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*Original Research*

# Brain, lung, and heart oxidative stress assessment of an over-the-counter pyrethroid insecticide product in Nigeria

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**ABSTRACT: We evaluated the brain, lung, and heart oxidative stress in rats exposed to aerosol of an over-the-counter pyrethroid insecticide product in Nigeria. The experimental animals were randomly divided into four groups: group I (control) was not exposed to the insecticide aerosol, while groups II, III, and IV were exposed to 6.0 mL $m^{-3}$, 12.0 mL $m^{-3}$, and 18 mL $m^{-3}$ of insecticide aerosol respectively. Exposures were carried out in wooden-glass chambers one hour daily for six weeks. Malondialdehyde (MDA) and reduced glutathione (GSH) concentrations, as well as catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GPx), and glutathione S-transferase (GST) activities were determined. The brain, lung, and heart showed no significant difference in their weights and relative weights compared with the control. A significant increase in brain lipid peroxidation (LPO) was seen in groups III and IV, while there was no significant increase in lung and heart LPO compared with control. Significant decrease in the brain and lung GSH were observed in all the treatment groups when compared with the control, but only group IV showed significant reduction in heart GSH. Also, activities of lung GST and SOD were decreased compared with control, while the activity of GPx in the lung was significantly increased in group III. Lastly, non-significant increase in lung CAT activity was recorded in groups II and III, but decreased in group IV compared with control. Prolonged and incessant exposure to the insecticide aerosol over a long period of time may lead to tissue oxidative stress. These findings suggest that the use of insecticide aerosol for domestic purposes should be regulated.**

**KEYWORDS: Insecticide aerosol, pyrethroid, oxidative stress, lipid peroxidation, rats.**

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## INTRODUCTION

Malaria is a common disease in tropical and subtropical regions, which includes parts of Africa, Asia, and America. Approximately 350-500 million cases are reported for malaria each year, of which one to three million death cases are recorded, majority of the incidents are among children in Sub-Saharan Africa (Snow *et al*., 2001). Malaria leads to poverty by impeding economic growth, thereby promoting conditions that enhance malaria transmission (Okrah *et al*., 2002; Sachs & Malaney, 2002; Malaney *et al*., 2004). Eliminating mosquito vectors of the malaria parasite is one of the most effective measures against malaria.

Pyrethroid insecticide products are commonly used in the control of mosquitoes in Nigeria. The active insecticidal ingredients of pyrethroid insecticide product used in this study include cyfluthrin, imiprothrin, and prallethrin.

A recent survey of household pesticide use conducted for the U.S. Environmental Protection Agency (EPA) showed that cyfluthrin use is extensive. While cyfluthrin was used by less than 2 percent of the households surveyed, this represented almost 40 million applications annually in the U.S. The bulk of these treatments (over 33 million annually) were made indoors (Whitmore *et al*., 1992). Many synthetic pyrethroids,

including cyfluthrin, are complex molecules and have a variety of three-dimensional isomeric configurations. All of the isomers, however have the same mode of action (Cremlyn, 1991). Cyfluthrin has a complex mode of action and affects normal nerve function in several ways. It induces alterations in nerve membranes, causing abnormal sodium and potassium flows (US EPA, 1986). This results in the repetitive discharges from the neurons, causing convulsions and also blockage of further nerve impulses (Cremlyn, 1991). Cyfluthrin also affects calcium concentrations in nervous tissue by inhibiting an enzyme involved in calcium transport. This in turn increases the amount of the neurotransmitter acetylcholine released at the junction between nerves (Al-Rajhi, 1990). In addition, two receptors found in nervous tissue, the gamma-aminobutyric acid receptors and the peripheral benzodiazepine receptors, are inhibited by cyfluthrin. Inhibition of either of these receptors can cause convulsions (Ramadan *et al*., 1988a; 1988b). Cyfluthrin is also acutely toxic when inhaled. Exposure of laboratory animals to 0.7−0.9 mg per liter of air caused convulsions, excess salivation, incoordination, decreased activity, and death (US EPA, 1986). Other studies of laboratory animals exposed to cyfluthrin noted symptoms of labored breathing, reduced movement, nasal discharge, and ungroomed fur (Pauluhn *et al*., 1988). People are exposed to cyfluthrin by eating contaminated food, from residues persisting after indoor or outdoor applications, and through making applications of cyfluthrin containing products (Cox, 1994).

Imiprothrin is specifically targeted at waterbugs, ants, silverfish, cockroaches, crickets, and spiders in commercial products. A study with rats indicates that repeated non-contiguous inhalation of an insecticide that contains imiprothrin could have immunotoxic effects in sites distal to the lungs (Emara & Daz, 2007).

Prallethrin, the third active insecticidal ingredients, has wide application in the treatment of domestic pets. It is used in household insecticide products against cockroaches, mosquitoes, and houseflies (Matsunaga *et al*., 1987). Findings with human volunteers who were exposed regularly to prallethrin containing mosquito repellent include alterations in the biochemical composition of erythrocyte membranes, erythrocytic osmotic haemolysis, and plasma levels of nitrite and nitrate (Narendra *et al*., 2007).

In addition to the active insecticidal ingredients, insecticide aerosols also contain ‘‘inert’’ ingredients which are referred to as “trade secrets” by their manufacturers. Inert ingredients may not be inert in the usual sense of the word; often they are not chemically, biologically, or toxicologically inert. For instance, ethylbenzene, trimethylbenzenes, crystalline silica, and xylenes are common inert ingredients in cyfluthrin containing products, being used as solvents. Occupational exposure to these solvents has been associated with an increased rate of leukemia and a range of lymphoma types (McMichael, 1988; Cocco *et al*., 2010).

Information on toxicological consequences of frequent exposure to household insecticide aerosols is still needed. In this study, we assessed the risk and the hazard associated with exposure to aerosols of a commonly used over-the-counter pyrethroid insecticide product, using rats as an experimental animal model. We assessed the oxidative stress of the multi-purpose insect killer in rats exposed to the aerosols by monitoring the activities of lung CAT, SOD, GPx, and GST, as well as concentrations of GSH and MDA in brain, lung, and heart of the exposed and control groups.

## MATERIALS AND METHODS

### Test materials and chemicals

Baygon™ multi-purpose pyrethroid insecticide product of Johnson Wax Nigeria Limited, Lagos (composition Cyfluthrin, 0.015%; Imiprothrin, 0.05%; Prallethrin, 0.05%; and undisclosed inert ingredients, 99.885%) was purchased from a local supermarket near the university. All other reagents and chemicals were of analytical grade, products of Sigma Chemical Co., Saint Louis, MO, USA or BDH Chemical Ltd, Poole, England.

### Exposure of rats: exposure chamber design

Four identical wooden-glass exposure chambers each with internal volume of 0.167 $m^3$ (0.405 m x 0.800 m x 0.515 m) were used. Into each chamber (containing five rats) was sprayed 0, 1, 2, or 3 mL respective volume of the pyrethroid product multi-purpose insect killer. This is equivalent to 0, 6.0, 12.0, and 18.0 mL $m^{-3}$ of the exposure chamber respectively. The chambers were closed for 1 hour immediately after spraying. A glass top enabled observations to be made of reactions of the animals to the aerosols. These procedures were carried out once a day for 6 weeks. Effective light usage of the insecticide in Nigerian homes ranges from about 3.5–6.0 mL $m^{-3}$. Three different doses, multiples of this light usage, were experimented with in different groups of rats exposed to the insecticide aerosols thereby giving allowance for heavy aerosols spray and high level of exposure to the insecticide. The volume of the insecticide sprayed as aerosols usually depend on the users and the perceived population of insects in the house.

### Experimental animals and treatments

Twenty male wistar albino rats with an average weight of 150 g used for this study were obtained from the animal house of the College of Veterinary Medicine, Federal University of Agriculture, Abeokuta, Nigeria. They were housed in steel metal cages in the animal house of our department. The rats were divided randomly into four groups (I–IV) of five animals per group based on the treatment received in the exposure chamber (internal volume 0.167 $m^3$) as below:

**Table 1. Brain, lung, and heart weights of control and experimental rats exposed to pyrethroid insecticide aerosols.**

| | Brain Weight (g) | Lung Weight (g) | Heart Weight (g) |
|---|---|---|---|
| I (Control) | 1.47 ± 0.11 | 1.87 ± 0.30 | 0.68 ± 0.05 |
| II (6.0 ml/m$^3$) | 1.37 ± 0.20 | 1.41 ± 0.12 | 0.66 ± 0.03 |
| III (12.0 ml/m$^3$) | 1.54 ± 0.14 | 1.40 ± 0.07 | 0.61 ± 0.02 |
| IV (18.0 ml/m$^3$) | 1.52 ± 0.13 | 1.54 ± 0.11 | 0.69 ± 0.03 |

Values of the treatment are expressed as ml/m$^3$ of insecticide aerosols. Each value is a mean of 5 rats ± SEM. No Significant difference from control group ($p > 0.05$).

**Table 2. Relative brain, lung, and heart weights of control and experimental rats exposed to pyrethroid insecticide aerosols.**

| | Relative Brain Weight (%) | Relative Lung Weight (%) | Relative Heart Weight (%) |
|---|---|---|---|
| I (Control) | 0.69 ± 0.02 | 0.86 ± 0.10 | 0.32 ± 0.01 |
| II (6.0 ml/m$^3$) | 0.71 ± 0.13 | 0.73 ± 0.05 | 0.34 ± 0.01 |
| III (12.0 ml/m$^3$) | 0.82 ± 0.04[a] | 0.74 ± 0.04 | 0.32 ± 0.01 |
| IV (18.0 ml/m$^3$) | 0.76 ± 0.04 | 0.78 ± 0.08 | 0.35 ± 0.01 |

Values of the treatment are expressed as ml/m$^3$ of insecticide aerosols. Each value is a mean of 5 rats ± SEM. [a]Significantly different from negative control group ($p<0.05$). Relative organ (brain/lung/heart) weight = (organ weight/final body weight) x 100.

**(1)** Group of rats not exposed to insecticide aerosols.

**(2)** Rats in this group were exposed to 6.0 mL of the aerosols per m$^3$ treatment chamber volume (i.e., 1mL of the insecticide product in 0.167 m$^3$ exposure chamber).

**(3)** Animals in this group were exposed to the aerosols at 12.0 mL m$^{-3}$.

**(4)** Rats in this group were exposed to the aerosols at 18.0 mL m$^{-3}$.

### Sample preparation

At the end of the experimental period, the animals were sacrificed and the brain, lung, and heart were harvested. The organs were washed in ice-cold saline (0.9 % w/v) solution, and were blotted dry, after which they were suspended in ice-cold 0.1 M phosphate buffer (pH 7.4) and homogenized, followed by centrifugation at 5000 rpm for 10 minutes. The homogenate was then used immediately for analysis of biochemical parameters.

### Assay for biochemical parameters

Catalase (CAT) activity was determined by the method of Sinha (1972). The reaction mixture (1.5 ml) contained 0.01 M phosphate buffer, pH 7.0, tissue homogenate (0.1 ml) and 2 M $H_2O_2$ (0.4 ml). The reaction was stopped by the addition of 2 ml dichromate-acetic acid reagent (5% potassium dichromate and glacial acetic acid mixed in 1:3 ratios), followed by heating in boiling water for 10 minutes, and then cooled at room temperature. The absorbance was read at 570 nm. Superoxide dismutase (SOD) was determined by

the method of Misra and Fridovich (1972). The method is based on the ability of superoxide dismutase to inhibit auto-oxidation of adrenaline to adrenochrome at alkaline pH. The unit of enzyme activity is defined as the enzyme required for 50% inhibition of adrenaline auto-oxidation. Glutathione peroxidase (GPx) was determined by the method of Paglia and Valentine (1967) which depends on the oxidation of NADPH at 340 nm using hydrogen peroxide, and Glutathione S=transferase (GST) was determined by the method of Habig *et al*. (1974) based on enzyme-catalysed condensation of glutathione with the model substrate, 1-chloro-2,4-dinitrobenzene. The product formed (2,4-dinitrophenyl-glutathione) absorbs light at 340 nm. Malondialdehyde (MDA) levels, a marker of lipid peroxidation (LPO) was determined by the method of Beuge and Aust (1978). In this procedure, 1.0 ml of the supernatant was added to 2 ml of tricarboxylic acid–thiobarbituric acid–hydrochloric acid (TCA/TBA/HCl) (1:1:1 ratio) reagent, boiled at 100 $^{o}$C for 15 minutes and allowed to cool. Flocculent materials were removed by centrifuging at 3000 rpm for 10 minutes. The supernatant was removed and the absorbance read at 532 nm against blank. MDA concentration was calculated using the molar extinction coefficient for MDA-TBA complex of 1.56 × $10^{5}M^{-1}cm^{-1}$, while GSH levels was determined by the method of Moron *et al*. (1979) where the color developed was read at 412 nm.

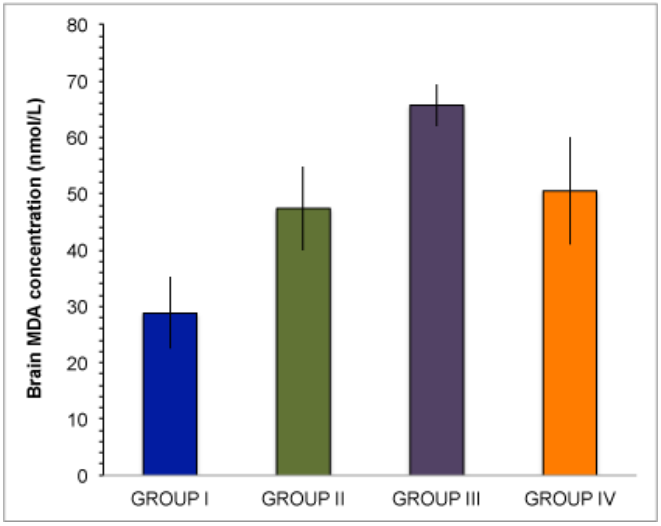


**Figure 1. Effects of pyrethroid insecticide product aerosols on rats' brain lipid peroxidation.** I: Group of rats not exposed to aerosols. II: Rats in this group were exposed to 1 mL of the insecticide product aerosols in 0.167 $m^3$ treatment chamber (equivalent to 6.0 mL $m^{-3}$ treatment chamber volume). III: Animals in this group were exposed to 2 mL of the aerosols (equivalent to 12.0 mL $m^{-3}$ treatment chamber volume). IV: Rats in this group were exposed to 3 mL of the aerosols (equivalent to 18.0 mL $m^{-3}$ treatment chamber volume). Values are mean ± SEM; n = 5.

Note: *Significantly different from control group I ($p < 0.05$).

### Statistical analysis

Data were analyzed by one-way analysis of variance (ANOVA), followed by least significant difference (LSD) to test for significant differences among the groups of rats using Statistical Package for Social Sciences program version 17.0. Data were expressed as mean ± standard error of mean. P values less than 0.05 were considered statistically significant.

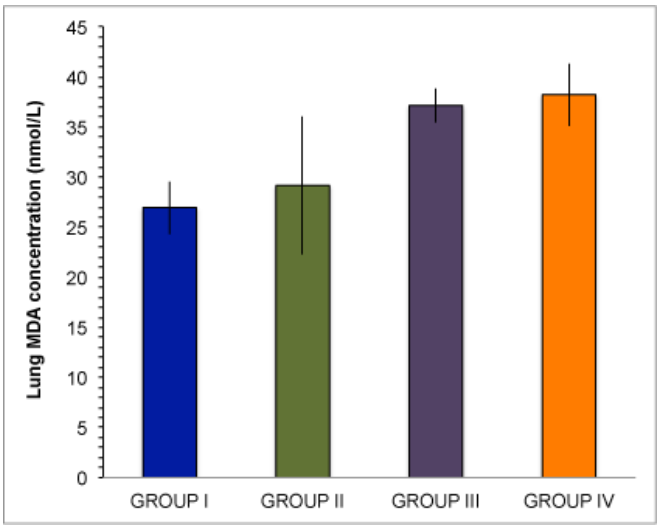


**Figure 2. Effects of pyrethroid insecticide product aerosols on rats' lung lipid peroxidation. I**: Group of rats not exposed to aerosols. II: Rats in this group were exposed to 1 mL of the insecticide product aerosols in 0.167 $m^3$ treatment chamber (equivalent to 6.0 mL $m^{-3}$ treatment chamber volume). III: Animals in this group were exposed to 2 mL of the aerosols (equivalent to 12.0 mL $m^{-3}$ treatment chamber volume). IV: Rats in this group were exposed to 3 mL of the aerosols (equivalent to 18.0 mL $m^{-3}$ treatment chamber volume). Values are mean ± SEM; n = 5.

## RESULTS

The brain, lung, heart weights and the relative weights of control and experimental rats exposed to pyrethroid insecticide aerosols are shown in Table 1 and Table 2 respectively. Exposure of rats to the insecticide aerosol did not cause any significant effect ($p > 0.05$) on brain, lung and heart weights compared to control. Apart from 12.0 mL $m^{-3}$ of the aerosol that produced a significant difference ($p < 0.05$) in relative brain weight, there was no significant difference ($p > 0.05$) in lung and heart relative weights compared to control.

The effects of pyrethroid insecticide aerosol on brain, lung, and heart MDA concentrations are shown in Figures 1, 2, and 3 respectively. The results obtained showed that the 12.0 mL $m^{-3}$ and 18.0 mL $m^{-3}$ concentrations of pyrethroid insecticide aerosol significantly increased ($p<0.05$) the brain MDA concentration, while no significant increase ($p>0.05$) in MDA concentration in lung and heart was recorded compared with control.

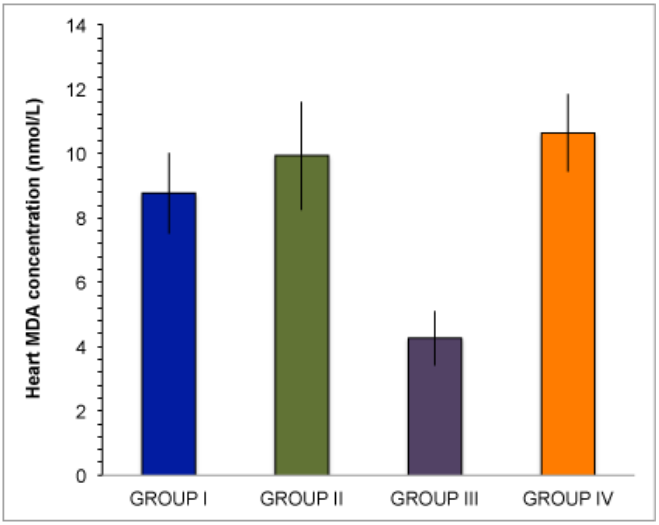


**Figure 3. Effects of pyrethroid insecticide product aerosols on rats' heart lipid peroxidation.** I: Group of rats not exposed to aerosols. II: Rats in this group were exposed to 1 mL of the insecticide product aerosols in 0.167 $m^3$ treatment chamber (equivalent to 6.0 mL $m^{-3}$ treatment chamber volume). III: Animals in this group were exposed to 2 mL of the aerosols (equivalent to 12.0 mL $m^{-3}$ treatment chamber volume). IV: Rats in this group were exposed to 3 mL of the aerosols (equivalent to 18.0 mL $m^{-3}$ treatment chamber volume). Values are mean ± SEM; n = 5.

Note: *Significantly different from control group I ($p < 0.05$).

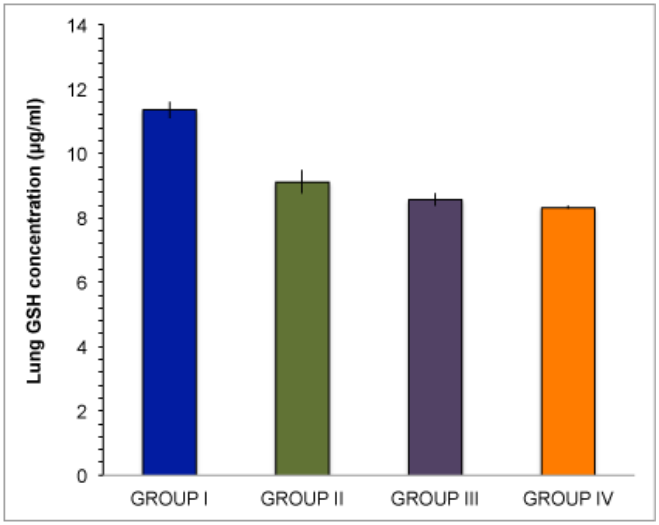


**Figure 5. Effects of pyrethroid insecticide product aerosols on rats' lung GSH level.** I: Group of rats not exposed to aerosols. II: Rats in this group were exposed to 1 mL of the insecticide product aerosols in 0.167 $m^3$ treatment chamber (equivalent to 6.0 mL $m^{-3}$ treatment chamber volume). III: Animals in this group were exposed to 2 mL of the aerosols (equivalent to 12.0 mL $m^{-3}$ treatment chamber volume). IV: Rats in this group were exposed to 3 mL of the aerosols (equivalent to 18.0 mL $m^{-3}$ treatment chamber volume). Values are mean ± SEM; n = 5.

Note: *Significantly different from control group I ($p < 0.05$).

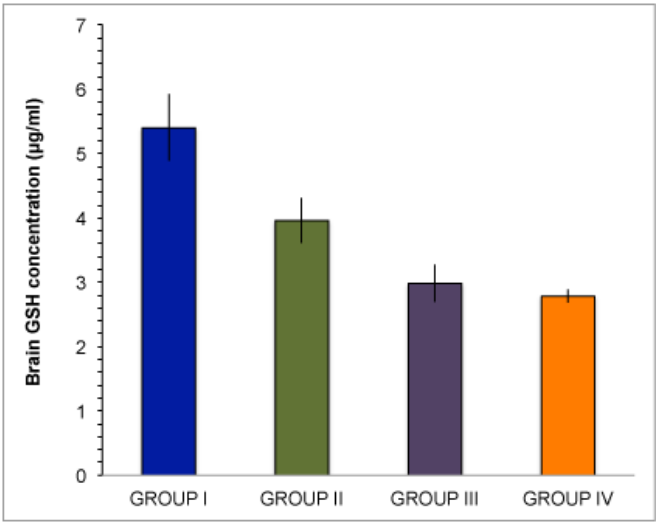


**Figure 4. Effects of pyrethroid insecticide product aerosols on rats' brain GSH level.** I: Group of rats not exposed to aerosols. II: Rats in this group were exposed to 1 mL of the insecticide product aerosols in 0.167 $m^3$ treatment chamber (equivalent to 6.0 mL $m^{-3}$ treatment chamber volume). III: Animals in this group were exposed to 2 mL of the aerosols (equivalent to 12.0 mL $m^{-3}$ treatment chamber volume). IV: Rats in this group were exposed to 3 mL of the aerosols (equivalent to 18.0 mL $m^{-3}$ treatment chamber volume). Values are mean ± SEM; n = 5.

Note: *Significantly different from control group I ($p < 0.05$).

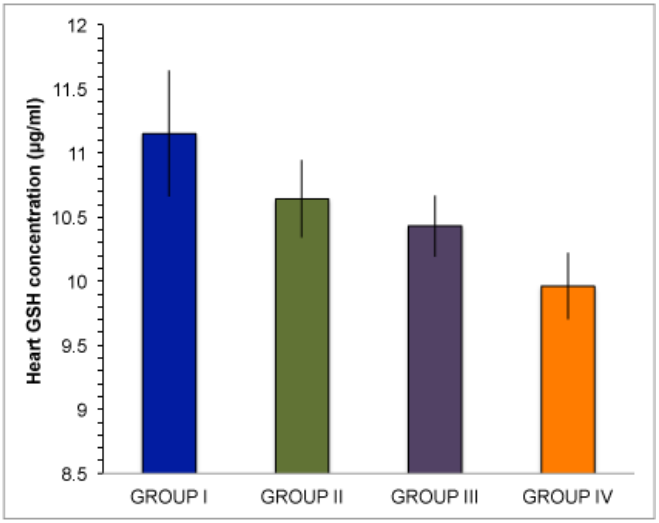


**Figure 6. Effects of pyrethroid insecticide product aerosols on rats' heart GSH level.** I: Group of rats not exposed to aerosols. II: Rats in this group were exposed to 1 mL of the insecticide product aerosols in 0.167 $m^3$ treatment chamber (equivalent to 6.0 mL $m^{-3}$ treatment chamber volume). III: Animals in this group were exposed to 2 mL of the aerosols (equivalent to 12.0 mL $m^{-3}$ treatment chamber volume). IV: Rats in this group were exposed to 3 mL of the aerosols (equivalent to 18.0 mL $m^{-3}$ treatment chamber volume). Values are mean ± SEM; n = 5.

Note: *Significantly different from control group I ($p < 0.05$).

The effects of the insecticide aerosol on brain, lung, and heart levels of GSH are shown in Figures 4, 5, and 6 respectively. All the concentrations of insecticide aerosol assessed (group II–IV) significantly reduced ($p<0.05$) the levels of GSH in brain and lung compared to control, in a dose dependent manner, while only 18.0 mL $m^{-3}$ of the insecticide significantly reduced ($p<0.05$) the heart GSH level compared to control.

Exposure to the insecticide aerosol did not result in significant reductions ($p>0.05$) in lung GST and SOD activities (Figures 7 and 8) compared to control, while 12.0 mL $m^{-3}$ of the pyrethroid insecticide aerosol significantly raised ($p < 0.05$) the lung GPx activity (Figure 9) compared to control. For CAT, 6.0 mL $m^{-3}$ and 12.0 mL $m^{-3}$ concentrations of the insecticide caused no significant increase ($p>0.05$), while 18.0 mL $m^{-3}$ of the aerosol reduced its activity (Figure 10).

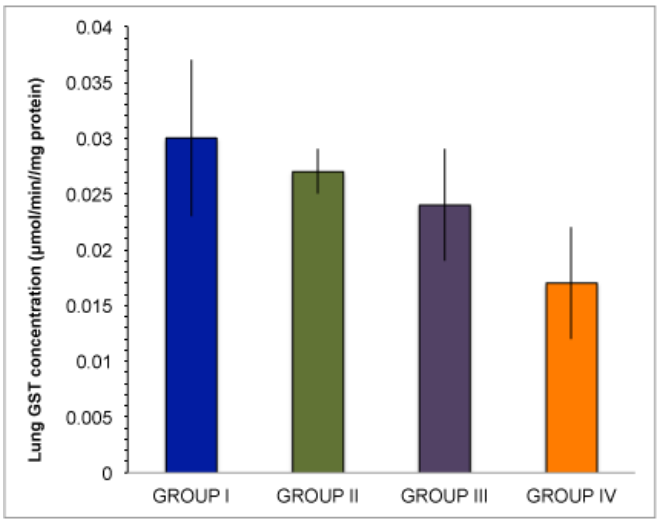


**Figure 7. Effects of pyrethroid insecticide product aerosols on rats' lung GST activity.** I: Group of rats not exposed to aerosols. II: Rats in this group were exposed to 1 mL of the insecticide product aerosols in 0.167 $m^3$ treatment chamber (equivalent to 6.0 mL $m^{-3}$ treatment chamber volume). III: Animals in this group were exposed to 2 mL of the aerosols (equivalent to 12.0 mL $m^{-3}$ treatment chamber volume). IV: Rats in this group were exposed to 3 mL of the aerosols (equivalent to 18.0 mL $m^{-3}$ treatment chamber volume). Values are mean ± SEM; n = 5.

## DISCUSSION

Misuse of pyrethroids insecticides could cause toxicity in non-target species (Cantalamessa, 1993). Insecticides exposure constitutes a source of potent hazard especially in children and animals (Eisler, 1989; Nebeker *et al*., 1992; Menegaux *et al*., 2006). Non-biodegradable materials such as plastic bags and bottles, used automobile wheel tires in the environment provide increasing breeding grounds for mosquitoes, the vector of malarial parasites. These factors consequently lead to increasing use of insecticides to fight home infestation of mosquitoes. This results in increased production of existing insecticides and development of new ones.

The multipurpose insect killer used in this study is a pyrethroid insecticide product. It is a popular brand for the eradication of mosquito in households in Nigeria and in some cases it is used daily in homes. This increases the exposure of people, especially children, to the aerosols and the resulting consequent effects on their health.

Organ weights are measured in toxicity studies to evaluate a broad range of physiological and biochemical functions, as well as tissue injury assessment. Long-term exposure of laboratory animals to cyfluthrin has been reported to caused adverse effects that range from diarrhea to reduced body temperature and weight loss (Cox, 1994). Cyfluthrin-contaminated diets over longer periods (four weeks) caused weight loss, changes in several blood chemistry parameters, and changes in liver weights (Cox, 1994). In our findings, the insecticide aerosol increased the brain weight and relative weights, decreased the lung weight and relative weight, and had no effect on the heart weight compared with control. It was reported that prallethrin treatment in rats increased relative liver weight compared to control group (Mossa *et al*., 2013).

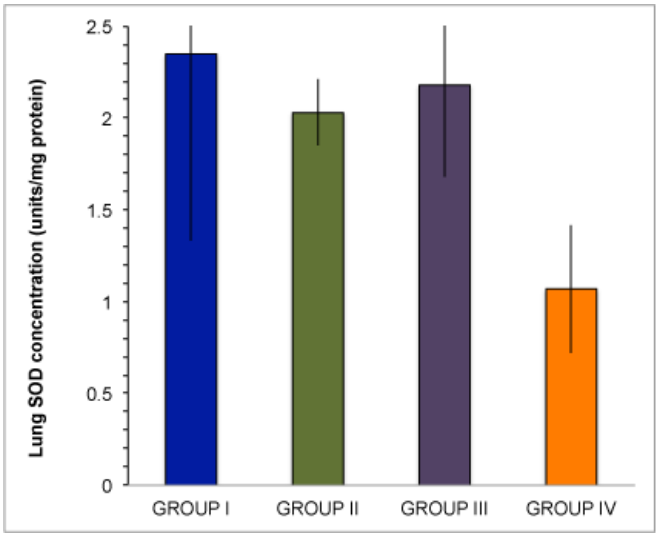


**Figure 8. Effects of pyrethroid insecticide product aerosols on rats' lung SOD activity.** I: Group of rats not exposed to aerosols. II: Rats in this group were exposed to 1 mL of the insecticide product aerosols in 0.167 $m^3$ treatment chamber (equivalent to 6.0 mL $m^{-3}$ treatment chamber volume). III: Animals in this group were exposed to 2 mL of the aerosols (equivalent to 12.0 mL $m^{-3}$ treatment chamber volume). IV: Rats in this group were exposed to 3 mL of the aerosols (equivalent to 18.0 mL $m^{-3}$ treatment chamber volume). Values are mean ± SEM; n = 5.

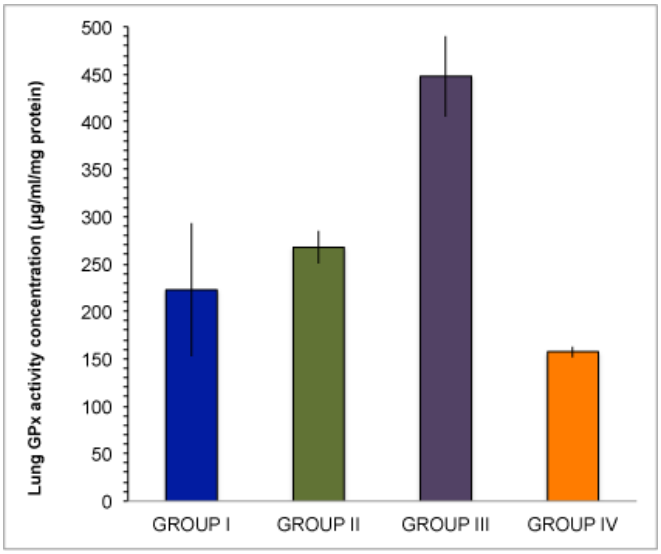


**Figure 9. Effects of pyrethroid insecticide product aerosols on rats' lung GPx activity.** I: Group of rats not exposed to aerosols. II: Rats in this group were exposed to 1 mL of the insecticide product aerosols in 0.167 $m^3$ treatment chamber (equivalent to 6.0 mL $m^{-3}$ treatment chamber volume). III: Animals in this group were exposed to 2 mL of the aerosols (equivalent to 12.0 mL $m^{-3}$ treatment chamber volume). IV: Rats in this group were exposed to 3 mL of the aerosols (equivalent to 18.0 mL $m^{-3}$ treatment chamber volume). Values are mean ± SEM; n = 5.

Note: *Significantly different from control group I ($p < 0.05$).

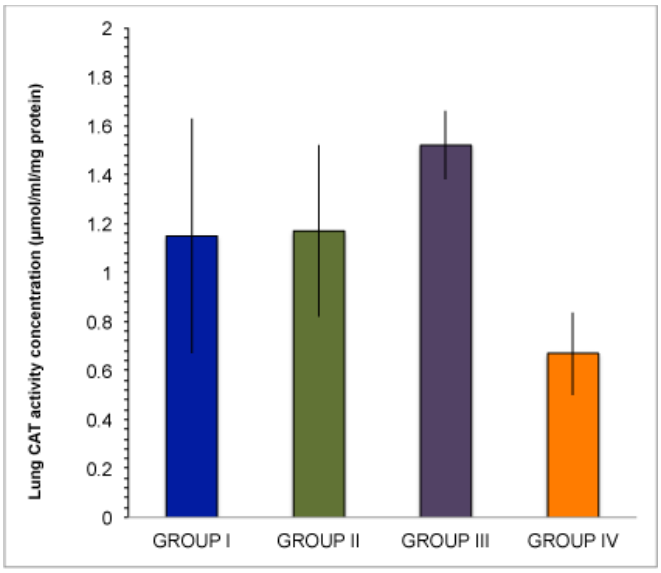


**Figure 10. Effects of pyrethroid insecticide product aerosols on rats' lung CAT activity.** I: Group of rats not exposed to aerosols. II: Rats in this group were exposed to 1 mL of the insecticide product aerosols in 0.167 $m^3$ treatment chamber (equivalent to 6.0 mL $m^{-3}$ treatment chamber volume). III: Animals in this group were exposed to 2 mL of the aerosols (equivalent to 12.0 mL $m^{-3}$ treatment chamber volume). IV: Rats in this group were exposed to 3 mL of the aerosols (equivalent to 18.0 mL $m^{-3}$ treatment chamber volume). Values are mean ± SEM; n = 5.

The measurement of thiobarbituric acid reactive substances (TBARS) is commonly used to monitor lipid peroxidation and indirectly, oxidative stress *in vitro* and *in vivo* (Beltowski *et al*., 2000). Lipid peroxidation is initiated by free radical attack on electron-rich membrane polyunsaturated fatty acids leading to their transformation and fragmentation to alkanes and reactive aldehyde compounds. In the present study, the increase ($p<0.05$) in the concentration of brain, lung, and heart MDA induced by the pyrethroid insecticide aerosol could be as a result of the generation of reactive oxygen species (ROS) that attacked the unsaturated lipids, thereby causing the generation of lipid peroxides leading to alteration of membrane permeability and cell function. The lipid-rich nature of the brain could be responsible for the significant increase ($p<0.05$) in its lipid peroxidation. Deltamethrin, a pyrethroid insecticide, has been reported to cause an induction in the level of lipid peroxidation and MDA (Yarsan *et al*., 2002; Rehman *et al*., 2006). Cypermethrin exposure to rats caused free radical-mediated tissue damage as indicated by elevated cerebral and hepatic lipid peroxidation (Giray *et al*., 2001). Cypermethrin and fenvalerate increased the oxidative stress and LPO in liver, kidneys, and heart tissues of rats (Kale *et al*., 1999).

Pesticides induce oxidative stress as well as alter the defense mechanisms of detoxification and scavenging enzymes (Rasoul *et al*., 2012; Mossa *et al*., 2012; Mansour & Mossa, 2010; Mansour & Mossa, 2011; Marzouk *et al*., 2011). These toxic compounds impair the cellular function, enzymes activity and produce cytotoxic changes through generation of ROS (Rasoul *et al*., 2012; Mossa *et al*., 2012; Abbassy & Mossa, 2012). These free radicals also damage the cell components including proteins, lipids and DNA (Persson *et al*., 2014). The antioxidant enzymes such as SOD, CAT and GPx are the main enzymes that act as defenses, as well as non-enzymatic antioxidants such as GSH (Tomlin, 1994). They protect against the destructive effects of ROS. SOD is responsible for catalytic dismutation of highly reactive and potentially toxic superoxide radicals to hydrogen peroxide ($H_2O_2$) and $O_2$. CAT and GPx are responsible for the catalytic decomposition of $H_2O_2$ to molecular oxygen and water (Tomlin, 1994). Glutathione is a small tripeptide (made up of glutamate, cysteine and glycine) protein synthesized in the liver (Kaplowitz *et al*., 1985). It is a potent antioxidant with high redox potential and it also serves as a co-factor for several oxidative stress detoxifying enzymes (Valko *et al*., 2007; Parris, 1997). Glutathione also helps in the regeneration of some important antioxidant vitamins such as C and E, and its depletion has been reported in apoptosis and many degenerative conditions (Parris, 1997). GSH participate in the elimination of ROS, acting both as non-enzymatic oxygen radical scavenger and as a substrate for various enzymes such as GPx (Ashar & Muthu, 2012). GST is a detoxifying enzyme that catalyzes the conjugation of a variety of electrophilic substrates to the thiol group of GSH, producing less toxic forms (Hayes & Pulford, 1997).

The significant decrease in the levels of brain, lung and heart GSH, as well as decrease in the activities of lung GST, SOD, GPx, and CAT due to treatment with the aerosol of the pyrethroid insecticide could be due to oxidative stress, resulting into generation of free radicals, particularly superoxide radical. SOD in response to this radical, could dismutate it to $H_2O_2$, which is then subsequently detoxified by CAT and GPx to $H_2O$ and molecular oxygen. GSH is a substrate for GPx. The detoxification of $H_2O_2$ causes GSH oxidation to the oxidized form (GSSG), which can be reduced back by glutathione reductase (GRd). Therefore, the decreased levels of brain, lung and heart GSH could be due to diminished GRd activity as a result of increased ROS assault. It has been reported that 14 days exposure to beta-cyfluthrin caused a significant attenuation in CAT and SOD activity compared to control in a dose dependent manner (Verma *et al*., 2013). Cyfluthrin has been reported to increase the generation of free radical and decrease SOD and CAT activity in mice (Omotuyi *et al*., 2006; Eraslan *et al*., 2007). and in cultured human erythrocytes (Sadowaska-Woda *et al*., 2010). Deltamethrin treatment decreased SOD and CAT activity in mice (Yarsan *et al*. 2002; Rehman *et al*., 2006) Kale *et al*. (1999) previously demonstrated an increase in erythrocytes SOD and CAT activities in rats following fenvalerate and cypermethrin treatment. Also, it was recently reported that the activities of kidney SOD and GPx, as well as activities of liver SOD, GST, and CAT were significantly decreased by prallethrin administration in rats (Mossa *et al*., 2013; Refaie *et al*., 2014).

We therefore conclude from this study that prolong and incessant exposure to the insecticide aerosol over a long period of time may lead to tissue oxidative stress, which may pose health risk in humans. Hence, its use domestically or occupationally should be with caution and subjected to closer regulation by environmental and health protection agencies.

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