate non-significant changes

Histopathology results

liver

Microscopically the liver in 1/10 LD50 group showing severe congestion in the hepatic sinusoids (arrow) (figure15) Meanwhile the liver in 1/20 LD50 showing coagulative necrosis in hepatic lobule (arrow) and dialation of portal veins (figure16) also the liver is displaying vacuolation of the hepatocytes (arrow) beside congestion of portal vein and hemorrhage (figure17) in addition liver is displaying mild portal inflammation and eosinophilic recruitment (arrow) (figure18).

kidney

Microscopically the kidney in two treated groups showing proliferative glomerulonephritis and presents of blood clots in the glomeruli (arrow) (figure19)

DISCUSSION

Insecticides are widely used in most countries of the world, and it is necessary not only to avoid the side effects of chemical agents but also to know their harmful effects. In the current study, erythrogram results showed that organic insecticides, including deltamethrin, cause hematological damage in various clinical and experimental studies [17].

Exposure of rats to deltamethrin induced hematological changes with decreased erythrocyte, Hb, PCV, MCH, and MCHC parameters. The decreases in erythrocytes, Hb and PCV could be attributed to inhibition of erythropoiesis and blood synthesis, as well as to an increased rate of erythrocyte destruction in hematopoietic organs. The decrease in erythrocytes, Hb, and PCV and the increase in MCV observed in rats exposed to deltamethrin were manifestations of erythrocyte swelling and macrocytic erythroblastic anemia [18].

In this study, deltamethrin-treated animals also showed significantly higher WBC than control animals. It has been shown that the increase in WBC is due to increased leukocyte recruitment, which may be directly proportional to the severity of the causative stress condition [19]. Deltamethrin insecticide may also cause increases in serum AST, ALP, and ALT activity [20]. When hepatocyte transport is impaired as a result of hepatic injury, the permeability of the cell membrane is altered, causing enzymes to leak out of the cell [21].
It is suggested that deltamethrin causes liver injury. The etiology is likely due to free radical (02-) formation. Deltamethrin undergoes metabolism in the liver via hydrolytic ester cleavage and oxidative pathway by the cytochrome P system [22]. Elevated serum enzyme levels indicate increased permeability, injury or necrosis of hepatocytes.
Decrease in total plasma protein and albumin This decrease in plasma protein may be due to altered metabolism of proteins and free amino acids and their synthesis in the liver. The observed decrease in plasma protein may also be due to the damaging effects of deltamethrin on hepatocytes [23].
Serum levels of creatinine and urea were used as indicators of renal function. Elevated blood urea is known to be associated with increased protein catabolism to urea as a result of increased synthesis of arginase enzymes involved in urea production [24]. In this study, elevated serum creatinine and urea levels reflect a diagnosis of renal failure.

CONCLUSION

Through this study, we can conclude that the use of deltamethrin for plants or animals has a very harmful effect. It is recommended that its use be prohibited or to increase the withdrawal period for treatment in the veterinary and agricultural field

Conflict of Interest

There are no financial, personal, or professional conflicts of interest to declare.

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التأثير السمي للدلتامثرين على بعض الصفات الدموية والكيميائية الحيوية لذكور الجرذان

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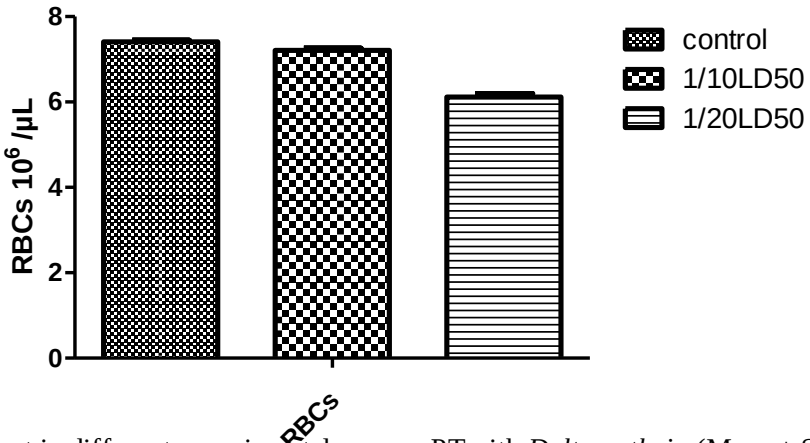
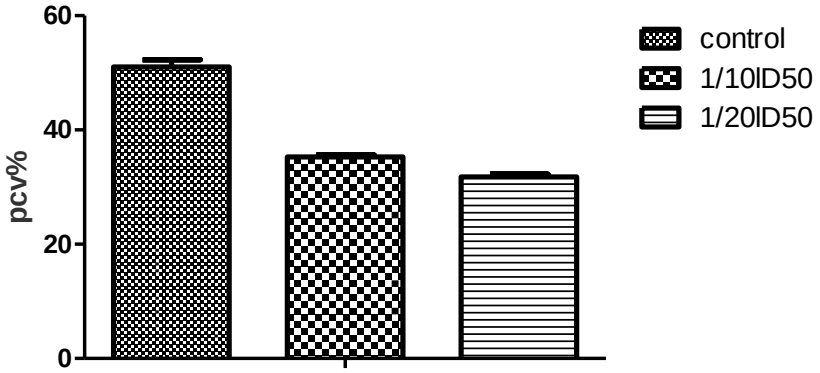
المستخلص

الخلفية والأهداف. دلتامثرين (Dm) هو مبيد حشري اصطناعي من مادة البيرثرويد يستخدم في جميع أنحاء العالم في الزراعة ومكافحة الآفات المنزلية وحماية المواد الغذائية ومكافحة ناقلات الأمراض. كان الهدف من هذه الدراسة هو دراسة مدى ميل الدلتامثرين لتحفيز الإجهاد التأكسدي والتغيرات في أمراض الدم والمعايير البيوكيميائية والتأثير المسخي في ذكور الجرذان. **طُرق الدراسة**. تم تقسيم خمسة عشر ذكرًا بالغًا من فئران ويستار البيضاء إلى ثلاث مجموعات، وكانت المجموعة الأولى بمثابة مجموعة ضابطة وتم تلقي الماء المقطر عن طريق الفم. تلقت المجموعة 2 10/1 LD 50 (0.6 مجم/كجم من وزن الجسم) عن طريق الفم لمدة 30 يومًا، وتلقت المجموعة 3 1/20 DM LD 50(0.3 مجم/كجم من وزن الجسم) عن طريق الفم لمدة 30 يومًا. **النتائج**. تسبب دلتامثرين في حدوث تغيرات معنوية في بعض مؤشرات الدم) خلايا الدم الحمراء(RBC) ، الهيموجلوبين(Hb) ، الهيماتوكريت(PCV) ، متوسط حجم الكريات(MCV) ، متوسط هيموجلوبين الكريات(MCH) ، متوسط تركيز الهيموجلوبين الكرياتي (MCHC) والدم الأبيض. خلايا ((WBC) في الفئران المعالجة مقارنة بالضوابط. زيادة معنوية في مستويات إنزيمات العلامات الكبدية (ألانين أمينوترانسفيراز(ALT) ، الأسبارتات أمينوترانسفيراز (AST) والفوسفاتيز القلوي .(ALP) علاوة على ذلك، ارتفعت العلامات الكلوية مثل اليوريا والكرياتينين في الجرذان المعالجة بالدلتامثرين. **الاستنتاج**. الدلتاميثرين ضار على صحة الحيوان والإنسان.

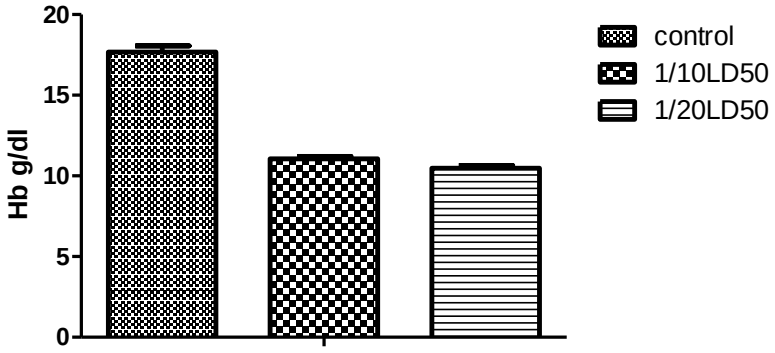
الكلمات الدالة. دلتامثرين، أمراض الدم، الكيمياء الحيوية، التشريح المرضي، الفئران.



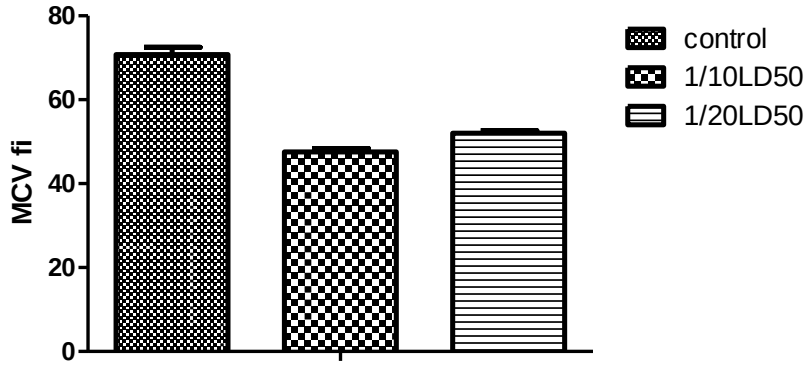
Figure(1):RBCs count in different experimental groups PT with *Deltamethrin* (Mean ± SE)



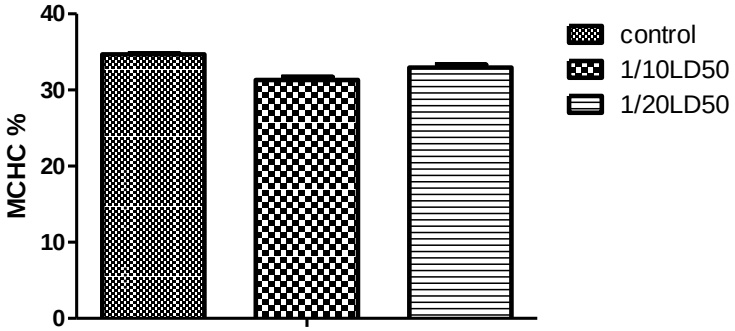
Figure(2):PCV count in different experimental groups PT with *Deltamethrin* (Mean ± SE)



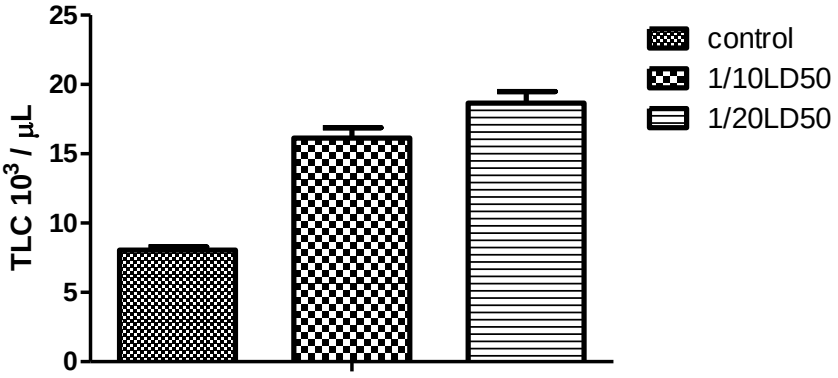
Figure(3):Hb concentration in different experimental groups PT with *Deltamethrin* (Mean ± SE)



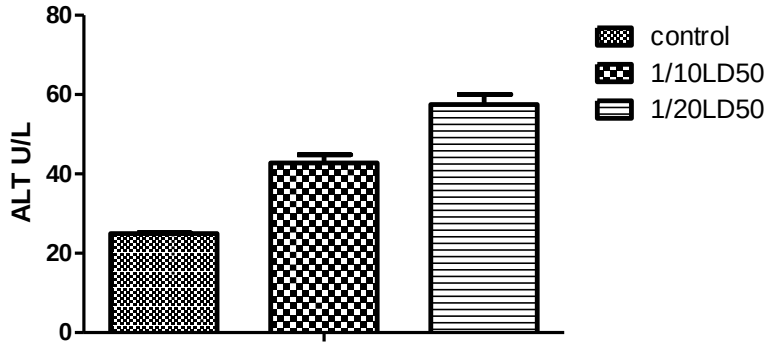
Figure(4):MCV volume in different experimental groups PT with *Deltamethrin* (Mean ± SE)



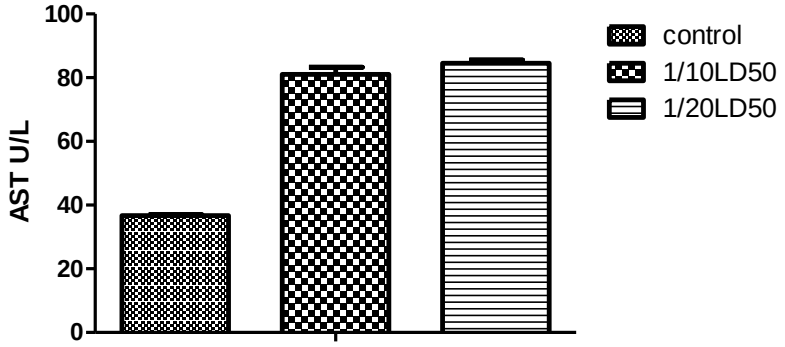
Figure(5):MCHC concentration in different experimental groups PT with *Deltamethrin* (Mean ± SE)



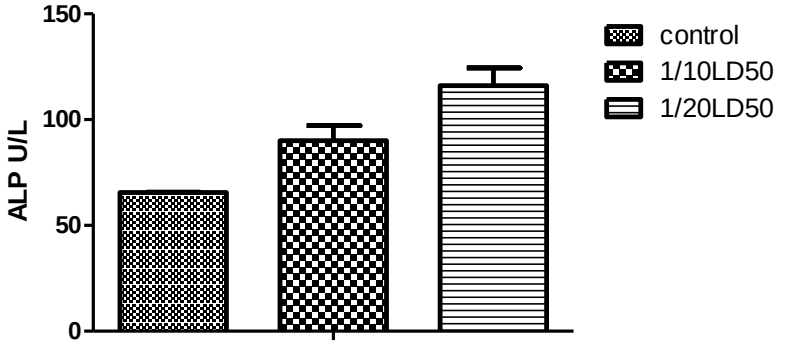
Figure(6):TLC count in different experimental groups PT with *Deltamethrin* (Mean ± SE)



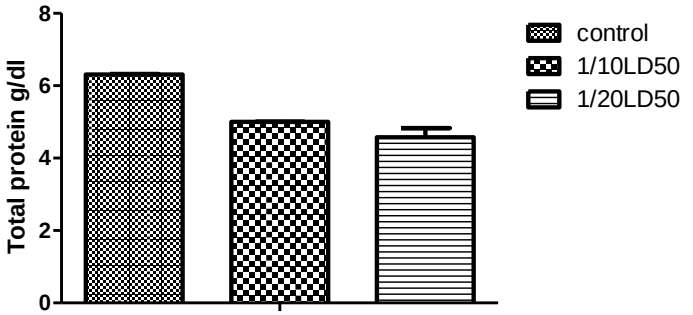
Figure(7):ALT concentration in different experimental groups PT with *Deltamethrin* (Mean ± SE)



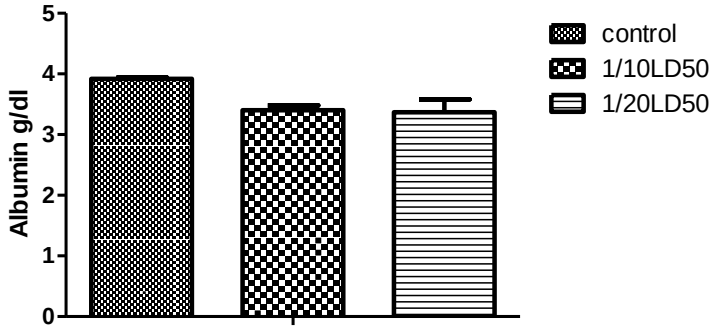
Figure(8):AST concentration in different experimental groups PT with *Deltamethrin* (Mean ± SE)



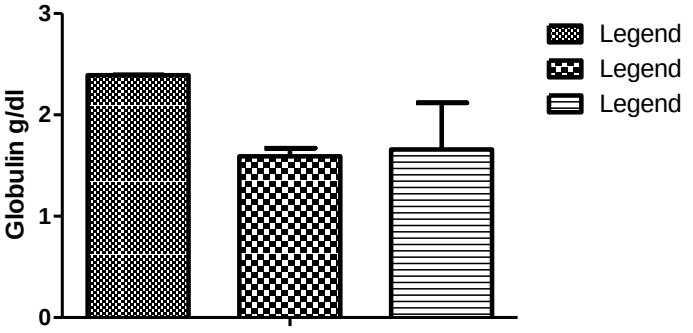
Figure(9):ALP concentration in different experimental groups PT with *Deltamethrin* (Mean ± SE)



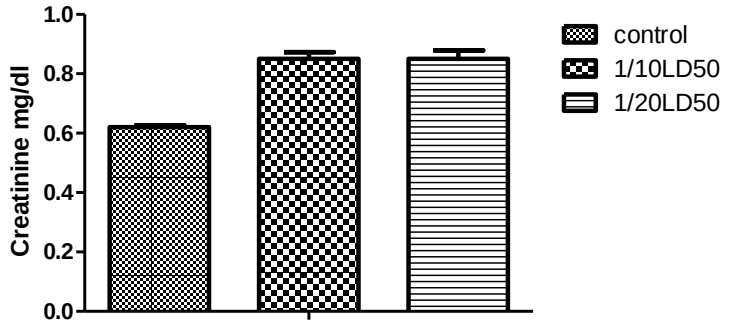
Figure(10):Total protein concentration in different experimental groups PT with *Deltamethrin* (Mean ± SE)



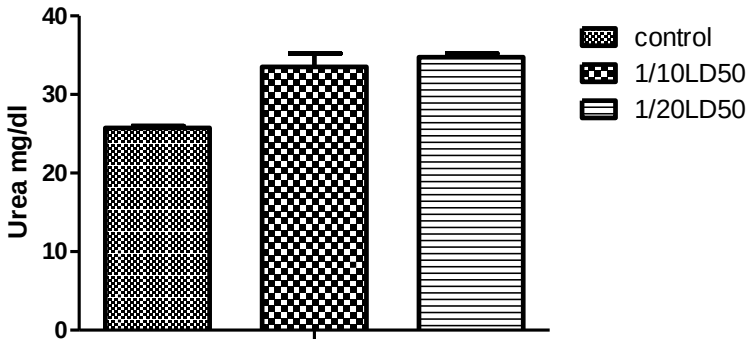
Figure(11):Albumin concentration in different experimental groups PT with *Deltamethrin* (Mean ± SE)



Figure(12):globulin concentration in different experimental groups PT with *Deltamethrin* (Mean ± SE)



Figure(13):creatinine concentration in different experimental groups PT with *Deltamethrin* (Mean ± SE)



Figure(14):Urea concentration in different experimental groups PT with *Deltamethrin* (Mean ± SE)

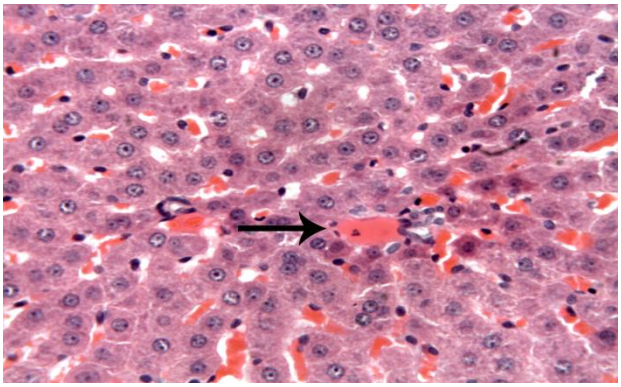


Figure (15): Liver is displaying severe congestion in the hepatic sinusoids (arrow). (HE, 400x)

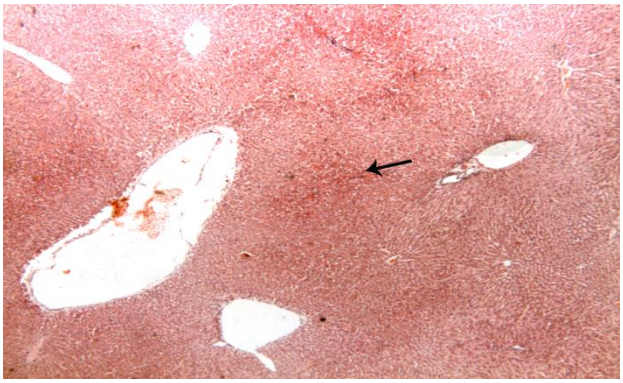


Figure (16): Liver is displaying coagulative necrosis in hepatic lobule (arrow) and dialation of portal veins. (HE, 40x)

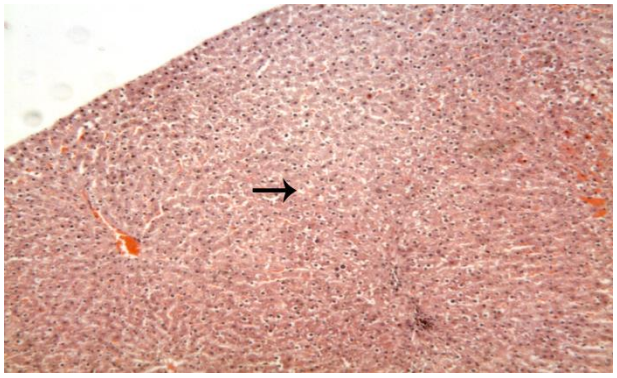


Figure (17): liver is displaying vacuolation of the hepatocytes (arrow) beside congestion of portal vein and haemorrhage. (HE, 100x)

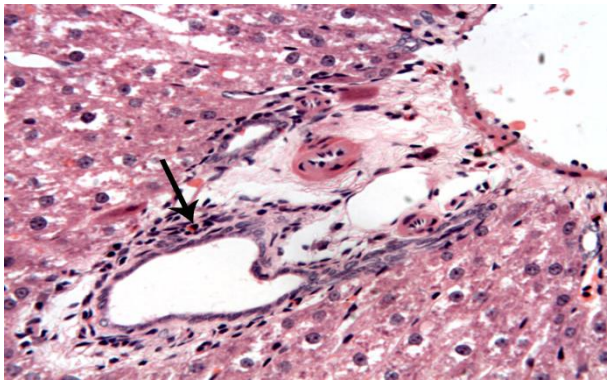


Figure (18): liver is displaying mild portal inflammation and eosinophilic recruitment (arrow). (HE, 400x)

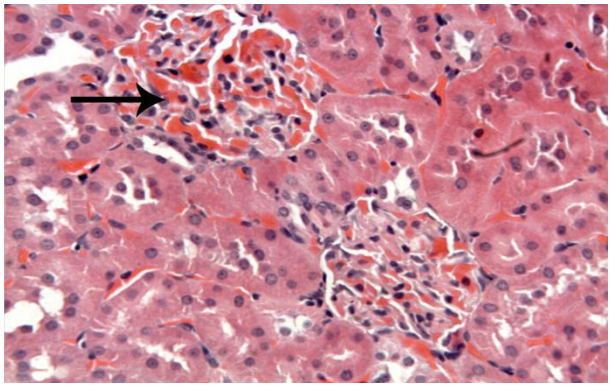


Figure (19): Kidney is displaying proliferative glomerulonephritis and presents of blood clots in the glomeruli (arrow). (HE, 400x)