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Effects of Subchronic Intoxication with Propoxur on Acid-Base Status in Pigeon (*Columba livia domestica*)

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Abstract: Propoxur (2-isopropoxyphenyl N-methyl carbamate) is a widely used broad spectrum insecticide. Despite the increasing use of propoxurin Egypt, there is no complete information on the toxic effects of this insecticide in birds. Pigeons are usually feed on the seeds that may be contaminated by the insecticide (propoxur), mean while their meat is greatly required as food for people. Therefore, the purpose of this study is to investigate the effects of subchronic oral dosage of propoxur (1/10 LD50) on acid-base status. The bird employed in the present study is the rock pigeon (*Columba livia domestica*), weighing between 320 – 380g. Birds were classified into four groups each consists of 5 animals as follow:1- Control group, 2- Three doses group, pigeons in this group treated with a repeated oral dose (1/10 LD_{50}) of propoxur for three consecutive doses. 3- Six doses group, pigeons in this group treated with a repeated oral dose (1/10 LD_{50}) of propoxur for six consecutive doses. 4 – Nine doses group, Pigeons in this group treated with a repeated oral dose (1/10 LD_{50}) of propoxur for nine consecutive doses. (two-days interval between each two consecutive doses in treated groups) and birds were sacrificed after 24 hours after the last dose.This study concluded that, propoxur intoxication leads to Significant elevation in arterial and venousPCO_2in all intoxicated groups, and significant decrease in arterial and venous blood pH as compared to control,

decrease in arterial and venous blood HCO_3^- and a significant decrease in calculated $HCO_3^-/\alpha\ PCO_2$ in arterial and venous blood compared to control in all intoxicated groups.

Key words: Propoxur, Acid-base, Pigeon, Carbamate, Toxicity.

1. INTRODUCTION

The use of pesticides to manage pests in land and water has posed health hazards to live stock and wildlife. Problems and outbreaks have been reported to occur among animals and human from insecticide exposure [1]. Prolonged exposure to insecticides is known to cause chronic neurological syndrome, malignant tumors, immunosuppressive action, teratogenic effect, abortion and decreased fertility in experimental animals[2]. Pesticides may cause reproductive toxicity through direct damage to cells, interference with biochemical processes necessary for normal cell function and biotransformation resulting in toxic metabolites[3].

Propoxur (2-isopropoxyphenyl N-methyl carbamate) is a widely used broad spectrum insecticide. In addition to the control of cockroaches, mosquitoes, bugs, fleas, ants, millipedes, this insecticide is also used against pests in food stores, open areas, and households. Propoxur exhibits a toxic effect characterized by the inhibition of the enzyme cholinesterase [4]. Although mildly toxic to humans and domestic animals (class II), propoxur is highly toxic to birds, fish and honeybees [5]. Several cases of suicidal and occupational poisoning have also been reported [6].

propoxur have a common mechanism of action toward insect pests and unintended toxicity to non target organisms including humans, that is, acetylcholinesterase (AChE) inhibition by carbamylating the serine hydroxyl group in the active site of the enzyme in the nervous system, leading to the persistent action of the neurotransmitter, acetylcholine, on cholinergic postsynaptic receptors [7].

It is possible that carbamates may be involved in oxidative stress through the generation of free radicals and changes in antioxidant enzymes. Lipid peroxidation is known to be one of the molecular mechanisms of carbamate-induced toxicity [8]. The study of Waly *et al*. [9] concluded that exposure of animals to diazinon or propoxur are capable of including marked hazardous alterations. The generation of excessive levels of free radicals is one of the basic underlying mechanisms of these changes. Changes observed in oxidative stress markers as reduction in catalase and SOD activities and GSH concentration support this. Propoxur might also influence general physiological and pathological condition, nutritional status, hormonal function and hepatic metabolism, which may affect immune system [10].

Chronic exposure to a combination of propoxur and permethrin in the study of Liang [11] leads to induction of hepatotoxicity and nephrotoxicity. Results of Liang [12] study showed that propoxur, even at low dose levels can induce oxidative stress, impair liver function, enhance ketogenesis and fatty acid β-oxidation, and increase glycolysis, which contribute to the hepatotoxocity. The study of Mehta *et al*. [13] concluded that Carbamate pesticides like propoxur have been shown to adversely affect memory and induce oxidative stress on both acute and chronic exposure.

Propoxurhas been shown to adversely affect memory and induce oxidative stress on both acute and chronic exposure. Propoxur produced a statistically significant increase in the brain MDA levels and decrease in the brain GSH levels and catalase activity [13]. Results of the study of Ruiz et al [35] suggest that carbamates induce GSH depletion, leading to oxidative stress. However, the induction of the antioxidant

enzyme GST produced by aldicarb sulfone and propoxur in CHO-K1 cells, suggests that the enzyme provides adequate protection to mammals cells through the detoxification of these carbamates. Studies have shown that sub-chronic exposure to propoxur can cause oxidative stress and immuno-suppression in rats. Lethal cardiac complications leading to death and various arrhythmias have been reported after organophosphate and/or carbamate poisonings. Increased the oxidative stress and oxidative modifications in the genomic DNA content of the cardiac tissues [14].

Despite the increasing use of propoxurin Egypt, there is no complete information on the toxic effects of this insecticide in birds. Pigeons are usually feed on the seeds that may be contaminated by the insecticide (propoxur), mean while their meat is greatly required as food for people. Therefore, the purpose of this study is to investigate the effect of subchronic oral dosage of propoxur (1/10 LD50) on acid-base status in pigeon.

2. MATERIALS AND METHODS

2.1. Experimental Animal:

The bird employed in the present study is the rock pigeon (*Columba livia domestica*) which belongs to order columbiformes, weighing between 320 – 380g. Experimental birds purchased from local market of Benha city, Egypt. They were apparently healthy, active and free from any abnormalities. Birds were kept for one week under normal conditions of feeding with free access to water before experiments in order to assure their acclimatization.

2.2. Insecticide:

The carbamate insecticide used in the present work was propoxur. The chemical names are 2-isopropoxyphenyl–N–methyl-carbamate and 2-(1-methylethoxy) phenylmethyl carbamate). The common names are propoxur and PHC .Propoxur has also been called IMPC and IPMC. Ttrade names have included Baygon, Balttanex, Invisi-Gard, Propogon, Sendra, Sendran, Suncide, Tendex, Tugon, Fliegenkugel, Unden and Undene [15].

2.3. Dosage of propoxure:

The required dose of propoxur was mixed with 1gm of wheat dough, formed as pellets, dried, and was given to pigeons by obligatory oral feeding.

2.4. Determination of LD_{50} of propoxur for pigeon (*Columba liviadomestica*)

Five groups of pigeons (7 birds each) were treated with a single oral doses of propoxur 30, 36, 42, 48, and 52 mg / kg body weight, respectively. The pigeons died were watched by the end of 24 hrs., and the mortality percentage was determined according to the method of Litchfield and Wilcoxon [16]. This experiment was repeated twice and the average of mortality was taken. The calculated median lethal concentration (LD_{50}) of propoxur for the rock pigeon, *Columba liviadomestica* ,at a period of 24 hrs. was 38.83 mg/kg body weight .

2.5. Experimental Groups: Birds were classified into four groups each consists of 5 animals as follow:

(a). Control group: This group, non-treated pigeons, were not subjected to oral administration of the insecticide.

(b). Three doses group: Pigeons in this group treated with a repeated oral dose (1/10 LD_{50}) of propoxur for three consecutive doses. (two-day interval between each two consecutive doses) and birds were sacrificed after24 hours after the last dose.

(c). Six doses group: Pigeons in this group treated with a repeated oral dose (1/10 LD_{50}) of propoxur for six consecutive doses. (two-day interval between each two consecutive doses) and birds were sacrificed after24 hours after the last dose.

(d) Nine doses group: Pigeons in this group treated with a repeated oral dose (1/10 LD_{50}) of propoxur for nine consecutive doses. (two-day interval between each two consecutive doses) and birds were sacrificed after24 hours after the last dose.

2.6. Determination of Acid-base status:

2.6.1. Blood sampling: For analysis of acid-base status, birds were anaesthetized by ether inhalation. Arterial and venous blood samples were taken anaerobically from dorsal aorta and post caval veins respectively by means of 1 ml tuberculin syringes with 18-22ψ gauge needles. Heparin was used as an anticoagulant (1000 USP units of heparin per 1 ml blood). The needle was held in a horizontal position with the blood vessels so that the blood flows into the syringe partially without coming into contact with the atmospheric air [17]. The syringe was sealed with a rubber cap and placed on ice water for a maximum period of ten minutes.

2.6.2. Analysis acid-base status: For acid-base status analysis**,** 238 M. Ciba Corning pH Blood Gas Analyzerwas used to measure blood pH and carbon dioxide partial pressure (PCO_2) in mmHg, and calculate bicarbonate (HCO_3^-), total carbon dioxide (TCO_2) and base excess (BE) in mmol/l for both arterial (a) and venous (v) blood taken from dorsal aorta and post caval vein, respectively. Each determination required 0.25 - 0.3 ml blood. The apparatus incorporates a calculator which accurately calculate values for anaerobic plasma, bicarbonate according to the Henderson-Hasselbaleh equation and total CO2 from the relation

$$\left(pH = pK + Log \frac{HCO_3^-}{\alpha\, PCO_2} \right)$$

$TCO_2 = \alpha\, PCO_2 + HCO_3^-$

wherepK is the negative logarithm of the H^+ concentration at which half of the carbonic acid molecules are associated and half dissociated and it equals 6.1, α is the solubility coefficient of CO_2 and it equals 0.03 .

2.7. Determination of kidney function tests

2.7.1. Blood sampling: Blood samples were collected by making a puncture in the wing vein, large enough to ensure a free flow, making sure not to take the first drops which contain haemolysed blood, in non-heparinized tubes, and left overnight at 4°C to obtain a full separation of clott. Serum was obtained by centrifugation of the tubes at 5000 r.p.m. for 10 minutes then stored in deep freeze (at -20^0 C) for kidney function tests.

2.7.2. Determination of kidney function tests: Urea was determined by urease Berthelot reaction according to Patton and Crouch[18].Uric acid was determined by Uricase-PAP method

(enzymatic colorimeteric test)using Diamond Kit-Egypt according to Barham and Trinder [19] and Fossati *et a*l [20].

Creatinine was measured using kinetic JAFFE method according to Henery [21].

2.8. Statistical Analysis: Data are expressed as mean ± SE. The level of statistical significance was taken at $P < 0.05$, using one way analysis of variance (ANOVA) test followed by Dunnett test to detect the significance of differences between each group and control. All analysis and graphics were performed by using graph Pad Prism software version 5.

RESULTS

Table (1) illustrates the effects of repeated oral doses of proxour (1/10 LD_{50} each) on blood acid-base status parameter of pigeons after administration of 3, 6 and 9 doses compared to those of control group. The pH value of arterial and venous blood of pigeons treated with 3, 6 and 9 doses of propoxur (1/10 LD_{50} each) were exhibited significantly lower values compared to those of the control pigeons group. The percent arterio-venous difference of pH was significantly lower after 3 doses, significantly higher after 9 doses and non-significantly changes after 6 doses compared with the value of the control pigeons group.

arbon dioxide partial pressure of arterial and venous blood ($PaCO_2$ & $PvCO_2$ in mm Hg) of pigeons treated with propoxur after 3, 6 and 9 doses (1/10 LD50 each) were significantly higher than that of control pigeons group, the percentage arterio-venous difference of carbon dioxide partial pressure (%P(a-v)CO_2) was significantly increased after 3 doses and significantly decreased after9 doses administration as compared to that of control pigeons. Arterial blood bicarbonate (HCO_3^-), total carbon dioxide (TCO_2) and base excess(BE) were found to be significantly lower in the intoxicated pigeon groups than in control group after administration of 3, 6 and 9 doses of propoxur (1/10 LD_{50} each). Venous blood bicarbonate and total carbon dioxide were significantly decrease after administration of 3 and 9 doses, and decreased non-significantly after 6 doses as compared to those of the control group. Venous blood base excess was decreased significantly after administration of 6 doses and non-significantly after 3 and 9 doses compared to the control group. The percentage arterio- venous administration of bicarbonate (%(a-v) HCO_3^-) was increased significantly 3 doses post-treatment and significantly decrease after 6 and 9 doses as compared to the control group .The percentages arterio- venous difference of total carbon dioxide (%(a-v) TCO_2) was decreased significantly 6 and 9 doses post- treatment, while, it was insignificantly increased 3 doses post- treatment compared to that of the control group. The percentage arterio-venous difference of base excess (BE) of all treated pigeon groups (3, 6 and 9 doses) were significantly decreased as compared to control pigeons group.

The calculated $HCO_3^-/\alpha PCO_2$ ratios of arterial and venous blood after 3, 6 and 9 doses were significantly lower than that of the control pigeons group. The percentagearterio- venous difference of the calculated $HCO_3^-/\alpha PCO_2$ ratio was found to be significantly lower in treated birds than in control group. The calculated buffer values (Log PCO_2/pH) of arterial and venous blood were significantly increased in treated pigeons after administration 3, 6 and 9 doses of propoxur (1/10 LD_{50} each) as compared to that of the control group. The percentage arterio-venous difference of buffer value was significantly increased 3 doses and decreased 6 doses post-treatment, while that of treated pigeons treated with 9 doses was non-significantly decreased as compared to that control pigeons group.

Table-1: Effect of subchronic oral dosage (1/10 LD_{50}) of propoxur on blood acid– base status of pigeon.

Parameter Mean ± SE		Number of oral doses			
		Control	Three doses	Six doses	Nine doses
pH (Unit)	a	7.49 ± 0.02	7.39 ± 0.02 *	7.36 ± 0.03 *	7.42 ± 0.01 *
	v	7.36 ± 0.01	7.30 ± 0.01 *	7.24 ± 0.02 *	7.20 ± 0.02 *
	% (a-v)	1.76 ± 0.06	1.13 ± 0.09 *	1.74 ± 0.16	2.90 ± 0.25 *
PCO_2 (mmHg)	a	27.17 ± 1.78	38.33 ± 1.15 *	30.0 ± 0.86 *	30.83 ± 1.20 *
	v	36.50 ± 0.89	43.17 ± 1.78 *	48.50 ± 1.34 *	43.83 ± 0.70 *
	% (a-v)	-40.97 ± 2.56	-12.40 ± 1.45 *	-61.70 ± 0.65 *	-44.95 ± 1.87
(HCO_3^-) (mM/L)	a	27.25 ± 0.52	22.40 ± 0.73 *	23.55 ± 0.65 *	21.78 ± 0.89 *
	v	28.77 ± 1.15	22.55 ± 0.36 *	26.27 ± 1.23	25.23 ± 0.84 *
	% (a-v)	-5.08 ± 0.20	-2.02 ± 0.41 *	-14.05 ± 1.20 *	-15.97 ± 0.66 *
TCO_2 (mM/L)	a	29.28 ± 0.61	24.63 ± 1.46 *	24.48 ± 0.63 *	22.72 ± 0.92 *
	v	30.33 ± 1.16	23.90 ± 0.38 *	27.77 ± 1.24	25.80 ± 1.35 *
	% (a-v)	-5.47 ± 0.61	-1.65 ± 1.96	-13.28 ± 1.22	-13.73 ± 1.13
BE. (mM/L)	a	1.40 ± 1.26	-2.87 ± 0.16	-4.25 ± 0.96	-2.67 ± 0.63
	v	-4.88 ± 0.17	-6.08 ± 0.46 *	-7.35 ± 0.58	-5.63 ± 1.15
	% (a-v)	46.37 ± 14.50	-111.93 ± 7.24 *	-98.48 ± 16.33 *	-75.68 ± 3.94 *
$\frac{(HCO_3^-)}{\alpha PCO_2}$	a	34.84 ± 2.52	19.51 ± 0.52 *	26.3 ± 1.18 *	23.57 ± 0.53 *
	v	26.32 ± 1.10	17.58 ± 0.85 *	18.15 ± 1.04 *	19.16 ± 0.90 *
	% (a-v)	29.48 ± 0.21	11.44 ± 0.49 *	34.02 ± 0.60 *	18.77 ± 1.59 *
$\frac{\text{Log PCO2}}{\text{pH}}$	a	0.19 ± 0.004	0.22 ± 0.002 *	0.20 ± 0.002 *	0.20 ± 0.002 *
	v	0.213 ± 0.002	0.224 ± 0.003 *	0.234 ± 0.002 *	0.23± 0.002 *
	% (a -v)	-11.87 ± 0.53	-3.58 ± 1.04 *	-16.83 ± 1.01 *	-14.12 ± 0.96 *

(a)arterial blood, (v) venous blood, (a - v) arterio – venous difference; (*) significant difference compared to control group (P < 0.05).

Table (2) illustrates the effects of repeated oral doses of proxour (1/10 LD_{50} each) on kidney function tests. Serum urea concentrationwas increased significantly in pigeons treated with a repeated dose (1/10 LD_{50}) of propoxur; after 3 doses, 6 doses 9 doses as compared to control pigeons group. Variations in serum uric acid concentration .in pigeons treated with repeated doses (1/10 LD_{50}) of propoxur; after 3, 6

and 9 doses compared with control pigeons group as illustrated in **Table-2** showed significant increase in serum uric acid concentration after 6 doses and 9 doses of treatment when compared with control group. There are no any significant changes were observed in serum creatinine concentration in all intoxicated groups.

Table-2: Effect of subchronic oral dosage (1/10 LD_{50}) of propoxur on kidney function tests of pigeon.

Parameter Mean ± SE	Number of oral doses			
	Control	Three doses	Six doses	Nine doses
Urea (mg/dl)	6.72 ± 0.23	39.04 ± 0.77 *	41.1 ± 0.99 *	38.01 ± 1.13 *
uric acid (mg/dl)	5.68 ± 0.10	6.05 ± 0.32	7.50 ± 0.31 *	6.84 ± 0.27 *
Creatinine (mg/dl)	1.63 ± 0.02	1.63 ± 0.02	1.66 ± 0.02	1.66 ± 0.01

(*) significant difference compared to control group (P < 0.05).

DISCUSSION

Acid–base homeostasis is concerned with maintaining the proper balance between acids and bases in the body (i.e., pH). The body is extremely sensitive to changes in pH, and, as a result, powerful mechanisms exist to tightly regulate the body's acid–base balance to maintain it in a very narrow range. Outside the acceptable range of pH, proteins are denatured, and enzyme activity and nerve and cardiac function are altered, which ultimately results in death [22].

Acids are continuously produced in the body and threaten the normal pH of the extracellular fluid and intracellular fluid. Physiologically, acids fall into two groups, H_2CO_3 (carbonic acid) and all other acids (noncarbonic; also called "nonvolatile" or "fixed" acids). The distinction between these groups arises because H_2CO_3 is in equilibrium with the volatile gas CO_2, which can leave the body via the lungs. The concentration of H_2CO_3 in arterial blood is, therefore, set by respiratory activity. By contrast, noncarbonic acids in the body are not directly affected by breathing. Noncarbonic acids are buffered in the body and are then excreted by the kidneys [22].

The body contains several different buffers that reversibly bind H^+ and blunt any change in pH. These buffers include bicarbonate, protein, phosphate, and others.The bicarbonate buffering system is especially important, as carbon dioxide (CO_2) can be shifted through carbonic acid (H_2CO_3) to hydrogen ions and bicarbonate (HCO_3^-). Buffering is accomplished by chemical buffers, the lungs, and the kidneys.Chemical buffers in ECF and ICF and in bone are the first line of defense of blood pH. Chemical buffering minimizes a change in pH but does not remove acid or base from the body. The respiratory system is the second line of defense of blood pH. Normally, breathing removes CO_2 as fast as it is produced. Large loads of acid stimulate breathing (respiratory compensation), which removes CO_2 from the body and thus lowers the H_2CO_3 in arterial blood, reducing the acidic shift in blood pH. The kidneys are the third line of defense of blood pH. Although chemical buffers in the body can bind H+ and the lungs can change the H_2CO_3 of blood, the burden of removing excess H+ falls directly on the kidneys. Hydrogen ions are excreted in combination with urinary buffers. At the same time, the kidneys add new HCO_3^- to the ECF to replace HCO_3^- used to buffer strong acids. The kidneys also excrete the anions

(phosphate, chloride, and sulfate) that are liberated from strong acids. The kidneys affect blood pH more slowly than other buffering mechanisms in the body; full renal compensation may take 1 to 3 days [23].

The decrease in pH, HCO_3^-, TCO_2, BE and HCO_3^- /αPCO_2 ratio and increase in PCO_2 indicated the presence of respiratory acidosis, which induced by treatment of pigeons with propoxur. This was also reported for the gold skink [24]. In the present study pigeons treated with propoxur showed the respiratory acidosis i.e. increase in blood PCO_2 and decrease in blood pH that cannot be compensated (decrease the HCO_3^- /αPCO_2 ratio). Also the disturbances in the kidney function (serum urea, uric acid and creatinine) may verify the decrease of the compensative activity of the kidney. Moreover, the decreases of HCO_3^- and TCO_2 on long exposure to propoxur can be explained by continuous trans-epithelial elimination with the steady state production of non –volatile metabolic end products. In the present study, the observed respiratory acidosis may confirm the disturbances in blood gases transport mechanisms that may affected by hypoventilation and disturbances in pulmonary diffusing capacity under the effect of propoxur.

The non-protein nitrogens include urea, uric acid, creatinine, and a few less important compounds. These, in general, are the end products of protein metabolism and must be removed from the body to ensure continued normal protein metabolism in the cells. The concentrations of these, particularly of urea, can rise to as high as 10 times normal during 1 to 2 weeks of total renal failure. With chronic renal failure, the concentrations rise approximately in proportion to the degree of reduction in functional nephrons. For this reason, measuring the concentrations of these substances, especially of urea and creatinine, provides an important means for assessing the degree of renal failure [25].

Each day the Human body normally produces about 50 to 80 mill moles more metabolic acid than metabolic alkali. Therefore, when the kidneys fail to function, acid accumulates in the body fluids. The buffers of the body fluids normally can buffer 500 to 1000 mill moles of acid without lethal increases in extracellular fluid hydrogen ion concentration, and the phosphate compounds in the bones can buffer an additional few thousand mill moles of hydrogen ion. However, when this buffering power is used up, the blood pH falls drastically, and the patient will become comatose and die if the pH falls below about 6.8 [23].

Non-protein nitrogenous substances such as uric acid, urea and creatinine are increased only when renal function is below 30% of its original capacity in birds [26]. Plasma urea appears to be the single most useful variable for early detection of pre-renal causes of renal failure [26]. The elevation of serum urea concentration after a repeated oral doses (1/10 LD_{50}) administration of propoxur to pigeons shows an alteration in normal kidney function which might be related to the propoxur – induced renal dysfunction or may be due to heap to cellular disorder .

A similar elevations in serum urea was observed with the chlorinated insecticide in rats [27], and with the carbamate insecticide in mice [28] and in rats [29]. In addition, Cerôn et al., [30] observed elevation of plasma urea level at 72 hours of exposure of eel (*Anguilla anguilla*) to a sub-lethal diazinon concentration of 0.042 mg/L. This suggests that probably proteins are being used to meet the increases energy demands during pesticides intoxication. Moreover, the overall effect of glucocorticoids (secreted after a stressful stimuli) on metabolism will supply glucose to the organism by the trans formation of proteins in the liver [31]. An accelerated rate of protein catabolism would result in an increase of amino groups released from amino acids. These groups are converted firstly to uric acids, and secondly to urea in the detoxification process that takes place in liver [30]. Jayasree *et al.*, [26] recorded an increase in serum urea in day old male broiler chicks fed on deltamethrin (100 mg/kg feed) for 6 weeks, which may be due to the oxidative damage by free radicals. The elevation of serum urea and uric acid in the present study may be

due to the decrease in the glomerular filtration rate induced by kidney dysfunction as a result of the action of propoxur

El-Missiry and Othman [32] reported that in-significant changes in blood urea nitrogen was observed after 1 hrs .and 7 days of treatment of rats with a subcutaneously injection with 3.3 mg / kg body weight with lannate . The present results showed significant increase in the serum uric acid after 6 and 9 doses of propoxur (1/10 LD_{50}). Similar observations were reported with pyrethroid insecticide in pigeons [29,33]and with the carbamate insecticides in rats[27].

Creatinine is the anhydrides of creatine (methyl guanidinoacetic acid) and a constant constituent of normal human urine and is found in serum in a small amount [29,34] . Jayasree *et al.*[26] recorded an increase in serum creatinine in day old male broiler chicks fed on deltamethrin (100 mg/kg feed) for 6 weeks, which may be due to the oxidative damage by free radicals.

In the present study, repeated oral doses of propoxur administration to pigeons showed nonsignificant changes in serum creatinine. Similar observation was reported in rats treated with methomyl except for a slight, but significant, decrease after the 3rd week of methomyl treatment [29].

CONCLUSION

This study concluded that, propoxur intoxication leads to Significant elevation in arterial and venous PCO_2 in all intoxicated groups, and significant decrease in arterial and venous blood pH compared to control, decrease in arterial and venous blood $HCO_3^-$and a significant decrease in calculated HCO_3^-/α PCO_2 in arterial and venous blood compared to control in all intoxicated groups.

REFERENCES

1. N F Salih, M S. Jaafarm Heavy metals in blood and urine impact on the woman fertility. Chem. Mat. Res. 2013; 3(3): 81-89.
2. J.D. Meeker, L.Ryan, D.B. Barr, R .Hauser, Exposure to non-persistent insecticides and male reproductive hormones. Epidemiol. 2006; 17: 61–68.
3. G K. Sangha, K. Kaur, K. S. Khera, Cypremethrine-induced pathological and biochemical changes in reproductive organs of female rats. J. Environ. Biol. 2013; 34: 99-105.
4. Y .Shukla, S.M. Baqar, N.K. Mehrotra, Carcinogenicity and cocarcinogenicity studies on propoxur in mouse skin, Food Chem. Toxicol. 1998; 36: 1125-1130.
5. S.Kaya, Insektisitler. In: VeterinerHekimligindeToksikoloji. MedisanYayinevi, Ankara. 2002; 401-454.
6. B.D.Banerjee, S.T. Pasha, Q.Z.Hussain, B.C. Koner, A. Ray, A. comparative evaluation of immunotoxicity of Malathion after subchronic exposure in experimental animals. Indian J ExpBiol. 1998; 36(3): 273-282.
7. J.B. Knaak, C.C. Dary, M.S.Okino, F.W.Power, X. Zhang, C.B. Thompson, R. Tornero-Velez., Blancato, J. Parameters for carbamate pesticide QSAR and PBPK/PD models for human risk assessment. Rev. Environ. Contam. Toxicol. 2008; 193:53–210.

8. M.Ott, V. Gogvadze, S Orrenius, Zhivotovsky, B. Mitochondria, oxidative stress and cell. death. Apoptosis.2007; 12: 913-922.
9. M.Waly, H A. El-mezayen, M.Mohyee, Potential Role of Curcumin and Garlic Acid against Diazinon and Propoxur Hepatotoxicity. Int. J. Pharm. Sci. Rev. Res.2015; 33(2): 50-57.
10. S G. Suke, R. Pathak, R. Ahmed, A. K. Tripathi, and B.D. Banerjee, Melatonin treatment prevents modulation of cell mediated immune response induced by propoxur in rats. Indian journal of Biochemistry and Biophysics, 2008; 45 (August): 278-281.
11. Y.J. Liang, H.P Wang, D.X. Long, Y.J. Wu, Applying biofluidmetabonomic techniques to analyze the combined subchronic toxicity of propoxur and permethrin in rats. Bioanalysis.2012; 4(24):2897-907.
12. Y.J. Liang, H.P. Wang, D.X. Long, Y.J. Wu, H NMR-based metabonomic profiling of rat serum and urine to characterize the subacute effects of carbamate insecticide propoxur. Biomarkers 2012; 17(6):566-74.
13. K.D. Mehta, A.K. Mehta, S. Halder, N.Khanna, A.K. Tripathi, K.K. Sharma, Protective effect of melatonin on propoxur-induced impairment of memory and oxidative stress in rats. Environ Toxicol. 2014; 29(6):705-13.
14. A.Zafiropoulos, K.Tsarouhas , C.Tsitsimpikou, P. Fragkiadaki, I.Germanakis, M. Tsardi, , G Maravgakis, N.Goutzourelas, F. Vasilaki, D. Kouretas, A. Hayes, A. Tsatsakis, Cardiotoxicity in rabbits after a low-level exposure to diazinon, propoxur, and chlorpyrifos. Hum ExpToxicol, 2014; 33(12):1241-52.
15. Hayes, W.J. and Laws, E.R., 1991. Handbook of Pesticide Toxicology".Academic Press, Inc.
16. J.T. Litchfield, and F.Wilcoxon, A simplified method of evaluating dose effect experiments. J. Pharmacol. Exp. Therap.1949; 96: 99 -113.
17. A. A. M. El-Shafey, M. M. E. Seleim, M. E. Abdel–Halim, and A. M .Awad, Effect of bromadiolone on some blood parameters and respiratory functions in the albino rat .Egypt J. Zool. 2000;35 : 385 – 400 .
18. C.J. Patton and S.R. Crouch, enzymatic colorimetric method of urea. Anal.Chem.1977; 49: 464 - 469.
19. D.Barham and P. Trinder, Enzymatic determination of uric acid. Analyst.1972; 97: 142-145.
20. P.Fossati, L.Principe, and G.Berti, Enzymatic colorimetric method of uric acid. Clin. Chem. 1980; 26 (2): 227-273.
21. R.J. Henery, Kinitic method of creatinine determination. Clin. Chem. Acta.1974; 37: 193-197.
22. A. A. Rhoades, and D.R. Bell, Medical Physiology Principles for Clinical Medicine 4th Ed. Lippincott Williams Wilkins, New York. 2013, 451-470.
23. A.A.M. El-Shafey, Effect of γ- irradiation on respiratory functions of blood of two Egyptian lizards .Proc . 1st Int. Con. On Low Cost Exper. On Biophy. Cairo Univ. 1989; 105 – 112.

24. A C. Guyton, and J E Hall, Textbook of Medical Physiology 12th Ed. Saunders Elsevier. 2011; pp: 379-409.

25. C. M. Porth, Essentials of Pathophysiology 4th Ed. Lippincott Williams&Wilkins, New York. 2015; 614-635.

26. U.Jayasree, A. R. Gopala, K.S Reddy, Y. Anjaneyulu, and B.Kalakumar, Evaluation of vitamin E against deltamethrin toxicity in broiler chicks. Indian J. Physiol. Pharmacol.2003; 47 (4): 447, 452.

27. A.R Shakoori, Y.G Rasul, and S.S. Ali, The effect of long term administration of dieldrin on biochemical compounds in blood serum of albino rats. Folia Biol. 1984; 32: 213 – 222.

28. M.Gupta, S.Mukherjec, S.D. Gupta, A.K. Dolui, S.N. Dey, and D.K. Roy, Changes of lipids spectrum in different tissues of furadan treated mice. Toxicol. 1986; 38: 69, 79.

29. F.Saleh, Metabolic effects of the carbamate insecticide (methomyl) on rats. III. Changes in some blood biochemical indices in the rats poisoned with the insecticide. Egypt. J. Physiol. Sci. 1990; 24: 65-74

30. 30. J.J. Cerộn, E. Sancho, M.D Ferrando, Gutierrez, C. and Andren, E. Metabolic effects of diazinon on the European eel (Anguilla anguilla). J. Env. Sci. Health. 1996; 31 (5): 1029 – 1040.

31. A.Rijnberk, and J.A. Mol, Adrenocortical function. In Kaneko, J. J., Clinical biochemistry of domestic animals. 4 th .Ed. Academic press, San- Diego .1989; 610, 626.

32. M.A.El-Missiry, and A.I. Othman, Influence of lannate on biochemical and haematologicalparametersin old rats. J. Egypt. Ger. Soc. Zool. 1993; 11: 2 1 9-229.

33. F.Saleh, A.A. El-Shater, and E. N. Nasr, Effect of synthetic pyrethroidcypermethrin on protein metabolism in the pigeon .J. Egypt. Ger. Soc. Zool.1991; 3: 63 .73.

34. Oser, B. L. Hawk's physiological chemistry.14 th. Ed. Tata, Mc-Graw – Hill Publ. Comp. LTD. New Delhi 1979; 1167.

35. M.J. Ruiz, E.Maran, H. Berrada, M. Fernandez, Effects of carbamates as oxidative stressors on glutathione level and lipid peroxidation in CHO-K1 cells. J. Toxlet. 2007; 7:148.

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