

Original Research Article

## **Toxicological Influence of Propoxur on Respiratory Functions of the Blood in Pigeon (*Columba livia domestica*)**

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**Abstract:** Propoxur is a non-systemic insecticide which was introduced in 1959. It is used against mosquitoes in outdoor areas, against flies in agricultural settings, against fleas and ticks on pets, as an acaricide, on lawns and turf for ants, on flowering plants, and in private dwellings and public buildings. However, nontarget organisms such as honey bees, birds and fish have sensitive toxicity responses to carbamates in the environment, and propoxur has also been classified in group B, a probable human carcinogen. Despite the increasing use of propoxur in 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), meanwhile 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 LD<sub>50</sub>) on respiratory functions of blood. 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, this group, non-treated pigeons, were not subjected to oral administration of the insecticide. 2- Three doses group, pigeons in this group treated with a repeated oral dose (1/10 LD<sub>50</sub>) of propoxur for three consecutive doses.. 3- Six doses group, pigeons in this group treated with a repeated oral dose (1/10 LD<sub>50</sub>) of propoxur for six consecutive doses. 4 – Nine doses group, Pigeons in this group treated with a repeated oral dose (1/10 LD<sub>50</sub>) 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. Results of this study, showed significant decreases in arterial and venous blood oxygen partial pressure, percentage of oxygen saturation and alveolar oxygen partial pressure in all intoxicated groups, also there were significant elevations in arterial and venous blood carbon dioxide partial pressure, alveolar- arterial oxygen partial pressure difference, percentage of venous admixture (% shunt), and the percentage arterio – venous difference of percentage oxygen saturation, oxygen partial pressure and carbon dioxide partial pressure in all intoxicated groups.

**Keywords:** Propoxur, blood gases, respiratory functions, Pigeon.

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### **INTRODUCTION**

Propoxur (2-isopropoxy-phenyl-N-methylcarbamate) is a non-systemic insecticide which was introduced in 1959 [1]. It is used against mosquitoes in outdoor areas, against flies in agricultural settings, against fleas and ticks on pets, as an acaricide, on lawns and turf for ants, on flowering plants, and in private dwellings and public buildings. It is also used as a molluscicide. It is effective against cockroaches, aphids and leafhoppers [2].

Propoxur is one of the chemicals that have, to a large extent, replaced DDT in the control of black flies and mosquitoes [3]. However, nontarget organisms such as honey bees and fish have sensitive toxicity

responses to carbamates in the environment, and propoxur has also been classified in group B, a probable human carcinogen [4, 5].

Carbamates are another class of pesticides that have been increasingly used worldwide. Carbamates, e.g., propoxur, are similar to organophosphates in their action of inhibiting acetylcholinesterase, but unlike organophosphates, the carbamates are transient cholinesterase inhibitors and are hydrolyzed from the cholinesterase enzymatic site within 48 hours [6]. Thus, carbamate toxicity tends to be of shorter duration compared to the organophosphates, although the mortality rates associated with exposure to these chemical classes are still similar [7]. Due to their lower

toxicity and shorter half life, carbamates have been used widely in place of organophosphates, particularly for home pesticides. Carbamates are also known to exhibit inhibitory effect on cholinesterase activity, which is directly related to their cholinergic effects [8]. Oral administration of propoxur (10 mg/kg b.wt.) resulted in a significant reduction of brain and blood AChE activity. A significant prolongation of the acquisition as well as retention transfer latency was observed in propoxur-treated rats [9].

Chronic exposure to a combination of propoxur and permethrin in the study of Liang [10] leads to induction of hepatotoxicity and nephrotoxicity. Results of Liang [11] study showed that propoxur, even at low dose levels can induce oxidative stress, impair liver function, enhance ketogenesis and fatty acid  $\beta$ -oxidation, and increase glycolysis, which contribute to the hepatotoxicity. The study of Mehta *et al* [12] concluded that Carbamate pesticides like propoxur have been shown to adversely affect memory and induce oxidative stress on both acute and chronic exposure.

Propoxur (a carbamate pesticide) has 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 CAT activity [13]. Results of the study of Ruiz *et al* [14] 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 immunosuppression 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 [15].

The study of Ngoula *et al* [16] concluded that, propoxur increased food consumption, relative weights of testes, epididymis, ventral prostate, seminal vesicles, liver and kidneys; decreased body weight gain and sperm density per gram of cauda epididymis without affecting the reproductive performances in male rats. The data of in vitro study of Pandy and Guo [17] suggest a low acute cytotoxicity, genotoxicity, and embryotoxicity of propoxur on cultured flounder gill cells and zebrafish embryo.

Despite the increasing use of propoxur in 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), meanwhile 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 LD<sub>50</sub>) on respiratory functions of blood.

## MATERIALS AND METHODS

### 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.

### 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. Trade names have included Baygon, Balttanex, Invisi-Gard, Propogon, Sendra, Sendran, Suncide, Tendex, Tugon, Fliegenkugel, Uden and Undene [1].

### 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.

## METHODS

### Determination of LD<sub>50</sub> of propoxur for pigeon (*Columba livia domestica*)

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 [18]. This experiment was repeated twice and the average of mortality was taken. The calculated median lethal concentration (LD<sub>50</sub>) of propoxur for the rock pigeon, *Columba livia domestica* , at a period of 24 hrs. was 38.83 mg/kg body weight .

### Experimental Groups

Birds were classified into four groups each consists of 5 animals as follow:

#### 1- Control group

This group, non-treated pigeons, were not subjected to oral administration of the insecticide.

### 2 – Three doses group

Pigeons in this group treated with a repeated oral dose (1/10 LD<sub>50</sub>) of propoxur for three consecutive doses. (two-days interval between each two consecutive doses) and birds were sacrificed after 24 hours after the last dose.

### 3 – Six doses group

Pigeons in this group treated with a repeated oral dose (1/10 LD<sub>50</sub>) of propoxur for six consecutive doses. (two-days interval between each two consecutive doses) and birds were sacrificed after 24 hours after the last dose.

### 4 – Nine doses group

Pigeons in this group treated with a repeated oral dose (1/10 LD<sub>50</sub>) of propoxur for nine consecutive doses. (two-days interval between each two consecutive doses) and birds were sacrificed after 24 hours after the last dose.

## Determination of blood gases

### Blood sampling

For analysis of blood gases, 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 18-22 gauge needles. Heparin was used as an anticoagulant (1000 USP units of heparin per 1 ml blood). It does not affect the pH of blood sample [19, 20]. 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 [21]. The syringe was sealed with a rubber cap and placed on ice water for a maximum period of ten minutes.

### Analysis of blood gases

For blood gases 238 M. Ciba Corning pH Blood Gas Analyzer was used to measure oxygen partial pressure (PO<sub>2</sub>) and carbon dioxide partial pressure (PCO<sub>2</sub>) in mmHg both arterial (a) and venous (v) blood taken from dorsal aorta and post caval vein, respectively. Each determination required 0.25-0.03 ml blood.

The effective alveolar capillary blood oxygen partial pressure (P<sub>A</sub> O<sub>2</sub>) and alveolar arterial blood PO<sub>2</sub> gradient (P<sub>A</sub> - a O<sub>2</sub>) were calculated using the alveolar gas equation from Farver *et al.*, [22].

$$P_A O_2 = P_1 O_2 - P_a CO_2 / R.$$

Assuming a respiratory gas exchange ratio (R) of 0.8 and P<sub>1</sub> is The inhaled gas oxygen partial pressure.

$$P_{(A-a)} O_2 = P_A O_2 - P_a O_2$$

The percentage of venous admixture (% shunt) was calculated as previously described [20,23-25].

$$\% \text{ shunt} = \frac{PAO_2 - PaO_2}{PAO_2 - PvO_2} \times 100$$

## Determination of Blood Oxygen Equilibrium Curve (OEC)

Oxygen equilibrium curve and P<sub>50</sub> were determined as previously described [26] at the animal blood PCO<sub>2</sub> without addition of buffers, dilution of blood or other alternations. Blood was drawn from the heart into a heparinized syringe and one drop of 1 % sodium fluoride was added for every 3 ml of blood to reduce the rate of glycolysis and to stabilize the pH [19]. The blood was kept at 0-2 °C. A two ml volume of the agitated blood was drawn into a 30 ml graduated syringe followed successively by nitrogen, oxygen and carbon dioxide appropriate to the different gas mixtures previously used [26], with a blood to gas volume ratio of 1:14. The syringe probe was closed with a short blind length of small pore rubber tubing. The syringe was rotated for 15 min in a water bath at 0 °C. Care was taken to ensure that the plunger of the syringe was free to move inside the barrel so that the gas was at atmospheric pressure. Then, the syringe was removed from the water bath and the gas was expelled. A fresh gas mixture of the same composition was introduced into the syringe and the blood was re-equilibrated for another 15 min. the use of a two-stage equilibrium made it easier to control the final partial pressure. The equilibrated blood were transferred from the syringe into the sample chamber of the blood gas analyzer to measure its PO<sub>2</sub>. Each determination is the mean of five measurements of PO<sub>2</sub>. the Hill n value for each OEC was obtained [27] by plotting log [Y/(100-Y)] against log PO<sub>2</sub> where Y is % O<sub>2</sub> sat. The value changes at the saturation extremes when the Hill plot departs from linearity, the recorded value covers the saturation range of 30-70 %.

## Determination of Some Haematological Parameters

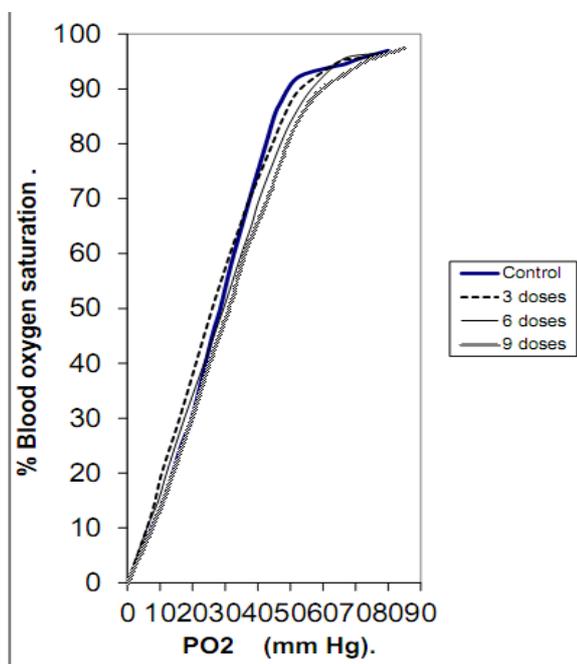
### Blood sampling and analysis

Heparinized blood samples, for blood indices, 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). Red blood cells count, Hematocrit, Hemoglobin and blood indices were determined according to methods in Cheesbrough [28].

## 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 graphPad Prism software version 5.



**Fig-1: Effect of subchronic oral dosage (1/10 LD<sub>50</sub>) of propoxur on blood oxygen equilibrium curve of pigeon**

**RESULTS**

**Blood Gases**

The effect of repeated oral doses (1/10 LD<sub>50</sub> each) of propoxur on the blood gases (PO<sub>2</sub> & PCO<sub>2</sub>) of both arterial and venous blood of the pigeons after 3, 6 and 9 doses of propoxur administration compared to control group are shown in table (1). The calculated P<sub>A</sub>O<sub>2</sub>, P<sub>A-a</sub>O<sub>2</sub> and the percent venous admixture (% Shunt) are also presented in table (1). Analysis of the data declared that both arterial and venous oxygen

partial pressure (P<sub>a</sub>O<sub>2</sub> & P<sub>v</sub>O<sub>2</sub>) were decreased significantly subsequent to 3, 6 and 9 doses of propoxur administration as compared to those of control group. Also, alveolar oxygen partial pressure (P<sub>A</sub>O<sub>2</sub>) was significantly decreased after 3 doses while, it was non-significantly decreased after 6 and 9 doses as compared to that of the control group.

The percent arterio-venous difference of oxygen partial pressure was significantly increased after 6 and 9 doses while it was non-significantly changed after 3 doses as compared to that of the control group. The percentage of venous admixture (% shunt) after 3, 6 and 9 doses was increased significantly compared to that of control pigeons group. Alveolar-arterial oxygen partial pressure difference was increased significantly after 3 and 6 doses and non-significantly after 9 doses of propoxur administration as compared to control pigeons group. Percent oxygen saturation (% O<sub>2</sub> sat.) of arterial and venous blood after administration 3, 6 and 9 doses of propoxur (1/10 LD<sub>50</sub> each) were significantly decreased as compared to those of control group. The percentage arterio-venous difference of percent O<sub>2</sub> saturation (%(a-v) O<sub>2</sub> sat.) after at 3, 6 and 9 doses of propoxur administration was increased significantly compared to that of control group.

Carbon dioxide partial pressure of arterial and venous blood (P<sub>a</sub>CO<sub>2</sub> & P<sub>v</sub>CO<sub>2</sub> in mm Hg) of pigeons treated with propoxur after 3, 6 and 9 doses (1/10 LD<sub>50</sub> each) were significantly higher than that of control pigeons group, the percentage arterio-venous difference of carbon dioxide partial pressure (%P(a-v)CO<sub>2</sub>) was significantly increased after 3 doses and significantly decreased after 9 doses administration as compared to that of control pigeons.

**Table 1: Effect of subchronic oral dosage (1/10 LD<sub>50</sub>) of propoxur on blood gases of pigeon .**

Parameter Mean ± SE	Number of oral doses				
	Control	Three doses	Six doses	Nine doses	
PO <sub>2</sub> (mmHg)	a	74.67 ± 2.40	54.67 ± 0.84*	64.0 ± 0.93 *	68.67 ± 1.78 *
	v	50.50 ± 1.20	37.00 ± 1.44*	36.83 ± 0.70 *	39.83 ± 1.20 *
	% (a-v)	32.25 ± 0.78	32.41 ± 1.85	42.47 ± 0.36 *	41.93 ± 1.41 *
	A	125.04 ± 2.22	111.17 ± 1.42	121.50 ± 1.07	120.44 ± 1.49
	A-a	50.38 ± 2.18	56.49 ± 0.93*	57.50 ± 1.85 *	51.78 ± 1.67
	%shunt	52.38 ± 1.92	76.22 ± 1.28 *	67.84 ± 1.34*	64.22 ± 1.88 *
% O <sub>2</sub> Sat.	a	96.08 ± 0.24	90.38 ± 0.37*	94.57 ± 0.39 *	93.87 ± 0.80 *
	v	77.08 ± 1.05	63.20 ± 2.56*	62.53 ± 1.86 *	68.98 ± 1.49 *
	% (a-v)	19.79 ± 0.92	30.16 ± 2.61*	33.93 ± 1.72 *	26.52 ± 1.05 *
PCO <sub>2</sub> (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

a)arterial blood, (v) venous blood, (a - v) arterio - venous difference, A = alveolar blood, (A-a) alveolar - arterial difference . (\*) significant difference compared to control group (P < 0.05)

**Blood Oxygen Equilibrium Curve (OEC)**

The blood oxygen equilibrium curve (OEC) of pigeon groups post-treatment with 3, 6 and 9 oral doses (1/10 LD<sub>50</sub> each) of propoxur were found to be shifted to the left after 3 doses and shifted to the right after 6 and 9 doses in relation to that of the control pigeons group. The blood oxygen half saturation pressure (P<sub>50</sub>)

as a measure of blood oxygen affinity found to be 28.5, 26.2, 29 and 30.5 mm Hg in control, 3, 6 and 9 doses respectively with significant differences (Table 2). Hill's constant (n value in Hill's equation) was found to be 2.5, 3.8, 3.68 and 3.45 for control and 3, 6 and 9 doses post-treatment, respectively (Table 2).

**Table 2: Effect of subchronic oral dosage (1/10 LD<sub>50</sub>) of propoxur on blood oxygen half saturation pressure (P<sub>50</sub>) and Hill's constant (n value) of pigeon**

Parameter Mean ± SE	Number of oral doses			
	Control	Three doses	Six doses	Nine doses
P <sub>50</sub> (mm Hg)	28.50 ± 0.33	26.20 ± 0.42 *	29.00 ± 0.49 *	30.50 ± 0.36 *
n	2.50 ± 0.03	3.80 ± 0.07 *	3.68 ± 0.07 *	3.45 ± 0.03 *

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

**Hematological parameters**

The data obtained are presented in table (3), it is apparent from the result that the administration of a repeated oral dose (1/10 LD<sub>50</sub>) of propoxur to pigeons induced significant depression in RBCs count after 6 doses, and 9 doses as compared with controls. Haemoglobin Content was reduced in pigeons treated with a repeated oral dose (1/10 LD<sub>50</sub>) of propoxur after 3 doses, 6 doses 9 doses groups, when compared with control. The data shown in table (3) also indicated a

decrease of Hct value in all intoxicated groups as compared with control. Mean cell volume was significantly decreased after 3 doses and 6 doses ) of propoxur treatment. Mean cellular haemoglobin exhibited significant decreases in response to administration of a repeated oral dose (1/10 LD<sub>50</sub>) of propoxur in 3 doses and 6 doses groups, while after 9 doses non-significantly changed as compared with control. There were no any significant alterations were observed in MCHC in all intoxicated groups.

**Table 3: Effect of subchronic oral dosage (1/10 LD<sub>50</sub>) of propoxur on hematological parameters of pigeon**

Parameter Mean ± SE	Number of oral doses			
	Control	Three doses	Six doses	Nine doses
RBCs (× 10 <sup>6</sup> Cell/mm <sup>3</sup> )	3.25 ± 0.09	3.08 ± 0.04	2.54 ± 0.04 *	2.05 ± 0.06 *
Hb (g / dl)	14.64 ± 0.15	12.37 ± 0.67*	10.76 ± 0.16*	10.73 ± 0.24 *
Hct (%)	45.20 ± 0.53	32.00 ± 0.55 *	30.80 ± 0.37*	31.6 ± 1.44 *
MCV (μ <sup>3</sup> )	154.62 ± 7.11	103.98 ± 2.26*	121.58 ± 3.39*	154.20 ± 3.36
MCH (Pg)	51.54 ± 1.34	40.12 ± 1.80 *	42.43 ± 0.79 *	52.56 ± 1.26
MCHC (%)	36.31 ± 1.84	38.78 ± 2.44	34.97 ± 0.82	34.18 ± 1.39

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

**DISCUSSION**

Changes in blood constituents are routinely used to determine various states of the body for clinical purposes or physiological studies. Blood constituents can be used to determine stresses due to intoxication with pesticides, and other environmental pollutants, nutritional and pathological factors.

The pesticides tend to become concentrated as they move up the food chain. They accumulate in organism body (target and non-target organisms) which content them. The pesticides don't kill the individual birds often but do affect their bodies so that they lay eggs with very thin shells often these thin-shelled eggs break or the birds are unable to reproduce. Pesticides also affect bird's physiological functions. Natural conservation committee and royal Society for birds protection suggested that indirect effect of pesticides was a major cause of decline birds species [29].

The calculated median lethal concentration (LD<sub>50</sub>) of propoxur for the rock pigeon, *Columba livia*, at period of 24 hr. was 38.83 mg/kg body weight with confidence limits 32.52- 46.35 mg/kg body weight. The literature has reported variable toxicity of propoxur for different animal species. LD<sub>50</sub> of propoxur for rat ranged from 80 to 191 mg/kg body weight [30, 31]. Haley *et al.*, [32] found that LD<sub>50</sub> of propoxur for mouse ranged from 37 to 109 mg/kg body weight. WHO [33] reported that LD<sub>50</sub> of propoxur for guinea pig was 40 mg/kg body weight.

The amount of oxygen carried by blood depends on the partial pressure of oxygen to which it is exposed. The total CO<sub>2</sub> content in circulating blood depends on its buffering capacity, carbon dioxide in the tissues and the control of the acid-base balance by the kidney and respiratory organs. In most vertebrates,

especially birds and mammals the sensitivity of the carotid and aortic bodies to changes in blood  $PO_2$  is modified by changes in blood  $PCO_2$ . Higher  $PCO_2$  producing greater sensitivity to drops in  $PO_2$ . Propoxur exposure reduced the ability of arterial blood to transport oxygen, while venous blood lost its unloading capacity indicated by the decrease of  $PaO_2$  and  $PvO_2$  throughout the experimental periods.

The observed decrease of  $PaO_2$  &  $PvO_2$  and increase of  $PaCO_2$  &  $PvCO_2$  may be a result of the decrease of erythrocytes count, haematocrite value and haemoglobin contents observed in this study or may be due to the increase of oxygen demands by the pigeon tissues and the disturbances in metabolic rate.

The observed decrease in arterial and venous blood oxygen partial pressure, percentage oxygen saturation, alveolar oxygen partial pressure and the increase in  $PCO_2$ , the percentage arterio-venous difference of percentage oxygen saturation,  $PO_2$  and  $PCO_2$  after all experimental periods and doses may be due to the increases of the % shunt occurred by the effect of propoxur. When unoxygenated mixed venous blood does not come in contact with gas exchange surfaces (shunted blood), it mixes with oxygenated blood as it leaves the lungs in the pulmonary veins. The result is a lowering of the  $PO_2$  in the arterial blood, the amount depending on the fraction of the cardiac output that has been shunted, there is normally a small right-to-left shunt resulting from the bronchial circulation to the parenchyma of the lung. Right- to- left shunts can also occur in the heart because of blood entering the left ventricle from the basin veins in the wall of that heart chamber. Right- to- left shunts are present in regions of the lung where no gas exchange occurs, but where there is still blood flow or if there are anatomical anastomosis between pulmonary arteries and pulmonary veins [34].

A high  $PCO_2$  or low pH tends to dissociate oxygen from haemoglobin and to promote gas exchange (Bohr effect). The oxygen affinity of blood is decreased by lowering the pH and increased by raising it. Variations of  $PCO_2$  from the normal tension modify the position of the oxygen equilibrium curve. Bohr effect is independent on the oxygen saturation, but depends on the temperature at any oxygen saturation value [35].

The interaction of  $O_2$  and  $CO_2$  transport mechanism is mainly through the Haldane effect i.e., deoxygenated blood having a greater capacity for  $CO_2$  than oxygenated blood. This is directly due to the formation of carbamino groups and also the fact that deoxygenated blood binds relatively more proton than oxygenated blood this forms the basis for the linkage between the Bohr and Haldane effects [36].

Blood  $PO_2$ ,  $O_2$  saturation, and oxygen content are three closely related indices of oxygen transport. The relationship between  $PO_2$ , oxygen saturation, and oxygen content is illustrated by the oxyhemoglobin–equilibrium curve, an S-shaped curve over a range of arterial oxygen tensions from 0 to 100 mm Hg. The shape of the curve results because the hemoglobin affinity for oxygen increases progressively as blood  $PO_2$  increases [35]. The shape and position of the oxygen equilibrium curve (OEC) partly determine the uptake of oxygen in the respiratory organ and its delivery to the tissues. Functioning of gas exchange systems must adjust to the changes in the environmental condition [37]. Propoxur caused acidosis of blood of the pigeon shifting its oxygen equilibrium curve to the right and increasing the  $P_{50}$ . It may be attributed to the increased blood  $PCO_2$  accompanied by a lowering of pH [35]. Propoxur may cause qualitative and quantitative variation of the haemoglobin compounds, each with its own oxygen binding properties and has specific relation with oxygen affinity modulates.

Propoxur may also stimulate the intraerythrocyte anaerobic glycolysis with increased production of organic phosphate which decrease the blood oxygen affinity and aid in shifting the  $O_2$  EC to the right. Not only the location of the blood oxygen equilibrium curve, blood oxygen affinity and  $P_{50}$ , but also the shape of the curve was affected by exposing the pigeon to propoxur, this changes in the shape of the curve was confirmed by change in the Hill's coefficient. This effect is a result of disturbances in the blood gas transport and exchange mechanisms [38], which was also previously reported for other animals by different effectors [39,40]. The changes in the n value may also confirm that propoxur may affect the haemoglobin multiplicity and functional heterogeneity in the pigeon. It was also previously reported for other animals by different effectors [21,39,40].

The present study revealed that erythrocyte count decreased significantly after treatment of pigeon with propoxur. Similar results were observed in pigeon exposed to fenitrothion [41] and to methomyl and trichlorofon [42]. Moreover, a reduction in erythrocyte count was observed in different animal species exposed to organophosphorus insecticides: in rats [43] and in rabbits [44]. The present significant decrease in erythrocyte count of pigeon after propoxur administration may be attributed to haemorrhage caused by injury to the vascular wall [42].

The present data demonstrate that blood haemoglobin level of pigeon decreased significantly after 3, 6 and 9 repeated dose. The decrease of the haemoglobin level accompanied with decrease in erythrocyte count may be due to elimination of erythrocytes from the circulation as a result of

extravasations of blood. The calculated blood indices (MCV, MCH and MCHC) have a particular importance in describing anaemia in most animals. In the present study, the development of anaemia in pigeon could be due to propoxur interference with haemopoiesis and / or alteration of the membrane integrity, it is also possible that the diminution of incorporation rate of iron in the porphyrin ring and the depression of iron absorption of the treated animals could take place [43].

## CONCLUSION

Subchronic intoxication with propoxur leads to significant decreases in arterial and venous blood oxygen partial pressure, percentage of oxygen saturation and alveolar oxygen partial pressure in all intoxicated groups, also there were significant elevations in arterial and venous blood carbon dioxide partial pressure, alveolar-arterial oxygen partial pressure difference, percentage of venous admixture (% shunt), and the percentage arterio-venous difference of percentage oxygen saturation, oxygen partial pressure and carbon dioxide partial pressure in all intoxicated groups.

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