ROLE OF VITAMIN E IN REDUCTION OF OXIDATIVE STRESS INDUCED BY PYRETHROIDS ON RAT LIVER

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ABSTRACT

Pyrethroids account for over than 30% of insecticide use worldwide, a new generation of pyrethroid, is widely used in agriculture, home pest control and protection of foodstuff. Some pyrethroid insecticides last a long time in the environment (days or weeks) and the others may break down within a few minutes to a few hours after application. Extensive application of pesticides is usually accompanied with serious problems of pollution and health hazards. Antioxidants have shown that they inhibit the free radical formation produced by pyrethroid, that may effectively decrease lipid peroxidation in biological systems. So, the present work studied the toxic effect of permethrin on rat liver cells and to evaluate the role of vitamin E in reduction of these effects. The study was carried out on 40 male albino rats. Permethrin was obtained from El-Nasr Co. Intermediate Chem., Egypt. It was obtained in a concentration of (75mg/ml) dissolved in corn oil. Vitamin E was obtained from Arab Company for Pharmaceutical and Medicinal Plants (MEPACO), Egypt, in Capsular form. Rats were assigned to the following experimental groups; Group A: Control group: included 10 rats. They were divided into two subgroups (subgroup A_A: negative control group: included 5 rats on usual diet and had no any addition of medications or drugs; subgroup A_B: positive control group: included 5 rats on usual diet and 0.5 ml of corn oil, to test if it has any effects on the rat liver cells). Group B: Permethrin-treated group: include 15 rats, treated with permethrin in 150 mg/kg/day for 4 months, and had no any other treatment. Group C: include 15 rats, treated with permethrin in 150 mg/kg/ day for 4 months plus vitamin E 100mg/kg/ day for 4 months.; then blood samples were collected for different laboratory analysis from inner canthus of the eye by capillary tubes. The following biochemical parameters had been estimated as: liver function tests, serum glutathione reductase and glutathione peroxidases and alfa–feto protein, then after 4 months liver samples were taken and divided into two samples, one for electron microscopy examination and the other for the histopathological examination by hematoxylin and eosin. In general the results of the present study show that pyrethroids exposure introduces significant oxidative stress in hepatic tissues. In addition, vitamin E exerted a protective effect against oxidative stress damage to liver tissue. It was recommended that expanding more effort on most groups of insecticides with testing the effects of others antioxidants such as (zinc, selenium, glutathione, vitamin C) in reduction of oxidative stress on the liver and others organs.

INTRODUCTION

The synthetic pyrethroids represented a unique group of pesticides that had pyrethrin-like structures with better effects and account for over 30% of insecticide use worldwide **(1).**

Synthetic pyrethroids such as permethrin and deltamethrin are used for indoor pest control because of their high toxicity to insects and considerable low mammalian toxicity compared with other pestiorcides **(2).** Regarding mechanism of their action, pyrethroids act on the axons in the peripheral and central nervous systems of insects, causing prolonged opening of sodium channels **(3).**

Permethrin [3-phenoxy-benzyl (±) cis / trans-3-(2,2- dichloro-vinyl)-2,2-di-methyl-cyclo-propane-1-carboxylate], a pyrethroid insecticide, is widely used worldwide as a wide-spectrum insecticide for numerous crops and for indoor pest control. Its wide use is largely because of its presence in two forms cis and trans permethrin and due to its high activity in insects and relative low toxicity for humans and mammals **(4,5).**

Although it was believed that permethrin had low mammalian toxicity, a high number of studies have shown that permethrin can also cause a variety of toxicities such as neurotoxicity **(6),** cardiotoxicity **(7),** hepatotoxicity **(8),** digestive system toxicity

(9), endocrine disrupting effects **(10,11).**
Pyrethroids are photostable, but they are considered to be safe because they are easily converted to relatively non-toxic derivatives by hydrolysis in mammalian species **(12)**.

However, the pesticide and its metabolites have not been proved definitively to be safe in mammals. For example, some authors have indicated that hydrolysis products of permethrin are more cytotoxic than the parent compound, and show endocrine-disrupting properties **(13).**

In liver, it had been showed that, alcohol dehydrogenase (ADH) and aldehyde dehydrogenase (ALDH) in cytosolic fraction catalyze the oxidations to 3-phenoxybenzyl alcohol (PBAlc) and 3-phenoxybenzaldehyde (PBAld), respectively **(14).**

Involvement of reactive oxygen species is postulated as one of the mechanisms by which pesticides like permethrin exert their deleterious effects on animal tissue **(15).**

Studies carried out with antioxidants such as α-Tocopherol, have shown that they inhibit free radical formation **(16)** and may effectively minimize lipid peroxidation in biological systems **(17).**

AIM OF THE WORK

The aim of the present work is to study the toxic effect of permethrin on rat liver cells and to evaluate the role of vitamin E in reduction of these effects in faculty of medicine, Al-azhar university (New Damietta).

METHODS

The present study was carried out on 40 male albino rats. They were ranged between 150 and 225 gram in weight. They were housed in stainless steel cages under conventional standard conditions (up to five rats per cage, 12 hours light–dark cycle, 22±2 °C, 70±10% humidity).

They were kept under good ventilation and standard hygienic conditions and allowed free access to balanced food and tap water. At the start, rats were left in their housing for 2 weeks, for acclimatization to the environmental condition and to displace the diseased ones. Permethrin was obtained from El-Nasr Co. Intermediate Chem., Cairo, Egypt.

It was obtained in a concentration of (75mg/ml) dissolved in corn oil, that was prepared by company itself on behalf of the researchers. Vitamin E was obtained from Arab Company for Pharmaceutical and Medicinal Plants (MEPACO), Egypt, in Capsular form. Each capsule contains 400mg, equal to 400IU (Alpha tocopherol acetate).

Rats were assigned to the following experimental groups;

Group A: control group: included 10 rats. They were divided into two subgroups;

subgroup A_A: negative control group: included 5 rats on usual diet and had no any addition of medications or drugs and

subgroup A_B: positive control group: included 5 rats on usual diet and 0.5 ml of corn oil, to test if it has any effects on the rat liver cells.

Group B: Permethrin-treated group: include 15 rats, treated with permethrin in 150 mg/kg/day orally for 4 months, and had no any other treatment **(18).**

Group C: include 15 rats, treated with permethrin in 150 mg/kg/ day orally for 4 months plus vitamin E 100mg/kg/ day for 4 months **(19).**

Blood samples were collected for different laboratory analysis from inner canthus of the eye by capillary tubes **(20).**

The following biochemical parameters had been estimated **(20), (21).**

1) liver function tests (including total bilirubin, AST, ALT and alkaline phosphatase enzyme),

2) serum glutathione reductase and glutathione peroxidases were determined on erythrocytes and,

3) alfa–feto protein (AFP). The enzymatic tests were performed on Vita Lab Micro-200 analyzer. This is a quantitative automated and well-programmed biochemical analyzer that can be programmed for 40 different test methods. (AFP) was determined by the method of **(20).** The activity of erythrocyte glutathione reductase (GSH-R) and erythrocyte glutathione peroxidase (GSH-Px) was determined by the method of **(21).**

Histopathological and electron microscopy examination:

After 4 months, the animals were deeply anesthetized by diethyl-ether inhalation in a ball jar. Immediately after deep anesthesia

was achieved, the whole animal was weighted on a sensitive ***FRJ5000*** scale, graduated by 5 g, with the capacity up to 1 kg. The specimens (whole liver) had been taken from control and treated groups and prepared for histopathological examination. A midline skin incision extended from the xiphoid process to the symphysis pubis was made and the abdominal muscles were incised longitudinally. The abdominal viscera were retracted and the liver was exposed. Bouin's fluid was used as a standard fixative, because it keeps the tissue well, penetrated rapidly and caused little shrinkage. The fixative was prepared as follow: 75 ml picric acid, 25 ml formalin and 5 ml glacial acetic acid. 10% neutral buffered formalin was used as the other fixative. A sharp knife to allow rapid penetration of the fixative cuts. Transverse and longitudinal sections of the liver were taken. The specimens were left in the Bouin's solution and 10% neutral buffered formalin for 24 – 48 hours. Each sample (liver) was divided into two samples, one for electron microscopy examination (uranyl acetate enbloc stain, 2%) and the other for the histopathological examination by hematoxylin and eosin stain **(22).**

STATISTICAL ANALYSIS

The collected data were statistically analyzed using SPSS compute package version 16 (SPSS Inc. Chicago, USA). For quantitative data, the mean and standard deviations were calculated and for comparison between more than 2 means, the one way analysis of variance (ANOVA) test was used and $P \leq 0.05$ was considered significant.

RESULTS

Biochemical result:

Both negative and positive control groups showed no significant difference as regard to any of laboratory investigations. Thus, both included as one group (control group) in statistical analysis.

In the present work, body weight was significantly reduced in permethrin and permethrin plus vitamin E groups when compared to control group. However, the difference between permethrin and permethrin plus vitamin E was statistically non-significant. Here, permethrin affected body weight to significant level even if associated with vitamin E. On the other hand, liver weight was significantly increased in each of permethrin and permethrin plus vitamin E groups when compared to control group and in permethrin when compared to permethrin plus vitamin E group. Here, addition of vitamin E reduced the increase in liver weight to a significant level when compared to permethrin alone. In addition, each of total bilirubin, ALT and AST were significantly increase in both permethrin and permethrin plus vitamin E groups when compared to control group and in permethrin group when compared to permethrin plus vitamin E groups. Also, alkaline phosphatase significantly increase in permethrin group when compared to either control or permethrin plus vitamin E groups; but the difference between control and permethrin plus vitamin E was statistically non-significant. On the other hand, albumin was significantly reduced in both permethrin and permethrin plus vitamin E when compared to control group and in permethrin group when compared to permethrin plus vitamin E groups. These results indicated that, vitamin E protects the liver but not to normal levels, i.e., the toxic manifestations still to develop even with vitamin E but to lesser extent. Alfa-fetoprotein significantly increased in permethrin and permethrin plus vitamin E groups when compared to control group and in permethrin when compared to permethrin plus vitamin E group. Finally, glutathione reductase was significantly reduced in permethrin and permethrin plus vitamin E groups when compared to control group but the difference was statistically non-significant between permethrin and permethrin plus vitamin E group (i.e., Vitamin E cannot reserve glutathione reductase). In addition, glutathione peroxidase was significantly increased in permethrin group when compared to either control or permethrin plus vitamin E groups, but the difference between permethrin plus vitamin E and control groups was statistically non-significant (i.e., vitamin E prevents the oxidative stress of permethrin to a significantly higher level) (table 1).

Histopathological results

By light microscopy, histological analysis of the liver of control animals showed hepatocytes with a round, clear nucleus that contained

scarce chromatin and a conspicuous nucleolus. The cytoplasm was granular and a few cells showed lucid vesicles at the periphery. Hepatocytes with abundant but small mitochondria were observed. The rough endoplasmic reticulum was seen throughout the cytoplasm and in larger amounts around the nucleus. In permethrin treated group, there were histopathological changes of liver including dilated central veins, areas of congestion and necrosis and increased mitotic figures. In vitamin E treated group, the pathological changes were less evident than that observed in the permethrin treated groups. The central vein is slightly dilated; no areas of congestion or necrosis were observed (Figures 1-4).

By electron microscopy:

The ultra-structural analysis of the liver of control animals showed hepatocytes with a round, clear nucleus which contained scarce chromatin and a conspicuous nucleolus. The cytoplasm was granular and a few cells showed lucid vesicles at the periphery. Hepatocytes with abundant but small mitochondria were observed. The rough endoplasmic reticulum was seen throughout the cytoplasm and in larger amounts around the nucleus (Figures 5). In permethrin treated group, mitochondria were found discretely dilated, and some small mitochondria contained dense inclusions. Endoplasmic reticulum cisternae were associated with the mitochondria. The liver parenchyma showed hepatocytes with clear vesicles of different sizes. At the ultrastructure level, there were a large number of round, ovoid mitochondria, with short christae and clear matrix. Some small mitochondria, that were also damaged, showed dense inclusions. There was also an increase in smooth endoplasmic reticulum. The proliferation and swelling of the smooth endoplasmic reticulum were more evident (Figures 6). . The liver of the animals treated with vitamin E showed slight damage to the hepatocytes organelles. An increase in the smooth endoplasmic reticulum was observed, a slight swelling of the mitochondria and an increase in the number of secondary lysosomes, which indicates a strong endocytotic activity. The protective effect exerted by vitamin E in this study was observed in the inner membrane of the mitochondria and in the endoplasmic reticulum of the liver cells (Figures 7).

Table (1): Comparison between studied groups as regards laboratory data by using (ANOVA) test

	Control		Permethrin		Per + Vit-E		p1	p2	P3
	Mean	SD	Mean	SD	Mean	SD	0.007*	0.27	0.008*
Weight (g)	195.40	18.14	175.80	15.02	189.13	9.81	<0.001*	0.02*	<0.001*
Liver weight(g)	10.78	0.85	15.80	3.09	12.13	1.50	<0.001*	<0.001*	<0.001*
Total bilirubin(mg/dl)	0.41	0.12	1.19	0.25	0.86	0.16	<0.001*	<0.001*	<0.001*
ALT(IU/L)	18.90	2.60	97.73	12.47	53.00	21.77	<0.001*	<0.001*	<0.001*
AST(IU/L)	25.10	3.78	43.33	3.43	31.86	4.01	<0.001*	<0.001*	<0.001*
Alkaline phosphatase (IU/L)	64.90	21.24	116.46	15.86	77.20	11.28	<0.001*	0.07	<0.001*
Albumin (g/dl)	4.64	0.21	3.72	0.22	3.96	0.12	<0.001*	<0.001*	0.002*
Alfa-fetoprotein (µg/ml)	2.06	0.23	12.0	2.80	6.00	2.13	<0.001*	<0.001*	<0.001*
Glutathione reductase (U/g Hb)	11.19	2.14	3.76	0.54	4.01	0.42	<0.001*	<0.001*	0.16
Glutathione peroxidase (U/g Hb)	69.70	8.51	103.46	8.65	66.46	13.77	<0.001*	0.51	<0.001*

*P1 = Comparison between control and permethrin groups; P2= Comparison between control and permethrin plus vitamin E groups; P3= comparison between permethrin and permethrin plus vitamin E groups; * = significant difference*

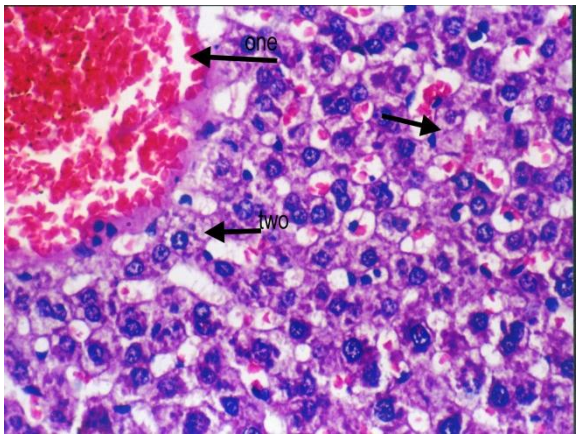

Figure (1): Photo from control group showing normal hepatic lobule with normal hepatocytes and normal central vein (H&E x 400).

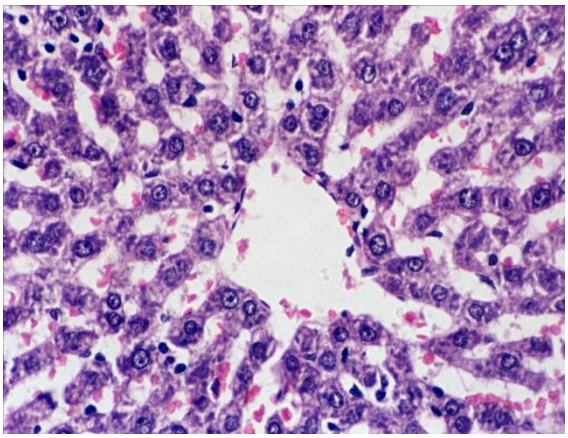

Figure (2): Photo from Permethrin-treated group revealed marked central vein congestion (arrow one); cell swelling up to ballooning of centri-zonal hepatocytes (arrow two) and areas of necrosis (arrow) (H&E x 400).

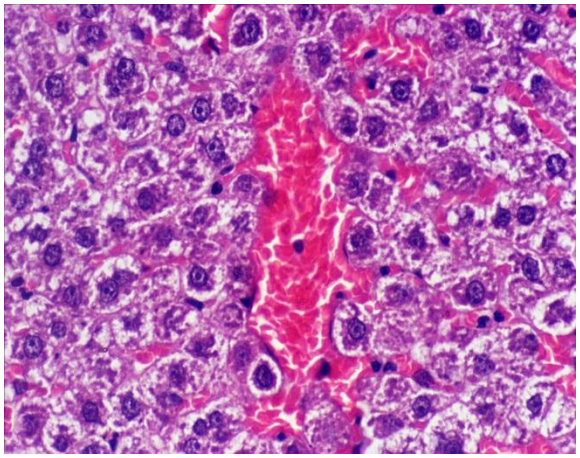

Figure (3): Photo from permethrin treated group showing cell swelling; central vein congestion and areas of necrosis (H & E x 400).

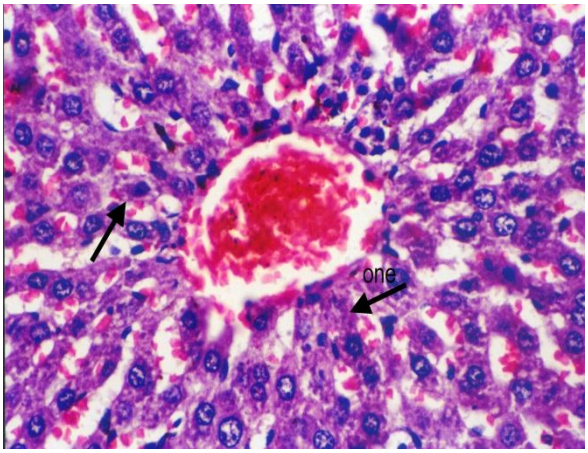

Figure (4): Photo from permethrin+ vit E–treated group showing mild cell swelling (arrow) and mild necrobiosis (arrow one) (H&E x 400).

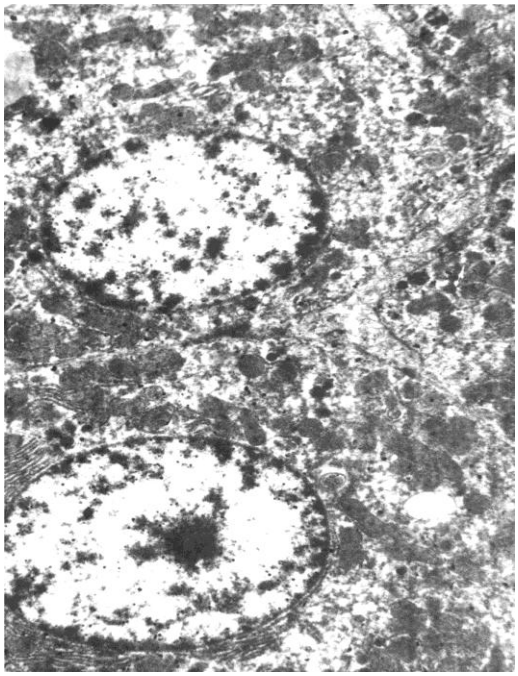

Figure (5): Photo of control rat in showing normal ultrastructure of hepatocytes (UA x4000).

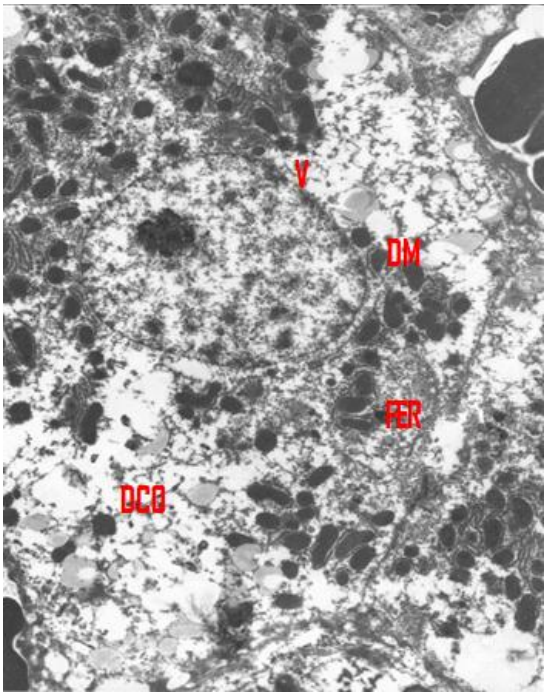

Figure (6): Photo of permethrin treated group showing highly vacuolated cells **(V),** with high degenerated cytoplasmic organelles **(DCO),** fragmented endoplasmic reticulum (**FER**) and highly electron dense mitochondria (**DM**) (UA x 4000).

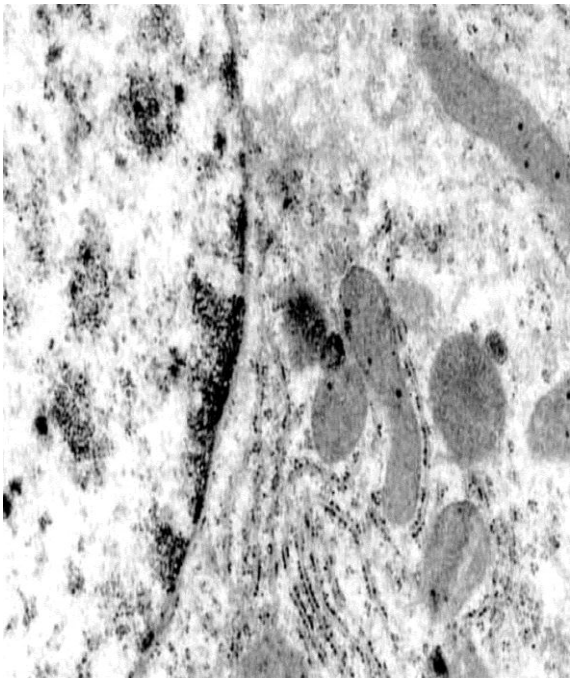

Figure (7): Photo of permethrin treated group + vitamin E showed slight damage to the organelles of hepatocytes (UAx 4000)**.**

DISCUSSION

Pyrethroid insecticides were used preferably over organochlorines, organophosphates and carbamates due to their high effectiveness against a wide range of insects, low toxicity to non-target organisms (mammals) and easy biodegradability. In spite of claims of low mammalian toxicity of synthetic pyrethroids, evidence is gradually accumulated against it **(23).**

Several studies were carried out to evaluate the potential role of antioxidant vitamins, such as, vitamin C, vitamin E, and β-carotene **(24)**, and antioxidant minerals, such as, zinc and selenium **(25)** for the protection of cells against oxidative damage due to pesticides toxicity.

The present study was designed to investigate the oxidative stress possibly exerted by pyrethroids (permethrin) on the liver of the white albino rat and the possible protective effects of vitamin E against toxic effects of permethrin the liver of the rat.

In the present work, body weight was significantly reduced in permethrin and permethrin plus vitamin E groups when compared to control group. However, the difference between permethrin and permethrin plus vitamin E was statistically non-significant. Here, permethrin affected body weight to significant level even if associated with vitamin E. On the other hand, liver weight was significantly increased in each of permethrin and permethrin plus vitamin E groups when compared to control group and in permethrin when compared to permethrin plus vitamin E group. Here, addition of vitamin E reduced the increase in liver weight to a significant level when compared to permethrin alone.

(38) reported that body weights at the end of the study were significantly lower in pyrethroid treated groups in comparison to control group. In addition, liver relative weights were significantly higher than that of control.

In addition, **(26)** reported that a statistically significant decrease in body weight, when compared with the control animals, was found. The relative liver weight of pyrethroid-treated animals showed a significant increase. They also reported that, when rats were treated with vitamin E treatment protects against increase of liver weight in pyrethroid treated group. The

increase in relative liver weights in rats exposed to pyrethroids is in agreement with **(27)** in rats and **(28)** in sheep. The inhibitory effects of antioxidant (genistein) on cell growth targets only proliferating cells, leaving quiescent, and non-dividing cells unaffected, which are likely mediated by inhibition of tyrosine kinases **(29).**

In addition, each of total bilirubin, ALT and AST were significantly increase in both permethrin and permethrin plus vitamin E groups when compared to control group and in permethrin group when compared to permethrin plus vitamin E groups. Also, alkaline phosphatase significantly increase in permethrin group when compared to either control or permethrin plus vitamin E groups; but the difference between control and permethrin plus vitamin E was statistically non-significant. On the other hand, albumin was significantly reduced in both permethrin and permethrin plus vitamin E when compared to control group and in permethrin group when compared to permethrin plus vitamin E groups. These results indicated that, vitamin E protects the liver but not to normal levels, i.e., the toxic manifestations still to develop even with vitamin E but to lesser extent. These results are in agreement with **(30),** who indicated that treatment with pyrethroid caused significant increase ($P<0.05$) in plasma total bilirubin concentrations, ALT and AST compared to control animals. In addition **(31),** reported that low dose pyrethroid altered (decrease) marker enzyme activity.

The increase in plasma total bilirubin concentrations of rats treated with permethrin are in accordance with the previous study of **(32)** in workers exposed to pesticides.

(33), reported that the induction in the plasma bilirubin indicates malfunction in the liver of examined animals. In addition **(34),** reported that treatment with isoflavones alone (Antioxidant) had significant effect on these parameters and counteracted or minimized the toxic effect of pyrethroids. This can be attributed to the vital role of isoflavones as antioxidant factor **(35).**

As regard to serum albumin, our results are supported by the study of **(36),** who reported that albumin decreased by 27% with pyrethroid treatment and it recovers with vitamin E supplementation by about 11%. In addition, **(26),** reported that pyrethroids resulted in a significant ($P<0.05$) decrease in plasma albumin. These results are also in agreement with those of **(37)** in rabbits, **(38)** in sheep, and **(39)** in rats.

(40), found that sheep treated with pyrethroids showed a significant decrease in serum total protein and albumin.

(41), reported that the reduction in plasma protein, particularly albumin, in animals treated with pesticides could be attributed to changes in protein and free amino acid metabolism and their synthesis in the liver. Additionally, the protein depression in the blood was also reported to be mainly due to excessive loss through nephrosis **(42).**

In addition, the decrease in blood protein may be due to loss of protein either by reduce protein synthesis or increased proteolytic activity or degradation **(43).**

Also, the observed decrease in plasma proteins could be attributed in part to the damaging effect of pyrethroids on liver cells as confirmed by the increase in the activities of serum AST and ALT as shown in the present study.

Regarding the protective effects of antioxidant vitamin E on albumin levels, it was in agreement with **(50),** who reported that antioxidant species may act in vivo to decrease oxidative damage to DNA, protein and lipids.

In the present work, alfa-fetoprotein significantly increased in permethrin and permethrin plus vitamin E groups when compared to control group and in permethrin when compared to permethrin plus vitamin E group. These results are in agreement with **(44),** who reported that pyrethroids have the potential to initiate or promote the process of carcinogenesis.

Finally, in the present work, glutathione reductase was significantly reduced in permethrin and permethrin plus vitamin E groups when compared to control group but the

difference was statistically non-significant between permethrin and permethrin plus vitamin E group (i.e., Vitamin E cannot reserve glutathione reductase). In addition, glutathione peroxidase was significantly increased in permethrin group when compared to either control or permethrin plus vitamin E groups, but the difference between permethrin plus vitamin E and control groups was statistically non-significant (i.e., vitamin E prevents the oxidative stress of permethrin to a significantly higher level). It is possible that pyrethroids can be transported through blood to the liver for metabolism and may produce cellular damage in erythrocytes **(8).**

In an extensive review, **(45)** reported that, the generation of reactive oxygen species (ROS) or reactive nitrogen species (RNS) might play critical roles in oxidative stress and the related toxicities induced by permethrin. The oxidative stress induced by permethrin might be dose- and tissue-dependent. In addition, it was reported that, PER could decrease the antioxidant defence system resulting in damage to cellular macromolecules, such as DNA, lipids, and proteins. Following oxidative stress, cell death can occur via apoptotic or necrotic mechanisms. During this process, DNA damage, enhanced lipid peroxidation and protein damage may occur **(46).**

The results of the present study are in agreement with **(39)**, who reported that, when compared study with the control group, administration of pyrethroids to rats caused increases in glutathione peroxidase activities of liver and erythrocytes. In addition, **(47)** observed that the liver can be accepted as source of glutathione peroxidase, and therefore a higher activity was found in this organ compared to the other organs.

The induction of oxidative stress and alteration of antioxidant system by pyrethroids in animals and fishes have been reported. Investigators showed that lipid peroxidation in erythrocytes increased with pyrethroid treatment and antioxidant enzyme activities **(48).**

(49) reported that pretreatment of rats with Vitamin- provided significant protection against the elevation of MDA concentrations in cerebral and hepatic tissues, induced by pyrethroids.

The histological and ultrastructure analysis of the liver of control animals showed hepatocytes and liver lobules with normal architecture. In permethrin treated group, there were histopathological and ultrastructure changes indicated harmful effects on the liver hepatocytes and liver lobules; the changes which markedly reduced by pretreatment of vitamin E. **(30),** reported that pyrethroid produced prominent vacuolation and nuclear de-arrangement of the hepatocytes.

In addition, **(36)** reported that rats of control group did not show any histopathological alteration in liver tissue. In pyrethroid-treated group, hepatocytes were swollen and had cytoplasmic vacuoles. Some hepatocytes had pyknotic nuclei suggesting individual cell necrosis. These changes accompanied by cellular swelling and disorganized hepatic cord pattern. Similar ultrastructure changes were observed by **(51).**

The findings of histological and ultrastructure changes in the liver of animals exposed to pyrethroids, agree with those published by **(50).**

It was reported that pyrethroids administered orally to adult albino rats produced necrotic areas in hepatocytes and cell swelling, cytoplasmic hypertrophy and intracytoplasmic vacuoles were seen. In the in vivo study with pyrethroids in the black Bengal goat resulted in congestion in portal and central veins of the liver and hepatocytes, hydropic degeneration, and a few cases of karyolysis of the liver cells **(51).**

In addition, **(52)** reported that pyrethroids can act as a tumor promoter in rat liver cells. The effect exerted by vitamin E in the study of **(31)** was observed at the inner membrane of the mitochondria and in the endoplasmic reticulum of liver cells. This finding may be explained by the fact that these are sites where vitamin E is accumulated in higher concentrations **(52).**

In conclusion, the results of the present study

show that pyrethroids exposure introduces significant oxidative stress in hepatic tissues. In addition, vitamin E exerted a protective effect against oxidative stress damage to liver tissue. It was that recommended that expanding more effort on most groups of insecticides with testing the effects of others antioxidants such as (zinc, selenium, glutathione, Vitamin C) in reduction of oxidative stress on the liver and others organs.

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تأثير البيرميثرين على خلايا كبد الفئران وتقيم دور فيتامين (ه) في خفض هذه التأثيرات دراسة

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إن نسبة انتشار المبيدات الحشرية البيرثرويد 30% من نسبة المبيدات الحشرية على مستوى العالم، ومع التوسع في اكتشاف انواع جديده من مبيد الحشرات البيرثرويد للتحكم في الحشرات المنزلية وذلك لحماية المواد الغذائية. بعضا من هذه المبيدات يظل عالقا في البيئة لعدة أيام أو أسابيع والبعض الاخر منها يتحلل في خلال دقائق أو ساعات، لذا فالتوسع في استخدام هذه المبيدات، عادة ما يصاحب ذلك من تأثيرات خطيره سواء على البيئة أو على صحة الإنسان. نظرا لان مضادات الاكسدة تمنع تكوين الجزيئات الحرة الضارة الناتجة من مبيد الحشرات البيرثرويد والتي بدورها تقلل اكسد وتحلل الدهون فى الانظمة البيولوجية بالجسم. لذا كان الهدف من هذا البحث هو دراسة دور فيتامين (ه) في خفض الخلل الايضى الناتج عن المبيد الحشري (البيرميثرين) في كبد الفئران، حيث اجريت هذه الدراسة على اربعون ذكر من الفئران البيضاء. تم الحصول على البيرثرويد (البيرميثرن) تركيز75% من شركة النصر للكيماويات المتوسطة بالقاهرة، كما تم الحصول على كبسولات فيتامين (ه) من الشركة العربية للأدوية والنباتات الطبية بالقاهرة. تم تقسيم الفئران الى مجموعتين مجموعة ضابطة (A) وتشمل 10 حالات، تم تقسيمهم الى مجموعتين مجموعة (A_A) : و تشمل 5 فئران تم تناولهم غذاء عادى و مجموعة (A_B) : و تشمل 5 فئران تم تناولهم غذاء عادى بالإضافة الى زيت الذرة لاستبعاد تأثيره على كبد الفئران. مجموعة الدراسة تشمل 30 حاله. تم تقسيمهم الى مجموعة (B): تشمل 15 حالة من الفئران تم معالجتهم بما يعادل 150 مليجرام لكل كيلو جرام يوميا بمادة البيرميثرن لمدة أربعة شهور ومجموعة (C): تشمل 15 حالة من الفئران تم معالجتهم بما يعادل 150 مليجرام لكل كيلو جرام يوميا بمادة البيرميثرن بالإضافة الى فيتامين (ه) بما يعادل 100 مليجرام لكل لكل كيلو جرام يوميا لمدة أربعة شهور. تم سحب عينات الدم من جميع الفئران لعمل وظائف كبد، الجلوتاثيون الاختزالي والبيروكسيد، دلالات الأورام (البروتين الجنيني ألفا). تم أخذ عينات كبدية من الفئران بعد أربعة شهور لفحص النسيج خلويا وفحصة بواسطة الميكروسكوب الإلكتروني. وأسفرت نتائج الدراسة عموما عن وجود تأثير لمبيد الحشرات (البيرميثرن) ذو دلالة واضحة على خلايا الكبد بالإضافة الى الاثر الواضح لفيتامين (ه) وحمايته لخلايا كبد الفئران. لذا بناءا على ما سبق، نوصى بتوسيع العمل ليشمل عدد اكبر من المبيدات الحشرية واختبار عدد اكبر من مضاد الاكسدة مثل مركبات (الزنك، الجلوتاثيون السلينيوم، وفيتامين س) لخفض الاثر السيء والضار لهذه المبيدات على الكبد أو حتى باقي الاعضاء وتطبيقها على الإنسان.