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Impact of Fenitrothion Thermal Fogging on some Biological and Biochemical Parameters in New Zealand Rabbits as Non-target Organisms

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ABSTRACT

This study was conducted to investigate the effect of exposure to fenitrothion thermal fogging on some biological and biochemical parameters in New Zealand white rabbits as a non-target organism. Fenitrothion 50EC, diluted with diesel (1: 39), was applied by thermal fogging at the recommended rate 10 L ha^{-1}. Rabbits, individually caged, were exposed to the pesticide for 30 days, day after day. The results showed a significant reduction in the body weight (13.34%) compared with the control; on the contrary, weights of liver, heart and lungs increased by 23.37, 20.23 and 14.76%, respectively. A reduction in brain, blood, plasma, and erythrocytes cholinesterase (ChE) activity was observed after 15 and 30 days of exposure. The blood, plasma and RBCs' ChE was more sensitive than the brain enzyme. After 30 days of recovery, all tested biological parameters returned to their normal values.

Key Words: Fenitrothion; Thermal fogging; Cholinesterase; Body and organs weights; Rabbits

INTRODUCTION

Utilization of insecticides to control adult mosquitoes is an essential component in mosquito control programs (Najera & Zaim, 2002). According to the recommendation of WHO, mosquito adulticides are usually applied by the ULV or thermal fogging equipments (Itoh *et al.*, 1988; Warrell & Gilles, 2002). However, occupational exposure to pesticides causes many adverse health effects on pesticide workers (Ojajarvi *et al.*, 2000; Jenner, 2001; Mourad, 2005). In addition, there is a good relationship between exposure to organophosphorus insecticides and inhibition of acetylcholinesterase (AChE) activity (Tapia *et al.*, 2006; Gaafar *et al.*, 2008) therefore, the level of AChE activity has been considered a good biomarker for exposure to these pesticides (Worek *et al.*, 1999; Joshaghani *et al.*, 2007; Remor *et al.*, 2009). Chronic exposure to pesticides may also produce changes in some biological measurements (Farghaly *et al.*, 2007; Afshar *et al.*, 2008). Exposure to pesticides through the respiratory system is more toxic than exposure through other routes, since pesticides are absorbed more rapidly through the lungs. Nose inhalation of fenitrothion aerosols caused reduction in body weight and cholinesterase activity (Breckenridge *et al.*, 1982).

Fenitrothion ($C_9H_{12}NO_5PS$) is a slightly volatile, non-systemic organophosphothioate insecticide of low water-solubility, classified as fat-soluble and acetylcholinesterase inhibitor. It is used in agriculture, horticulture, forestry and public health against chewing and sucking insects on rice, cereals, fruits, vegetables, stored grains, cotton, etc., for agriculture and flies, mosquitoes and cockroaches in public health use (FAO, 2010).

Hayes and Laws (1990) reported that fenitrothion has a distinct cytotoxic effect on the lungs of rats. Hepatotoxicity of fenitrothion increased in a time and dose-dependent manner and marked damage of isolated hepatocytes in the oxidative and antioxidant parameters was observed (El-Shenawy, 2010). Fenitrothion exposure also significantly decreased the body and spleen weights in Wistar rats and apoptotic lymphocytes in spleen were observed under transmission electron microscope (Li *et al.*, 2010).

Fenitrothion is widely applied in mosquito control programs in the Kingdom of Saudi Arabia by both ULV and thermal fogging techniques; therefore, the aim of this study was to investigate the effect of exposure to fenitrothion thermal fogging on some biological and biochemical parameters in rabbits in order to evaluate some hazardous and side effects of this pesticide on pesticide workers.

MATERIALS AND METHODS

Tested insecticide and utilized reagents: Fenitrothion [(O,O-dimethyl O-(3-methyl-4-nitrophenyl) phosphoro-

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thioate)] was a generous gift in the form of emulsifiable concentrate 50% formulation (50 EC) from APCO company, Riyadh, Kingdom of Saudi Arabia. DTNB [5, 5-bis (2-nitro benzoic acid)] and acetylthiocholine iodide were purchased from BDH Chemicals Co. Ltd Pool, England.

The fogging machine: The portable thermal fogger SWINGFOG SN50 (nozzle No. 1, releasing rate 20.6 L ha^{-1}) was used in this work.

Experimental animals and exposure conditions: Thirty New Zealand white male rabbits weighing 3.50±0.1 kg were purchased from Animal Care Center, Faculty of Pharmacy, King Saud University, Saudi Arabia. The animals were maintained on standard laboratory diet and water *ad libitum* for one week for acclimation under the laboratory conditions (25±2°C). The rabbits were divided into three equal groups, each rabbit in a separate cage. The first group was used as control; the second group was exposed to the utilized vehicle (diesel), while the third group was exposed to fenitrothion diluted with diesel (1:39 v/v). Boxes were put on a woody table one meter above the ground and 10 meters distance from the discharge point. The required time to cover the treated area, 100 m^2, was determined by 2.56 min. The experiment continued for 30 days and rabbits were exposed day after day. The weather conditions during the experiment were recorded (Table I). After 30 min of the treatment, rabbits were transferred into other clean cages. At days 15 and 30 of treatment, blood samples were collected from the rabbit's ears in heparinized tubes to determine the ChE specific activity. After 30 days of exposure, five rabbits were weighed, sacrificed and dissected to record the weight of brain, heart, liver, lungs, spleen and kidneys; the change in weight was calculated using the following equation:

Reduction (-) or Increase (+) % =

[(Value of Treatment–Value of control)/Value of control] × 100.

The remaining five rabbits of each group were maintained without exposure for additional 30 days recovery period. At the end of the recovery period, all the previous parameters were recorded.

Determination of ChE activity: The specific activity of brain, plasma, blood and erythrocytes ChE was assayed according to the method of Ellman *et al*. (1961) and the protein content was determined according to Lowry *et al.* (1951). Reduction in ChE activity was calculated according to the above mentioned equation.

Statistical analysis: Significant differences between mean values of exposed and control groups were statistically analyzed using the Student's *t*-test, utilizing the computer program Sigma plot for windows (version 2.0).

RESULTS

Effect of fenitrothion on body and organs weight: The weight of liver, lungs and heart in the treated group was higher than the control organs by 23.37, 14.76 and 20.23%, respectively (Table II). On the contrary, a significant decrease in the body weight of treated animals (13.34%) was recorded. No significant differences were observed in the weight of the other organs compared to the control. In case of the diesel treatment, there were no significant differences in the weight of organs compared to the control except for the weight of heart, which was significantly higher than the control by 22.6%. After the recovery period, no significant differences were recorded between the values of the body and organs weight of the treated animals and those of the control (Table III). The liver weight of fenitrothion-treated animals showed 14.5% increase compared to the control, but this increase did not represent a significant difference.

Table I: The weather conditions during the application of fenitrothion and/or diesel oil through the experiment period

Application date	Temperature (°C)	Wind speed (km/hr)	Relative humidity (%)
02/04/2009	21.20 ± 1.31	1.38±0.9	64.00± 7.8
04/04/2009	25.15 ± 1.42	1.65 ±1.01	21.50 ± 0.58
06/04/2009	25.45 ± 2.00	1.26±1.39	17.25± 1.71
08/04/2009	25.575 ± 1.80	1.68 ±1.41	13.75 ± 1.89
10/04/2009	27.25 ± 1.76	1.65 ± 0.66	35.25 ± 11.59
12/04/2009	27.15 ± 2.09	1.43±0.93	16.25±2.22
14/04/2009	27.95 ± 1.01	1.68 ±0.78	17.00 ± 1.41
16/04/2009	27.00 ± 1.49	1.55±1.18	17.50± 2.65
18/04/2009	27.00 ± 1.12	1.75 ± 0.84	16.50 ±1.29
20/04/2009	27.97 ± 1.16	1.33 ± 0.37	9.75± 0.5
22/04/2009	27.15 ± 0.97	1.65± 0.44	10.75 ±1.71
24/04/2009	27.07 ± 1.66	1.68 ± 0.78	16.50± 2.08
26/04/2009	28.00 ± 0.99	1.33±0.37	13.00± 2.16
28/04/2009	26.11 ± 1.60	1.45 ±0.66	25.00 ± 4.08
30/04/2009	27.90 ± 1.80	1.65± 0.44	13.75±1.89

Each value of the recorded weather conditions represents the average of three replicates ± SD

Effect on cholinesterase activity: Table IV shows the specific activity of brain, blood, plasma and erythrocytes ChE at days 0.0, 15, 30 and 60, respectively. After 15 days of treatment, significant ($P<0.05$) differences were found between ChE activity (blood, plasma & erythrocytes) in the fenitrothion-treated group and the control group. However, the ChE activity in the diesel-treated group was not affected and was comparable to the control group. The highest reduction was in plasma ChE activity (28.7%), followed by blood and RBCs ChE, 17.8 and 15.1% reduction, respectively. After 30 days of the treatment, the inhibition of ChE activity was more obvious than after 15 days and correlated with the period of exposure. Significant ($P<0.001$) differences were found between the ChE actitvity in the fenitrothion-treated group and the control group and again, plasma ChE was the most susceptible (35.7% inhibition), followed by blood and RBCs ChE, 33.6 and 33.1% inhibition, respectively, whereas the brain enzyme was the least sensitive (22.2% inhibition). The diesel treatment had almost no effect on ChE activity. After 30

Table II: Body and organs weights of rabbits after 30 days of exposure to fenitrothion and diesel oil sprayed by thermal fogger

Organs	Control weight (g)	Diesel		Fenitrothion	
		Weight (g)	Change (%)[a]	Weight (g)	Change (%)[a]
Body	3476.0 ± 157.96	3142.5 ± 270.23	-9.59	3012.20 ± 182.14**	-13.34
Heart	7.66 ± 0.62	9.36 ± 1.91*	22.19	9.21 ± 1.19*	20.23
Lung	12.74 ± 0.78	11.65 ± 1.50	-8.55	14.62 ± 1.34*	14.76
Spleen	1.27 ± 0.45	1.24 ± 0.46	-2.36	1.62 ± 0.62	27.56
Kidneys	18.64 ± 2.22	18.03 ± 0.75	-3.27	17.97 ± 0.89	-3.59
Brain	9.79 ± 0.51	9.84 ± 0.39	0.51	9.39 ± 0.99	-4.08
Liver	82.34 ± 9.26	71.32 ± 13.34	-13.38	101.58± 12.02**	23.37

Data are presented as means of five replicates ± SD

* Significantly different from control at $P \leq 0.05$

** Significantly different from control at $P \leq 0.01$

[a] Percentages of increase or decrease in treatment weights compared to control

Table III: Body and organs weights of rabbits after 30 days recovery period of exposure to fenitrothion and diesel oil

Organs	Control weight (g)	Diesel		Fenitrothion	
		Weight (g)	Change (%)[a]	Weight (g)	Change (%)[a]
Body	3565.8 ± 188.89	3419.2 ± 205.02	-4.11	3476.0 ± 252.27	-2.52
Heart	9.04 ± 0.42	9.8 ± 0.11	8.40	9.0 ± 0.95	-0.40
Lung	15.17 ± 4.33	15.25 ± 1.78	0.52	16.84 ± 3.89	11.01
Spleen	1.34 ± 0.63	1.62 ± 0.13	20.89	1.24 ± 0.23	-7.46
Kidneys	19.7 4± 2.03	20.38 ± 1.82	3.24	19.92 ± 1.48	0.91
Brain	9.11 ± 0.67	10.34 ± 0.97	13.50	9.86 ± 0.16	8.23
Liver	87.6 ± 8.81	86.18 ± 6.89	-1.62	100.26 ± 13.71	14.45

Data are presented as means of five replicates ± SD

No significant difference from control ($P > 0.05$)

[a] Percentages of increase or decrease in treatment weights compared to control

Table IV: Specific activity of acetylcholinesterase in brain, blood, plasma and RBCs in the rabbits exposed to diesel oil and diesel-diluted fenitrothion

Time of Measurement (days)	Enzyme source	Specific activity (µmol/min/mg protein)				
		Control	Diesel	Change (%)[a]	Fenitrothion	Change (%)[a]
0	Brain	-	-		-	
	Blood	22.96 ± 2.09	22.64± 1.83	-1.3	22.25± 2.20	-3.1
	Plasma	4.37 ± 0.42	4.07 ± 0.39	-6.9	4.11 ± 0.59	-5.9
	RBCs	18.59 ± 1.67	18.57± 1.44	-0.1	18.14± 1.61	-2.4
15	Brain	-	-		-	
	Blood	23.20 ± 1.57	23.37± 1.65	0.73	19.08 ± 1.94*	-17.75
	Plasma	4.53 ± 0.30	4.66 ± 0.19	2.87	3.23 ± 0.35*	-28.69
	RBCs	18.67 ± 1.27	18.71± 1.46	0.21	15.85 ± 1.59*	-15.10
30	Brain	24.77 ± 2.75	23.16 ± 1.92	-6.49	19.26 ± 0.74***	-22.24
	Blood	22.58 ± 1.62	22.91 ± 1.13	1.46	15.00 ± 2.16***	-33.56
	Plasma	4.17 ± 0.23	4.30 ± 0.14	3.12	2.68± 0.39***	-35.73
	RBCs	18.41 ± 1.39	18.61 ± 0.99	1.08	12.32 ± 1.77***	-33.08
60	Brain	24.42 ± 1.34	24.14 ± 2.92	-1.15	25.49 ± 4.77	4.38
(30 day recovery)	Blood	23.48 ± 2.31	23.09 ± 1.74	-1.66	22.73 ± 2.63	-3.19
	Plasma	4.67 ± 0.58	4.50 ± 0.42	-3.64	4.12 ± 0.55	-11.76
	RBCs	18.81 ± 1.73	18.59 ± 1.32	-1.17	18.41 ± 2.18	-2.13

Data are presented as means of five replicates ± SD

* Significantly different from control at $P \leq 0.05$

*** Significantly different from control at $P \leq 0.001$

[a] Percentages of increase or decrease in treatment weights compared to control

days recovery period, no significant differences were found among all three groups and ChE activity in the fenitrothion-treated group returned to normal values.

DISCUSSION

The significant increase in the weights of liver, lung and heart of fenitrothion–treated animals was expected because fenitrothion was shown to cause hepatomegaly, pulmonary edema and cardiomegaly. Several authors reported that fenitrothion causes significant degradation and necrosis of the paranchymal cell of the liver, and this leads to liver bleeding (Hays & Law, 1990; Farghaly *et al.*, 2007; Afshar *et al.*, 2008). The alveolar epithelial type I pneumocytes were damaged and replaced by proliferation of the type II pneumocytes in fenitrothion-treated rats

(Chevalier *et al.*, 1982). It was reported that lungs and heart are sensitive to fenitrothion due to their high affinity to this compound; consequently, the fenitrothion accumulates in these organs more than in other organs (Hayes & Law, 1990; Briggs, 1992). Also, Soltaninejad and Abdollahi (2009) showed that treatment with fenitrothion causes oxidative stress, lipid peroxidation reactions in the liver tissues, accumulation of lipids and hepatomegaly.

Cholinesterase (ChE) is the main target for organophosphorus insecticides (Nigg & Knaak, 2000). The inhibition of ChE in pesticides-exposed workers and animals has been indicated in previous studies. Inhalation of fenitrothion for 30 days (2 h/day) caused a reduction in ChE activity in treated rats and the reduction increased with the period of exposure; the ChE activity returned to the normal value after 30 days of recovery (Breckenridge *et al.*, 1982). ChE activity was reduced in rats given fenitrothion at 5, 10, or 20 mg/kg body weight for 30 days and recovery was faster in case of the low doses than in the high doses (Durham *et al.*, 1982). Rats fed fenitrothion-treated soybean showed reduction in plasma and erythrocyte ChE activity (Farghaly & El-Maghraby, 2008). The diesel oil did not affect the ChE activity. Clark *et al*. (1989) reported that the diesel oil causes dermal irritations, which rapidly disappeared soon after ending the exposure.

In conclusion, these results prove the importance of ChE as a biomarker to monitor the workers exposure to pesticides to take effective measures before having serious adverse health effects.

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