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Haemato-biochemical changes following inhalational exposure to commercial grade pyrethroid mixture in male Wistar rats

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ABSTRACT

Introduction: Pyrethroid insecticides are widely used for control of insects such as ticks and flies which may act as disease vectors. During usage, these pyrethroids are absorbed not only by the target parasites but also by the host. We investigated the haematological and some biochemical changes that may occur as a result of daily exposure to pyrethroids via inhalation for seven days in male Wistar rats at varying concentrations.
Methods: A total of sixteen male Wistar rats used for this investigation were divided into four groups: A-D. Group A served as the control unexposed while groups B-D were exposed to 0.04; 0.08 and 0.16mg/ml of pyrethroid (0.05% imiprothrin, 0.05% prallethrin and 0.015% cyfluthrin) respectively daily for seven days.
Results: The results showed a significant reduction in packed cell volume, mean corpuscular haemoglobin and haemoglobin concentrations, while there was also a significant increase ($p < 0.05$) in activities of aspartate aminotransferase and alanine aminotransferase while protein, creatinine and urea concentrations were equally elevated.
Significance: Repeated exposure to pyrethroid continuously over a period of seven days resulted in alteration of haematological and biochemical parameters predisposing the rats to microcytic hypochromic anaemia and perturbation of protein metabolism.

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Introduction

One of the major sources of potential hazard to the environment is the use of insecticides. Insecticides may significantly damage certain physiological and biochemical processes when they enter into the blood stream and then transported to various organs where they are accumulated. Pyrethroids are synthetic chemical analogues of pyrethrins which are naturally occurring insecticidal compounds produced in the flowers of *Chrysanthemum cinerariaefolium.* (Adhikari *et al*., 2006; John, 2007). These pyrethroids include cypermethrin, phyrethrin, allerthrin, tetramethrin and resmethrin among others. The major routes by which these pyrethroid gain access to the body are through inhalation, intradermal or via body orifices. Pyrethroids are considered as comparatively safe pesticides, but their increased utility due to enhanced toxic potential and easy biodegradability, necessitate non-target toxicity assessment (Salama *et al*., 2005; Addy-Orduna *et al*., 2011). Long term exposure to these products causes countless abnormalities and reduces the life span of organisms (Hussain *et al*., 2011; Naz *et al*., 2011).
Various chemicals have been used as insecticides or pesticides in public health programs, veterinary and agriculture. In the use of these synthetic pyrethroids either solely or in combination, there is every tendency that humans are consciously or unconsciously exposed to these pyrethroids. Hence, there is need to determine some haematological and biochemical changes that may arise upon exposure to these chemical agents.
The aim of the present study was to evaluate the toxicity of pyrethroids in male Wistar rats, by estimation of haematological and some biochemical parameters upon exposure to graded doses pyrethroid daily for seven days.

Materials and methods

Experimental animals
A total of sixteen male Wistar rats were used for this investigation. The average weight of the rats was 152±3.50g. They were provided with laboratory animal feed (Fat/oil 6%, crude fibre 5%, calcium 1%, Available phosphorus 0.4%, Lysine 0.85%, Methionine 0.35%, Salt 0.3%, Crude protein 18%, Metabolisable Energy 2900Kcal.kg^{-1}), manufactured by TOPFEEDS®, (Lagos, Nigeria) and water provided. Experimental animals were acclimatized to their environment before the start of the experiment.

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Animal ethics

All experimental protocols carried out on the animals were in accordance with the international accepted principles for laboratory animal use and were approved by the Ethics Committee (UIL/FVERC/001/2018) on Laboratory animal use of the Faculty of Veterinary Medicine, University of Ilorin, Nigeria.

Experimental chemical

The pyrethroid used for this investigation contains 0.05% imiprothrin, 0.05% prallethrin and 0.015% cyfluthrin (all synthetic pyrethrin) in a 300ml pressurized liquid canister.

Chemical exposure

A total of sixteen male Wistar rats were used for the experiment. They were randomly divided into four groups (A-D) of four animals per group.
Group A was the control non exposed group to the pyrethroid while groups B to D were exposed to 0.04mg/ml, 0.08mg/ml and 0.12mg/ml of pyrethroid insecticides via inhalation in a separate desiccator for each group daily for seven days.

Haematological effects

At the end of exposure period, blood samples were collected via the *Media canthus* into heparinized tubes for haematological studies. Packed cell volume, red and white blood cell counts along with differentials and platelets counts were determined as described by Jain (1986). The haematological indices such as mean corpuscular volume, mean corpuscular haemoglobin and mean corpuscular haemoglobin concentration were calculated.

Plasma preparation

The blood samples were centrifuged at 4000rpm for 10 minutes to separate the plasma from the cellular components. The plasma was then pipetted out and stored in Eppendorf tubes for further analysis.

Biochemical analysis

Total plasma protein and albumin concentrations were estimated according to the methods of Tietz (1995) and Grant (1987) respectively, while blood urea nitrogen and creatinine concentrations were estimated as described by Henry (1974) using commercial kits (Randox®, Spain). The aspartate and alanine aminotransferases activities were assayed as described by Reitman and Frankel (1957).

Statistical analysis

Results were expressed as mean ± SEM. Analysis of the data was done using one-way analysis of variance followed by the Duncan multiple range test. A p-value < 0.05 was considered significant. All analyses were done using GraphPad Prism version 5.

Results

Clinical observations

Exposure of rats to the pyrethroids produced varying degrees of clinical observations and these were in a dose dependent manner. There were both nasal and ocular discharges, chemotactic response to the source of the pyrethroids, ruffled body coat, scratching of the nostril and the irritation of the eyes along with frequent mild watery stool.

Erythrocytes and erythrocytic indices

Table 1 shows the erythrocytes and erythrocytic indices of male Wistar rats treated with graded doses of pyrethroid. There was a significant decrease in red blood cell counts (RBC), packed cell volume (PCV), mean corpuscular haemoglobin (MCH), mean corpuscular haemoglobin concentration (MCHC) and the haemoglobin concentrations (HGB) of rats exposed to the pyrethroid in dose dependent.

Hepatic and renal parameters

Table 2 shows some hepatic and renal parameters of male Wistar rats treated with graded doses of pyrethroid**.** There was a significant ($p < 0.05$) increase in the activities of both aspartate amino transferase and alanine amino transferase while corresponding increase was also recorded in the creatinine concentration. These increases were dose dependent.
Table 3 shows mean protein, albumin and urea concentrations of male Wistar rats treated with graded doses of pyrethroid. There was a significant decrease in plasma total protein concentrations of the treated rats compared to the control group. However, there was a marginal increase in the albumin concentration. The alterations observed were dose dependent.

Table 1. Erythrocytes and erythrocytic indices of male Albino rats treated with graded doses of pyrethroid.

Groups	RBC $\times 10^{12}$ (L)	PCV (%)	MCV (Fl)	MCH (Pg)	MCHC (g/dl)	HGB (g/dl)
Control	7.06 ± 0.71^{a}	42.75 ± 4.31^{a}	60.50 ± 0.29^{a}	17.70 ± 0.67^{a}	29.20 ± 1.14^{a}	12.35 ± 0.86^{a}
0.04 mg/ml	6.53 ± 0.30^{b}	39.75 ± 1.75^{b}	55.00 ± 1.87^{b}	15.40 ± 0.55^{b}	26.98 ± 0.25^{b}	11.98 ± 0.42^{b}
0.08 mg/ml	5.00 ± 0.31^{b}	33.50 ± 2.26^{b}	50.00 ± 0.71^{b}	13.45 ± 0.24^{b}	24.43 ± 0.52^{b}	10.20 ± 0.45^{b}
0.16 mg/ml	4.31 ± 0.26^{b}	30.50 ± 1.56^{b}	40.50 ± 0.29^{b}	12.50 ± 0.27^{b}	22.45 ± 0.30^{b}	9.80 ± 0.26^{b}

Values within the same column with different superscripts are significantly different at $p < 0.05$.

Table 2. Some hepatic and renal parameters of male Albino rats treated with graded doses of pyrethroid

Group	AST (mmol/L)	ALT(mmol/L)	Creatinine (mmol/L)	Urea (mmol/L)
Control	27.15 ±1.08[a]	27.80±0.96[a]	92.48±3.55[a]	2.88±0.11[a]
0.04 mg/ml	33.25±2.96[b]	35.43±2.21[b]	93.10±2.99[b]	3.28±0.35[b]
0.08 mg/ml	37.33±2.90[b]	38.38±2.88[b]	101.13±5.53[b]	3.40±0.41[b]
0.16 mg/ml	39.30±4.95[b]	42.05±0.77[b]	103.00±3.69[b]	3.45±0.36[b]

Values within the same column with different superscripts are significantly different at $p < 0.05$

Discussion

Pyrethroids constitute major source of potential environmental hazards not only to animals but also to humans when they become part of food chains or as a result of exposure to them during insecticidal applications (Abd-Alla *et al*., 2002). Pyrethroids are preferred to organophosphates, carbamates and organochlorines as they have high efficiency, low toxicity and easy biodegradability (Sharaf *et al.*, 2010). However, repeated long term exposure to these pyrethroids causes various abnormalities and reduces the life span of organisms (Hussain *et al*., 2011; Naz *et al*., 2011).

Table 3. The mean protein, albumin and urea concentration of male Albino rats treated with graded doses of pyrethroid.

Group	Protein (mmol/L)	Albumin (mmol/L)
Control	8.48±1.30[a]	2.65±0.10[a]
0.04 mg/ml	7.83±0.22[b]	3.35±0.24[b]
0.08 mg/ml	6.60±0.44[b]	3.70±0.13[b]
0.16 mg/ml	5.33±0.55[b]	3.78±0177[b]

Values within the same column with different superscripts are significantly different at $p < 0.05$

Haematological findings are important for the assessment of various systemic functions and health of animals under various environmental conditions and most importantly, for diagnosis of drug or chemical induced haemolysis (Atamanalp and Yanik, 2003). The result of the present study shows that exposure via inhalation to pyrethroid results in decreased haematological parameters – red blood cell counts, packed cell volume, haemoglobin concentration and calculated erythrocytes indices such as mean corpuscular volume, mean corpuscular haemoglobin and mean corpuscular haemoglobin concentration. This is suggestive of microcytic hypochromic anaemia because of the decrease packed cell volume and the mean corpuscular haemoglobin concentration. Also, substantial decrease in total erythrocyte counts and haemoglobin concentration could possibly be due to suppression of erythropoiesis and haem synthesis, with concomitant devastation of erythrocyte in haemopoietic tissue (Manna *et al*., 2004; Fetoui *et al*., 2008). Haemolysis is produced by agents that injure the red cell membrane, leading to oxidative damage to haemoglobin or suppression of the antioxidative protective mechanism. The results of our study is consistent with the reports of Atamanalp and Yanik (2003), Ahmad *et al*.(2009) and Hussain *et al*. (2011) who reported that when pyrethroids are used in excessive dosage they become part of food chain, triggering a series of haematological alterations leading to abnormalities in respiratory, nervous, immune and endocrine systems. Anaemia due to decrease in haemoglobin concentrations was reported in mice treated with fenvalerate (EPA, 1991) while total erythrocytes counts in female rats and decrease in packed cell volume in male rats fed cypermethrin have also been reported (EPA, 1989).

Liver and kidney are important organs in terms of xenobiotic detoxification and excretion respectively. Alanine aminotransferase (ALT), aspartate aminotransferase (AST) are two key enzymes present in liver cells. Our results showed increase in the activities of the liver transaminases with corresponding increase in the indicators such as creatinine and urea. The degree of elevation therefore indicates marked degree of hepatic cellular damage and kidney dysfunction. Manna *et al.* (2003) reported that increase of serum ALT and AST activities are related to liver damage and change in hepatic function. Increase in the activities of these enzymes is attributed to the leakage of these enzymes to the blood stream. Also, the hepatic injury could be due to oxidative damage by free radicals (Manna *et al*., 2003; Muthuviveganandavel *et al*., 2008). Yousef *et al.* (2006) have reported an increase in ALT, AST and LDH following pyrethroid exposure indicating hepatotoxicity.

Urea is a nitrogenous waste product resulting from deamination of amino acids in the liver, while a metabolic product of creatine phosphate dephosphorylation in the muscle is creatinine. The increased urea and creatinine concentrations following

pyrethroid exposure may be attributed to their low clearance indicating diminished ability of the kidneys to filter these waste products from the blood and excrete them in the urine. Our result is consistent with that of the other workers Ahmad *et al*. (2011) and Ravel (1995) that reported increased urea and creatinine concentrations in blood of pyrethroid treated animals.

Proteins constitute the building block and the basic molecules for any biochemical reaction. They are intimately related with almost all physiological processes in a biological system. The physiological and biochemical alterations observed in an animal under any physiological stress can be correlated with the structural and functional changes of cellular proteins. Proteins occupy a unique position in the metabolism of cell because of the proteinaceous nature of all the enzymes which mediate the various metabolic pathways Michacla and David (2008). The decrease in plasma protein concentration shows dose dependent changes with pyrethroid treatment. This could be ascribed to the harmful effect of pyrethroids on hepatocytes bringing about alterations in the metabolism of protein and free amino acids. Previous study of pyrethroid toxicity has witnessed inconsistent results. Khan *et al*. (2009) reported decrease in total serum proteins following pyrethroid exposure; however Hussain *et al*. (2009) and Aslam *et al*. (2010) reported increased protein concentrations while Sayim *et al*. (2005) reported no effect on protein concentration.

Conclusion

From these observations made in the rats under pyrethroid inhalation it can be concluded that the severity in the changes of the lesion are dependent on the dose of the pyrethroid. High dose caused more alterations to the haematological and biochemical activities of the rats than the moderate and lower dosages. Further works expounding the exact mechanism underlying these biochemical changes and determining the genotoxic effects of the pyrethroids are essential. It is recommended that pyrethroid users should handle this substance with care.

Conflict of interest

There is no conflict of interest.

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