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ASCORBATE AND ALPHA-TOCOPHEROL MITIGATE TOXIC PATHOLOGICAL CHANGES IN ADULT WISTAR RATS EXPOSED TO CYPERMETHRIN

Temidayo Daniel Adeniyi, Akinpelu Moronkeji*, Osetohanmen Flourish Ralph-Okhiria

Department of Medical Laboratory Science, University of Medical Science, Ondo, Nigeria

ABSTRACT

The excessive and uncontrolled use of pyrethroids, such as cypermethrin (CP), for pest control in Nigeria could adversely affect humans. This study aimed to investigate the oxidative stress response to cypermethrin exposure, focusing on measuring the parameters (i.e., malondialdehyde (MDA), superoxide dismutase (SOD), glutathione peroxidase (GPx), and catalase (CAT)) and the potential therapeutic effects of single and co-administration of ascorbate and alpha-tocopherol. The lungs and hearts of the animals were histologically examined for cypermethrin-induced cytopathic changes. Twenty-five adult male Wistar rats weighing 180–200 g were randomly assigned to five groups, each consisting of five animals. Group I was the control group that was not subjected to any treatment. Group II was orally exposed to cypermethrin at a dosage of 10 mg/kg bw without any additional treatment. Groups III, IV, and V received cypermethrin at standard doses of 10 mg/kg bw and were orally administered with ascorbate (5,000 mg/kg bw), alpha-tocopherol (3,000 mg/kg bw), and a co-administration of ascorbate (5,000 mg/kg bw) and alpha-tocopherol (3,000 mg/kg bw), respectively. The animals were euthanized after 28 days, and samples were processed for histological analysis using hematoxylin and eosin staining. Analysis of variance (ANOVA) and Duncan's multiple range test were used to compare categorical variables of the biochemical parameters and determine the levels of MDA, SOD, GPx, and CAT. The data analysis revealed that the cypermethrin-exposed, untreated rats had elevated MDA levels and a concurrently marked decrease in SOD, GPx, and CAT activities ($p<0.05$). Additionally, the histopathological examination of the organs indicated inflammation and congestion. The co-administration of ascorbate and alpha-tocopherol restored the biochemical parameters more effectively compared to when the substances were administered individually. In conclusion, co-administration of ascorbic acid and alpha-tocopherol ameliorates cypermethrin-induced oxidative damage more effectively than a single administration of either substance. This may be due to the synergistic antioxidant properties of the substances.

Keywords: Agricultural practices; cypermethrin; oxidative stress; healthy lifestyle; farmers

***Correspondence:** Akinpelu Moronkeji, Department of Medical Laboratory Science, University of Medical Science, Ondo, Nigeria. Email: amoronkeji@unimed.edu.ng

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Highlights:
1. This study provides insight into the detrimental effects of cypermethrin exposure on the human cardiopulmonary system as well as the beneficial roles of ascorbate and alpha-tocopherol in cypermethrin-induced toxicity.
2. This study investigated the effectiveness of ascorbate and alpha-tocopherol as affordable vitamin supplements for Ondo farmers to protect against cypermethrin-induced oxidative damage.
3. The co-administration of ascorbate and alpha-tocopherol mitigates cypermethrin-induced oxidative damage better than a single administration of either subtance.

INTRODUCTION

Pyrethrins are insecticidal compounds obtained from the flowers of the plant *Tanacetum cinerariaefolium*, which is also known as *Chrysanthemum cinerariaefolium* or *Pyrethrum cinerariaefolium*. Pyrethroid insecticides, which can be produced from the plant, are highly effective against a wide range of pests found on both animals and livestock (Ensley 2018). When sprayed and exposed to the environment, pyrethroids (e.g., cypermethrin) can come into contact with the skin, nostrils through inhalation, and mouth through ingestion. These substances have been shown to exert negative effects on both animals and humans (Kaur & Singh 2021). Humans can be exposed to

pesticides in a variety of ways, particularly in environments that encompass farmlands and water bodies. The extent to which cypermethrin affects human health and the environment is determined by the amount of the substance present and the duration and frequency of exposure (Ye et al. 2017). In Nigeria, the uncontrolled use of pyrethroid pesticides has constituted a public health problem. Pyrethroids are rapidly metabolized, resulting in the production of easily excretable metabolites. This characteristic allows them to be a safer alternative to organochloride pesticides. However, this does not fully deny the fact that pyrethroids have the potential to bioaccumulate in various organs (Atere et al. 2021).

Cypermethrin is a type II pyrethroid commonly used in agriculture and households as an insecticide. Despite its advantageous uses, numerous pieces of evidence have indicated that exposure to cypermethrin at either acute or chronic levels may lead to health problems, including respiratory issues, cancer, and neurological diseases (Huang et al. 2018). Although pyrethroids are considered safer than relatively carcinogenic organochloride pesticides, they have been found to induce some adverse effects in mammals. Earlier studies have reported that acute and chronic exposure to pyrethroids may result in neurotoxicity, increased oxidative stress, and a wide variety of toxic effects such as hepatotoxicity and nephrotoxicity (Chrustek et al. 2018, Bouabdallah et al. 2021, Atere et al. 2021). A study by Sandhu et al. (2010) indicated the presence of toxic symptoms, which ranged from mild to moderate, and behavioral changes in rats orally administered with repeated doses of cypermethrin at 5 and 20 mg/kg/day for 30 days. The histopathological examination of the cardiac tissues did not reveal any cytopathic changes in rats receiving lower cypermethrin doses. Meanwhile, hemorrhages, disruption in the branching structure with loss of striations, and early necrotic changes in the myocardium were evident in rats receiving higher cypermethrin doses.

Cypermethrin may predispose local farmers and individual users to its effects via inhalation and the oral route. This sometimes occurs inadvertently when the farmers consume contaminated food and drink while working. Previous research has shown that the cardiopulmonary system is susceptible to toxicity from pesticide exposure. Additionally, it is a well-established fact that pesticides, such as cypermethrin, have the propensity to bioaccumulate, particularly in the lungs and heart (Ratanachina et al. 2020, Yu et al. 2022). Against this background, we aimed to examine the effect of ascorbate and alpha-tocopherol on cypermethrin-induced oxidative damage in adult male Wistar rats. The concern associated with uncontrolled pyrethroid exposure necessitated this study to determine whether ascorbate and alpha-tocopherol can mitigate toxic pathological changes caused by cypermethrin exposure.

MATERIALS AND METHODS

A total of 25 adult male Wistar rats weighing around 180–200 g was obtained from the Animal House, Faculty of Basic Medical Sciences, University of Medical Science, Ondo, Nigeria. The rats had a two-week acclimation period and were adequately housed in a well-ventilated and clean space. They were properly fed with standardized rat pellets sourced from the university's animal holding facility. Daily monitoring was carefully carried out throughout the experiments. The experimental animals were handled in accordance with the International Humane Animal Care Standards (Hau & Schapiro 2013).

The rats were divided into five groups consisting of five rats each. The rats in Group I served as controls, meaning they were unexposed to cypermethrin and did not receive any treatment. Group II consisted of rats that were orally exposed to cypermethrin at a standard dosage of 10 mg/kg bw without any treatment given. Groups III, IV, and V were administered cypermethrin at standard doses of 10 mg/kg bw. Group III was treated with ascorbate at a dose of 5,000 mg/kg bw. Group IV received alpha-tocopherol at a dose of 3,000 mg/kg bw. Meanwhile, Group V received a co-administration of ascorbate (5,000 mg/kg bw) and alpha-tocophero (3,000 mg/kg bw). Cypermethrin was administered twice a week, while ascorbate and alpha-tocopherol were given daily for 28 days (Hassan 2019, Oladele et al. 2022).

The experiments used a cypermethrin-based pesticide of commercial grade with an effect concentration (EC) of 10%. Cypermethrin [(RS)-cyano-(3-phenoxyphenyl) methyl-(IRS)-cis-trans-3-(2,2-dichloroethenyl)-2,2-dimethyl cyclopropane carboxylate] with the trade name Avestrin® was manufactured in Lagos, Nigeria, by Harvestfield Industries Ltd. The substances used to mitigate the effects of cypermethrin exposure were ascorbic acid and alpha-tocopherol (Pisoschi & Pop 2015). The alpha-tocopherol capsules manufactured in Dabhel, India, by Olive Healthcare were purchased from Ever Destiny Pharmaceuticals Ltd., Lagos, Nigeria. Each soft gelatin capsule contained 1000 IU of vitamin E acetate, as specified by the United States Pharmacopeia (USP) Reference Standard. Vitamin C tablets, produced in Lagos, Nigeria, by Chemo-Pharma Laboratories Ltd. and registered with the National Agency for Food and Drug Administration and Control (NAFDAC) under the number 04-3486,

were purchased from Uche Care Pharmaceuticals, Ondo, Nigeria. Each tablet contained 100 mg of ascorbic acid, in accordance with the British Pharmacopoeia (BP) Reference Standard.

Upon completion of the experiments, the rats were euthanized by means of cervical dislocation. The hearts and lungs of the rats were immediately excised to collect specimens, which were then transferred into freshly prepared 0.1 mol/L phosphate buffered saline (PBS) with a pH of 8.0. The specimens were homogenized and centrifuged at 3,000 revolutions per minute for 20 minutes at 4°C. The obtained supernatants were stored at -80°C for the analysis of biochemical markers, i.e., malondialdehyde (MDA), catalase (CAT), superoxide dismutase (SOD), and glutathione peroxidase (GPx). The histopathological samples were transferred into freshly prepared 10% neutral buffered formalin and processed for microscopic analysis following the method outlined by (Suvarna et al. 2019).

As described by Kalinovic et al. (2021) and Oladipo et al. (2018), the lung and heart tissue homogenates were prepared for the analysis of malondialdehyde (MDA). The biochemical indicators were analyzed using the enzyme-linked immunosorbent assay (ELISA) following the protocols provided in the kits. The ELISA kits were manufactured in the USA by Elabscience Biotechnology, Inc. The ELISA analysis was performed to assess the activities of catalase (CAT), superoxide dismutase (SOD), and glutathione peroxidase (GPx). The detection ranges for CAT, SOD, and GPx were 1.12-150 U/mL, 0.2-14.4 U/mL, and 17.7-518.32 U/mL, respectively (Kang et al. 2020, Huang et al. 2022, Li et al. 2023).

The prefixed lungs and heart tissues were prepared with an automatic tissue processor machine before being observed under a light microscope. The stained sections were examined using a binocular light microscope (model XSZ-107BN, No. 071771, Olympus, Japan), while micrographs were taken at 100X magnification with a digital camera (model Easyshare C183, Kodak, USA) (Suvarna et al. 2019, Akinpelu et al. 2023). The collected data were subjected to statistical analysis using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, N.Y., USA). The categorical variables were compared using analysis of variance (ANOVA) and Duncan's multiple range test. A value of $p<0.05$ was considered statistically significant, with a confidence level of 95%.

RESULTS

The histopathological examination of the lung section of the control rats that were not exposed to any substances showed no abnormalities. The bronchioles appeared normal, and the intralveolar spaces were devoid of inflammation or congestion. This indicated the absence of pulmonary toxicity, as cypermethrin was not administered (Figure 1a). The untreated rats that were exposed to cypermethrin exhibited peribronchiolar inflammation and congestion, coupled with a focal area of inflammation where the intra-alveolar spaces collapsed. This indicated that exposure to cypermethrin caused pulmonary toxicity in these rats (Figure 1b). The bronchioles of the rats treated with ascorbate did not show signs of inflammation. However, there was mild inflammation in the intraalvolar spaces (Figure 1c). The rats treated with alpha-tocopherol had a normal bronchiole, with a mild infiltration of the intra-alveolar spaces by mononuclear inflammatory cells (Figure 1d). On the other hand, the rats co-administered with ascorbate and alpha-tocopherol exhibited a normal bronchiole with mildly inflamed intra-alveolar spaces (Figure 1e).

The cardiac section of the unexposed control rats exhibited a normal appearance, with a typical myocardial layer and healthy-looking myocytes. This result indicated that there was no cardio-toxicity, considering cypermethrin was not provided to these rats (Figure 2a). The cypermethrin-exposed rats that did not receive any treatment had a mildly congested myocardium, suggesting a presence of cardiotoxicity induced by cypermethrin exposure (Figure 2b). The cypermethrin-exposed rats that were treated with ascorbate showed a congested myocardial layer (Figure 2c), while those treated with alpha-tocopherol had congested myocardium (Figure 2d). The co-administrative treatment using ascorbate and alpha-tocopherol resulted in a normal myocardium devoid of pathological lesions (Figure 2e).

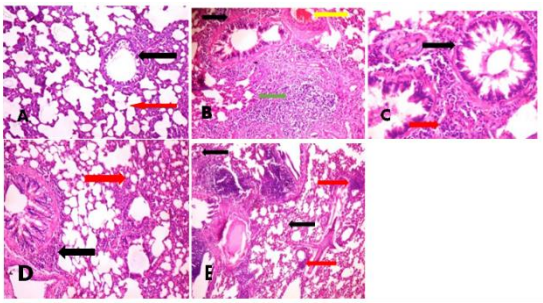

Figure 1. (a) Normal bronchiole (black arrow) and intra-alveolar spaces (red arrow) in Group I; (b) peribronchiolar inflammation and congestion (black arrow), inflammed and collapsed intra-alveolar spaces (green arrow), and mild vascular congestion (yellow arrow) in Group II; (c) normal bronchiole (black arrow) and mildly infiltrated intra-alveolar spaces (red arrow) in Group III; (d) normal bronchiole (black arrow) and infiltrated intra-alveolar spaces (red arrow) in Group IV; (e) normal bronchiole (red arrows), mildly infiltrated intra-alveolar spaces in Group V (100X magnification).

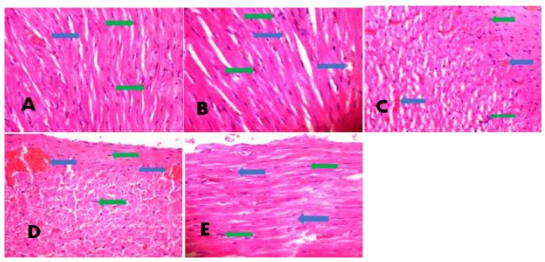

Figure 2. (a) Normal myocardial layer (blue arrow) and myocytes (green arrow) in Group I; (b) mildly congested myocardium (blue arrow) and myocytes (green arrow) in Group II; (c) congested myocardium and myocytes (green arrow) in Group III; (d) congested myocardium (blue arrow) and myocytes (green arrow) in Group IV; (e) normal myocardium (blue arrow) and myocytes (green arrow) in Group V (100X magnification).

The biochemical evaluation of the oxidant and antioxidant parameters demonstrated the effect of cypermethrin on the lung tissue homogenates and the variations in the levels of the oxidant MDA and the antioxidants SOD, GPx, and CAT among the different groups. The rats that were exposed to cypermethrin exhibited significantly higher levels of MDA compared to the unexposed control rats. Conversely, the rats that were treated with a single administration of either ascorbate or alpha-tocopherol showed significantly decreased levels of MDA. The co-administration of ascorbate and alpha-tocopherol resulted in a significant decrease in MDA levels compared to the other treatment groups (Table 1). The SOD levels were reduced significantly in the cypermethrin-exposed rats that did not receive any therapy. Conversely, the co-administration of both vitamins resulted in superior treatment outcomes compared to the single administration of either ascorbate or alpha-tocopherol. The levels of GPx and CAT significantly decreased in the rats exposed to cypermethrin, compared to the control rats that were not treated as well as the other groups receiving vitamin treatment. However, a marked increase in antioxidant levels was observed in the rats that received both ascorbate and alpha-tocopherol, indicating the therapeutic effect of co-administering these two substances (Table 1).

The biochemical evaluation of the effect of cypermethrin on heart tissue homogenates revealed a significant rise in the oxidant MDA levels in the treatment groups compared to the control group that was not exposed to the substance. Additionally, the levels of the antioxidants SOD, GPx, and CAT were found to be significantly different across the treatment groups. The rats that were given a combination of ascorbate and alpha-tocopherol showed the most significant reversal of the oxidative damage. The levels of SOD, GPx, and CAT in all treatment groups were significantly lower compared to the controls. However, the co-administration of ascorbate and alpha-tocopherol more effectively restored the levels of SOD, GPx, and CAT in comparison to the other groups receiving different treatments (Table 2).

DISCUSSION

Pesticides, including pyrethroids, are beneficial for pest control in various environments, such as farmlands or households. However, the unregulated use of pyrethroids potentially induces oxidative stress and cardiopulmonary toxicity when food and water sources for human consumption become contaminated (Shaffo et al. 2018, El-Nahhal & El-Nahhal 2021). The experiment in this study used oral administration of cypermethrin to simulate a major route of contamination, specifically via the ingestion of contaminated food and drink. This means of cypermethrin exposure frequently occurred among local farmers who made use of the

Table 1. Biochemical parameters in the lung tissue homogenates across the various groups.

Parameters	Group I	Group II	Group III	Group IV	Group V
MDA (µmol/mg protein)	0.3482 ± 0.08446^{c}	3.2594 ± 0.46949^{a}	1.5796 ± 0.37563^{b}	1.4726 ± 0.60105^{b}	0.6396 ± 0.25314^{c}
SOD (U/mg protein)	7.874 ± 0.92813^{a}	3.347 ± 0.14764^{c}	4.2912 ± 0.18541^{bc}	5.235 ± 0.70549^{b}	6.846 ± 1.62827^{a}
GPx (µmol/min/mg protein)	94.5962 ± 2.81905^{a}	17.1548 ± 1.92755^{d}	47.9164 ± 5.44814^{c}	51.2416 ± 6.25599^{c}	72.6032 ± 5.91337^{b}
CAT (mmol/mg protein)	17.728 ± 2.08951^{a}	4.4058 ± 1.79837^{c}	7.8166 ± 1.85901^{b}	9.2802 ± 1.20953^{b}	15.4152 ± 3.66585^{a}

Notes: The mean±SD values with different superscripts represent significant differences at a 5% level, with a>b>bc>c>d. The significant values for each superscript are as follows: a=0.000, b=0.015, bc=0.025, c=0.034, d=0.043.

Table 2. Biochemical parameters in the heart tissue homogenates across the various groups.

Parameters	Group I	Group II	Group III	Group IV	Group V
MDA (µmol/mg protein)	0.1336 ± 0.03231^{c}	1.4544 ± 0.30831^{a}	0.6886 ± 0.1459^{b}	0.6266 ± 0.21744^{b}	0.2458 ± 0.09742^{c}
SOD (U/mg protein)	3.0312 ± 0.35739^{a}	0.5063 ± 0.22603^{c}	1.3362 ± 0.31807^{b}	1.6884 ± 0.58682^{b}	2.6356 ± 0.62685^{a}
GPx (µmol/min/mg protein)	37.1448 ± 2.01953^{a}	8.3302 ± 1.69969^{d}	16.1076 ± 1.66911^{c}	16.4278 ± 2.32259^{c}	34.142 ± 2.86812^{b}
CAT (mmol/mg protein)	6.8248 ± 0.80443^{a}	1.4958 ± 0.32051^{c}	3.408 ± 0.4293^{b}	3.6814 ± 0.25831^{b}	5.9344 ± 1.41127^{a}

Notes: The mean±SD values with different superscripts represent significant differences at a 5% level, with a>b>c>d. The significant values for each superscript are as follows: a=0.001, b=0.019, c=0.028, d=0.040.

pesticide for farming. The dose for the administration of cypermethrin was determined by a thorough analysis of multiple prior studies (Abdus Sallam et al. 2020, Akinpelu et al. 2023).

The findings of tests conducted on rats by Akorede et al. (2020) and Abdel-Razik et al. (2021) demonstrated that the administration of cypermethrin at doses between 5 mg/kg bw and 20 mg/kg bw could induce oxidative damage. Therefore, we opted for a dosage of cypermethrin within this range to be applied in this experiment. The dose was also determined by considering the ratio of the median lethal dose (LD50). The LD50 of cypermethrin was determined to be 250 mg/kg bw (Bouabdallah et al. 2021). The determination of the cypermethrin doses to be administered was conducted as a preventive measure against unnecessary animal mortality.

We reasoned that the contamination we attempted to replicate was sufficient, given that the farmers did not directly consume the chemicals but were inadvertently exposed through food and drink contamination instead. In addition, the farmers used pesticides not on a daily basis but rather on a seasonal basis. As a result, we deduced that the chosen dose would be adequate to induce the expected toxic effects.

Studies have suggested that vitamins can act as a form of therapy to tackle oxidative stress. Ascorbate and alpha-tocopherol are among these beneficial vitamins (Pisoschi & Pop 2015, Wang & Dong 2018, Akinpelu et al. 2023). Oxidative stress arises from an imbalance between the presence of oxidants in the body and the body's ability to combat them. In the presence of oxidants, the body needs to be able to regulate reactive oxidants or repair the resulting damage produced by them (Choudhury & MacNee 2017). In this study, we investigated the oxidative stress response in adult male Wistar rats exposed to cypermethrin, which is a type of pyrethroid often used by farmers in Ondo, Nigeria. Additionally, we evaluated the protective effects of ascorbate and alpha-tocopherol when administered singly or in combination.

This study examined the histological changes in the lungs and hearts of the cypermethrin-exposed rats to identify the cytopathic alterations induced by cypermethrin. The findings obtained from the biochemical and histological analyses provide valuable insights into the extent of oxidative stress caused by cypermethrin exposure and the potential ameliorative effects of the antioxidant treatments. The control group that was not subjected to any interventions showed no signs of oxidative distress or response throughout the experiment. This finding was supported by the absence of a significant increase in MDA levels as well as the steadiness of normal SOD, GPx, and CAT levels without any noticeable decrease. These results are consistent with the findings reported by (El-Okda et al. 2017).

The histoarchitectural analysis of the control rats revealed that their lungs were devoid of pathological lesions, as typified by normal bronchioles and alveolar spaces. Similarly, the heart tissues exhibited normal epicardial and myocardial layers, and the myocytes were normal without any signs of inflammation or congestion. This was consistent with the findings reported by Ghazouani et al. (2020). The results obtained from the cypermethrin-unexposed control group established a baseline for comparing them with the treatment groups. This enabled a comprehensive evaluation of cypermethrin-induced oxidative stress and the protective effects of ascorbate and alpha-tocopherol.

The cypermethrin-exposed, untreated rats exhibited significant alterations in both biochemical and histological parameters, indicating damage induced by oxidative stress. Biochemically, elevated levels of MDA were observed in this group, suggesting increased lipid peroxidation and oxidative damage to the cellular membranes (Hassan 2019). Concurrently, the activities of essential antioxidant enzymes, i.e., SOD, GPx, and CAT, were significantly reduced. This indicated an imbalance between reactive oxygen species (ROS) production and antioxidant defense mechanisms. In a previous study conducted by Ghazouani et al. (2020), it was observed that cypermethrin exposure reduced the levels of SOD, GPx, and CAT. The histopathological analysis of lung tissues in the group exposed to cypermethrin revealed inflammation and congestion, which were indicative of cypermethrin-induced lung injury.

The heart tissue examination revealed mild congestion, signifying the onset of cardiotoxicity due to cypermethrin exposure. In contrast, the group solely treated with ascorbate demonstrated improved biochemical and histological parameters, suggesting a potential ameliorative effect against cypermethrin-induced oxidative stress. The biochemical analysis revealed a decrease in MDA levels, indicating the attenuation of lipid peroxidation. This finding is consistent with the study conducted by Akorede et al. (2020), who documented a significant reduction in MDA levels in adult male Wistar rats treated with ascorbate to alleviate carbamazepine-induced oxidative stress. Furthermore, the activities of SOD, GPx, and CAT were restored, highlighting the effectiveness of ascorbate in enhancing antioxidant defenses. The histological examination of lung tissues in the group treated with ascrobate showed a reduction in inflammation and congestion when compared to the

exposed, untreated group. This provides more evidence for the beneficial effects of ascorbate on cypermethrin-induced lung injury. Similarly, the heart tissues showed enhanced architecture with decreased congestion, suggesting a protective function of ascorbate against cypermethrin-induced cardiotoxicity.

The results of this study aligned with those of Kaushik et al. (2018), who reported the protective effect of ascorbate on cypermethrin-induced organ damage. The group treated with alpha-tocopherol demonstrated notable improvements in both biochemical and histological parameters. Biochemically, decreased MDA levels in the lungs and heart indicated the attenuation of lipid peroxidation. The restoration of the enzymes SOD, GPx, and CAT further demonstrated the effectiveness of alpha-tocopherol in combating cypermethrin-induced oxidative stress. The histopathological analysis of lung tissues showed reduced inflammation and congestion. This finding corroborated the protective effects of alpha-tocopherol against cypermethrin-induced lung injury. Moreover, the heart tissues displayed strengthened architecture accompanied by a reduction in congestion, buttressing the cardio-protective role of alpha-tocopherol. It can be inferred that even though exposure to cypermethrin causes histopathological changes, the use of alpha-tocopherol helps to ameliorate the toxic effects (Abdus Sallam et al. 2020).

Interestingly, the co-administration of ascorbate and alpha-tocopherol demonstrated the most robust antioxidant effect among all experimental groups. The co-administration group displayed the lowest MDA levels, indicating the most effective mitigation of lipid peroxidation and oxidative damage. Additionally, this group exhibited elevated levels of SOD, GPx, and CAT activities, which suggest a synergistic antioxidant action of both ascorbate and alpha-tocopherol. Such synergistic action has also been documented in earlier research (Bhardwaj et al. 2018). The histological examination of the lungs in the treatment groups revealed mild peribronchiolar inflammatory reactions. However, the co-administration group showed a notable reduction in inflammation and a lack of congestion, suggesting enhanced protection against cypermethrin-induced lung injury. These results correspond with those of a previous study conducted by Oladele et al. (2022). The rats that received both vitamins exhibited the most favorable outcomes, according to the heart tissue examination. They showed a significant reduction in inflammation and congestion, underscoring the synergistic cardioprotective effects of both antioxidants.

Food contaminated with insecticides, such as cypermethrin, has an increased risk of harming both humans and domesticated animals. The prophylactic use of vitamins as a preventive measure in medical intervention for pathological conditions can be beneficial due to their ability to mitigate oxidative stress induced by cypermethrin exposure (Oladele et al. 2022, Akinpelu et al. 2023). Overall, this study underscores the detrimental effects of cypermethrin on the cardiopulmonary system. Therapeutic interventions using a combination of ascorbate and alpha-tocopherol effectively mitigate oxidative damage. The co-administration of both antioxidants provides the strongest protective effects (Pisoschi & Pop 2015, Huang et al. 2018). The biochemical and histological findings from this study support the potential use of ascorbate and alpha-tocopherol as protective agents against cypermethrin-induced oxidative stress. These substances were found to boost antioxidant defense mechanisms and enhance tissue architecture. This highlights the importance of antioxidant supplementation in combating oxidative stress induced by pesticides, thus warranting the need for more research to investigate potential clinical applications.

Strength and limitations

This study reflects the practical implications of cypermethrin exposure on local farmers in the Ondo community of Nigeria. It was done by simulating their exposure to the pesticide during farming activities through the use of animal models. The findings of this study provide evidence for the robust effect of ascorbate and alpha-tocopherol supplementation in combating pesticide-induced oxidative stress. However, the use of cypermethrin in this study merely represented a limited degree of the harmful effects of cypermethrin on the local farmers. The overall cytotoxicity of pyrethroids experienced by the local farmers might not be accurately reflected.

CONCLUSION

The administration of ascorbate and alpha-tocopherol provides protective effects against cypermethrin exposure by reducing oxidative damage. Furthermore, the co-administration of the vitamins has robust effectiveness. The combined use of these substances can boost the overall antioxidant capacity through a synergistic effect. Antioxidant supplementation is important in protecting against pesticide-induced oxidative stress. Further investigation is required to explore the potential clinical applications of ascorbate and alpha-tocopherol concerning cypermethrin exposure.

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Conflict of interest

None.

Ethical consideration

The Research Ethics Committee (REC) of the University of Medical Sciences, Ondo, Nigeria, approved this study under reference No. NHREC/TR/UNIMED-HREC-Ondo St/22/06/21 on 3/6/2022. Appropriate measures were implemented to ensure minimal discomfort for the rats used in this study.

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None.

Author contribution

AM conceptualized, designed, and drafted the article. AM analyzed and interpreted the data as well as performed a critical revision of the manuscript for important intellectual content. TDA granted final approval for the article. TDA provided the study materials. OFR collected and compiled the data. AM conducted the statistical analysis. TDA provided administrative, technical, and logistic support.

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