



Hematological and Biochemical Effects of Sub-Acute Doses of Lambda-Cyhalothrin, Imidacloprid, and Emamectin-Benzoate Insecticides on Albino Rats

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Abstract

A toxicant may induce several types of injuries, and the severity of its effects is usually related to the dose and duration of exposure to the chemical under a specified exposure. Therefore, this study aimed to assess the impact of $1/10$ LD₅₀ of lambda-cyhalothrin, imidacloprid, and emamectin-benzoate insecticides on hematological and biochemical parameters in albino rats. No significant changes were observed in the treated rat's body weight compared with control, except for emamectin, which caused a significant decrease after the recovery period. Emamectin-benzoate induced a significant increase in WBCs after the 5th and 10th doses, and imidacloprid caused a significant increase after the 10th dose (+ 89.5%); at the same time, lambda-cyhalothrin caused a slight increase. After the recovery period, white blood cell counts decreased in all treated rats compared to the treatment period but did not return to the control level. Imidacloprid caused a significant decrease in red blood cells (RBC) after the 5th dose (-6.6% below the control level). In contrast, after the recovery period, a significant decrease in RBCs was observed in rats treated with lambda-cyhalothrin and emamectin benzoate. The data also revealed a significant increase in GOT and GPT activities after the 5th and 10th doses in treated rats, while no significant differences in GPT activity were found in emamectin-benzoate-treated rats compared with control rats at the same time points. After the recovery period, the activity of both enzymes in all treated rats decreased but did not return to the control level. Similarly, lambda-cyhalothrin and emamectin benzoate had the greatest effect on kidney function compared to imidacloprid. Generally, there is no fixed pattern of the ill effects of different classes of pesticides on hematological and vital parameters. Therefore, it is of utmost importance to check and reduce the indiscriminate use of pesticides and to look into other environmentally friendly agrochemical approaches to increase crop productivity.

Keywords: Insecticides, Subacute, Hematological, Biochemical Parameters, Rats.

INTRODUCTION

Chemical pesticides pose potential health risks to humans, with effects ranging from immediate to long-term, based on exposure levels and methods. The level of toxicity varies among pesticide types and their intended purposes. For instance, products designed to eliminate insects generally present a higher risk to human health compared to those targeting plants. The impact of a single compound can differ depending on the dosage, which refers to the amount of the chemical an individual encounters. Additionally, the manner in which exposure occurs, whether through ingestion, inhalation, or skin contact, can influence the toxic effects on the human body [1]. Environmental contamination from pesticides has become a widespread issue, presenting significant dangers to the health of humans and animals

alike. In recent times, there has been growing concern about the potential health hazards associated with pesticide contamination. Studies show that annually, over 3 million people globally experience pesticide poisoning due to various causes [2]. Understanding the various ways pesticides interact should be applied to assess potential risks to human health. As a result, experiments on animals in laboratory settings have become the primary source of toxicological information. A toxic substance can cause multiple forms of damage, and the intensity of its effects typically correlates with the amount and length of exposure to the chemical under specific conditions [3,4]. Acute pesticide poisoning poses a significant and immediate danger, potentially leading to serious harm or even death. These poisonings usually result from either deliberate self-harm or unintentional exposure. Globally, pesticide poisoning affects an estimated

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350,000 to 440,000 people each year, representing about 30% of all suicides [5,6]. One of the more sensitive markers of early health changes brought on by environmental pesticide exposure may frequently be the variations in biochemical parameters as assessed in different bodily fluids[7]. The liver, a vital organ for the biotransformation-based metabolism of several substances, is the main site of xenobiotic toxicity. Toxic metabolites are disposed of in part by the kidneys. Transaminases, such as glutamic-pyruvic transaminase (GPT) and glutamic-oxaloacetic transaminase (GOT), are secreted by hepatocytes and are particular markers of liver injury because they are involved in the production of amino acids. They can seep into the bloodstream when liver tissue is injured, which raises their levels and activity in plasma. Together, the liver and kidney are regarded as the organs that pesticide poisons are most likely to target[8]. Important enzymes called transaminases are involved in many biological processes. They are crucial for the production and catabolism of amino acids. Glutamic and pyruvic acids are created when alpha ketoglutaric acid receives the amino groups of alanine and aspartate from ALT and AST. The treated animals' livers showed increased AST and ALT activity. Because transaminases are involved in the detoxification process, metabolism, and production of energy macro-molecules for several vital processes, their deviation from normal values indicates biochemically significant lesions of tissues and cellular function[9]. The majority of the data on pesticide nephrotoxicity comes from studies conducted on experimental animals. In experimental animal investigations, exposure to particular pesticides has been shown to cause renal damage and

functioning in a dose-dependent and/or exposure duration-dependent manner. Numerous pesticide types, such as triazine and chlorophenoxy herbicides, organophosphate, organochlorine, carbamate, and pyrethroid insecticides, have been demonstrated to harm and malfunction the kidneys of animals [10]. Nowadays, pesticide components are always present in our atmosphere and have contaminated our food, water, and soil, posing acute and long-term health risks. High doses of pesticides can be inhaled, consumed, or come into contact with the skin or eyes, resulting in acute toxicity. Chronic toxicity is caused by repeated or protracted exposure to pesticides. Different forms of toxicity, such as neurotoxicity, mutagenicity, carcinogenicity, teratogenicity, and endocrine disruption, are produced by pesticides. The presence of inert or synergistic components that may alter or increase the toxicity of a pesticide formulation, as well as the active ingredient itself, can affect the toxicity of the product. To reduce the health risks associated with modern pesticides, safety considerations are urgently needed [11]. People who are exposed to pesticides suffer serious hemotoxic effects, according to numerous studies [12]. Therefore, this study aimed to investigate the possible adverse effects of sublethal doses of tested insecticides on liver and kidney functions and hematological parameters.

MATERIALS AND METHODS

Insecticides Used

Three insecticides which are commonly used in pest control programs in Egypt, were selected in the present study: imidacloprid (neonicotinoids), lambda-cyhalothrin (pyrethroids), and emamectin-benzoate (Avermectin).

Table 1. Insecticides common and trade names, chemical groups and pamphlet median lethal doses (LD₅₀)

No.	Common name	Trade name	Chemical group	LD ₅₀ (mg/kg b.w) *
1	Imidacloprid	Joun@70% WG	Neonicotinoids	450.0
2	Lambda-cyhalothrin	Icton 2.5 % EC	Pyrethroids	56.0
3	Emamectin-benzoate	Proclaim 5% SG	Avermectins	82.5

*According to Anonymous [13]

Animals Used

Male albino rats (*Rattus norvegicus*) weighing 120±10 g was obtained from the Animal Breeding House of the National Research Center (NRC). The rats were kept at a temperature of 25 ± 2 °C and 48% relative humidity in the laboratory. The rats were acclimated for 1 week before the start of the experiment. Animals were handled and treated in accordance with the guidelines and welfare regarding animal protection in the Animal Breeding House of NRC, which was approved by the NRC Local Ethical Review Committee and was conducted in conformity with “the Guide for the Care and Use of Laboratory Animals [14].

Experimental Design

The animals were divided into four groups (5 rats each).

The 1st, 2nd and 3rd groups were treated with 1/10 LD₅₀ of the pamphlet median dose [13] for each tested pesticide (Table 1). The pamphlet LD₅₀ values used were: 5.6, 45.0 and 8.25 mg/kg body weight, respectively for imidacloprid, lambda-cyhalothrin, and emamectin-benzoate. While the fourth group was served as a control. Lambda-cyhalothrin and imidacloprid were dissolved in corn oil while emamectin was dissolved in water and administered orally by convenient use of a stomach tube, every three days for 30 day- period (equal 10 doses). Then, the pesticide treatments were withdrawn for 10 days to allow the animals to recover from toxicity. Treated animals were observed daily for signs of clinical or toxicological effects [15].

Bleeding Regimen

On days 15 and 30, three rats for each group were bled after

24 h. of the 5th and 10th dose of administration and after the recovery period (10 days after the last dose). Blood was withdrawn from the retro-orbital plexus [16] of anesthetized rats using heparinized and non-heparinized ampoules. Hematological evaluation and biochemical analysis were carried out at the Medical Research Centre Excellence, National Research Centre, Dokki, Giza.

Hematology Assay

The blood in heparinized ampoules was analyzed for white blood cells (WBC), red blood cells (RBC), hemoglobin (Hb), and platelet (PLT) counts by using Med Source Fully Automatic Euro-count 5L 5-Part Hematology Analyzer, For Laboratory, User Input: Touch.

Biochemical Analysis

Sera were separated from coagulant blood (un-heparinized ampoules) after centrifugation at 3000 rpm for 10 min and kept at -20 °C until analysis. Hepatic injury was assessed by measuring the activity of aminotransferase enzymes, and renal injury by measuring urea and creatinine concentrations. These parameters were analyzed spectrophotometrically using kits purchased from the Bio-Marieux Company (France). An XL-180 Fully Automated Random Access Clinical Chemistry Analyzer was used for automated clinical chemistry.

Statistically Analysis

All results were expressed as mean ± standard error (S.E.) for the indicated number of experiments. The significance of the difference among groups was analyzed using ANOVA one-way, followed by the Least Significant Difference Test (LSD) for mean separation. A *p* value ≤ 0.05 was considered significant. All statistical analyses were made using the software CoStat [17].

Table 2. Mean values of body weights of rat males exposed via sub chronic assay to 1/10 LD₅₀ of treated pesticides.

Treatments	Avg. body weight (g) at different pesticide dosing intervals*				
	Pretreatment	5 th dose	10 th dose	After recovery period	Average (%change)*
Lambda-cyhalothrin	139.4 a ± 9.4 (-3.72)	180.4 a ± 12.4 (-4.65)	190.2 a ± 18.5 (-1.24)	222.6 a ± 9.7 (+4.54)	183.1 (-0.97)
Imidacloprid	144.6 a ± 10.4 (-0.14)	194.8 a ± 8.9 (+2.96)	198.8 a ± 12.6 (+3.22)	222.6 a ± 13.8 (+4.54)	190.2 (+2.86)
Emamectin benzoate	136.6 a ± 19.4 (-5.66)	182 a ± 23.8 (-3.8)	191.2 a ± 19.9 (-0.72)	198.3 b ± 14.6 (-6.9)	177 (-4.27)
Control	144.8 a ± 7.6	189.2 a ± 13.5	192.6 a ± 17.4	213 ab ± 12.12	184.9
LSD 5%	16.848	21.058	23.25	23.928	

*+/- % above or below the control treatment. Values within each column followed by the same letter are not significantly different at *p* > 0.05 (LSD test).

Similar, data was obtained by Madkour *et al.* [23] who found that treated rats with 9mg/kg b. w of emamectin-benzoate day after day for 6 weeks caused a significant decrease in rats' body weight. Also, Shalaby *et al.* [24] reported that treated rats

RESULTS AND DISCUSSION

Signs of Toxicity

During the experiment, animals from all groups were checked daily for signs of toxicity. Slight sensitivity was observed in rats administered the tested compounds 4-5 hours after dosing. These signs gradually decreased over the next few hours. Some adverse effects, such as general weakness and fatigue, were observed in lambda-cyhalothrin treated-rats. No mortality was recorded in treated rats.

Effect of Tested Pesticides on Body Weight

Generally, the increase or decrease of body weight is yet considered as a simple index of toxic effects [18]. Data listed in Table 2 and revealed that there are no significant differences in body weight of treated rats during the experiment periods, except in case of emamectin-benzoate at recovery period, there is a significant decrease compared with other treatments. Generally, all treated rat weight was increased during the experiment, the highest average happened in imidacloprid treated rats (+2.86 % above the control level), followed by untreated rats (184.9 g), then lambda-cyhalothrin (-0.97% below the control level), while the lowest was noticed in emamectin benzoate treated rats (-4.27%). Many researchers reported body weight decreases in experimental animals including rabbits, mice and rats due to exposure to different insecticides [19,20]. Mahmoud and Mahmoud [21] reported that repeated oral administration of thiamethoxam at 100 mg/kg b.w day and emamectin benzoate at 5 mg/kg b.w day caused a significant decrease in body weight gain of animals compared with untreated animals. Data obtained by Kašuba *et al.* [22] revealed that there is a significant lower body weight was noticed in male rats treated with 0.015, 0.157 and 0.786 mg/kg b.w/ day of α-cypermethrin for 28 days compared with untreated rats.

with expired malathion and chlorpyrifos caused a significant decrease in body weight after the 5th dose compared with non-expired formulations. At 15 days after the last dose (the recovery period), an increase in body weight was noticed in all groups.

Hematological Effects

Data in Table 3 showed the effects of subchronic exposure of tested pesticides on the blood profile in treated animals. The 1/10 LD₅₀ of emamectin-benzoate induced a significant increase in WBCs after the 5th and 10th doses (+ 97.3 and 104.5% above the control level), and imidacloprid induced

a significant increase also after the 10th dose (+ 89.5%); at the same time, lambda-cyhalothrin caused a slight increase. After the recovery period, the white blood cell counts slightly decreased in all treated rats but did not return to the control level. Emamectin-benzoate had the highest average, followed by imidacloprid and lambda-cyhalothrin (+ 75, 56.8, and 29.5 % above the untreated rats, respectively).

Table 3. Hematological parameters in rat males exposed to 1/10 LD₅₀ of tested pesticides for 30 days compared to the untreated control

Treatments	Blood cell counts at different pesticide dosing intervals*							
	White blood cells (WBC, 10 ³ /μl)				Red blood cells (RBC, 10 ⁶ /μl)			
	5 th dose	10 th dose	After recovery period	Average	5 th dose	10 th dose	After recovery period	Average (change)*
Lambda-cyhalothrin	5.25 ab±1.2 (+37.4)	6.55 ab±0.6 (+42.7)	5.19 a±1.54 (+7.4)	5.7 (+29.5)	3.59 ab±0.1 (-2.7)	4.16 a±0.26 (-0.23)	3.3 c±0.28 (-23.9)	3.7 (-8.6)
Imidacloprid	6.1 ab±1.33 (+59.9)	8.7 a±2.18 (+89.5)	5.96 a±2.1 (+23.4)	6.9 (+56.8)	3.44 b±0.06 (-6.6)	4.0 a±0.33 (-4.1)	4.32 a±0.1 (-0.4)	3.92 (-3.2)
Emamectin benzoate	7.54a±3.8 (+97.3)	9.39 a±1.33 (+104.5)	6.28 a±4.8 (+30.0)	7.7 (+75.0)	3.52 ab±0.29 (-4.6)	4.3 a±0.43 (+3.1)	3.95 b±0.12 (-8.8)	3.93 (-3.0)
Control	3.82 b±2.4	4.59 b±7.13	4.83 a±6.31	4.4	3.69 a±0.35	4.17 a±0.42	4.34 a±0.20	4.05
LSD 5%	2.315	3.55	3.97		0.445	0.688		0.358

*+/- % above or below the control treatment; Values within each column followed by the same letter are not significantly different at p >0.05 (LSD test).

At the same Table for the red blood cells (RBC), the results indicated that imidacloprid caused a significant decrease in RBC counts after the 5th dose (-6.6% below the control level), while other treatments induced slight changes (increase or decrease) after the 5th and 10th doses compared with untreated animals. After the recovery period, a significant decrease in RBCs was noticed in treated rats with lambda-cyhalothrin and emamectin (-23.9 and 8.8 %, below the control level). The results showed convergence in the RBC average of rats treated with tested insecticides, and there is a slight decrease compared with untreated rats.

process in the body, and their origin is in the bone marrow. Thrombocytopenia is a subnormal number of platelets in the circulating blood. It is the most common inducer of abnormal bleeding in living organisms [4,24]. Data presented in Table 4 showed the effect of tested insecticides on platelet (PLT) count and hemoglobin (Hb) values in treated rats.

The obtained data showed in significant decrease in PLT counts in treated rats by tested insecticides after all experimental periods. The highest average of PLT counts was noticed in untreated rats (959.4 x 10³μl⁻¹), followed by imidacloprid treatment, then emamectin and lambda-cyhalothrin (-2.75, -4.4 and -4.8 %, below the control level, respectively).

Platelets play a vital role in homeostasis and the coagulation

Table 4. Effect of tested compounds on platelet (PLT) counts and hemoglobin (Hb) values of treated rats

Treatments	Platelet counts and Hemoglobin levels at different pesticide dosing intervals*							
	PLT (10 ³ /μl)				Hb (mg/dL)			
	5 th dose	10 th dose	Recovery period	Average 10 ³ /UL	5 th dose	10 th dose	Recovery period	Average(change)* g/dL
Lambda-cyhalothrin	909.66 a ±13.5 (-4.8)	903.6 a±217.5 (-1.8)	924.6 a±53.5 (-7.7)	912.6 (-4.8)	13.6 ab±0.6 (-1.8)	15.1 ab±0.9 (-2.3)	15.2 a±2.18 (-1.2)	14.6 (-2.0)
Imidacloprid	901.0 a±37.5 (-5.7)	874.6 a±61.5 (-5.0)	968.6 a±28.5 (-3.3)	933.0 (-2.75)	13.15ab±0.35 (-5.0)	14.15 b±0.45 (-8.4)	12.56 c±0.1 (-18.4)	13.28 (-10.8)
Emamectin benzoate	926.0 a±50 (-3.09)	874.6a±55.5 (-5.0)	904.6 a±168.5 (-9.7)	917.1 (-4.4)	12.86 b±0.25 (-7.2)	15.7 a±0.3 (+1.5)	14.06 b±0.15 (-8.7)	14.2 (-4.7)
Control	955.66 a±75	920.6 a±4.5	1002 a±0	925.8	13.85 a±0.55	15.46 a±0.35	15.4 a±0.55	14.9
LSD 5%	92.784	219.150	168.582		0.867	1.042		0.546

*+/- % above or below the control treatment. Values within each column followed by the same letter are not significantly different at p >0.05 (LSD test).

A slight reduction in the numbers of both RBCs and platelets for treated rats was noticed, probably due to suppressive and toxic effects on bone marrow and hematopoiesis. Since platelets are synthesized in bone marrow, the double suppressing effect on RBCs and platelets would be explained [25, 6, 24]. The high increase of leucocytes may be due to the inflammatory response induced as a defense mechanism. Also, the emamectin-benzoate compound may affect the WBC counts by the stressogenic effect of this compound on the reticuloendothelial system [24]. Data showed also, that the emamectin caused a significant decrease in Hb value after the 5th dose (-7.2 %, below the untreated animals), and imidacloprid after the 10th dose (-8.4%), while other treatments caused a negligible change in Hb values. After the recovery period, a significant decrease in Hb value happened in imidacloprid and emamectin-treated rats (-18.4 and -8.7%, below the untreated animal's level, respectively). The highest Hb average was noticed in untreated rats (14.9 mg dl⁻¹), followed by lambda-cyhalothrin, emamectin, and imidacloprid (14.6, 14.2 and 13.28 mg dl⁻¹). On the other hand, the reduction in erythrocyte counts and consequently hemoglobin concentration may be attributed to more than one factor, i.e. the failure to provide the blood circulation with cells from hemohepatic tissues, since the liver has an major role in the regeneration of erythrocyte and the possible destructive effect on erythrocyte by the toxicants [26, 21]. El-Sheikh and Galal [27] reported that emamectin benzoate treatment significantly decreased body weight, RBC count, Hb concentration, and reduced total leukocyte, lymphocyte, monocyte and platelet count but significantly increased granulocyte count.

Effects on Liver and Kidney Functions

The impact of pesticides on biochemical parameters, tissues, and organs is commonly used to assess their toxicity in humans and animals [26, 24]. Assessing enzymatic activity in the blood is commonly used to determine pesticide toxicity because of its high sensitivity and time efficiency.

Data presented in Table 5 revealed that $1/_{10}$ LD₅₀ of lambda-cyhalothrin, imidacloprid, and emamectin-benzoate insecticides caused a significant increase in glutamic-oxaloacetic transaminase (GOT) activity after the 5th dose compared with untreated rats. This trend was noticed after the 10th dose. After the recovery period (10 days after the last dose), GOT activity did not return to normal level in lambda-cyhalothrin and imidacloprid. However, in emamectin-benzoate-treated rats, the enzyme activity was still high compared with untreated rats but insignificant (+12.1% above the control level). Data also, showed that GOT activity in all treated rats was above the control level, the highest average was noticed in lambda-cyhalothrin-treated rats (+32.4%), followed by imidacloprid (+23.2%), the emamectin-benzoate (+18.4% above the control level).

A similar trend was observed in the case of GPT activity; lambda-cyhalothrin and imidacloprid induced a significant increase in GPT activity after the 5th and 10th doses, whereas no significant difference in enzyme activity was observed in emamectin benzoate-treated rats compared with the control. After the recovery period, the activity of GPT enzyme of all treated rats decreased but didn't return to the control level. Generally, lambda-cyhalothrin had the highest average (+21.6 % above the untreated level) of enzyme activity, followed by imidacloprid (+15.5) and emamectin-benzoate (+8.5%). The liver plays an important role in the decomposition and elimination of toxic compounds, such as pesticides, whereas the kidneys are responsible for the removal of metabolic waste from the body [28]. The liver is the primary target of xenobiotic toxicity and is essential for the biotransformation of many chemicals. Hepatocytes secrete transaminases (GPT and GOT enzymes), which play a major role in amino acid biosynthesis and are, thus, specific indicators of liver injury. GPT and GOT are normally found in hepatocytes; however, when liver tissue is damaged, they leak into the bloodstream, leading to an increase in their levels and activity in the plasma [29, 30]. Some enzymes in the blood serum have been considered as a measure of hepatic dysfunction and destruction [31].

Aminotransferases (AST and ALT) are important and critical enzymes in biological processes. These enzymes are involved in the breakdown of amino acids into α -keto acids, which are routed for complete metabolism through the Krebs cycle and electron transport chain. Consequently, they are considered specific indicators of liver damage [18] and are responsible for detoxification processes, metabolism, and biosynthesis of energetic macromolecules for different essential functions. Similarly, data obtained by Madkour et al. [23] revealed that treating rats with 9 mg/kg b.w of emamectin-benzoate day after day for 6 weeks caused a significant increase in ALT and AST enzyme activities compared with untreated rats. In addition, Mahmoud and Mahmoud. [21] reported that serum biochemical parameters such as AST, ALT, and ALP were not significantly changed in female rats orally administered thiamethoxam at doses of 25 and 50 mg/kg b.w day and emamectin benzoate at doses of 1.25, 2, and 5 mg/kg b.w day as compared to the control. However, a significant increase ($p < 0.05$) was noted in serum AST, ALT, and ALP levels in animals exposed to 100 mg/kg b.w dose of thiamethoxam and 5 mg/kg b.w of emamectin compared with untreated control groups. These alterations in ALT and AST activities could be due to necrotic changes in the hepatic tissue, as observed in histopathological examination. In addition, the damage could be attributed to the toxic effects of emamectin benzoate, primarily by the generation of reactive oxygen species, which damage various membrane components of the cell and lead to the leakage of cytoplasmic enzymes [27].

The liver, as a central organ, is responsible for the detoxification

of xenobiotics, metabolism, and biosynthesis of energetic macromolecules for different essential functions [32]. Therefore, hepatotoxicity is a crucial endpoint for evaluating the effects of a particular xenobiotic. Clinical chemistry and histopathological evaluations are commonly used to detect organ-specific effects related to chemical exposure [33]. GOT and GPT are vital enzymes that serve as specific indicators of liver injury because they are secreted into the blood and increase with hepatocellular damage. After 10 doses of treated rats with lambda-cyhalothrin, imidacloprid, and emamectin-benzoate, GOT and GPT levels markedly increased, supporting the hypothesis that pesticide exposure results in subtle biochemical liver toxicity [34]. Moreover, the

increase in these enzyme activities as bioindicators of liver injury after sub-chronic or chronic exposure to emamectin benzoate has also been experimentally observed (El-Sheikh and Galal, [27]). Shalaby et al. [24] reported that GOT and GPT enzymes transfer the amino group of alanine and aspartate to alpha-ketoglutaric acid and form glutamic and pyruvic acids. The activity of these enzymes was measured in the blood serum and livers of the treated animals. The activity deviations of these enzymes from average values indicate biochemical impairment and injury to tissues and cell functions, as they are involved in the metabolism, biosynthesis, and detoxification of active macromolecules for different vital functions.

Table 5. Effect of tested insecticides on Glutamic-Oxaloacetic Transaminase (GOT) and Glutamic Pyruvic Transaminase (GPT) activities of treated rats

Treatments	GOT and GPT activities at different pesticide dosing intervals*							
	GOT (u/L)				GPT (u/L)			
	5 th dose	10 th dose	Recovery period	Average	5 th dose	10 th dose	Recovery period	Average (change)*
Lambda-cyhalothrin	58.5 a ±2 (+37.6)	50.0 a±1 (+29.8)	50.8 a±4.5 (+28.6)	53.1 (+32.4)	36.5 a±1 (+27.6)	48.0 a±10 (+24.6)	38.0 a±6 (+20.2)	40.8 (+21.6)
Imidacloprid	51.2b±4.5 (+20.4)	48.3a±6.5 (+25.4)	48.8ab±5 (+23.5)	49.4 (+23.2)	33.0b±1.5 (+15.4)	45.5ab±2.5 (+18.2)	35.6 a±2.5 (+12.6)	38.0 (+15.5)
Emamectin benzoate	51.0b±3 (+20.0)	47.3a±0 (+22.8)	44.3bc±8.5 (+12.1)	47.5 (+18.4)	28.6 c±4 (0.0)	42.0 b±0.5 (+9.1)	36.6 a±0.5 (+15.8)	35.7 (+8.5)
Control	42.5 c±6	38.5b±9	39.5 c±2.5	40.1	28.6c±7.5	38.5 bc±6	31.6 b±5	32.9
LSD 5%	3.96	5.25	5.24		3.180	4.244	3.744	

*+/- % above or below the control treatment. Values within each column followed by the same are not significantly different letter at p >0.05 (LSD test).

The kidneys participate in the disposal of toxic metabolites in the body. The data presented in **Table 6** show insignificant changes in creatinine concentrations in animals exposed to sublethal doses of the tested insecticides after the 5th dose. After the 10th dose, all tested insecticides caused a significant increase in creatinine levels compared those to in the untreated rats. A significant increase was observed after the recovery period in lambda-cyhalothrin- and emamectin-treated rats, and a slight increase was observed in imidacloprid-treated rats (+5.26 % above the control level) during the same period compared with the control. In addition, the highest average concentration of creatinine was observed in rats treated with lambda-cyhalothrin and emamectin, followed by imidacloprid (+18.9, 16.2%, and 10.8 % above untreated animals). Date also indicated that Sub-chronic exposure to tested insecticides induced a significant increase in urea concentration after the 5th dose, and these effects increased with repeated doses; the urea concentration was high after the 10th dose. After the recovery period, the urea concentration decreased in all treatments but did not return to the control level. The highest effect was

observed in emamectin- benzoate treated rats (+34.3%), followed by lambda-cyhalothrin and imidacloprid (20.5 and 18.5% above untreated animals, respectively).

These changes may be due to epithelial necrosis of the renal tubules with nuclear and chromatin changes in the epithelium of the cortical tubules [35, 4]. The failure of kidney function as a result of exposure to pesticides has been reported by many investigators. Similarly, Bilalet al. [36] reported that orally administering fipronil (9.7 mg/kg b.w) and emamectin-benzoate (8.8 mg/kg b.w) three times for eight weeks caused a significant increase in serum AST, ALT, creatinine, and urea concentrations compared with untreated rats. The sharp increase in creatinine and urea concentrations may be due to the role of insecticides in glomerular filtration, which subsequently increases serum creatinine levels and uremia. This suggests that these compounds may induce renal damage or toxicity, leading to renal failure [24]. An increase in creatinine concentration is considered a biomarker of renal damage and can be attributed to liver function, and the increase in urea may be due to a disturbance in protein metabolism.

Table 6. Effect of tested pesticides on creatinine and urea concentration of treated rats

Treatments	Creatinine and urea levels at different pesticide dosing intervals							
	Creatinine (mg/dL)				Urea (mmol/L)			
	5 th dose	10 th dose	Recovery period	Average	5 th dose	10 th dose	Recovery period	Average(change)*
Lambda-cyhalothrin	0.39 a±0.03 (+2.8)	0.47 a±0.01 (+6.8)	0.45 a±0.05 (+18.42)	0.44 (+18.9)	44b±2.5 (+14.3)	59.6 b±3.5 (+38.6)	41 a±3 (+6.2)	48.2 (+20.5)
Imidacloprid	0.36 a±0.02 (0.0)	0.46 a±0.02 (+4.54)	0.4 bc±6.8 (+5.26)	0.41 (+10.8)	45.5 b±1.5 (+18.2)	57.6 b±0.6 (+34.0)	39 a±2 (+1.0)	47.4 (+18.5)
Emamectin benzoate	0.38 a±0.005 (+5.6)	0.48 a±0.05 (+9.1)	0.44 ab±0.04 (+15.78)	0.43 (+16.2)	52 a±2 (+35.1)	65 a±9 (+51.2)	44 a±1.5 (+14.0)	53.7 (+34.3)
Control	0.36 a±0.03	0.38b±0.04	0.36c±0.04	0.37	38.5c±4	43.0c±1	38.6 a±5	40.0
LSD 5%	0.046	0.036	0.048		5.026	4.160	5.978	

*+/- % above or below the control treatment. Values within each column followed by the same are not significantly different letter at p >0.05 (LSD test).

CONCLUSION

The results indicated that sub chronic exposure of rat males to sublethal dose of the tested pesticides significantly disturbed the hematology and vital parameters of rats. Generally, there is no fixed pattern of the ill effects of different classes of pesticides on hematological parameters. However, the toxicity of most pesticides results in anemia and leukocytosis in rats. Therefore, it is of utmost importance to check and reduce the indiscriminate use of pesticides and to look into other environmentally friendly agrochemical approaches to increase crop productivity.

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