Evaluation the repeated exposure of fipronil on liver and kidney tissues with oxidative stress status in male albino rats

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Abstract: Fipronil (FPN) is a phenylpyrazole class insecticide, which is widely used to control pests in agriculture, and domestic health. The aim study aim to investigate the effect of repeated exposure of formulated FPN on the examination of hepatotoxicity, nephrotoxicity and extended to assess the oxidative stress parameters in adult albino rats. The acute toxicity of formulated FPN and its sublethal effects by oral repeated exposure for 28 days were performed. Three dose levels high, middle and low doses as 1/20, 1/50 and 1/100 of estimated LD_{50} respectively were administrated to rats for repeated exposure study. The results of acute toxicity indicated that FPN exhibited moderate toxicity toward the treated rats. The estimated LD_{50} of formulated FPN was 610 mg/kg. The repeated exposure of FPN induced oxidative stress by increase the level of the lipid peroxidation at high and middle dose. The low dose did not induce significant change. The defense system began to play a role to reduce the effect of the oxidative stress by significant increase in the level of total antioxidant capacity at high, middle and low doses in comparison with the control group. In addition, the level of catalase activity as an antioxidant enzyme increased at high, middle and low doses. Also the activity of glutathione-s-transferase which is a multifunctional enzyme and plays a key role in cellular detoxification increased at the high dose group. According to the histopathological findings in this study, exposure to high and middle doses led to destructive effects only on the kidney tissues. The low dose led to slight effects on the kidney tissues. On the contrary there were no histopathological alterations were observed in the liver tissues at three dose levels. Creatinine and uric acid assays as a kidney function parameters, indicated increase in the level of uric acid and serum creatinine at the high and middle dose but no increasing at low dose in comparison with the control group. The result is complementary with previous findings if the quantity of dose and the variation in tolerance between the species take in consideration.

Keywords: Fipronil, oxidative stress, histopathology, nephrotoxicity

1. Introduction

Fipronil, is a pesticide that belongs to the phenylpyrazole chemical group. It is an insecticide with widespread use in the control of many agricultural and domestic pests. Over the last decade, the usage of Fipronil has increased considerably because it was developed to replace conventional pesticides, such as organophosphates, carbamates and pyrethroids insecticides, which becoming have no action against resistant pest strains **(Narahashi *et al.*, 2010)**. More addition, the fipronil has a broad spectrum of action against insects, being used to control fleas, ticks, termites, mole crickets, ants, rootworms, beetles, cockroaches and other insects **(Tingle *et al.*, 2003)**. Also, fipronil now is used in home applications as a public health pesticide. Fipronil toxicity is attributed to its ability to act at the GABA receptor as a noncompetitive inhibitor of the GABA-gated chloride channels of neurons in the central nervous system. Non conducting of the outflow of the chloride ions affects the transmission of nervous impulses, causing death by neuronal hyperexcitation and paralysis **(Zhao *et al.*, 2004)**. Fipronil is binding stronger to the chloride channels of insects than to those of mammals, resulting in an insecticide with selective toxicity. Thus, fipronil has a greater ability to block GABA-gated Cl channels of insects than those of vertebrates, therefore it is considered safe and is widely used in veterinary medicine **(Gunasekara *et al.*, 2007**).

So, the information on the toxicity and the adverse health effects of the formulation of this active ingredient is very important. As well-known that, the histopathology is a critical part of the toxicological and risk assessment of foods, drugs, chemicals, biologics, and medical devices **(Crissman *et al.*, 2004)**. Therefore, determination of the histopathologic effects of any toxic chemical by using different organisms is remarkable in environmental studies. Investigation of histopathological changes in animal tissues is a sensitive and rapid method, commonly used to detect effects of pesticides on various tissues and organs and to evaluate toxic potential and risk assessment of chemicals in the environment **(Al-Sharqi *et al.*, 2012; Al-Qudsi, and Linjawi, 2012).** In addition, **Tukhtaev *et al.*, (2012)** reported that pro-longed exposure to low doses of fipronil leads to oxidative stress in pregnant rats and their offspring. Moreover, repeated exposure of fipronil for 28 days induced oxidative stress in kidney and brain of mice but vitamin E and vitamin C made protective effect **(Badgujar *et al.*, 2015)**. Therefore, the present study was aimed to evaluate the adverse effects of repeated exposure of formulated fipronil on examination of hepatotoxicity,

nephrotoxicity and some parameters that covered oxidative stress parameters in adult albino rats.

2. MATERIALS AND METHODS

2.1 The tested insecticide (FPN)

The tested insecticide used in this study was a commercial insecticide with active ingredients of Fipronil 80%, the IUPAC name: (±)-5-amino-1-(2,6-dichloro-α,α,α-trifluoro -p-tolyl)-4-trifluoromethylsulfinylpyra-zole-3-carbonitrile. The formulation was supplied as water-dispersible granules (WG) by the Mammalian Toxicology Department, Central Agricultural Pesticides Lab, Dokki, Egypt.

2.2 Animals

Healthy male albino rats (*Rattus norvigieus*) of Wistar strain weighing 120g+10% were used throughout the whole study. The animals were obtained from the laboratory animal house of the Modern Veterinary Office, Giza, Egypt. Animals were kept under full hygienic conditions, had free access to fresh water and fresh well-balanced diet, and kept under supervision for two weeks before commencing the experimental work. The animals were housed in all groups of five rats per cage.

2.3 Experimental design

2.3.1 Median lethal dose (LD50) study

A total of 25 apparently rats were randomly divided into five groups. The first group was used as a pilot test to determine the range of dose levels of the main study. The other four groups were treated orally by gavage four dose levels 401.65, 586.41, 856.16, and 1250.00 mg/kg respectively. The rats were observed individually at least once during the first 30 minutes after dosing, then periodically during the first 24 hours and daily for a total of 14 days. The signs of toxicity and mortality were recording during the observation period.

2.3.2 Repeated oral exposure study

A total of 20 apparently rats were randomly divided into four groups. The first group was kept as control. The other three groups were treated by three dose levels. The first one (high dose) was administered by gavage at dose of 30.5 mg/kg. This equivalent to 1/20 of estimated LD50 of the FPN. The second group (middle dose) received in the same way a dose of 12.2 mg/kg which equivalent to 1/50 of LD50. The third group (low dose) received a dose of 6.1 mg/kg which equivalent to 1/100 of LD50. In all three groups, the administration of FPN was daily and did not stop until the end of the experiments (28 days). The signs of toxicity and the body weights of rats were recorded periodically **(OECD, 2008**).

2.4 Determination of the median lethal dose, LD_{50}

Estimation of the oral LD_{50} (median lethal dose) should be performed to provide preliminary information on the toxic nature of the tested insecticide for which no other toxicology information is available for this formulation. The method described by **(Weil, 1952)**. When the mortality data (***r*-values**) and the ***f*-values** were obtained from the tables. The LD50 can be calculated from the following equation:

log m = log D + d (f + 1), Where: **log m** = the logarithm of the LD50, **log D** = the logarithm of the lowest dose used, **d** = the logarithm of the constant ratio (=1.46) between dosage levels.

2.5 Blood collection and tissue preparation

Rats were sacrificed at the end of treatments through cutting of their neck veins after they were slightly anaesthetized by diethyl ether. Blood samples were collected in sodium heparin tubes for plasma samples while other part (serum samples) was left to clot for 30 min. Then all samples were centrifuged at 3000 rpm for 20 min and stored at −20◦C. Plasma and serum samples were used for oxidative stress and kidney function parameters. Liver and kidney were immediately removed and washed using chilled saline solution then were preserved in formalin (10%, w/v) for histological parameter.

2.6 Oxidative stress parameters

2.6.1. Total antioxidant capacity

The antioxidant capacity which represents the sum of all antioxidant enzymes can be measured by the reaction of antioxidants in the sample with a defined amount of hydrogen peroxide (H_2O_2). The antioxidants in the sample eliminate a certain amount of (H_2O_2) and the residual is determined colorimetrically by an enzymatic reaction **(Koracevic *et al*., 2001).**

2.6.2. Lipid peroxidation

The end-products of lipid peroxidation, is malondialdehyde (MDA) which reacts with thiobarbituric acid reactive substances (TBARS) in acidic middle at temperature of 95°C for 30min to form thiobarbituric acid reactive product which has a pink color and can be measured at 534 nm **(Okhawa *et al*., 1979).**

2.6.3. Catalase (CAT)

The activity of Catalase (CAT) which is one of the antioxidant enzymes was estimated by the method based on the CAT reacts with a known quantity of (H_2O_2) and the reaction is stopped after exactly one minute with catalase inhibitor. Remaining (H_2O_2) react with 3,5-dichloro-2 -hydroxybenzene sulfonic acid (DHBS) and 4-aminophenazone to form chromophore with a color intensity inversely proportional to the amount of catalase in the sample **(Aebi H.,1984).**

2.6.4. Glutathione-S-transferase

The enzyme protects cells against toxicants by conjugating them to glutathione. The glutathione conjugates are metabolized further to mercapturic acid then excreted. The

method based on measuring the conjugation of 1-chloro-2,4-dinitrobenzene (CDNB) with reduced glutathione. The conjugation is accompanied by an increase in absorbance at 340 nm. The rate of increase is directly proportional to GST activity in the sample **(Habig *et al*., 1974).**

2.7 kidney function parameters

2.7.1. Uric acid

Uric acid is the waste product produced from the degradation of purines. In healthy human, uric acid is filtered and removed from the blood by the kidneys and excreted into urine. Because a number of kidney diseases are known to affect uric acid levels, uric acid determination is thus important and useful in diagnosing and evaluating kidney diseases. Increased levels of uric acid are also known to be associated with uremia, leukemia and pneumonia. The method based on measuring the conjugation 3,5-dichloro-2-hydroxybenzene sulfonate and uricase to form chromophore with a color intensity inversely proportional to the amount of uric acid in the sample **(Sanders *et al*., 1980).**

2.7.2. Creatinine

Creatine is a substance found in the muscles, and when creatine is broken down, creatinine is formed. Creatinine is eliminated from the body in urine, through the kidneys. High levels of creatinine in serum or plasma may indicate impairment of functions of the kidneys. The purpose of this test, therefore, is determination of proper functioning of the kidneys. The method based on the creatinine in alkaline solution reacts with picric acid to form a colored complex. The amount of the complex formed is directly proportional to the creatinine concentration **(Bartels *et al*., 1972).**

2.8. Histological section preparation

Liver and kidney specimens were obtained from rats, and immediately fixed in 10% formalin for 24 hrs and decalcification was occurred on formic acid then washed in tap water. Serial dilutions of alcohol (absolute ethyl) were used for dehydration. Specimens were cleared in xylene and embedded in paraffin at 56°C in hot air oven for 24 hr. Paraffin bees wax tissue blocks were prepared for sectioning at 4 microns thickness by sledge microtome. The obtained tissue sections were collected on glass slides, deparaffinized, stained by Hematoxylin & Eosin stain then examination was done through the light microscope **(Banchroft *et al*., 1996).**

2.9 Statistical analysis

The data obtained in this study were calculated and statistically analyzed, according to Studen's t-test **(Venables and Ripley, 2002)**, using SigmaPlot statistics software, Ver. 11. Data were reported as mean ± SE.

3. Results and Discussion

3.1. Median lethal study, LD_{50}

The estimated oral LD_{50} of FPN is 610 mg/kg for adult male rats. Formulated FPN exhibited moderate toxicity toward rats. The symptoms of toxicity manifested by the animals were appeared 6 hours after the administration. The animals showed ataxia, tremor, and convulsions and some cases showed twitching, and nodding. Finally, paralysis was happened then followed by death after 24hrs. No mortality occurred in the animals which were survived after 2 days from administration and during the observation period (14 days). Our result is complementary with report of **(Anonymous, 2006)** which reported that the toxicity of fipronil is moderately hazardous and classified as Class II in WHO pesticide classification. This moderately toxicity of this insecticide due to the specificity of fipronil for insect GABA chloride channels is 700 to 1300 times greater than mammals, which permits the selectivity pest control of invertebrate **(Zhao *et al*., 2003; Zhao *et al*., 2004)**.

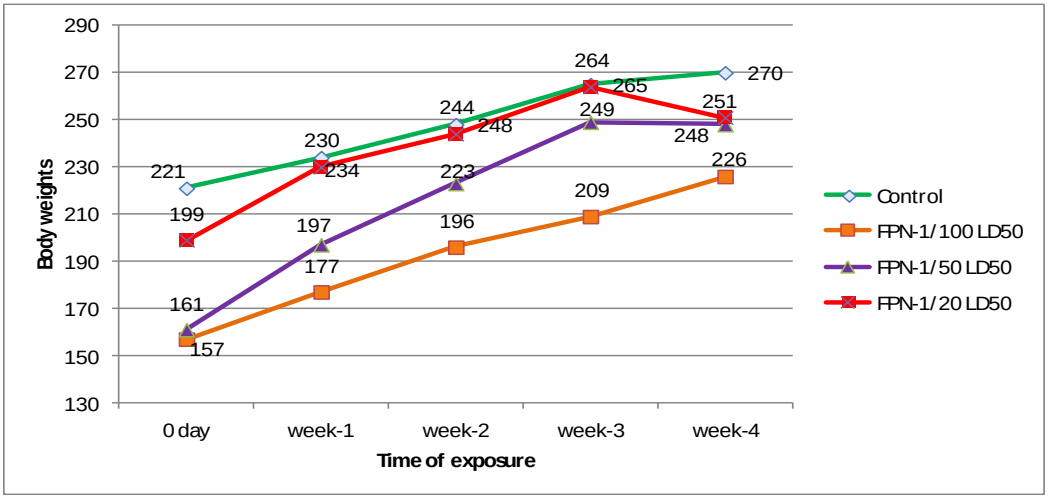

Fig (1). The correlation between the time of exposure of FPN and the mean of body weights of control and treatment groups

3.2. Effects of FPN on the body weight

The present study revealed that there are no signs of toxicity observed on rats after repeated doses of FPN. These observations are in agreement with **(Begymbetova *et al.*, 2011)** who administered fipron-il in the diet for four weeks in groups of five rats of each sex at concentrations ranged from 0 to 55 mg/kg body weights (bw) per day and found one female at 45 and one male at 55 mg/kg bw were died, and no accompanying signs of toxicity observed or pathological findings on the treated animals. Also found no decreased in bw in animals of each sex at doses < 13 mg/kg bw. Our results revealed that there were decrease in body weights after 4 weeks from repeated treatments in the dose of 1/20 and 1/50 of LD_{50} while at low dose 1/100 of LD_{50} did not induce any significant decrease in the body weights when each group was compared with the mean of the same group before and after one week, see (Fig 1). This result is apparently in agreement with **Hughes, (1997)** who found that slight loss of weight was seen on the first day after treatment and decreased in body -weight was gain up to day 3 after a single dose 25 mg/kg bw of FPN (purity, 97.9%). Our results also are in agreement with **Badgujar *et al.*, (2015)** they reported that there was no significant change in the body weight of mice treated with fipronil 2.5, 5 and 10 mg/kg bw respectively for 28 days as compared to control. On the other hand, the low dose which given to rats in this study did not induce significant decrease in the body weight. However, the lowest dose that produced adverse effects in body weight after repeated dose of FPN is equal 8.89 mg/kg/day for male rats **(Fipronil fact sheet, 1996**). So, according to our result it can be propose that the no observed adverse effects level (NOAEL) of this tested FPN is 6.1 mg/kg/day which is based on no decrease was happened in the body weights of the treated rats.

3.3. Effects of FPN on oxidative stress and antioxidant parameters

Oxidative stress induction involves an excessive production of reactive oxygen species (ROS) resulting from impaired balance between the ROS generation and antioxidant defense capability. Induction of oxidative stress is one of the main mechanisms of the action of many pesticides. The damage of membrane lipids is one of the endpoint of oxidative stress-inducing by the pesticides **(Tuzmen *et al.*, 2008).** In our study the results were summarized in Table (2) which indicated that the FPN induced oxidative stress through increase the level of the lipid peroxidation (MDA) at high and middle doses in comparison with control. On the other hand, the defense system began to play a role to reduce the effect of the oxidative stress by increase in the level of total antioxidant capacity (TAC) at high, middle and low. Also, the level of catalase (CAT) activity as an antioxidant enzyme significantly increased at high, middle and low doses. Also the activity of glutathione-s-transferase (GST) which is a multifunctional enzyme and plays a key

role in cellular detoxification increased at the high dose. These findings are apparently agreement with **Tukhtaev *et al.*, (2013)** they found that prolonged exposure (14-21 days) of pregnancy to low doses of fipronil (3.6 mg/kg) leads to oxidative stress in pregnant females and their offspring on 7-14 days after birth. They found significant increse in the level (MDA) and decrease in the activity of (CAT). Also **Badgujar *et al.*, (2015)** found that FPN exposure at three doses 2.5, 5 and 10 mg/kg bw, respectively for 28 days in mice caused significant increase in the lipid peroxidation in the brain and kidney tissues; while level of antioxidant enzymes superoxide dismutase (SOD) and catalase (CAT) were severely decreased. In addition **Wang *et al.*, (2016)** reported that the reactive oxygen species (ROS) and oxidative stress may be a result of FPN treatment and have correlated them with various types of toxicity.

3.4. Effects of FPN on the Liver tissues

Liver is a target organ for detoxification and is prone to various disorders as a consequence of exposure to environmental pollutants. Histopathological alterations in tissue may be used as a rapid method to evaluate the toxic effects of chemicals in different tissues and organs **(Bernet *et al.*,1999).** Histopathological examination of liver specimens taken from control group showed normal histological structure of the central vein and surrounding hepatocytes in the parenchyma Fig.2 (1-A). Also the

Table (1): Assessment of oxidative stress parameters in the plasma of rats treated with the FPN

Parameters	Control group	High dose =(30.5 mg/kg)	middle dose =(12.2 mg/kg)	Low dose =(6.1 mg/kg)
TAC (mM/L)	2.29 ± 0.09	$2.95 \pm 0.08^{(\uparrow)***}$	$2.69 \pm 0.07^{(\uparrow)**}$	$2.74 \pm 0.04^{(\uparrow)**}$
MDA (nmol/ml)	2.32 ± 0.17	$6.91 \pm 0.98^{(\uparrow)**}$	$4.83 \pm 0.58^{(\uparrow)**}$	$2.48 \pm 0.44^{(N.S)}$
CAT (U/L)	61.31 ± 2.62	$90.96 \pm 2.15^{(\uparrow)***}$	$76.38 \pm 5.09^{(\uparrow)*}$	$72.4 \pm 3.99^{(\uparrow)*}$
GST (U/L)	41.50 ± 3.58	$89.36 \pm 2.20^{(\uparrow)***}$	51.18 ± 3.42	49.83 ± 3.68

Values are from five replicates in each group and expressed as mean ± SE of each group; ***Significant at p<0.001; **Significant at p<0.01; *Significant at p<0.05 (N.S), non-significant; (-), Significant increase; (TAC), total antioxidant capacity; (MDA), malondialdehyde; (CAT), Catalase; and (GST), glutathione-s-transferase.

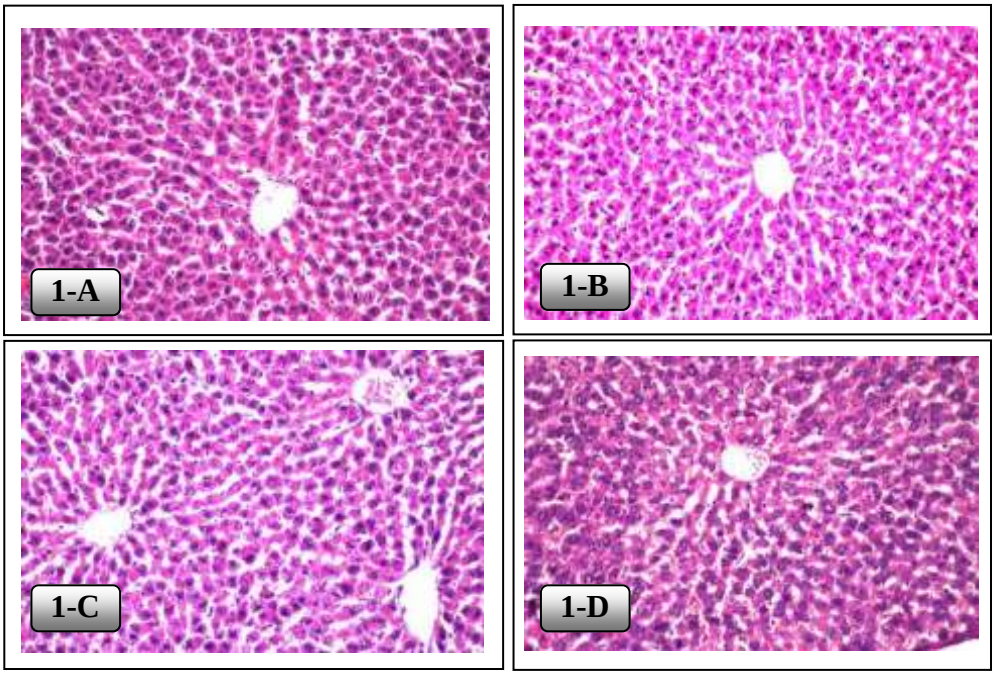

Fig (2) . Light micrographs of the rats liver tissue show as follow: (1-A), control group showing normal histological structure of hepatocytes; (1-B); (1-C), and (1-D) high, middle and low dose group respectively showing no histopathological alteration recorded.

histopathological examination of the three treated groups showed no histopathological alteration recorded in the hepatocytes Fig.2 (1-B), (1-C), and (1-D). Our results are agreements with **Begymbetova *et al.*, (2011)** who found that the microscopic examination of intact rat livers tissues of different age did not reveal any pathological changes after exposed three age groups of rats to aqueous solution of fipronil 10 mg/kg for 10 days. in contrast in fish study **(El-Murr *et al.*, 2015)** reported that the liver and gills of fish exposed to fipronil showed different histopathological alterations. Also similar findings in fish study **(Qureshi *et al.*, 2016)** reported that the exposure to sub-acute doses of fipronil and buprofezin in combinationor alone induces histopathological damage in liver of common carp. So, It seems that the FPN not induce adverse effect in the liver tissues of mammals but may be has harmful effects on aquatic organisms.

3.5. Effects of FPN on the kidney tissues

The kidney is the excretory organ shared the liver the main role of detoxification of the toxic chemicals. Both of them suffered from the stress of these injury compounds in the body. The histopathological examination of kidney specimens of control group showed normal histological structure of the glomeruli and tubules at the cortex Fig 3(2-A). In the our study, all three dose levels high, middle and low groups induced effects on the kidney tissues ranged from slight to severe effects. The low dose group showed congestion in glomeruli tuff with congestion in the intertubular blood vessels (2-B). the middle dose group induced swelling and vacuolization in the tubular lining endothelium and the high dose group induced congestion in the blood vessels and coagulative necrosis in the tubular lining epithelium (2-D). So, it seems the low dose of FPN treatment induced moderate histopathological lesions but the middle and high doses exhibited severe congestion in the glomerular tufts associated with coagulative necrosis in the tubular lining epithelium at the cortex of the kidney. In previous studies **(Mossaa *et al.*, 2015)** found that FPN caused histopathological alterations in liver and kidney of male rats at three concentrations 0.1, 1 and 10 mg/L in drinking water for 45 days. They thought that alterations in liver and kidney tissues could be due to the toxic effect of FPN that associated with a generation of free radicals. Moreover **(Badgujar *et al.*, 2015)** who reported that the mice treated with FPN 2.5, 5 and 10 mg/kg bw respectively for 28 days caused significant histopathological alterations in brain and kidneys of the mice. Also in fish study **(Qureshi *et al.*, 2016)** reported that the exposure to sub-acute doses of fipronil induced significant histomorphological alterations in the kidney tissue of all treatment groups in comparison to the control group. So, the above findings suggested that the kidney may be affected and suffered than the liver in detoxifying and eliminate the toxic agents.

3.6. Effects of FPN on the kidney function

Serum or plasma creatinine determines the glomerular filtration rate. Creatinine is derived mainly from the catabolism of creatine witch found in muscle tissue and its catabolism to creatinine. Severe kidney damage will lead to increase the creatinine levels. In the present study (table 2), the level of serum creatinine showed significant increase at the high dose but the middle and low dose did not induce significant changes. Previous study **(Ali *et al.*, 2016)** revealed that the creatinine and uric acid levels in

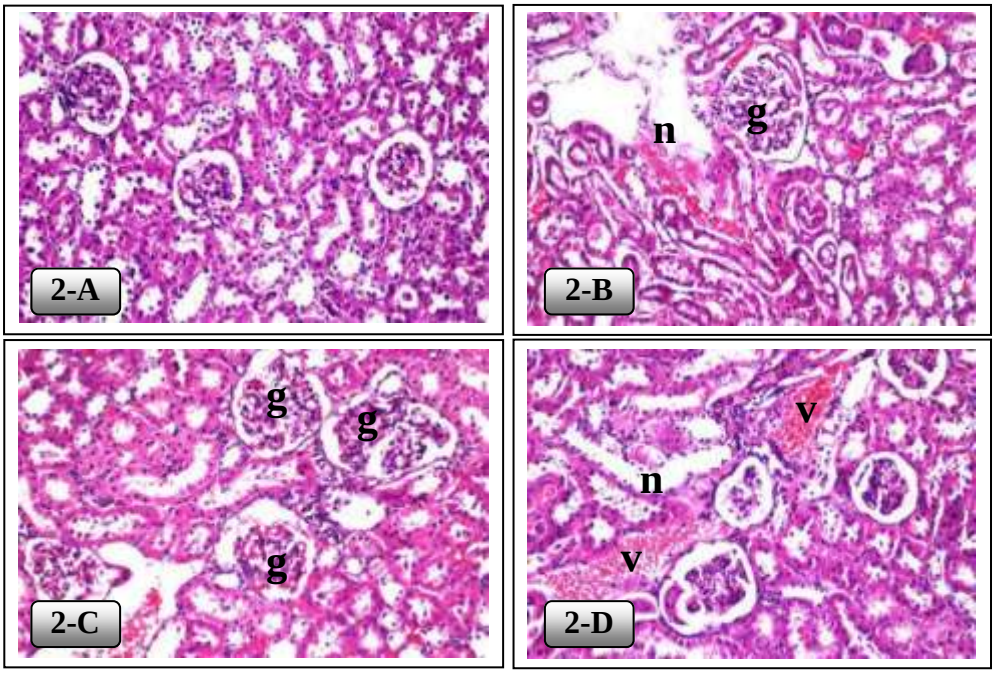

Fig (3) . Light micrographs of the rats kidney tissues show as follow: (2-A), control group showing normal histological structure of glomeruli and tubules at the cortex; (2-B), low dose group showing congestion in glomeruli tuff(g) with coagulative necrosis in the intertubular blood vessels(n); (2-C), middle dose group showing swelling and vacuolization in the tubular lining endothelium(g&n); (2-D), high dose group showing Sever congestion in the cortical blood vessels(v) and coagulative necrosis in the lining epithelium in most tubules(n).

Table(2): Uric acid and Creatinine levels in the serum of rats treated with the FPN

Parameters	Control group	High dose =(30.5 mg/kg)	middle dose =(12.2 mg/kg)	Low dose =(6.1 mg/kg)
Uric acid(mg/dl)	1.80 ± 0.08	$2.47 \pm 0.12^{(\uparrow)**}$	$2.10 \pm 0.09^{(\uparrow)*}$	$1.94 \pm 0.09^{(N.S)}$
Creatinine(mg/dl)	1.25 ± 0.08	$1.58 \pm 0.09^{(\uparrow)*}$	$1.48 \pm 0.06^{(N.S)}$	$1.47 \pm 0.09^{(N.S)}$

Values are from five replicates in each group and expressed as mean ± SE of each group.
**Significant at $p < 0.01$; *Significant at $p < 0.05$. (N.S), Non-significant; (↑), Significant increase.

Japanese quail was significant elevation after 15 days repeated gavage of fipronil. Also, **(Gill *et al.*, 2013)** found that the treatment for 98 days at dose of 0.5mg/kg/day of fipronil in buffalo calves made significant elevation in creatinine and uric acid levels. On the other hand, recent research has highlighted the pathogenic role of uric acid (UA) in renal and cardiovascular disease. Beyond being a marker of reduced glomerular filtration rate, serum UA level is associated with a faster progression of chronic kidney disease **(Busuioc *et al.*, 2007)**. Also, recent epidemiologic and experimental evidence suggests a role of UA not only as a marker of reduced kidney function but also as a causal risk factor for the development and progression of renal disease **Obermayr *et al.*, (2008)**. Our result revealed the level of (UA) was significant increased at the high and middle doses but it was in normal values in low dose. Although, the old theory about the increase level of (UA) in serum is recognized as a marker of oxidative stress because the production of the (UA) includes enzyme xanthine oxidase which is involved in producing of radical-oxygen species (ROS) and the last have a significant role in the increased vascular oxidative stress **(Higgins *et al.*, 2011).** Uric acid may play a predictive role as an antioxidant by scavenger a free radical and a chelator of transitional metal ions which are converted to poorly reactive forms **Settle and Klandorf, (2014)**. Also, UA can play a preventive anti-oxidation function through combination with iron and copper ions and also remove single oxygen and hydroxyl radicals directly **Pasalic *et al.*, (2012)**. But the increase of the UA levels could lead to increase the amount of nitric oxide (NO) synthesis **Robinson *et al.*, (2011).** Since the NO synthesis initiated the cascade of reactions, eventually leading to the destruction of tubular epithelial cells of kidney tissues, and development of acute renal failure **(Goligorsky *et al.*, 2002; Ruan *et al.*, 2015).**

Conclusion

It seems that the fipronil at the dose levels tested in the present study for a period of 28 days on male albino rats induced oxidative stress in these animals but the defense system was activated to reduce these effects according to the doses level. The histopathological findings in this study, revealed the exposure to high and middle doses led to destructive effects only on the kidney tissues. While the low dose led to slight effects on the kidney tissues. On contrary there were no histopathological alterations were recorded in the liver tissues at three dose levels. Kidney function parameters, creatinine and uric acid assays indicated increase in the level of uric acid and serum creatinine at the high and middle dose but no increasing at low dose in comparison with the control group. The result is complementary with previous findings if the quantity of dose and the variation in tolerance between the species take in consideration. So, it can be recommend to use this insecticide as long as using the recommended dose rates and safety applications.

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تقييم التعرض المتكرر لمبيد الفيبرونيل علي انسجة الكبد والكلي مع دراسة حالة الاجهاد التاكسدي في الفار الابيض

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الملخص العربي

مبيد الفيبرونيل ((Fipronil من مبيدات مجموعة فنيل بيرازول و هذا المبيد الجديد يستخدم حاليا على نطاق واسع في مكافحة العديد من الآفات الزراعية وكذلك يستخدم في مكافحة العديد من آفات الصحة العامة حيث لا توجد صفة مقاومة تكونت لهذا المبيد حتى الان. وتهدف هذه الدراسة الى التحقق من معرفة اثر التعرض المتكرر لاحد مستحضرات مبيد فيبرونيل على احداث السمية الكبدية والسمية الكلوية و الى تقييم قدرة المبيد علي احداث الاجهاد التأكسدي في فئران التجارب البيضاء. تم اجراء دراسة السمية الحادة اولا ومعرفة الجرعة القاتلة النصفية لهذا المستحضر من المبيد وبعدها تم اجراء دراسة السمية التحت حادة والمتكررة بإجراء التجريع اليومي عن طريق الفم من مستحضر المبيد للفئران المختبرة و لمدة 28 يوما متواصلة. التجريع كان علي ثلاثة مستويات من الجرعات، الجرعة العالية والمتوسطة والمنخفضة وكانت 1/20 ،1/50، 1/100من الجرعة القاتلة النصفية المتحصل عليها لهذا المستحضر. أظهرت نتائج دراسة السمية الحادة سمية معتدلة تجاه الفئران المعاملة وكانت قيمتها610 مليجرام لكل كيلوجرام من وزن الجسم. اظهرت نتائج الجرعات المتكررة من هذا المبيد اجهاد تأكسدي للفئران المعاملة بالجرعة العالية والمتوسطة وذلك بزيادة مستوى lipid peroxidation والجرعة المنخفضة لم تحدث تغيير معنوي في نسبة الاجهاد التأكسدي. ولكن الجهاز المناعي أظهر دور في تقليل نسبة الاجهاد التأكسدي وذلك بزيادة معنوية فى مستوى مجموع القدرة المضادة للأكسدة عند الجرعات الثلاثة العالية، المتوسطة ، المنخفضة وذلك بالمقارنة بالمجموعة الضابطة علاوة على ذلك فإن مستوى انزيم الكاتالاز كانزيم مضاد للأكسدة حدث له زيادة عند الجرعات الثلاثة ايضا بالإضافة الي زيادة في نشاط انزيم جلوتاثيون-اس- ترانسفيراز في الجرعة العالية فقط وهو انزيم متعدد الوظائف ويلعب دورا اساسيا فى التخلص من السموم الخلوية .وحسب النتائج الفحص النسيجي Histopathology التي تم التوصل اليها فى هذه الدراسة ان المعاملة بهذا المبيد ادت الى اثار مدمرة على انسجة.الكلي في الفئران المعاملة في الجرعات العالية والمتوسطة اما الجرعة المنخفضة ادت الى اثار طفيفة علي انسجة الكلى .ومن جهة اخري لم تكن هناك تغييرات فى انسجة الكبد عند الثلاثة مستويات من الجرعات. أظهرت النتائج ايضا ان نسبة حمض البوليك والكرياتينين بوصفها معلمات لوظائف الكلى الى زيادة مستوى حمض البوليك والكرياتينين عند الجرعة العالية والمتوسطة فقط ولم تحدث الجرعة المنخفضة زيادة معنوية .والنتيجة النهائية هى تتكامل مع النتائج السابقة اذا اخذ في الاعتبار مقدار الجرعة المعطاة والتباين في مستوى التحمل بين الكائنات المختلفة. وانه من الممكن التوصية باستخدام هذا المبيد عند الجرعات والمعاملات الموصي بها.

كلمات رئيسية: الفيبرونيل، الاجهاد التاكسدي، فئران التجارب، السمية الكبدية، السمية الكلوية