Digital Evaluation of Physiological, Histological, and Immunological Effects of Lambda-Cyhalothrin Exposure in Male Albino Rats

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Abstract: Pesticides primarily act to get rid of the harmful effects caused by rodents, insects, weeds, and others. This study aimed to investigate the adverse effects of varying lambda-cyhalothrin pesticide concentrations on several physiological, histological, and immunological parameters in male rats, including lipid profiles, liver and kidney functions, and Tumor Necrosis Factor Alpha, Lactate Dehydrogenase, and C-Reactive Protein levels. This study included 15 male albino rats, weighing 180-190g and 5-6 months of age, separated into the following three groups: group 1 was considered a control group and was given only water and food. The 2nd and 3rd groups were administered pesticides at concentrations of 15 and 30 mg/kg, respectively. The animals were orally administered 15 and 30 mg/kg pesticides for 30 days. The data revealed a significant increase in cholesterol, triglycerides, Low Density Lipoprotein, Very Low-Density Lipoprotein, Alanine Transaminase, Aspartate transaminase, and blood urea. creatinine, Tumor Necrosis Factor Alpha, Lactate Dehydrogenase, C-Reactive Protein, and a significant decrease in High Density Lipoprotein in the treated group with the two concentrations of pesticide compared with the control group. Liver and kidney tissue sections were taken as biomarkers for histopathological alterations after exposure to Lambda-Cyhalothrin pesticide. All findings in this study were digitally documented to ensure accurate recording and presentation of the physiological, histological, and immunological results.

1 INTRODUCTION

The Type II pyrethroid insecticide (lambda-cyhalothrin) exhibits unique acaricidal (Russet mites, gall mites, and leaf mites) and insecticidal (Lepidoptera, Diptera, and Coleoptera) properties [1]. Lice, ticks, mites, and fleas are among the described outdoor parasites that the pesticide lambda-cyhalothrin has been used to eliminate in cattle, poultry, and dogs, as well as pests in veggies, grains, and cotton [2]. Lambda-cyhalothrin (LCT) has been shown in earlier research to have remarkable cytotoxicity enhancement [3] and inflammation [4]. In vertebrates, there were clear signs of developmental toxicity and endocrine disruption [5]. LCT has a propensity to accumulate inside biological membranes, similar to other pyrethroids [6]. Produces oxidative stress damage and inflammatory mediators, and the vascular endothelium is activated by cytokines [7]. Additionally, to combat insects that might transmit illnesses, LCT can be utilized for general health purposes or fundamental pest administration. Scientific works confirmed that Type II pyrethroids, when they are orally administered, are mainly absorbed, especially by the digestive system, and are related to the presence of both halogen and α-cyano-3-phenoxybenzyl alcohol groups, as these represent the structural components of pyrethroids [8]. In the last decades, it was clear that the wide world utilization of LCT insecticide is causing severe environmental damage to the living organisms in these habitats [9] as well as being present in several ecological zones [10]. Several routes of entrance to the human body by the pesticide LCT can be enumerated, such as ingestion, inhalation, and the mouth. Thus, this action could be the main cause for people to be exposed to LCT; as a result of that, numerous diseases may occur [11]. Owing to oxidative stress, LCT is intimately linked to toxicity in organs related to the non-target organisms (aquatic and terrestrial animals). For instance, 6.12 mg/kg of body weight LCT enhanced alkaline phosphatase (ALP) activity, alanine aminotransferase (ALT), and aspartate aminotransferase (AST) levels

in the liver of male Sprague-Dawley rats; nevertheless, it can also interfere with the antioxidant status and induce oxidative damage, glutathione peroxidase (GPx) decline, catalase (CAT), superoxide dismutase (SOD), and glutathione S-transferase (GST) activity, accompanied by lipid peroxidation (LPO) and protein carbonyl (PCO) levels rising [12], [13]. As a scientific fact, male Wistar rats exhibit decreased CAT and SOD levels and increased malondialdehyde (MDA) levels when the experimental rats are therapeutically treated with LCT. The DNA of the thyroid gland shows fundamental damage as an outcome of the comet indications of the targeted pesticides [14]. The recent years have been very attractive for investigating the effect on the non-targeted organs by LCT; in fact, the studies indicate the side effects of pancreatic [15], [16], oxidative damage and hepatotoxicity in both mice and rats [13], [17], neurotoxicity in humans [18], acute toxicity in pigeons [19], toxicity to embryos [20], and fish injury from oxidation [21], [22].

2 MATERIALS AND METHODS

The experiment was held at the Research Centre of Biotechnology, Al-Nahrain University, Baghdad, Iraq.

The established time for the experiments was four months, from the first of March to May 25th. The experiment type falls under pure laboratory experiments, which were conducted in the laboratory of the Biotechnology Research Centre at Al-Nahrain University.

The study was approved by the ethical committee of the Department of Biology, College of Life Science, University of Baghdad (Ref.**:** CSEC/1025/0143).

2.1 Experimental Design

This investigation was conducted to ascertain the negative effects of one type of LCT on physiological and immunological parameters in male rats. This study included 15 albino rats, weighing 180-190g and 5-6 months' age, separated into the following three groups: Group 1 was considered the control group and was given only water and food. The 2nd and 3rd groups were administered pesticides at concentrations of 15 and 30 mg/kg, respectively. Treated animals were orally dosed for 30 days. The experiments were terminated after 30 days. Once the experiment reached its end, blood was drawn from the heart after anesthetizing the animals with 10% ketamine. Blood was separated by centrifugation for 15 min at 3000 rpm. The resultant serum was preserved in the refrigerator at -20 °C until biochemical analyses, which included lipid profile, ALT, AST, B. urea, Creatinine, TNF-α, LDH, and CRP, were performed. Then the kidneys and liver were separated and placed in a 10% formalin buffer for histological sectioning.

2.2 Biochemical Tests

A range of biochemical tests was conducted to evaluate lipid metabolism, liver and kidney function, and inflammatory biomarkers:

1) Lipid profile bio-Merieux\USA.
2) Liver function tests: Alanine transaminase (ALT) and Asepata Transaminase (AST) A GenWay Biotech, Inc.\ USA.
3) Kidney function:
   - Blood urea, LINEAR CHEMICALS S.L., Joaquim Costa Montgat, Barcelona, SPAIN.
   - Creatinine, LINEAR CHEMICALS, S.L.U. Joaquim Costa Montgat (Barcelona) SPAIN.
4) TNF-α (Tumor Necrosis Factor Alpha) ELISA Kit\ My BioSource/USA Catalog No: MBS2502004.
5) Lactate Dehydrogenase (LDH) kit (Xpress Bio Life Science Products).
6) C-Reactive Protein (CRP) My BioSource/USA.

All laboratory tests were performed using a spectrophotometer instrument (Apel PD-303, Japanese-manufactured).

2.3 Histological Study

Both the kidney and liver were instantly removed from the control group and the target rats, treated with a 10% formalin solution, and alcohol dehydrated immediately after tap water rinsing. Xylene clearance and tissue embedded in paraffin were applied. 4 microns is the paraffin sections that were performed. All procedure was performed according to the techniques used by Bancroft [23].

2.4 Statistical Analysis

Statistical significance was determined using one-way analysis of variance (ANOVA), and least significant differences (LSD) were used to explain the differences between means at ($P \leq 0.05$), ** ($P \leq 0.01$). The results were expressed as mean ± SE [24].

3 RESULTS

3.1 Biochemical Results

Table 1 shows a comparison between the different treatments for Blood Urea and Creatinine.

Blood Urea and Creatinine levels both increased significantly at the 30 mg/kg concentration compared to those in the control and 15 mg/kg groups.

The statistical tests showed the following: B. Urea differences are highly significant (LSD = 10.122). Creatinine differences are significant (LSD = 0.701).

Table 1: Comparison between different Treatments in B. Urea and Creatinine in groups that were treated with the targeted pesticide.

Conc. (mg/kg)	Means ±SE	
	Blood Urea (mg/dl)	Creatinine (mg/dl)
0 mg/kg	19.00 ±1.52 b	0.466 ±0.27 b
15 mg/kg	28.00 ±1.52 b	0.400 ±0.11 b
30 mg/kg	41.00 ±4.58 a	1.183 ±0.19 a
L.S.D.	10.122 **	0.701 *

Means with the different letters in the same column differed significantly. * (P≤0.05). Means having with the different letters in same column differed significantly. * (P≤0.05), ** (P≤0.01). Values are means ± SD (n = 5 rats per group). Different letters (a, b, c) within the same row indicate significant differences among groups at (P≤0.05, P≤0.01).

High increase showed by the results in the concentration of blood urea in the group treated with 30 mg\kg (41.00 ±4.58) mg/dl in contrast to the control group (19.00 ±1.52) mg/dl, and a substantial rise in the group's creatinine levels after receiving 30 mg\kg (1.183 ±0.19) mg/dl relative to the control group (0.466 ±0.27) mg/dl.

In Table 2, Statistical elevation was notable in cholesterol level in both groups treated with pesticide 15,30 mg\kg (97.00 ±3.05, 102.67 ±1.76) mg\dl, respectively, compared to the control group (87.33 ±2.18) mg\dl. The results of Triglyceride showed a marked increase in the group treated with pesticide 30 mg\kg (92.33 ±1.45) mg\dl compared to the control group (82.33 ±2.60) g\dl. Furthermore, HDL level in groups treated with pesticide 15 and 30 mg\kg revealed decreased statistically (21.00 ±2.08, 20.33 ±1.20) mg\dl, in contrast to the control group (28.00 ±1.15) mg/dl, the group treated with 30 mg/kg of pesticide had a significantly higher LDL level (64.33 ±4.67) than the control group (37.66 ±1.85). Additionally, the results showed that the group treated with 30 mg/kg showed that VLDL levels in the pesticide group were considerably higher (18.30±0.32) than in the control group (16.47±0.52) mg/dl.

Table 2: Comparison between different treatments in lipid profiles in groups treated with pesticides.

Conc. (mg/kg)	Means ±SE (mg/dl)				
	Cholesterol	Triglyceride	HDL	LDL	VLDL
0 mg/kg	87.33 ±2.18 b	82.33 ±2.60 b	28.00 ±1.15 a	37.66 ±1.85 b	16.47 ±0.52 b
15 mg/kg	97.00 ±3.05 b	87.66 ±1.85b	21.00 ±2.08 b	43.67 ±0.88 b	17.53 ±0.37 b
30 mg/kg	102.67 ±1.76 a	92.33 ±1.45 a	20.33 ±1.20 b	64.33 ±4.67 a	18.30± 0.32 a
L.S.D	6.291*	8.378*	5.327*	10.187*	1.629*

Means with the different letters in the same column differed significantly. * (P≤0.05). Values are means ± SD (n = 5 rats per group). Different letters (a, b, c) within the same row indicate significant differences among groups at (P≤0.05, P≤0.01).

Table 3: Comparison between different Treatments in ALT and AST in groups treated with pesticide.

Conc. (mg/kg)	Means ±SE	
	ALT (IU/L)	AST (IU/L)
0 mg/kg	22.67 ±2.03 b	28.67 ±2.60 b
15 mg/kg	33.00 ±4.58 b	34.00 ±2.31 b
30 mg/kg	53.00 ±5.51 a	43.00 ±2.64 a
L.S.D.	14.877 **	8.734 **

Means having with the different letters in same column differed significantly. ** (P≤0.01). Values are means ± SD (n = 5 rats per group). Different letters (a, b, c) within the same row indicate significant differences among groups at (P≤0.05, P≤0.01).

The results in Table 3 showed obtained markedly elevated ALT activity in the treatment group with 30 mg\kg (53.00 ±5.51) of pesticide compared to the control group (22.67 ±2.03) IU\l, Additionally, the findings revealed a noteworthy rise in AST activity in the group that received 30 mg\kg (43.00 ±2.64) IU\l mg/dl of pesticide compared to control group (28.67 ±2.60) IU\l.

In Table 4, Effects of varying treatment concentrations on three inflammatory or tissue-damage biomarkers: TNF (Tumor Necrosis Factor, pg/ml): a pro-inflammatory cytokine. LDH (Lactate Dehydrogenase, IU/L) – an enzyme that indicates

tissue damage or cellular injury. C-Reactive Protein (CRP, mg/kg), a general marker of inflammation**.**

Table 4: Comparison between different Treatments in TNF, LDH and CRP in groups treated with pesticide.

Conc. (mg/kg)	Means ±SE		
	TNF (pg/ml)	LDH (IU/l)	CRP (mg/ml)
0 mg/kg	510.67 ±14.42 c	149.33 ±2.91 b	2.82 ±0.45 c
15 mg/kg	674.67 ±17.40 b	195.00 ±7.02 a	4.21 ±0.22 b
30 mg/kg	810.00 ±13.07 a	216.00 ±9.64 a	6.40 ±0.21 a
L.S.D.	52.171 **	24.532 **	1.104 **

Means having with the different letters in same column differed significantly. ** (P≤0.01). Values are means ± SD (n = 5 rats per group). Different letters (a, b, c) within the same row indicate significant differences among groups at (P≤0.05, P≤0.01).

The results in Table 4 obtained highly raised increase in TNF, in both groups treated with pesticide 15 and 30 mg\kg (674.67 ±17.40, 810.00 ±13.07) pg/ml respectively compare to control group (510.67 ±14.42) pg/ml while the results showed remarkable increase in LDH in both groups treated with pesticide 15 and 30 mg\kg (195.00 ±7.02, 216.00 ±9.64) IU/l respectively compare to control group (149.33 ±2.91) IU/l. On the other hand, the results indicated a significant elevation in CRP levels in both groups administered 15 and 30 mg/kg (4.21 ±0.22, 6.40 ±0.21, respectively), in contrast to the control group (2.82 ±0.45) mg/kg.

3.2 Histological Study

The results of the liver tissue sections in concentrations (15 and 30) mg/kg are shown in Figures 1, 2, 5 and 6 that show mild congestion with dilation of portal vein, necrosis and focal aggregation of leukocytes, cellular swelling with nuclear pyknosis of hepatocytes, and the kidney tissue sections in concentrations (15 and 30) mg/kg are shown in Figures 3, 4 and 7 that show mild cellular swelling of lining cells, mild cellular vascular degeneration lining cells of renal tubules.

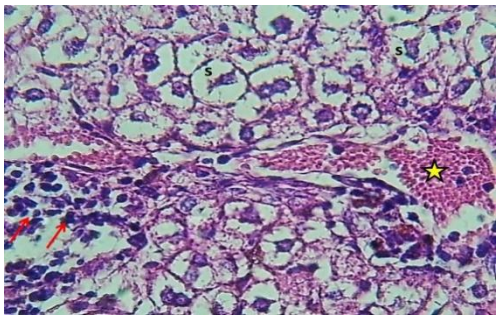

Figure 1: Section of hepatic lobule of group treated with 15 mg\kg of pesticide shows: mild congestion with dilation of the portal vein (asterisk), with periportal aggregation of MNCs (Arrow) & marked cellular swelling with nuclear pyknosis of hepatocytes (S). H&E stain. 400x.

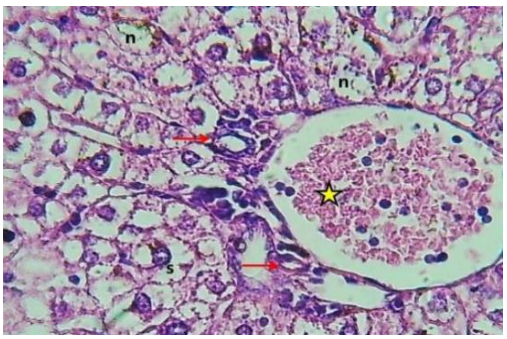

Figure 2: section of hepatic lobule 30 mg\kg of pesticide shows: mild congestion of central vein (Asterisk) with marked peri-central histogenesis of newly formed hepatocytes (Arrow) & marked cellular swelling with nuclear pyknosis of hepatocytes (s). & necrosis(n) H&E stain. 400x.

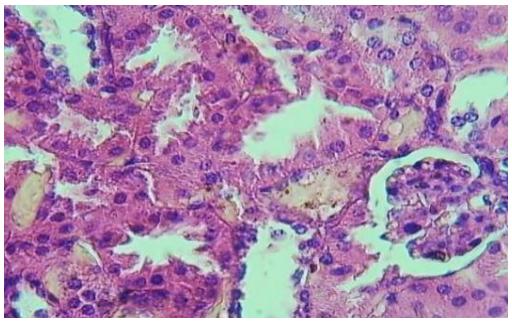

Figure 3: section of renal cortex 15 mg\kg of pesticide shows: mild cellular swelling of lining cells (Red arrow) with necrosis (Black arrow) of the lining cells of renal tubules, with little peri-glomerular aggregation of MNCs (Asterisk). H&E stain. 400x.

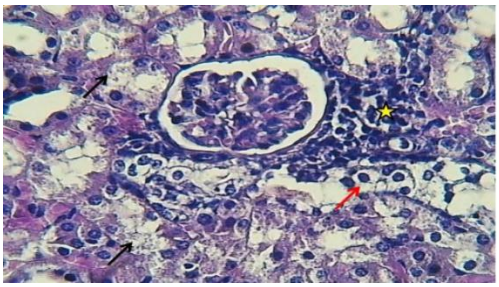

Figure 4: Section of renal medulla of group treated with 15 mg\kg of pesticide shows: mild cellular vascular degeneration lining cells of renal tubules, H&E stain. 400x.

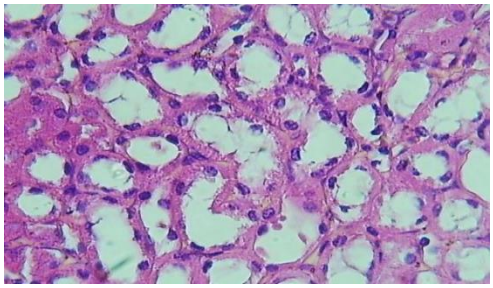

Figure 5: Section of hepatic lobule of group treated with 15 mg\kg of pesticide shows marked cellular swelling with nuclear pyknosis of hepatocytes (s). & necrosis (n) & focal aggregation of leukocytes (Arrows).

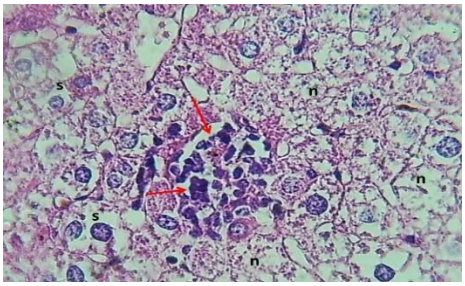

Figure 6: Section of hepatic lobule 30 mg\kg of pesticide shows marked cellular swelling with of hepatocytes (s). & necrosis (n) & little figures of apoptosis (Arrows) H&E stain. 400x.

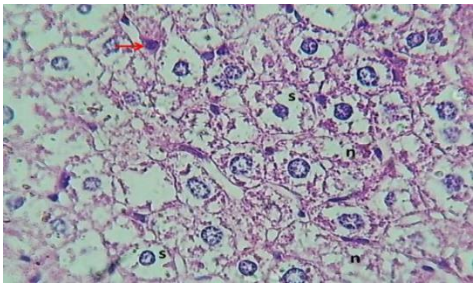

Figure 7: A segment of the renal cortex control group demonstrates normal renal tubule lining cells and normal glomerular cytoarchitecture. 400x H&E stain.

4 DISCUSSION

A wide range of people can be affected by pesticide exposure; however, agricultural workers and their families are especially vulnerable. Additionally, using household pesticides or eating food contaminated with pesticide residues may expose the broader public [25]. Notable increase in both blood urea and creatinine concentrations of 30 mg/kg was observed in the LCT-treated group. These substances prevent the incorporation of amino acids into proteins, which raises urea levels, the main product of protein metabolism that contains nitrogen [26]. The elevated plasma creatinine and urea levels in this investigation indicate renal failure [27]. Furthermore, it is well known that elevated blood urea levels are linked to increased protein catabolism and/or conversion of ammonia to urea, according to the increased synthesis of the urea-producing enzyme arginase. The elevation of blood urea and creatinine levels in LC-treated rats, as urea is the ultimate result of protein catabolism, is considered a significant marker of renal impairment and may be associated with metabolic anomalies in liver function. Moreover, xenobiotics alter sodium transport and enhance the acid-secreting function of the kidneys [28], [29]. The degree of liver damage seemed to be significant, as indicated by the increase in ALT and AST levels in our study, which showed that animals intoxicated with both low and high doses had marked elevations in liver marker enzymes. Histopathological investigations supported these findings, showing hepatocyte degeneration [25]. Serum triglyceride, VLDL cholesterol, and LDL cholesterol levels were all elevated in LCT-treated rats, whereas HDL levels were decreased. This could indicate that the LCT has a significant potential to change normal bodily physiology [30]. Redox-sensitive transcription factors, including NF-κB, are triggered by oxidative stress, which may be induced by toxicants, resulting in inflammatory responses [31]. The enhanced IL-6 and TNF-α levels observed may have resulted from these transcription factors being triggered by heightened oxidative stress caused by cypermethrin [32]. This is consistent with the results of Soliman et al, the rats' expression of the proinflammatory cytokines TNF-α and IL-6 was enhanced by CYP. Thus, the increase in TNF-α and IL-6 levels observed in CYP-exposed rats suggests that CYP exposure causes inflammation [33].

5 CONCLUSIONS

Studying the effect caused by the pesticide LCT has indicated the serious damage caused by direct exposure to the main concern pesticide, especially to the liver, kidney, and immune system of male albino rats, mainly at high dosage levels, as shown by altered biochemical markers and increased inflammatory responses. The data revealed a significant increase in cholesterol, triglycerides, Low Density Lipoprotein, Very Low-Density Lipoprotein, Alanine Transaminase, Aspartate transaminase, and blood urea. creatinine, Tumor Necrosis Factor Alpha, Lactate Dehydrogenase, C-Reactive Protein, and a significant decrease in High Density Lipoprotein in the treated group with the two concentrations of pesticide compared with the control group. Liver and kidney tissue sections were taken as biomarkers for histopathological alterations after exposure to Lambda-Cyhalothrin pesticide. Our results indicate that the insecticide LCT causes severe toxicity to the targeted tissues of both the Liver and the Kidney. Therefore, the overutilization of pesticides should be strongly monitored and regulated to minimize frequent exposure to poisons and toxins with maximum control.

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