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Research Article

Toxicity of Cypermethrin (Pyrethroid Insecticide) in Female Guinea Pig (*Cavia porcellus*)

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Abstract

This study aimed at evaluating the toxicity of Cypermethrin (Pyrethroid insecticide) in female Guinea pig after 60 days. For this purpose, 40 adult female guinea pigs with an average weight of 417 ± 19.21g were randomly allocated into four groups of 10 animals each. All animals were orally treated. T0 served as the control and received distilled water, while the three other groups T1, T2 and T3 were respectively given 92, 137.5 and 275 mg/kg of body weight (bw) of cypermethrin. The studied parameters included the blood concentration of estradiol, ovary and uterus menstruation, the weight and volume of kidney and liver, indicators of the renal (creatinine and urea) and hepatic (ASAT, ALAT, proteins, cholesterol, albumin, globulin) functions and the markers of oxidative stress (Superoxide dismutase, Catalase, total peroxidases, Malondialdehyde, and tissue proteins). The malondialdehyde concentration and the activities of superoxide dismutase, catalase and total peroxidases increased significantly ($p < 0.05$) in animals exposed to 137.5 and 275 mg/kg bw of cypermethrin compared to the control. The levels of ASAT, ALAT, creatinine and urea were significantly ($p < 0.05$) higher in cypermethrin-treated guinea pigs compared to the control. Meanwhile, the reverse was observed for the levels of proteins, cholesterol and globulin. The weights of the liver, kidneys, ovaries and uterus were comparable ($p > 0.05$) amongst treatments. The estradiol concentration significantly ($p < 0.05$) decreased in groups receiving 137.5 and 275 mg/kg bw of the insecticide with the reference to the control. Hence, cypermethrin has shown to be toxic in female guinea pigs by inducing oxidative stress and causing perturbations on the renal, hepatic and reproductive functions.

Keywords: *Cypermethrin; Female Guinea Pig; Oxidative Stress; Reproduction; Toxicity*

Introduction

The large growing population has brought about questions on efficient ways and methods to increase agricultural products in order to satisfy its alimentary needs. That is how the modernization of agriculture has led to the high utilization of chemicals among which pesticides. Many farmers nowadays use pesticides of one form or another in order to fight against numerous plant and animal parasites

thereby, considerably increasing agricultural yield [1]. Despite these advantages, their haphazard use is not highly selective, but is generally toxic to non-target species, including man and other animals. As such, their reproduction and production capacities are at risk [2].

Cypermethrin is a synthetic insecticide belonging to the pyrethroid family. Pesticides of this last family are worldwide used in the preservation of foodstuff and destruction of insects due to their high efficiency and low toxicity to man and other mammals compared to others like the organophosphorus insecticides [3]. They actually represent 17% of insecticides in the world's market [4].

The exposition of animals to cypermethrin has shown to cause serious health hazards in general and their reproduction in particular [5,6]. Studies showed that the toxicity of this insecticide caused morphological and functional changes in the female renal, hepatic and reproductive systems. Some include the decreased or increased weights of the ovaries, uterus, kidney and liver, the lengthening of the oestral cycle and the drop in the concentration of estradiol [7-9]. Indeed, studies showing the toxicity of cypermethrin on female organism of farm animals are scarce and many of them are necessary to better appreciate the toxicity of this insecticide used worldwide.

Aim of the Study

The present study aimed at investigating the reprotoxicity, the nephrotoxicity and the hepatotoxicity of cypermethrin, and its ability to induce oxidative stress in female guinea pigs.

Materials and Methods

Animal, lodging, feeding and pesticides

Forty adult female cavies (*Cavia porcellus*) aged 4 months, with a mean body weight of 417 ± 19.21g were obtained from the Teaching and Research Farm of the University of Dschang. They were identified using numbered ring attached on the ear and housed in clean mesh cages measuring 100 cm x 80 cm x 60 cm (length, width and height), under standard conditions with 12 hours photoperiod. They had free access to water and feed. They were handled according to ethical guidelines of the Cameroon National Veterinary Laboratory.

Animals were fed with *Pennisetum purpureum*-based ration and a supplement of provender diet whose composition and chemical characteristics are shown in table 1.

Ingredients	Quantity (%)
Maize	27.50
Wheat bran	8.00
Kernel cake	15.00
Soybean cake	4.00
Cotton cake	5.00
Premix 5%*	5.00
Palm oil	2.00
Fish meal	1.00
Sea shells	2.00
Salt	0.50
Total (kg)	100.00
Chemical characteristics	
Metabolisable energy (kcal/kg)	2175.18
Crude protein (% DM)	17.05
Crude cellulose (% DM)	8.17
Calcium (% DM)	1.34
Phosphorus (% DM)	0.76
Sodium (% DM)	0.26

Table 1: *Composition and chemical characteristics of the feed.*
***Premix: Mineral Nitrogen Mineral Complex: DM: Dried Matter.*

The pesticide used was cypermethrin 36% (360 g/L), commercially called Cigogne. It is in the liquid form with a pale yellow colour and was obtained from Louis Dreyfus Commodities Cameroon.

Experimental design

The 40 animals were divided into 4 groups of 10 animals each, comparable in body weight. Group 1 (T0) served as control and daily received distilled water, while the 3 other groups (T1, T2, T3) were orally given in 1 ml of solution, 92, 137.50 and 275 mg of cypermethrin/kg bw for 60 days. The animal body weight was recorded weekly and the doses of pesticide adjusted accordingly.

Collection of blood

Twenty-four hours after the last administration of the insecticide solutions, animals were anesthetised using ether vapour and blood was collected by cardiac puncture and stored at room temperature. Serum was collected 12 hours later for the dosage of estradiol, hepatic and renal biomarkers.

Data collection

Organs weights and volumes: The ovaries, uterus, liver and kidneys were weighed using a scale of 160g capacity and 10^{-3}g precision. Volumes of liver and kidneys were determined by their immersion in 0.9% NaCl solution contained in a graduated cylinder and any displacement of the solution was read.

Biochemical parameters: Estradiol was quantified in the serum, according to the instructions of Biorex kit (Certified to ISO 13485; Biorex Diagnostics Limited, Antrim, Northern Ireland, BT41 1QS, United Kingdom) and ALAT, ASAT, total protein, albumin, total cholesterol, creatinine and urea were quantified according to the instructions of Chronolab kits (Chronolab Systems S.L.; Travessia Prat de la Riba 34B 08849, Barcelona, Spain).

Oxidative stress markers

A 15% (W/V) homogenate was prepared using a piece of liver of each animal. The piece of liver was crushed in cold 0.9% NaCl followed by a centrifugation (3000 rpm, 30 min) and the supernatant was used for the oxidative stress markers analyses. The determination of malondialdehyde (MDA) concentration was done by the thiobarbituric acid method [10], while the superoxide dismutase activity was evaluated according to Misra and Fridovich [11]. The catalase (CAT) activity was assessed using the chromic acetate method as described in a previous work [12] and the total peroxidases (POX) activity was determined by the potassium iodate method [13].

Statistical analysis

Results were expressed as mean ± standard deviation. Differences between groups were assessed using one way ANOVA, followed by the Duncan's test at 5% significance.

Results

Oxidative stress indicators

The catalase activity increased significantly ($p < 0.05$) with an increasing dose cypermethrin. The activities of SOD and total peroxidases and the concentration of MDA were significantly ($p < 0.05$) higher in animals exposed to 137.5 and 275 mg/kg bw of the insecticide compared to the control Guinea pigs. The tissular proteins decreased in cypermethrin-treated females yet no significant ($p>0.05$) difference observed among treatments (Table 2).

Oxidative stress indicators	Dose of cypermethrin (mg/kg bw)				p
	0 (n = 10)	92 (n = 10)	137.5 (n = 10)	275 (n = 10)	
MDA (uM)	0.98 ± 0.66^{c}	1.11 ± 0.15^{bc}	1.25 ± 0.09^{b}	1.78 ± 0.25^{a}	0.000
SOD (U/min/g of hepatic proteins)	0.15 ± 0.03^{b}	0.16 ± 0.02^{b}	0.24 ± 0.06^{a}	0.24 ± 0.06^{a}	0.011
CAT (uM/min/g of hepatic proteins)	0.79 ± 0.03^{b}	1.05 ± 0.08^{a}	1.02 ± 0.14^{a}	1.17 ± 0.15^{a}	0.001
Tot POX (uM/min/g of hepatic proteins)	21.30 ± 4.21^{b}	25.57 ± 3.39^{b}	35.12 ± 9.21^{a}	39.17 ± 2.81^{a}	0.000
Hepatic proteins (g/dl)	2.53 ± 0.28	2.22 ± 0.26	2.36 ± 0.14	2.26 ± 0.29	0.246

***Table 2**: Effects of cypermethrin on oxidative stress markers in female Guinea pig.*
a, b, c: Within the same line, values with the same letters are not significantly (p > 0.05) different. n: Number of guinea pigs. bw: Body Weight; MDA: Malondialdehyde; SOD: Superoxide Dismutase; CAT: Catalase; Tot POX: Total Peroxidase. p = Probability Value.

Weight and volume of the liver and biomarkers of the hepatic function

The weight and volume of the liver increased in cypermethrin-treated cavies compared to control animals though no significant (p > 0.05) difference was observed (Table 3). The serum concentrations of ASAT and ALAT increased significantly (p < 0.05) in guinea pigs exposed to 137.5 and 275 mg/kg bw of cypermethrin with reference to animals receiving distilled water. In contrast, the levels of globulin, total cholesterol and protein globally declined significantly (p < 0.05) in cypermethrin-treated groups as compared to the control group. The albumin concentration decreased insignificantly (p > 0.05) in pesticide-administered animals, referring to the controls (Table 3).

Parameters	Dose of cypermethrin (mg/kg bw)				p
	0 (n = 10)	92 (n = 10)	137.5 (n = 10)	275 (n = 10)	
Weight and volume of liver					
Weight (g/100g bw)	2.39 ± 0.18	2.47 ± 0.10	2.64 ± 0.21	2.68 ± 0.29	0.207
Volume (ml)	11.50 ± 1.29	12.00 ± 0.82	13.25 ± 1.71	12.75 ± 0.96	0.248
Biomarkers of the hepatic function					
ALAT (IU)	87.65 ± 10.84^{c}	96.90 ± 12.30^{bc}	105.00 ± 9.51^{ab}	113.10 ± 9.56^{a}	0.010
ASAT(IU)	82.10 ± 12.83^{c}	91.70 ± 18.18^{bc}	109.85 ± 15.19^{ab}	127.40 ± 13.75^{a}	0.001
STC (mg/dl)	53.01 ± 5.44^{a}	50.44 ± 3.00^{ab}	46.02 ± 4.90^{bc}	42.49 ± 3.19^{c}	0.006
Total protein (g/dl)	5.56 ± 0.77^{a}	4.65 ± 0.56^{b}	4.54 ± 0.74^{b}	4.45 ± 0.66^{b}	0.044
Albumin (g/dl)	2.89 ± 0.27	2.86 ± 0.29	2.75 ± 0.15	2.56 ± 0.29	0.193
Globulin (g/dl)	2.76 ± 0.42^{a}	1.78 ± 0.48^{b}	1.79 ± 0.64^{b}	1.89 ± 0.43^{b}	0.019

***Table 3**: Effects of cypermethrin on the weight, volume and biomarkers of liver in female guinea pig.*
a, b, c: Within the same line, values with the same letters are not significantly (p > 0.05) different. n: Number of Guinea Pigs. bw: Body Weight; ALAT: Alanine Amino Transferase; ASAT: Aspartate Amino Transferase; STC: Serum Total Cholesterol. p = Probability Value.

Weight and volume of the kidney and biomarkers of the renal function

In table 4, the weight of kidneys was not affected ($p > 0.05$) no matter the dose of cypermethrin, while the volume of kidneys and concentrations of creatinine and urea significantly ($p < 0.05$) increased in groups exposed to the insecticide compared to the control.

Parameters	Dose of cypermethrin (mg/kg bw)				p
	0 (n = 10)	92 (n = 10)	137.5 (n = 10)	275 (n = 10)	
Weight and volume of kidneys					
Weight (g/100g bw)	0.71 ± 0.07	0.69 ± 0.07	0.69 ± 0.06	0.67 ± 0.06	0.799
Volume (ml)	2.75 ± 0.50^{b}	3.58 ± 0.51^{a}	3.83 ± 0.24^{a}	3.20 ± 0.25^{a}	0.012
Biomarkers of the renal function					
Creatinine (mg/dl)	0.70 ± 0.14b	1.12 ± 0.12^{a}	1.37 ± 0.28^{a}	1.12 ± 0.20^{a}	0.001
Urea (mg/dl)	49.21 ± 3.54^{b}	54.27 ± 4.00^{a}	52.10 ± 2.19^{ab}	57.17 ± 6.67^{a}	0.045

***Table 4**: Effects of cypermethrin on the weight, volume and biomarkers of kidneys in female guinea pig.*
a, b, c: Within the same line, values with the same letters are not significantly ($p > 0.05$) different.
n: Number of Guinea Pigs. bw: Body Weight. p = Probability Value.

Weight and measurements of reproductive organs

The weight and measurements of ovaries and uterus (Table 5) were comparable ($p > 0.05$) amongst different groups.

Measurements	Dose of cypermethrin (mg/kg bw)				p
	0 (n = 10)	92 (n = 10)	137.5 (n = 10)	275 (n = 10)	
Ovary weight (g/100g bw)	0.01 ± 0.00	0.01 ± 0.00	0.01 ± 0.00	0.01 ± 0.00	0.834
Uterus weight (g/100g bw)	0.20 ± 0.10	0.21 ± 0.06	0.17 ± 0.06	0.23 ± 0.08	0.742
Uterus length (mm)	40.83 ± 6.13	44.74 ± 5.74	41.73 ± 3.83	42.75 ± 2.77	0.699
Uterus width (mm)	7.45 ± 1.93	8.71 ± 1.06	8.18 ± 1.52	9.04 ± 1.43	0.496
Uterus thickness (mm)	5.80 ± 1.59	6.58 ± 0.95	6.00 ± 1.46	6.88 ± 1.23	0.647

***Table 5**: Effects of cypermethrin on the measurements of the ovary and uterus in female guinea pig.*
a, b, c: Within the same line, values with the same letters are not significantly ($p > 0.05$) different.
n: Number of Guinea Pigs. bw: Body Weight. p = Probability Value; mm: Millimetre.

Estradiol concentration

The estradiol concentration dropped with the increasing dose of cypermethrin. Meanwhile, only animals given 275 mg of cypermethrin/kg bw showed a significant ($p < 0.05$) difference compared to the control (Figure 1).

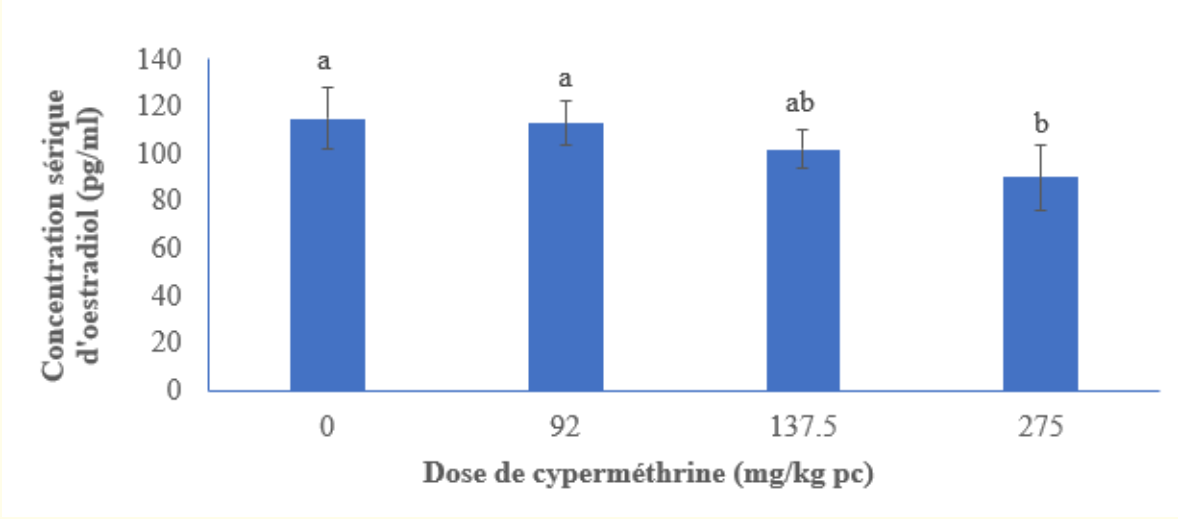

Figure 1: *Effects of cypermethrin on the serum concentration of estradiol in female guinea pig.*
a, b, c: Within the same line, values with the same letters are not significantly (p > 0.05) different.

Discussion

The level of MDA, the activities of SOD, CAT and total peroxidases are important markers used to put in evidence oxidative stress, which causes destruction of tissues [14]. In the present study, the concentrations of MDA and the activities of SOD, CAT and total peroxidases increased in cypermethrin-exposed animals. These results agree with the findings of Boufack., *et al*. [15] in male cavies expose to 1.33, 2 and 4 mg of paraquat/kg bw during 42 days. However, this result disagree with the observations of Zeinab., *et al*. [16] and Nithya and Elango [17] in rats treated respectively with 50 mg of bisphenol A/kg bw for 4 weeks and 5 mg of lindane/kg bw for 30 days. They observed an increased in MDA concentration followed by a decreased in antioxidant enzymes. The results of this study could be due to the fact that the prolonged administration (60 days) of cypermethrin might have caused an over production of free radicals which attacked the plasma membrane of cells, highly made up of polyunsaturated fatty acids thereby causing lipid peroxidation whose end product is MDA. This could explain its increased concentration in the liver [18]. Considering that the aim of antioxidant enzymes is to neutralize free radicals, the overproduction of these latter might therefore explain the increased activities of the studied antioxidant enzymes [19].

The weight of organs is one the basic criteria considered in toxicological studies [20]. Many pesticides have been shown to cause the reduction of the weight of organs by affecting the hypothalamus and/or the pituitary gland [21]. In the present work, the weight and volume of the liver insignificantly increased in cypermethrin-treated Guinea pigs. This could be explained by the fact that the liver is the main organ responsible for the metabolism of toxic substances like pesticides. Therefore, the increase weight of this organ might be due to the enhanced membrane permeability, a damage that comes from oxidative stress induced by cypermethrin [22,23]. The determination of ALAT, ASAT as well as total proteins, albumin and globulin are of great importance in the evaluation of the toxic effects of pesticides in the liver [24,25]. Indeed, the levels of ALAT and ASAT in serum give information on the state of hepatic cells and their increase in blood explains the hepatocellular damage [22,23,26]. In this study, the levels of ALAT and ASAT increased in female guinea pigs exposed to the insecticide. These results corroborate those of El-Shemi., *et al*. [9], who administered 6 and 12 mg of cypermethrin to sheep during 63 days. The rise of these enzymes in blood could be because of an increase in the secretory activity of hepatocytes following the damage of these cells induced by oxidative stress [27-29].

The administration of cypermethrin to females cavies brought about a significant decreased in the level of globulin, total proteins and cholesterol. These results are similar to that of Mokhtar., *et al*. [5] in female rats exposed for 28 days to 0.67, 1 and 2 mg of methomyl/kg bw. The reduction of total proteins and globulin could probably be due to the catabolism of proteins [30] or to the poor synthesis of proteins and their metabolism [31].

The weight of the kidneys was not affected by the administration of cypermethrin. Nevertheless, the kidney volume and the levels of creatinine and urea increased significantly in cypermethrin-treated Guinea pigs. This might be explained by the fact that the kidneys could have lost the ability to filter the toxic products out of blood because of the production of excess free radicals thus, reducing glomerular filtration [32]. Saber and Wael [33] obtained similar results after administering 0.6 mg of deltamethrin/kg bw to rat for 4 weeks.

The measurements of the ovary and uterus were not affected by cypermethrin. These results disagree with the findings of Mokhtar., *et al*. [5] in female rats exposed to 2 mg of methomyl/kg bw for 28 days, which revealed a decrease in the ovaries weight. The female sexual hormones regulate the oestral cycle and the reproductive functions. The concentration of oestradiol reduced significantly in animals given the highest doses of cypermethrin. These results corroborate the works of Obinna and Kagbo [34], who registered a decrease in oestradiol concentration in female rats exposed to 30 and 50 mg of beta-cypermethrin for 14 days. These results are contrary to that obtained by Mokhtar., *et al*. [5], who reported an increase concentration of oestradiol in female rats exposed to 2 mg of methomyl/kg bw for 28 days. In fact, cypermethrin belonging to the pyrethroid family is an endocrine disruptor and can compete with androgenic and oetrogenic receptors [35]. The present results might be due to the interference of cypermethrin with the synthesis, transport, metabolism and elimination of hormones, thereby reducing their natural concentration [36].

Conclusion

Cypermethrin was toxic to female Guinea pig after 60 days of treatment. The estradiol level diminished; the hepatic and renal functions were disrupted. It generated oxidative stress characterised by the increase in the activities of superoxide dismutase, catalase and total peroxidases, and the malondialdehyde concentration.

Conflict of Interest

The authors declare that they have no conflict of interest.

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