Hemato-biochemical and histopathological alterations induced by acute cypermethrin toxicity in rabbits.

H. Kh. Ulaiwi
Coll.of Vet.Med./ Univ of Al-Qadisyiah

Abstract

The present study was conducted to evaluate the acute toxicity of cypermethrin in rabbits. Twenty four rabbits were used in the study and kept under similar management conditions. After seven days of acclimatization, rabbits were randomly divided into two equal groups : the treated group (T) and control (C) group and the treated group was subdivided according to dose of administration of cypermethrin drug into 3 groups includes: T1, T2 and T3. The cypermethrin was administrated into treated group by oral administration of (15 mg/kg B.W.; 25 mg/kg B.W. and 50 mg/kg B.W.) to (T1, T2 and T3) respectively, while the control group(C) was received normal saline. Rabbits in each group received three treatments at an interval of seven days. All the animals were monitored twice daily for clinical signs. The blood was collected from control and treated group to evaluate the following blood parameters: Hb rate, PCV%, RBC counting number, WBC counting number and platelet counting number; also the plasma was separated to evaluate total protein concentration. Two rabbits from each treated group was sacrificed to study histopathological alteration in stomach, intestine, kidneys and lungs at the last day of experiment. The result of this study revealed that the erythrocytes count were decreased significantly ($P<0.05$) in all cyprmethrin treated groups, compared to control group. The concentration of Hb decreased significantly ($P<0.05$) in (T2 and T3) groups at periods of (21) and the result showed significant differences($P<0.05$) between (T3) and all other groups of study, while PCV decreased at day 14 in groups (T1 and T2) and at day 21 in group (T3) only, compared to control group, and the result revealed significant decreases($P<0.05$) in group (T3) as compared with other groups. Total white blood cells counts were significantly ($P<0.05$) increased specially at (21) in group (T3). Platelets count showed significant decreased ($P<0.05$) in all groups at 14 and 21 days of experiment as compared with control groups and (T3) revealed significant differences ($P<0.05$) as compared with other groups. The result ensured that there were significant decreased ($P<0.05$) in total protein in the (T2) and (T3) groups at period of (21) day. Gross investigation of stomach revealed eccymotic hemorrhage in the stomach and engorgement of blood vessels. The results of histopathological alteration revealed that there are engorgement of pulmonary capillary and congestion of pulmonary alveoli, thickening and congestion of the alveolar septa and swollen and tortuous of small vein, the pulmonary alveoli are full of amorphous eosinophilic fluid. In duodenum there are necrosis and destruction most of the superficial glands, with present some viable glandular tissue. In kidney there are destruction of few renal glomeruli and deposition of eosinophilic materials in the renal tubules with dilatation of the tubules. The renal tubules severely dilated and full with eosinophilic material. The renal glomeruli completely atrophied and destructed.

Introduction

Cypermethrin is a synthetic pyrethroid insecticide used to control many pests, including moth pests of cotton, fruit, and vegetable crops. It is also used for crack, crevice, and spot treatment to control insect pests in stores, warehouses, industrial buildings, houses, apartment buildings, greenhouses, laboratories, and on ships, railcars, buses, trucks, and aircraft. It may also be used in non-food areas in schools, nursing homes, hospitals, restaurants, hotels, in food processing plants, and as a barrier

treatment insect repellent for horses. Technical cypermethrin is a mixture of eight different isomers, each of which may have its own chemical and biological properties. Cypermethrin is light stable. It is available as an emulsifiable concentrate or wettable powder (1).Cypermethrin is a moderately toxic material by dermal absorption or ingestion (2). Symptoms of high dermal exposure include numbness, tingling, itching, burning sensation, loss of bladder control, incoordination, seizures, and possible death. Pyrethroids like cypermethrin may adversely affect the central nervous system (3). Symptoms of cypermethrin toxicity in laboratory animals include pawing, burrowing, salivation, tremors, writhing, and seizures (4). Cypermethrin has caused the cornea of laboratory animals to become opaque (5). Symptoms of high-dose ingestion include nausea, prolonged vomiting, stomach pains, and diarrhea which progresses to convulsions, unconsciousness, and coma. Cypermethrin is a slight skin or eye irritant, and may cause allergic skin reactions (6). Liver enlargement is often noted in laboratory animals that have ingested large doses of cypermethrin during their life span. Long-term feeding studies with laboratory animals have shown that cypermethrin causes adverse effects. In rats, it caused reduced growth rate and increased liver weight. In mice, it caused reduced weight gain, mild anemia, and increased liver weight. In dogs, it caused loss of appetite, incoordination, and tremors (7). In rabbits, it caused pathological changes in the thymus, liver, adrenal glands, lungs, and skin (8). Cypermethrin cause an increase in benign lung tumors in female mice at 1600 ppm in the diet. Pyrethroids like cypermethrin may cause adverse effects on the central nervous system.Skin irritation, itching, skin scratching, licking of legs and other body parts were observed in CY treated rabbits in dose dependent manner (9). Incoordination, muscular tremors, jerky movements, ataxia, staggering gait and dizziness were also observed in CY treated rabbits in dose dependent manner. Similar nervous signs like mild tremors, hyperexcitability or depression (10), grinding of teeth, hyperaesthesia, opisthotonus, spastic paralysis (11), muscle twitching, staggering gait, sunken eyes and thick eye discharge (12) have previously been reported.The toxicity of any compound depends on many factors, such as the chemical and physical form of the compound, route of administration, dose and duration of exposure, time elapsed after exposure, dietary level of the interacting elements, physiological conditions (pregnancy, lactation etc.), nutritional status, age and sex of the exposed individuals (13, 14, 15).

Study design:

This study was conducted in the clinical pathology laboratory, college of veterinary medicine, university of Al-Qadisyiah. The beginning was at 23/01/2010 and the finishing was 01/05/2010. Twenty four rabbits were used in the study and kept under similar management conditions. Food and water were available *ad libitum*. After seven days of acclimatization, rabbits were randomly divided into two groups : the treated group (T) and control (C) group and the treated group was subdivided according to dose of administration of cypermethrin(CY) drug into 3 groups includes: T1, T2 and T3. The cypermethrin was administrated into treated group by oral administration of (15 mg/kg B.W.; 25 mg/kg B.W. and 50 mg/kg B.W.) to (T1, T2 and T3) respectively, while the control group(C) was received normal saline. Rabbits in each group received three treatments at an interval of seven days(7, 14 and 21). All the animals were monitored twice daily for clinical signs like increased urination, licking of legs and face, ataxia, incoordination, head and neck tremor, staggering gait and dizziness that appearing after 30 minute and persisted for 60 to 90

minutes after each dose administration. The blood was collected from the control and treated group from the heart by using 5 ml sterile disposable syringe to evaluate the following blood parameters: Hb rate mg/dl, PCV%, RBC counting number million/ μL, WBC counting number thousand / μL and platelet counting number thousand / μL; also the plasma was separated to evaluate Total protein concentration. Two rabbits from each treated group was sacrificed at day (21) to study histopathological alteration in stomach, intestine, kidney and lungs (16).

Statistical Analysis:

Data were expressed as mean ±standard Error (SE) and analysed by two-way analysis of variance (ANOVA) for groups and days of treatment.

Results

Twenty to thirty minutes after the administration of cypermethrin dose, the animals started showing clinical signs like: restlessness, muscular tremors, incoordination, salivation and increased urination, licking of legs and face. Nervous signs consisted of incoordination, ataxia, staggering gait and dizziness and persisted for about 30 to 90 minutes. These clinical signs were very obvious in (T3) groups and appear more rapid than other groups.The result revealed that the RBCs count decreased significantly($P<0.05$) in all cypermethrin treated groups, on 14 and 21 days of experiment compared to control group (Table 1). The concentration of Hb decreased significantly ($P<0.05$) in (T2 and T3) groups at periods of (21) and the result showed significant differences($P<0.05$) between (T3) and all other groups of study, while PCV decreased on day 14 in groups (T1 and T3) and day 21 in group (T3) only, compared to control group, and the result revealed significant decreases($P<0.05$) in group (T3) as compared with other groups. Dose dependant gradual decrease in RBC counts, Hb concentration and PCV in all the treated groups was observed throughout the experiment. (Table 1).Total white blood cells counts were significantly ($P<0.05$) increased in (T2 and T3) groups in all periods compared to (T1) and control rabbits (Table 1). The WBCs count in (T3) at 21 days showed significant differences($P<0.05$) among all groups.(Table1).Platelets count showed significant decreased ($P<0.05$) in all groups at 14 and 21 days of experiment as compared with control groups and the result revealed that PLT count in (T3) group significantly different($P<0.05$) from other periods.(Table1).The result ensured that there were significant decreased ($P<0.05$) in total protein in the (T2) and (T3) groups at period of (21) day.(Table1).

Table(1): represent values of hematological and biochemical parameters in rabbits treated with cypermethrin (CY).The values represent (means±SE) at (P<0.05).

	Periods in days		
Parameters/ Groups	7	14	21
RBC count ($10^6/\mu L$) T1	$5.07x10^6 \pm 0.32$	$4.92x10^6 \pm 0.19$ Aa	$4.50x10^6 \pm 0.14$ Aa
T2	$5.24x10^6 \pm 0.16$	$4.74x10^6 \pm 0.13$ *Aa*	$4.63x10^6 \pm 0.08$ Aa
T3	$5.16x10^6 \pm 0.05$	$4.65x10^6 \pm 0.16$ Aa	$4.63x10^6 \pm 0.12$ Aa
C	$5.34x10^6 \pm 0.08$	$5.18x10^6 \pm 0.25$	$5.21x10^6 \pm 0.08$
Hb concentration(g/dL)			
T1	10.8 ± 0.19	11.3 ± 0.34	11.5 ± 0.31
T2	11.2 ± 0.34	10.86 ± 0.35	8.2 ± 0.09 Aa
T3	11.1 ± 0.42	10.83 ± 0.33	7.1 ± 0.40 Aab
C	11.4 ± 0.37	11.2 ± 0.34	11.2 ± 034
PCV%			
T1	42 ± 0.45	30 ± 0.53 a	34 ± 0.65
T2	37.6 ± 0.43	35.1 ± 0.54	33.6 ± 0.54
T3	38.8 ± 0.40	29 ± 0.37 a	28 ± 0.34 Aab
C	42 ± 0.45	42 ± 0.50	42 ± 0.45
WBC count$(10^3/\mu L)$			
T1	$4.08x10^3 \pm 0.46$ *A*	$4.38x10^3 \pm 0.48$	$4.89x10^3 \pm 0.56$ *a*
T2	$7.18x10^3 \pm 0.12$ *Aa*	$7.88x10^3 \pm 0.47$	$9.05x10^3 \pm 0.65$ *Aab*
T3	$6.56x10^3 \pm 0.45$ *A*	$8.90x10^3 \pm 0.53$ *Aa*	$10.18x10^3 \pm 0.70$ *Aab*
C	$4.72x10^3 \pm 0.72$	$4.08x10^3 \pm 0.46$	$4.08x10^3 \pm 0.44$
PLT$(10^3/\mu L)$			
T1	$206.75x10^3 \pm 0.83$	$164.15x10^3 \pm 0.64$a	$116.05x10^3 \pm 0.29$ *a*
T2	$250.75x10^3 \pm 0.78$	$136.75x10^3 \pm 0.66$ *a*	$124.05x10^3 \pm 0.29$ *Aa*
T3	$236.75x10^3 \pm 0.81$	$194.75x10^3 \pm 0.81$ *a*	$118.05x10^3 \pm 0.19$ *Aa*
C	$294.66x10^3 \pm 0.83$	$296.75x10^3 \pm 0.83$	$282.05x10^3 \pm 0.19$
Total protein(g/dL)	7	14	21
T1	13.77 ± 0.67	11.32 ± 0.56	11.73 ± 0.60
T2	9.4 ± 0.29	8.77 ± 0.32	8.71 ± 0.32 Aa
T3	8.03 ± 0.63	8.11 ± 0.64	7.77 ± 0.26 Aab
C	18.53 ± 0.43	18.09 ± 0.12	18.53 ± 0.53

- The small letter(a) represent the significant differences (P<0.05) between the days of the experiment in the same group.
- The capital letter (A) represent significant differences (P<0.05) between the days of the experiment in the different groups.
- Figure (6): Spleen, extramedullary hemopoiesis and Megakaryocytes (arrow) (H. and E; X400)

Results Histopathological alteration:

In gross appearance the stomach and kidneys as well as lungs undergo Eccymotic hemorrhage.(Figure 10).(Table2).Lungs: the result revealed that the lungs were edematous and congested (Figure 1). The small veins in the lung are swollen and tortuous and the alveolar septa markedly thickened (Figure 2). In (T3 group) the pulmonary alveoli are full of amorphous eosinophilic fluid which leaked from the congested capillaries (Figure 3) and a few eosinophilic strands (Probably fibrin) are also present in the lumen of some of the alveolar septa , also there were thickening of the alveolar septa that referred to inflammatory process therefore that bronchopneumonia was starting to develop.Stomach and intestine: the results revealed that there were no alteration in stomach and intestinal mucosa in (T1 group), while there were erosion and hemorrhage in group (T2) but erosion does not extend beyond the muscularis mucosa. There are necrosis and destruction of the superficial glandular tissue in group (T2 and T3). The erosion is very shallow and its floor consist largely of necrotic tissue and cells. There are few viable mucosa, beneath the necrotic tissue. The most superficial gland in the underlying (viable) mucosa are distorted partially necrotic. The mucosa usually atrophic and thinner than normal (Figure 4). Kidneys: the results showed that there were destruction of few renal glomeruli (Figure 6) and deposition of eosinophilic materials (may be fibrinous material) in the renal tubules with dilatation of the tubules in (T2 and T3). The renal tubules severely dilated and the eosinophilic material still present (Figure 7) and the renal glomeruli completely atrophied and destructed also there was congestion of renal veinules in group (T3) (Figure 8 and 9).

Table(2): represent necropsy finding in rabbits suffering from toxicity of cypermethrin

	Groups / Necropsy finding	T2	T3
1	Lungs	Petechial hemorrhage	Eccymotic hemorrhage
2	Kidneys	Normal kidney texture	Eccymotic hemorrhage
3	Stomach	Normal	Eccymotic hemorrhage
4	Intestine	Normal	Severe congestion

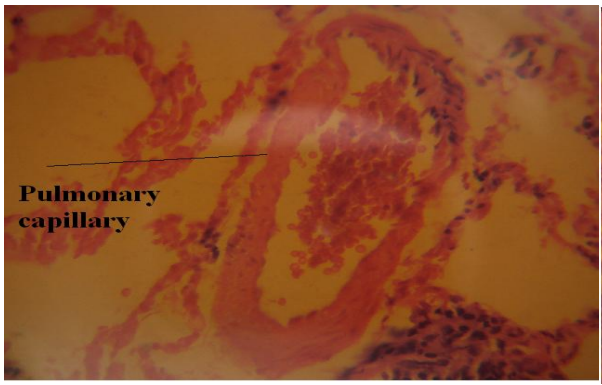
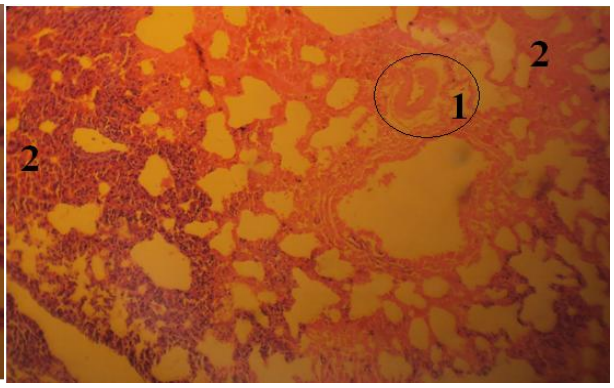


Figure (1) group (T2): engorgement of pulmonary capillary and congestion of pulmonary alveoli.(H&E) 400X



Figure(2) (T2 group): Thickening and congestion of the alveolar septa (2) and swollen and tortuous of small vein(1).(H&E stain).100X

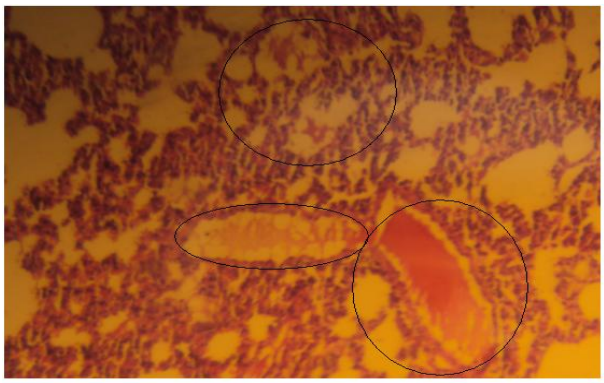
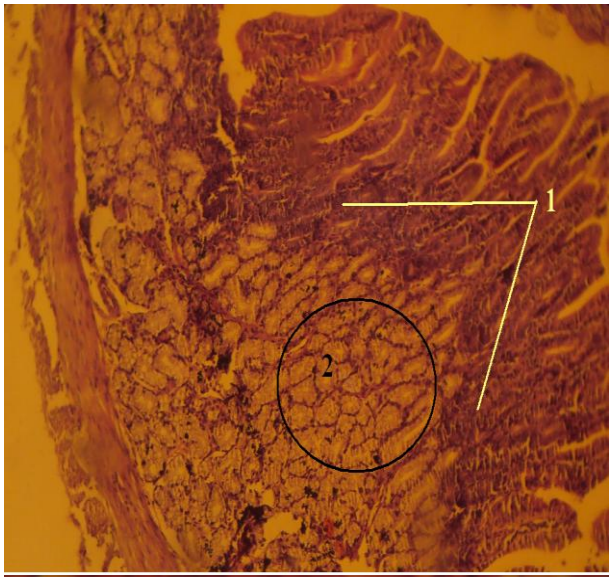


Figure (4) Group (T1)- Duodenum: necrosis and destruction most of the superficial glands(1), while (2) represent viable glandular tissue.(H&E stain). 100X



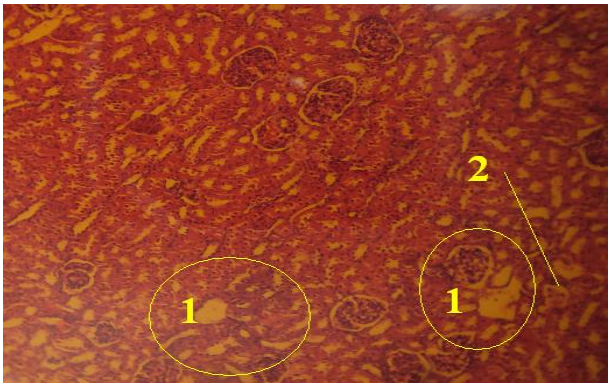
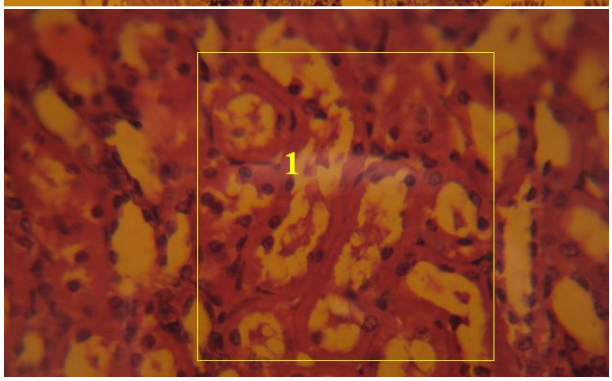
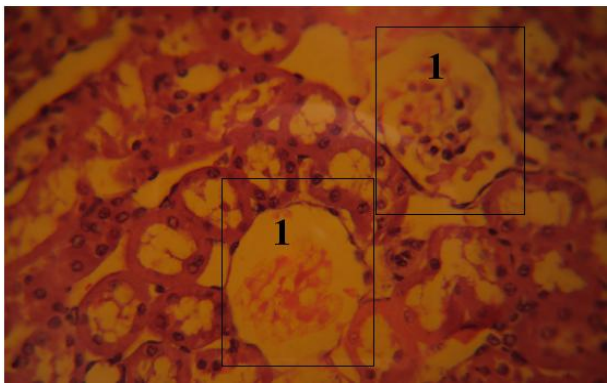


Figure (3) group (T3): the pulmonary alveoli are full of amorphous eosinophilic fluid(circles).(H&E stain).100X.

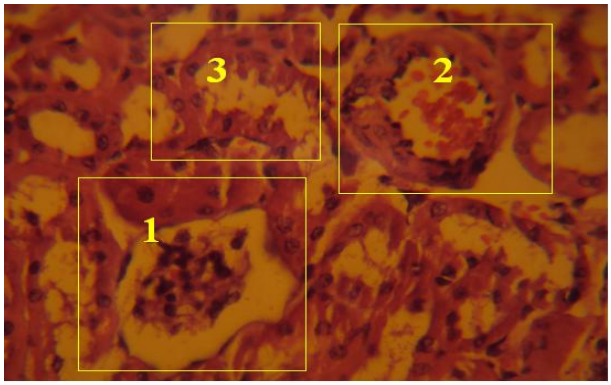


Figure(6) group(T2 and T3): destruction of few renal glomeruli (1) and deposition of eosinophilic materials in the renal tubules with dilatation of the tubules (2).(H&E stain).100X

Figure(7) group (T2 and T3): The renal tubules severely dilated and full with eosinophilic material (1).(H&E stain).400X.



Figure(8) group(T3): The renal glomeruli completely atrophied and destructed(1).(H&E stain).400X



Figure(9) group(T3): The renal glomeruli are atrophied and destructed(1) also there was dilatation of renal tubules(3) and congestion of renal veinules(2).(H&E stain).400X

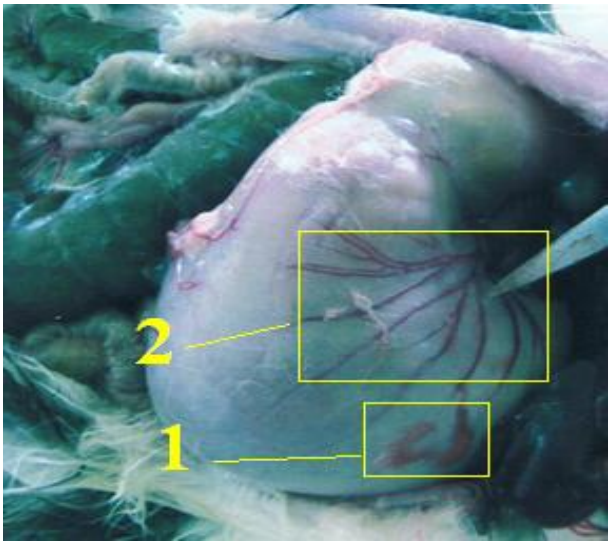


Figure (10): Eccymotic hemorrhage in the stomach(1) and engorgement of blood vessels(2).

Discussion

Clinical signs of CY toxicity in rabbits started during 30 minutes after CY administration and persisted for 60-90 minutes in all treated groups in the dose dependent manner in the present study.The results of this study indicated that cypermenthrin induced anaemia in rabbits. The decrease in RBC counts observed with CY treatment could be due to haemolysis as a result of type II pyrethroid which causes haemorrhages and reduced erythropoiesis this result are similar to the results of (17) that indicate presence of internal haemorrhages and some erythrocytes are absorbed by lymphatic vessels (autotransfusion) particularly in haemorrhages in body cavities. Remaining RBCs are lysed or phagocytosed (18). Various authors have reported similar results with the treatment of CY in rats (10), sheep (19), rabbits (20) and goats (21). Haemoglobin concentration significantly decreased in treated rabbits in the present study. Reduction in Hb contents could be

due to the impaired biosynthesis of haem in bone marrow (22), increased rate of destruction or reduction in rate of formation of RBCs. The decrease in red blood cells and haemoglobin contents could also be due to the disruptive action of the pesticides on the erythropoietic tissue as a result of which the viability of the cells might be affected. Alterations in the haematological parameters were brought about by CY as anemia due to decreased synthesis of red blood cells (23).The decrease in PCV in treated rabbits was obviously contributed by the decreased cellular counts in blood after CY treatment. In addition, the reduction in blood parameters (PCV, Hb and RBC) may be attributed to hyperactivity of bone marrow (24), leading to the production of red blood cells with impaired integrity which were easily destroyed in circulation by reticulo-endothelial system. Shakoori *et al.* (1990)(25) suggested that decrease in RBC counts is either an indicative of excessive damage to erythrocytes or inhibition of erythrocytes formation in rabbits. Luty *et al.*, (2001)(26) reported that irrespective of the dose, the deltamethrin and fenvalerate stimulated erythropoiesis and synthesis of Hb in male Swiss mice, while in female mice the administration of deltamethrin (25 mg.kg-1 b. wt.) resulted in anaemia. In accordance to the findings of the present study, Haratym-Maj, (2002)(13) reported anaemia in female mice, but not in males at CY doses 5 mg.kg-1 b. wt. He also reported that anaemia developed in female mice at low CY doses (5 mg.kg-1 b. wt.), whereas at high CY doses (25 mg.kg-1 b. wt.) no anaemia was observed. He alleged that female mice were principally susceptible to poisoning, particularly with low doses of pyrethroids used for long time. CY can induce oxidative stress in blood cells (27) or may accrue in cell membranes and disturb structure of membrane (28) which could lead to lysis of erythrocytes as a result their number would be low in circulation.Low Hb concentration could be due to enhanced Hb destruction or decreased Hb synthesis (20). Increased activity of bone marrow or haemolysis could lead to impaired Hb synthesis (29). Tissue receive inadequate oxygen (O2) if there is an insufficient supply in inspired air, impaired O2 transport from alveoli into blood stream, hypoventilation, inadequate Hb to carry O2, decreased arterial O2 saturation, abnormal blood flow or failure of haemoglobin to release bound O2 at tissue sites (6).Exposure to cypermethrin may produce convulsions, loss of consciousness and possible death. At higher doses rats exhibited signs of intoxication associated with pathology of the nervous system, decreased growth or increased liver and kidney weights. Short-term toxicity studies indicate that alpha-cypermethrin is approximately 2 to 3 times more toxic than cypermethrin in rats and dogs. Following oral administration to rats 90% of the dose was eliminated from the body over a 4-day period, 78% in the first day. residues in tissues were low except in fat tissue. In human volunteers 43% of an oral dose (0.25-0.75 mg) was excreted within 24 hours in the urine as free or conjugated cis-cyclopropane carboxylic acid. (30).Exposure to respiratory irritants may result in disease of the airways involving difficult breathing and related systemic problems. There is some evidence from animal testing that poisoning by natural pyrethrins may result in convulsion, paralysis with extreme muscle tone, rapid and uneven heart beat, liver and kidney damage, or death. (31).Leukocyte counts increased significantly($P<0.05$) in (T2 and T3) groups compared with control. The increase in WBC may be indicative of activation of defense and immune system of the body (19). This might result in an increase in release of WBC from bone marrow storage pool into the blood. Pathological leukocytosis may have resulted due to chemical, acute haemorrhages and acute hemolysis. Severe haemorrhages in lungs and liver may be the possible cause of

leukocytosis (18).The observed effects were dose-related and included (besides ataxia and hypersensitivity to external stimuli) liver changes and atrophy of the red pulp of the spleen (6).

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التغيرات الدمية–الكيماحيوية والنسيجية المرضية المستحثة بواسطة التسمم الحاد بمادة السايبرمثرين في الأرانب.

حسن خلف عليوي
كلية الطب البيطري /جامعة القادسية

الخلاصة

أجريت هذه الدراسة لتقييم السمية الحادة بمادة السايبرمثرين في الأرانب. استخدمت أربع وعشرون ارانباً في الدراسة وربيت في ظروف متماثلة. وكان الغذاء والماء متاحاً خلال طول مدة الدراسة. بعد سبعة أيام من التأقلم ، قسمت الأرانب عشوائيا إلى مجموعتين متساويتين المجموعة المعاملة (T) ومجموعة السيطرة (C)وقسمت المجموعة المعاملة بالاعتماد على كمية جرعة السايبرمثرين المعطاة الى ثلاثة مجاميع فرعية : T1، T2 و T3، حيث أعطيت جرع السايبرمثرين عن طريق الفم وبواقع (١٥ مغم / كغم ، و ٢٥ مغم / كغم و ٥٠ مغم / كغم) إلى (T1، T2 و T3) على التوالي ، في حين أعطيت مجموعة السيطرة (C) المحلول الفسلجي الطبيعي. تلقت حيوانات التجربة في كل مجموعة ثلاثة جرع في فاصل زمني مدته سبعة أيام. وتم مراقبة كل الحيوانات مرتين يوميا على الاقل لملاحظة ظهور العلامات السريرية. وتم جمع الدم من مجموعة المراقبة والمعالجة لتقييم المعايير الدمية التالية : معدل خضاب الدم ، نسبة حجم خلايا الدم الحمر المرصوصة ، عدد كريات الدم الحمر ، وعدد كريات الدم البيض و عدد الصفائح الدمية ؛ كما تم فصل البلازما لتقييم معدل البروتين الكلي. في اليوم الأخير من التجربة (٢١) تمت التضحية باثنين من الأرانب من كل مجموعة لدراسة التغيرات النسيجية المرضية في المعدة والأمعاء والكلى والرئتين. العلامات السريرية مثل زيادة كمية البول وعدد مرات التبول ، ولعق الساق والوجهه ، والترنح وعدم الاتساق وارتجاف والرأس والعنق ،وصعوبة المشي ظهرت بعد ٣٠ دقيقة واستمرت لمدة ٦٠ إلى ٩٠ دقيقة بعد اعطاء كل جرعة. أظهرت نتاج هذه الدراسة أن عدد الكريات الحمراء انخفضت بشكل ملحوظ ($P<0.05$) في جميع المجاميع المعاملة بمادة السايبرمثرين في الفترات ١٤ و ٢١ يوما من التجربة مقارنة مع مجموعة السيطرة. وانخفض تركيز خضاب الدم بشكل ملحوظ ($P<0.05$) في مجموعتي (T2 و T3) في الفترة (٢١) ، وأظهرت النتيجة فروق ذات دلالة إحصائية ($P<0.05$) بين مجموعة (T3) بقية المجاميع الأخرى للدراسة ، في حين انخفضت نسبة حجم خلايا الدم الحمر المضغوطة في الفترة ١٤ في مجموعتي (T1 و T2) والفترة ٢١ في المجموعة (T3) فقط ، مقارنة مع مجموعة السيطرة ، وكانت النتيجة كشفت انخفاض كبير ($P<0.05$) في المجموعة (T3) بالمقارنة مع المجموعات الأخرى. ولوحظ انخفاض تدريجي الحمرمعتمد على الجرعة في عدد خلايا الدم و معدل خضاب الدم ونسبة حجم الخلايا المرصوصة في جميع المجموعات المعالجة . وبلغ تعداد خلايا الدم البيضاء بدرجة كبيرة ($P<0.05$) ارتفاعً في الفترات ١٤ و ٢١ في مجموعتي (T2 and T3) مقارنة بمجموعة السيطرة. إن عدد كريات الدم البيض في مجموعة (T3) في فترة ٢١ يوما أظهرت فروقً ذات دلالة إحصائية ($P<0.05$) بين جميع المجاميع. وأظهرت النتائج انخفاضً كبيراً في عدد الصفائح الدمية ($P<0.05$) في كل المجاميع المعاملة في الفترات ١٤ و ٢١ يوماً من التجربة بالمقارنة مع مجموعة السيطرة وتبين أن الفرق الإحصائي ($P<0.05$) كان مميزاً في المجموعة (T3) بالمقارنة مع المجاميع الأخرى. كما أظهرت النتائج انخفاضً ملحوظً في معدل البروتينات الكلي ($P<0.05$) في مجموعتي(T2) و (T3) في الفترة (٢١) يوماً. وكشفت نتائج التغييرات النسيجية المرضية احتقان مع وذمة في الرئة مع تورم والتواء في الأوردة الصغيرة والشعيرات الدموية في الرئة. كما إن الاسناخ الهوائية في الرئتين مليئة بسائل ذو لون احمر ، كذلك وجود سماكة في الحواجز السنخية. وكشفت النتائج وجود تآكل ونزيف في الغشاء المخاطي للأمعاء مع نخر وتحطم للنسيج الغدي السطحي. مع وجود عدد قليل من النسيج الغدي الحي تحت الأنسجة المتنخرة. الغشاء المخاطي المعوي ضامر عادة وأكثر نحافة من المعتاد. في الكليتين كشف النتائج وجود تحطم قليل لكبيبات الكلى ، وترسب مواد حمراء اللون (من المحتمل أن تكون ليفية) في الأنابيب الكلوية مع توسع في الأنابيب. كذلك أظهرت النتائج حدوث ضمور وتحطم كامل لبعض من كبيبات الكلى.