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Histopathological Effects of Supercypermethrin in Liver of Albino rats

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ABSTRACT

Histopathological alterations histochemistry and Biochemical parameters were used to assess the toxicity of the commercial pesticide (cypermethrin) on the liver tissue of male albino rats. 48 rats were used in this study. Each set of six rats was separated into four groups in the acute experiment. The control group was subcutaneously injected with distilled water, while the other three were injected subcutaneously with the insecticide at different concentrations (0.050, 0.025, 0.10). At these different concentrations, acute toxicity was assessed. A)er 24 hours, the mortality rate and poisoning signs increased with the increase in the concentration of the pesticide. As for the subacute toxicity experiment, 4 groups were used in this experiment with 6 animals in each. a control group injected with distilled water only, and another group injected with 0.025 as a single daily dose for 10, 20, and 30 days, respectively. This pesticide In the three separate times, caused some histopathological and biochemical changes in the treated groups in liver tissues and some biochemical changes in liver function were recorded, including Alanine Transaminase(ALT), Aspartate Transaminase (AST), and the levels of protein were measured in the serum. The researchers determined that cypermethrin has acute and subacute toxic effects, which manifested as alterations in serum enzymes and histopathological abnormalities in liver tissue.

التأثيرات المرضية النسجية للسوبرسايبرين في كبد الجرذان البيضاء

لقاء حسين الدليمي

قسم علوم الحياة، كلية التربية للبنات، جامعة الموصل

الخلاصة

تم تشخيص التاثيرات المرضية النسجية والكيمياء النسجية وبعض المعايير الكيموحيوية لتقييم سمية المبيد التجاري (سايبرمثرين) في أنسجة الكبد لذكور الجرذان البيضاء. تم استخدام 48 جرذا في هذه الدراسة. تم فصل كل مجموعة من ستة جرذان إلى أربع مجموعات في التجربة الحادة. تم حقن مجموعة السيطرة تحت الجلد بالماء المقطر ، بينما تم حقنت المجاميع الثلاثة الأخرى تحت الجلد بالمبيد بتراكيز مختلفة (0.050 ، 0.025 ، 0.10). عند هذه التراكيز المختلفة ، تم تقييم السمية الحادة بعد 24 ساعة ازدادت معدلات النفوق وعلامات التسمم بزيادة تركيز المبيد. أما بالنسبة لتجربة السمية تحت الحادة ، فقد استخدمت في هذه التجربة 4 مجموعات بواقع 6 حيوانات في كل مجموعة. حقنت مجموعة السيطرة بالماء المقطر فقط ، وحقنت بقية المجاميع بتركيز 0.025 كجرعة يومية واحدة وللفترات 10 ، 20 ، 30 يوما على التوالي. تسبب هذا المبيد في ثلاث فترات منفصلة في احداث بعض التغيرات المرضية النسجية والكيميائية في المجاميع المعالجة في أنسجة الكبد وقياس بعض المعايير البيوكيميائية في

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وظائف الكبد Alanine Transaminase (ALT) و Aspartate Transaminase (AST) وكذلك قياس مستوى البروتين في مصل الدم. خلص الباحثون أن السايبرمثرين له تأثيرات سامة حادة وتحت حادة ، والتي تتجلى كتغيرات في إنزيمات وبروتين المصل والتغييرات النسجية المرضية في أنسجة الكبد.

الكلمات المفتاحية: تاثيرات نسجية مرضية للكبد، السوبرسايبرين، جرذان بيضاء.

Introduction

Pyrethroid insecticides are highly effective insecticides that are utilized in agricultural fields and residences all over the world. Cypermethrin is a pyrethroid that is used to control insects in the house and on farms. Despite its positive effects, its unregulated and repeated use has unintended consequences in non-target organisms (1). Its toxicity in humans is caused by inadvertent or deliberate exposure by inhalation, skin contact, or ingestion. Acute oral cypermethrin poisoning in humans or non-target organisms usually results in neurotoxicity due to delayed closure of voltage-sensitive sodium channels at higher dosages, as well as gastrointestinal symptoms (2).

However, even though pesticides have a variety of benefits, such as increased food production and a reduction in insect-borne diseases, their side effects on human health and the environment have become a major concern, including the effect on water quality, and pesticide use has become increasingly stimulating (3).

Cypermethrin produces neurotoxicity and motor impairments when it passes the blood-brain barrier. Cypermethrin causes excessive central nervous system stimulation by prolonging the opening of the sodium channel, which is one of its main sites of action. Cypermethrin regulates voltage-gated chloride, calcium, and potassium channels, modifies glutamate, acetylcholine, and adenosine triphosphate receptor function, and causes DNA damage and oxidative stress in neurons, in addition to the sodium channel (4). Cypermethrin also affects neurotransmitter levels, such as gamma-aminobutyric acid and dopamine. It's one of the most studied pesticides in neurotoxicology, and not simply because of its effectiveness (3).

The goal of this study is to determine the histopathological and histochemical changes in liver tissue, as well as their relationship to biochemical changes affecting liver function in albino rats treated with the insecticide (cypermethrin).

Materials and Methods

SUPER SAYBREN is a commercial cypermethrin product from Syngenta, and the diagnostic kits utilized for AST, ALT, and total protein, were from Biolabo in France.

Preparing the concentration

The stock solution of the cypermethrin was poured the needed volume of pesticide into a 10 mL cylinder. The container was filled with distilled water to 10 mL. Including five concentrations, based on the results of preliminary testing to calculate treatment doses (0.010, 0.025, 0.050, 0.075 and 0.10 mL) 9 mL D.W. to 1 mL stock solution (5), and solutions are kept in 10 mL glass bottles with airtight lids in the refrigerator at 4 °C until needed (the required concentrations listed above were prepared before starting each experiment).

Animals

This study employed white Wister rats that were one week old and weighed between 100 and 150 grams. They were raised in special plastic cages in the College of Veterinary Medicine's animal house, where they were given the water and food they needed throughout the study period, with a commitment to providing appropriate laboratory conditions of light and heat, as well as ethical methods in dealing with rats.

Cypermethrin acute toxicity study

24 rats were utilized in this study. The rats were placed into four groups, each with six rats. They were injected with subcutaneous dosages of 0.01, 0.025, and 0.05, and were divided into three groups.

First group: 0.2 ml D.W. control

The second group injected a concentration of 0.01.

The third group injected a concentration of 0.025

The fourth group is injected with a 0.05 concentration.

The number of dead animals and toxicity signs were estimated by using log probability analysis after 24 hours of treatment the lowest effective

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treatment concentration for rats was chosen, which was 0.025 of the pesticide which will be used in the sub-acute trial (5).

A sub-acute toxicity study of cypermethrin

In this experiment, rats were divided into four groups: the first one was given distilled water as a control, while the other three were injected with a concentration of 0.025 each animal, with the second group receiving treatment for 10 days, the third for 20 days, and the fourth for 30 days, respectively.

The rats were anesthetized with ether after the experiment was completed to extract blood from the eye socket and then blood was placed in clean plastic tubes. After 15 minutes, the blood samples were centrifuged at 3000 rpm for 10 minutes to extract the serum, which was then collected and refrigerated at -20 ° C until the Biochemical tests are performed.

Additionally, after the rats were sacrificed and the organs were washed, liver samples were collected, and some of them were placed in special plastic bags for freezing to conduct tissue homogeneity and biochemical tests on them. The organs were placed in plastic tubes with 10% formalin for the rest of their lives. Keep it until histopathological preparation is done (6,7).

Statistical analysis

The one-way ANOVA test was chosen, and then the LSD test was done using a special statistics application called SPSS. The arithmetic mean and standard error were used to describe the data, and the significant difference was less than 0.05.

Results

The results of the first experiment in acute treatment with several concentrations of the pesticide 0.01, 0.025, and 0.05 after 24 hours of treatment and after observing the toxic signs that were represented by severe inactivity in some rats with the death of several animals showed that the treatment with the following concentrations 0.01, 0.025, and 0.05. According to the logarithmic analytical software, a concentration of 0.025 was determined as the most suited for studying the harmful effect (Table 1).

Table 1: represents logarithmic concentrations using Probit Analysis

Group	Dose/Conc.	Total No.	Log Dose
Control	0.00	5	control
2	0.01	5	1.000
3	0.025	5	1.398
4	0.05	5	1.699
5	0.075	5	1.875
6	0.1	5	2.000

As a result of biochemical changes, Protein levels in the serum reduced significantly during the 20 and 30 days of toxicity as compared to the control group and the 10-day treatment group. In serum, ALT and AST levels decreased significantly after 20 and 30 days of treatment compared to the control group and 10 days of treatment, respectively, while in liver tissue, ALT and AST levels decreased significantly after 20 and 30 days of treatment compared to the control group and 10 days of treatment, respectively (Table2).

Table 2: The levels of protein, ALT, and AST enzymes in serum and liver tissue of animals treated with cypermethrin at different periods

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Sample	Exposure time (days)	Protein concentration (mg/dl)	ALT activity(U/L)	AST activity (U/L)
Serum	Zero time	9.4 ± 0.81	84.87 ± 1.28	113.58 ± 2.40
	10	8.7 ± 0.65	79.51± 1.41	102.31 ± 1.99
	20	7.1 ± 0.43 *a	74.81 ± 1.24 *	97.02 ± 1.52 *a
	30	5.2 ± 0.43 *a	68.92 ± 1.43 *a	87.95 ± 2.00*a
Liver tissue	Zero time	6.4 ±0.45	24.19 ± 1.44	91.04 ±1.70
	10	5.3 ±0.40	21.97 ±2.34 *	89.18 ±2.62
	20	5.1 ±0.26	20.46 ±2.05 *	84.85 ±1.94 *
	30	4.5 ±0.52 *	18.07 ±1.74 *	75.13 ±2.54 *a

The group consisted of 6 animals and the values represented the arithmetic mean ± SE
* The difference from control
a difference for a period of 10 days

Histopathological and histochemistry results:
H&E routine stain:

The liver of the control group revealed normal histological architectures (Figure 1,2) while the liver of the insecticide-treated group (after 10 days) showed mild pathological changes represented by congestion of the central vein and sinusoids with mild vacuolar degeneration of the hepatocytes in the liver comparing with the control group (Figure 3,4).

The lesions of the liver of cypermethrin insecticide treated group (after 20 days) were as in the cypermethrin-treated group (10 days) but severer representing necrosis of hepatocytes, dilation of sinusoids, and focal infiltration of inflammatory cells (Figure 5,6). The lesions of the liver of the cypermethrin-treated group (after 30 days) were less severe than group 2 represented by congestion of the central vein and portal vein, vacuolar degeneration of hepatocytes, and dilation of sinusoids in the liver (Figure 7,8).

PAS/Alcian blue stain:

The liver histological sections of the PAS/Alcian blue stain of the control group revealed the normal deposition of glycogen in the cytoplasm of hepatocytes with a positive reaction of magenta color in the liver (Figure 9).

The liver of the cypermethrin-treated group (after10 days) showed depletion of glycogen in the cytoplasm of hepatocytes with a negative reaction of magenta color (Figure 10,11).

The liver of the cypermethrin-treated group (after 20 days) revealed deposition of glycogen and mucopolysaccharides in the cytoplasm of necrotic hepatocytes with the moderate positive reactions of magenta color (Figure 12 ,13).

The liver of cypermethrin-treated group (after 30 days) revealed mild deposition of glycogen and mucopolysaccharides in the cytoplasm of degenerated or necrotic hepatocytes a with mild positive reaction of magenta color (Figure 14,15).

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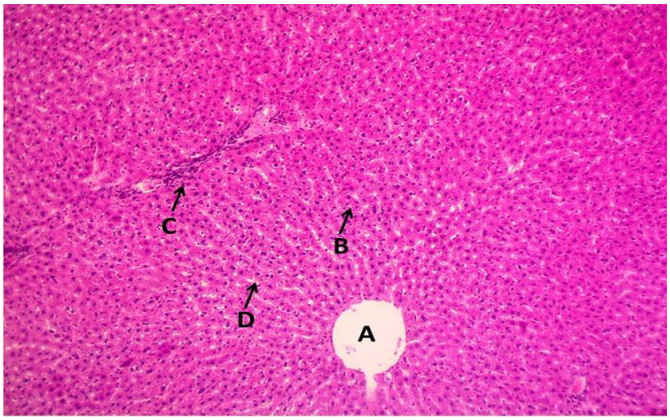

Figure 1: photomicrograph of rat liver of control group shows normal central vein (A), hepatocytes (B), portal area (C) and sinusoids (D). H&E stain, 100X.

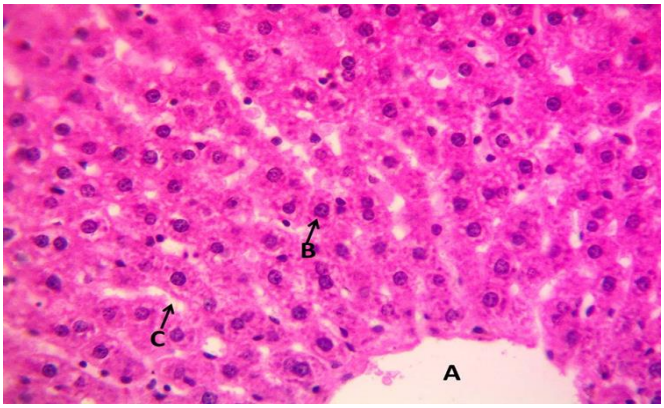

Figure 2: photomicrograph of rat liver of control group shows normal central vein (A), hepatocytes (B) and sinusoids (C). H&E stain, 400X.

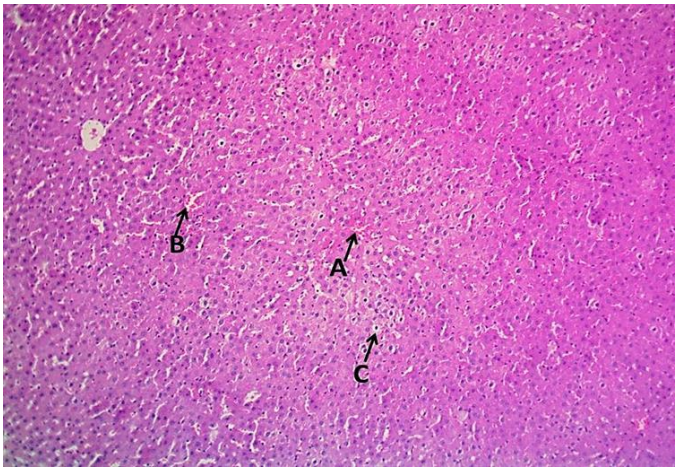

Figure 3: photomicrograph of liver of the Cypermethrin treated group (after 10 days) shows congestion of central vein (A) and sinusoids (B) with mild vacuolar degeneration of hepatocytes (C). H&E stain, 100X.

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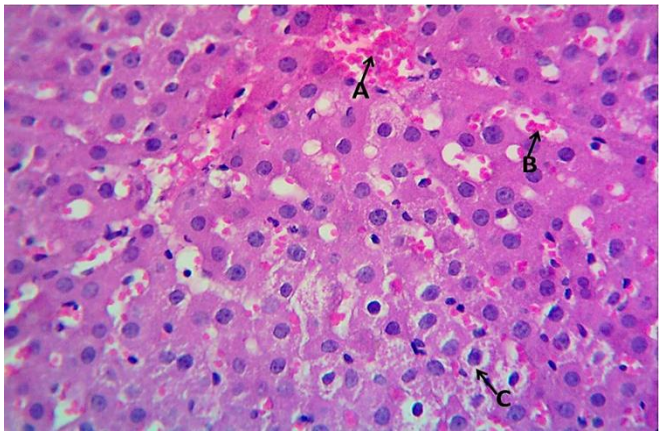

Figure 4: photomicrograph of liver of the Cypermethrin treated group (after 10 days) shows congestion of central vein (A) and sinusoids (B) with mild vacuolar degeneration of hepatocytes (C). H&E stain, 400X.

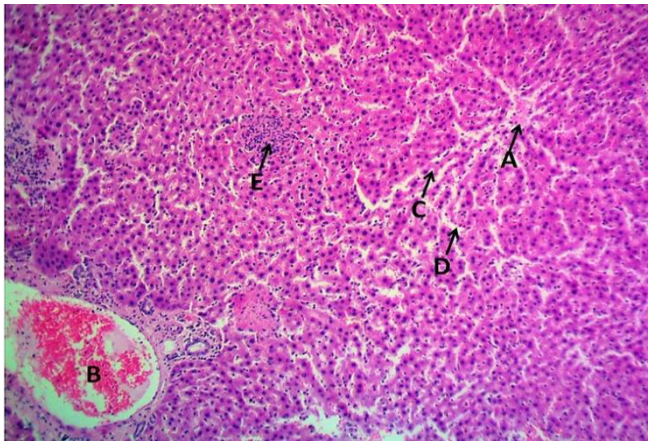

Figure 5: photomicrograph of liver of the Cypermethrin treated group (after 20 days) shows congestion of central vein (A) and portal vein (B), necrosis of hepatocytes (C), dilation of sinusoids (D) and focal infiltration of inflammatory cells (E). H&E stain,

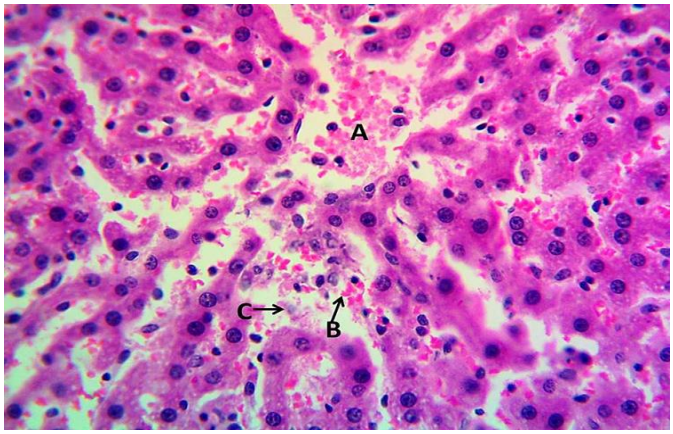

Figure 6: photomicrograph of liver of the Cypermethrin treated group (after 20 days) shows congestion of central vein (A) and sinusoids with dilation (B) and necrosis of hepatocytes (C). H&E stain, 400X.

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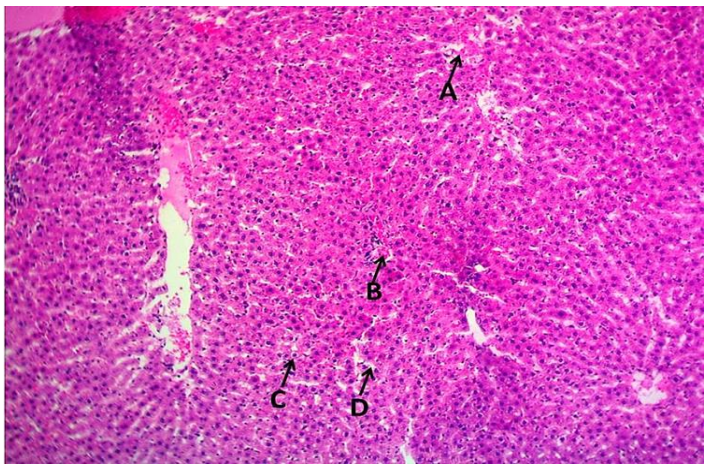

Figure 7: photomicrograph of liver of the Cypermethrin treated group (after 30 days) shows congestion of central vein (A) and portal vein (B), vacuolar degeneration of hepatocytes (C) and dilation of sinusoids (D). H&E stain, 100X.

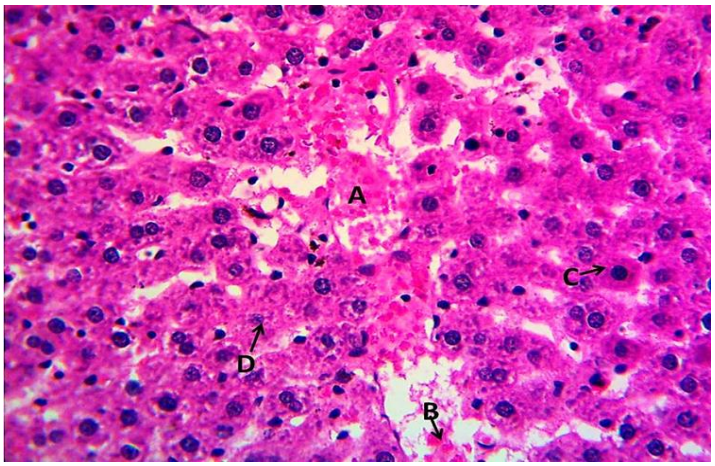

Figure 8: photomicrograph of liver of the Cypermethrin treated group (after 30 days) shows congestion of central vein (A) and sinusoids with dilation (B), cell swelling (C) and necrosis (D). H&E stain, 400X.

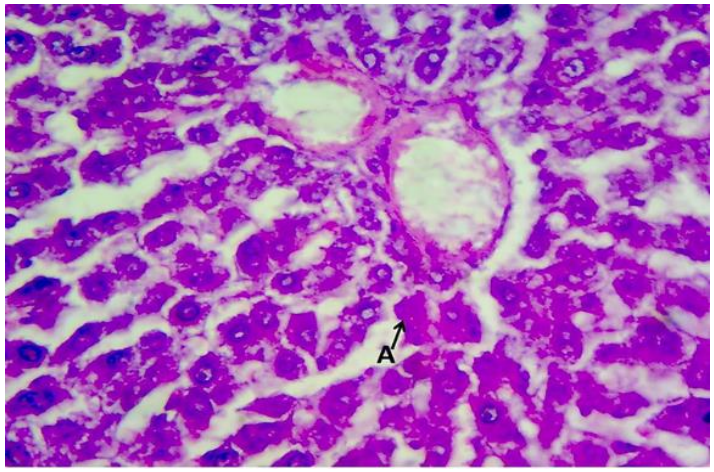

Figure 9: photomicrograph of liver of control group shows normal deposition of glycogen in the cytoplasm of hepatocytes with positive reaction of magenta color (A). PAS/Alcian blue stain, 400X.

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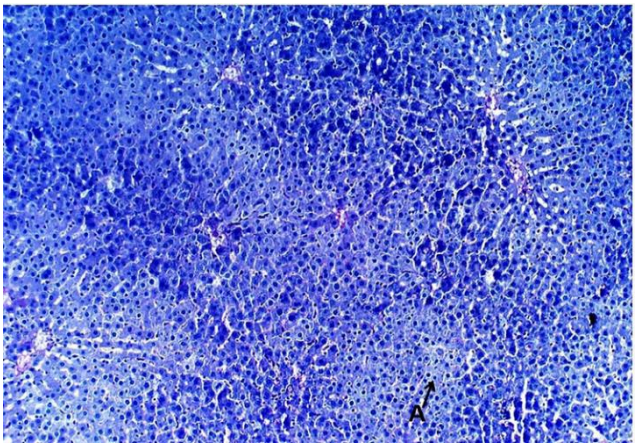

Figure 10: photomicrograph of liver of the Cypermethrin treated group (after 10 days) shows depletion of glycogen in the cytoplasm of hepatocytes with negative reaction of magenta color (A). PAS/Alcian blue stain, 100X.

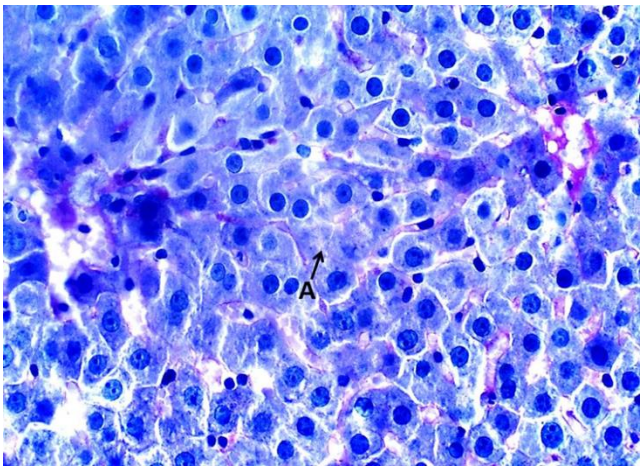

Figure 11: photomicrograph of liver of the Cypermethrin treated group (after 10 days) shows depletion of glycogen in the cytoplasm of hepatocytes with negative reaction of magenta color (A). PAS/Alcian blue stain, 400X.

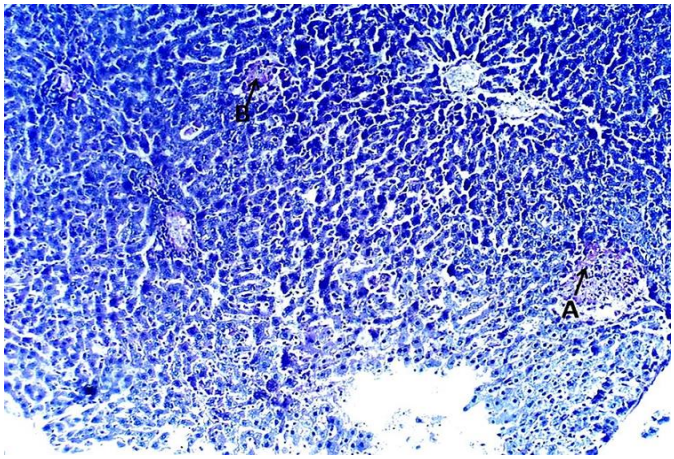

Figure 12: photomicrograph of liver of the Cypermethrin treated group (after 20 days) shows deposition of glycogen and mucopolysaccharides in the cytoplasm of necrotic hepatocytes (A) with moderate positive reaction of magenta color (B). PAS/Alcian blue stain, 100X.

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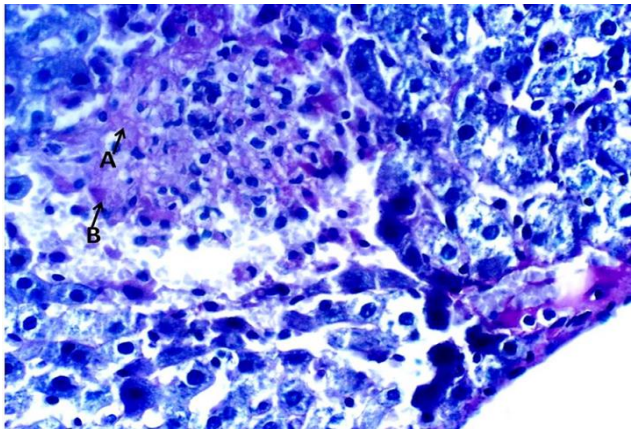

Figure 13: photomicrograph of liver of the Cypermethrin treated group (after 20 days) shows deposition of glycogen and mucopolysaccharides in the cytoplasm of necrotic hepatocytes (A) with moderate positive reaction of magenta color (B). PAS/Alcian blue stain, 400X.

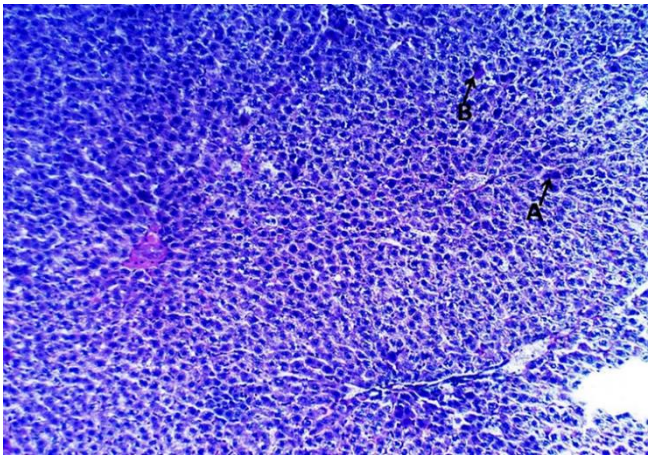

Figure 14: photomicrograph of liver of the Cypermethrin treated group (after 30 days) shows mild deposition of glycogen and mucopolysaccharides in the cytoplasm of degenerated or necrotic hepatocytes (A) with mild positive reaction of magenta color (B). PAS/Alcian blue stain, 100X.

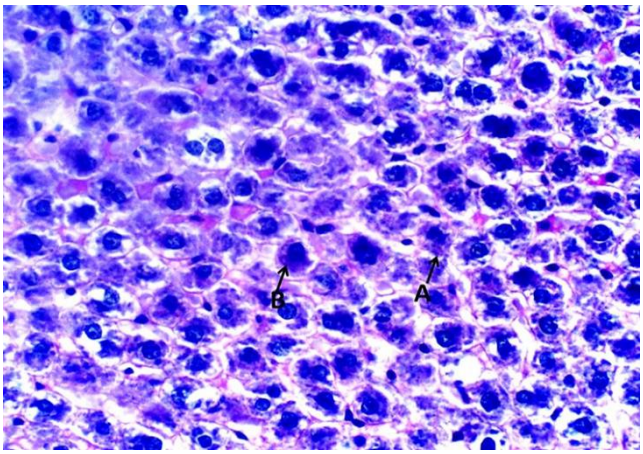

Figure 15: photomicrograph of liver of the Cypermethrin treated group (after 30 days) shows mild deposition of glycogen and mucopolysaccharides in the cytoplasm of degenerated or necrotic hepatocytes (A) with mild positive reaction of magenta color (B). PAS/Alcian blue stain, 400X.

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Discussion

The toxicity of pyrethroid insecticides to mammals has gotten a lot of attention recently, and our research found that they cause biochemical changes as well as other histopathological changes.

Pyrethroid metabolism takes place mostly in the liver, and prolonged exposure can cause liver damage. The researchers employed repeated oral dosages of cypermethrin for 10, 20, and 30 days to show that CYP causes alterations in liver function enzymes and total proteins. When employing routine staining with hematoxylin-eosin and PAS/Alcian blue stain in the tissues of the liver, it was discovered that pathological lesions formed.

Because of the fat-soluble nature of cypermethrin. It builds up in the liver, causing cell damage and degeneration. Cypermethrin produces a high level of free radicals, which produce abnormal oxygen species (ROS) and cause significant damage to cell structure, beginning with vital membranes, lipids, proteins, carbohydrates, and nucleic acids, as well as attacking and destroying mitochondria, which destroys energy stores in the cell and causes cell death (8). Pathological alterations in liver cells also could be caused by cypermethrin's inhibitory effect on total adenine triphosphate activity in the liver, which could lead to a defect in Na+, K transport +, and Ca^2, leading to hepatocyte injury (9).

The structure of the liver was determined to have changed. It's caused by a deficiency of glycogen in liver tissue, a significant inhibition in enzymes that break down esters (4,10). Hypoxia in liver cell tissue moreover, changes in the histopathology of liver tissue nutrition can be defined as a result of a defect in cells and protein catabolism (9), and Put a stop to the activity of The cytoplasmic protease that causes the hydrolyzed protein cascade's several stages, Pesticides' effect on tissues may be due to their effect on the liver's ATPase function, as evidenced by observed changes in liver tissue (11).

The study found that injury to liver tissue was a key cause of liver degeneration, Cypermethrin penetrates the lipid bilayer of the cell membrane, compromising its integrity and posing a risk of DNA damage through instability, DNA helices unravelling, and chromosomal lesions (12).

The results of the histochemistry study revealed glycogen depletion in hepatocytes, which was discovered through the use of PAS/Alcian blue stain, which confirmed the presence of different degrees of dye interaction with liver tissues, and the degrees of this interaction varied depending on the degree of cell damage and necrosis (13). Mucopolysaccharides, are long chains of sugar molecules present throughout the tissue and required for life. Itis plays a key role in preserving the structural integrity of organs, bones, cartilage, skin, elastic tissues, and membranes. Because it aids in the regulation of the flow of nutrients between capillaries in cell development, its depletion implies cellular damage. The results of using PAS/Alcian blue stain in the liver depend on the duration of exposure, and the logical reason for this result, is the removal of glycogen from hepatocytes, which explains the difference in the results between liver tissue (14, 9).

Hepatic proteolytic activity and glycogen decreased possibly due to the degradation of structural proteins and leakage of enzymes into the bloodstream (5). The biochemical data were consistent with the histological changes in our study.

In toxicological research, ALT levels are sometimes lowered. Reduced transaminases can be caused by a decrease in hepatocyte production and release, as well as an inhibitory effect of enzyme activity and a drop in the vitamin B-vitamin pyridoxal 5-phosphate (14).

The current investigation discovers that pyrethroids cause a decreasing trend in total protein concentration that is dose-dependent. Pyrethroids decrease adenine triphosphate synthesis by decreasing mitochondrial oxygen consumption and disrupting the Na+/K+ pump (15), with sodium and water in the cytosol causing cellular water pooling and protein synthesis disruption (9). The researcher found that total proteins are reduced by pyrethroids because of oxidative stress or increased urea enzyme activity; decreasing Total Protein can be caused by renal protein loss, intestinal hemorrhage, malabsorption, and hepatic failure, among other things (9, 16).

The protein depletion observed in this study due to the degradation of structural proteins is evident histologically as the hepatocyte membrane damage caused by the interference of the experimental compounds and their toxic metabolic intermediates (17, 18, 19). Indicate the active use of amino acids for energy and their entry into metabolic processes such as gluconeogenesis. Aminotransferases are enzymes sensitive to hepatocyte damage under oxidative stress induced by xenobiotic. The decreased activity of the hepatic liver enzyme in our study reflects a genetic abnormality in their production in order to overcome parathyroid-induced oxidative stress (20,21).

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Conclusion: The commercial insecticide SUPER SAYBREN (cypermethrin) has shown histological and some biochemical changes in liver tissue and functions, as evidenced by the histopathologically and biochemical changes described in the main text.

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Conflict of interest

In this field, there is no collaboration with anyone.

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