

Sokoto Journal of Veterinary Sciences



(P-ISSN 1595-093X; E-ISSN 2315-6201)

<http://dx.doi.org/10.4314/sokjvs.v20i5.11>



Idris *et al.*/Sokoto Journal of Veterinary Sciences, 20(Special): 97 – 105.

Effect of sodium selenite on sub-acute paraquat-induced toxicity in male rats

SY Idris^{1*}, HA Kakkaba¹, SJ Enam¹, LA Adekunle², I Abdullahi³ & S Adamu¹

1. Department of Veterinary Pathology, Ahmadu Bello University Zaria, Nigeria
2. Department of Veterinary Pathology, University of Ibadan Nigeria, Nigeria
3. Department of Community Medicine, Ahmadu Bello University, Zaria, Nigeria

*Correspondence: Tel.: +2347037865325; E-mail: drsheriffidris@gmail.com

Copyright: © 2022

Idris *et al.* This is an open-access article published under the terms of the Creative Commons Attribution License which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Publication History:

Received: 30-12-2021

Revised: 01-03-2022

Accepted: 11-04-2022

Abstract

Acute paraquat (PQ) toxicity induces redox cycling leading to fatality in both man and animals with clinical management being supportive therapy due to lack of specific and effective antidote. This study thus aimed at determining the sero-biochemical and pathological changes induced by acute PQ administration in male rats and the mitigating role of sodium selenite. Forty male rats were used for the study and were grouped into 5 of eight rats viz: Group I (control) administered distilled water (2 ml/kg), group II (15 mg/kg of PQ), group III (15 mg/kg of PQ + 0.3 mg/kg sodium selenite), group IV (30 mg/kg of PQ) and group V (30 mg/kg of PQ + 0.3 mg/kg sodium selenite). Administration were achieved per os and lasted for a week. Sera, lungs, liver and kidney samples were harvested at the end of the experiment. Result showed a significant ($p < 0.05$) higher liver enzymes, urea and creatinine in treated groups when compared to control. Biomarkers of oxidative stress revealed a significant ($p < 0.05$) increased superoxide dismutase and malonaldehyde activities of the lungs and liver. A dose-dependent pathologic lesion was also observed with milder lesions in selenium supplemented groups. The results demonstrate that selenium supplementation may be a promising therapy and should further be clinically validated.

Keywords: Oxidative stress markers, Paraquat, Pathology, Serum biochemistry, Sodium selenite

Introduction

The intensive and extensive use of herbicides to meet the current agricultural population demand is unavoidable and the misuse of these agrochemicals results in the degradation of the bio system (Sekhar *et al.*, 2011). PQ, holding the largest share of global herbicide market is one of the most widely used herbicides (Raghu *et al.*, 2013) and deaths have been reported following accidental consumption as well as suicides (Taylor *et al.*, 2001). The involvement of

oxidative stress in PQ-induced toxicity as the major culprit in experimental animals have been well elaborated (McCormack *et al.*, 2005; Patel *et al.*, 2006; Ahmad *et al.*, 2008; Gupta *et al.*, 2010). PQ, a quaternary nitrogen herbicide belonging to the bipyridium compounds (Raghu *et al.*, 2013) induces oxidative stress via depletion of natural endogenous antioxidant- glutathione (GSH) and increasing generation of free radicals (Bus and Gipson, 1984). It

is rapidly distributed in most tissues irrespective of the route of transmission, with the lungs and kidney having the highest concentrations (Suntres, 2002). Several therapeutic measures have been used to combat its toxicity and but no effective antidote adopted yet (Evans & Halliwell, 2001, Suntress, 2002). An imbalance between the biological system's anti-oxidative mechanism and the reactive oxygen species (ROS) production are involved in many diseases, therefore antioxidants are very important therapeutic agents (Prieser, 2021). It has been shown that selenium supplementation increases the expression of particular selenoproteins, which may play an important role in the effective counteracting of detrimental ROS levels in oxidative stress-related difficulties (Touat-Hamici *et al.*, 2014). Recognizing the fact that PQ induces its toxic effects via oxidative stress-mediated mechanisms, the goal of this study aims at investigating the possible protective role of sodium selenite against PQ-induced biochemical alterations and pathology in male rats.

Materials and Methods

Experimental animals

Forty adult male rats weighing between 150 – 200g were used for this study. They were housed using metal cages (600 x 300 x 250 mm) lined with saw dust in the Veterinary Physiology Department of Faculty of Veterinary Medicine, Ahmadu Bello University, Zaria. They were allowed to acclimatize for two weeks before the commencement of the study and fed on commercial pellets (Vital Feed® Growers) and water provided ad libitum. The experimental protocol and procedures used in this study were approved and obtained from the Ahmadu Bello University Committee on Animal Use and Care (ABUCAUC) with reference number ABUCAUC-2019-037.

Chemical source and Median lethal dose determination (LD₅₀)

The chemical used was sourced and LD₅₀ achieved as described by Idris *et al.* (2020).

Experimental design

Following 14 days of acclimatization, rats were randomly divided into five groups of eight rats each as described below:

Group I (DW): Were administered only distilled water at 2 ml/kg once daily.

Group II (P1): Were exposed to paraquat at 15 mg/kg.

Group III (P1 + S): Were exposed to paraquat at 15 mg/kg and supplemented sodium selenite at 0.3 mg/kg.

Group IV (P2): Were exposed to paraquat at 30 mg/kg.

Group V (P2 + S): Were administered paraquat at 30 mg/kg and supplemented with sodium selenite at 0.3 mg/kg.

The dose regimens were administered orally once daily for a period of one week.

Serum biochemical determination

At the end of the treatment, the rats were humanely euthanized via jugular venesection and 2 ml blood was collected in sterile test tube devoid of anticoagulant. The blood was left to stand for about 30 minutes to achieve clotting. Once clot was properly formed, test tubes were centrifuged at 2000 g for 10 minutes. Serum was removed gently using a micro pipette into a sterile serum vial and frozen at – 4 °C in a freezer until analysis. Alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), creatinine and blood urea nitrogen (BUN) were all assayed for using standard commercial kits (Randox) following manufacturer's recommendations.

Biomarkers of oxidative stress determination

Liver and lungs tissues were homogenized (10% w/v) with 0.01 M sodium, potassium phosphate buffered solution (pH 7.5). Homogenates were centrifuged at 3000 g for 20 minutes, and the supernatant collected in plain sample bottle, stored at – 4 °C in a freezer until analysis. Superoxide dismutase (SOD) and malondialdehyde (MDA) concentration were determined using the methods of Fridovich (1989) and Saleem *et al.* (2000).

Histopathology

Following a laparotomy on the rats, liver, lungs and kidney were harvested and observed for gross lesions and preserved in 10% neutral buffered formalin for histopathological processing.

Data analyses

Data were expressed as mean ± SEM. One way analysis of variance was used to compare means of each group and subjected to Tukey's post hoc test using Graph pad version 8.0 for Windows, GraphPad Software, San Diego California USA, www.graphpad.com. Values of p < 0.05 were considered significant.

Results

Rats administered distilled water showed no observable signs of toxicity. Compared to the control animals, rats in the PQ group exhibited respiratory

distress, rough hair coat, depression, weakness, anorexia and weight loss. A total of 7 rats died during the study, 3 rats from group IV, 2 from group II and 1 each from groups III and V.

The mean serum AST activities in the control and treated rats were as presented in Figure 1. There were significant ($p < 0.05$) higher serum AST activities in the treated groups II (8.3 ± 0.71 IU/L), III (7.5 ± 0.33 IU/L), IV (11.3 ± 0.67 IU/L) and V (9.8 ± 0.51 IU/L) when compared to the control (6.3 ± 0.35 IU/L).

ALT activities were significantly ($p < 0.05$) higher in group II (12 ± 0.48 IU/L) when compared to the control (7.2 ± 0.41 IU/L). However, groups III, IV and V have numerically higher values when compared to the control (Figure 2).

Mean serum ALP activities in the control and treated rats were as presented in Figure 3. A significant ($p < 0.05$) higher ALP activities were only observed in group IV (201 ± 9.4 IU/L) when compared to the control (158 ± 3.6 IU/L). However, groups II, III and V have numerically higher ALP activities when compared to the control group.

The mean serum BUN concentration for the control and treated rats were as presented in Figure 4. There was a significant ($p < 0.05$) increase in BUN concentration in group IV (4.1 ± 0.33 nm/mol) when compared to control group (3.3 ± 0.19 nm/mol). Also, a significant ($p < 0.05$) high serum creatinine concentration was observed in the treatment group II (50 ± 4.9 nm/mol), IV (52 ± 3.0 nm/mol) and V ($49 \pm$

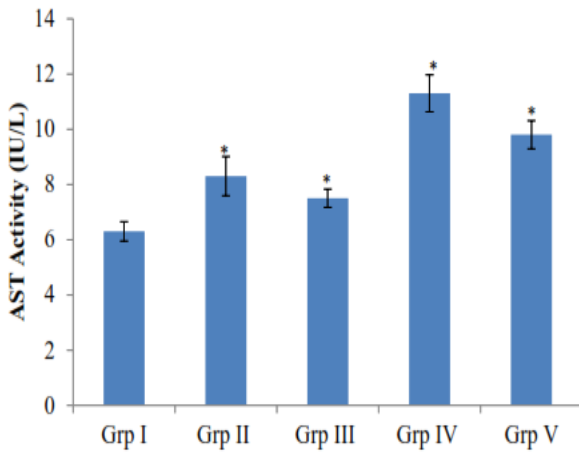


Figure 1: Aspartate aminotransferase activity of rats treated with distilled water, paraquat and selenium for a week. * Significantly different from control group (Grp I)

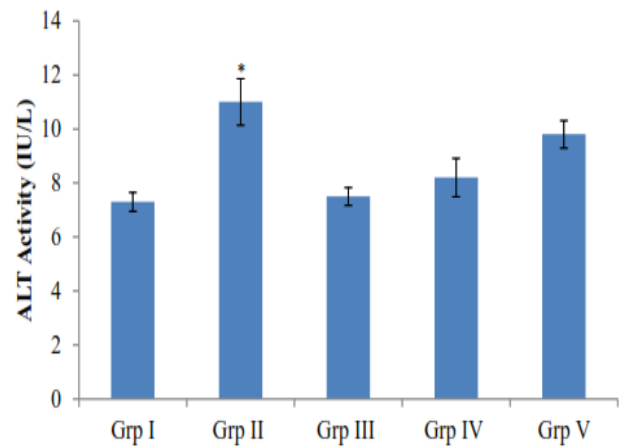


Figure 2: Alanine aminotransferase activity of rats treated with distilled water, paraquat and selenium for a week. * Significantly different from control group (Grp I)

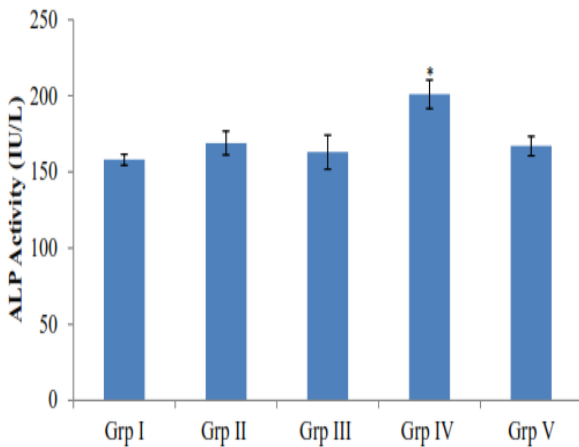


Figure 3: Alkaline phosphatase activity of rats treated with distilled water, paraquat and selenium for a week. * Significantly different from control group (Grp I)

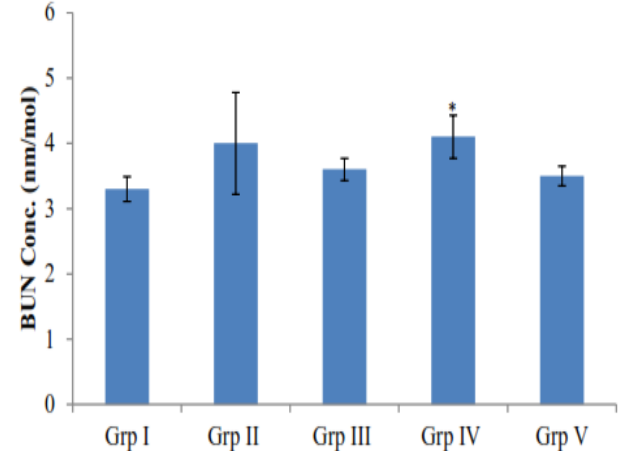


Figure 4: Blood urea nitrogen concentration of rats treated with distilled water, paraquat and selenium for a week. * Significantly different from control group (Grp I)

4.7 nmol/mol) when compared to the control (38 ± 2.8 nmol/mol). This is as presented in Figure 5.

The mean liver SOD activities for control and treated rats were as presented in Figure 6. There was no significant ($p > 0.05$) difference in SOD activity of liver in the treatment groups when compared to the control (41.1 ± 3.95 U/mg). However, a significant ($p < 0.05$) high lung SOD activities was observed in the treatment groups II (39.3 ± 4.51 U/mg), III (38.5 ± 3.44 U/mg), IV (41.2 ± 3.28 U/mg) and V (38.1 ± 2.56 U/mg) when compared to control (25.8 ± 4.05 U/mg). This is as presented in Figure 8.

The mean liver MDA level for the control and treated rats were as presented in Figure 7. There was a significant ($p < 0.05$) liver MDA level in treatment groups IV (5.1 ± 0.34 nmol/mg) and V (4.28 ± 0.27 nmol/mg) when compared to the control (2.41 ± 0.55 nmol/mg).

The mean lung MDA level for the control and treated rats were as presented in Figure 9. There was a significantly ($p < 0.05$) higher MDA level in treated groups II (4.86 ± 0.32 nmol/mg), III (3.92 ± 0.27 nmol/mg), IV (6.31 ± 1.10 nmol/mg) and V (6.2 ± 0.9 nmol/mg) when compared to the control (1.93 ± 0.53 nmol/mg).

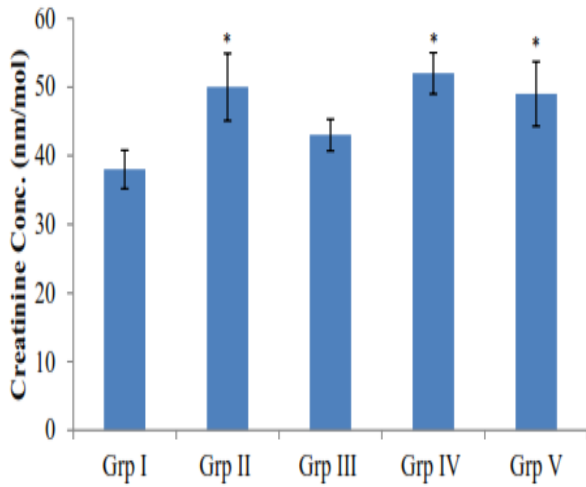


Figure 5: Creatinine concentration of rats treated with distilled water, paraquat and selenium for a week.
* Significantly different from control group (Grp I)

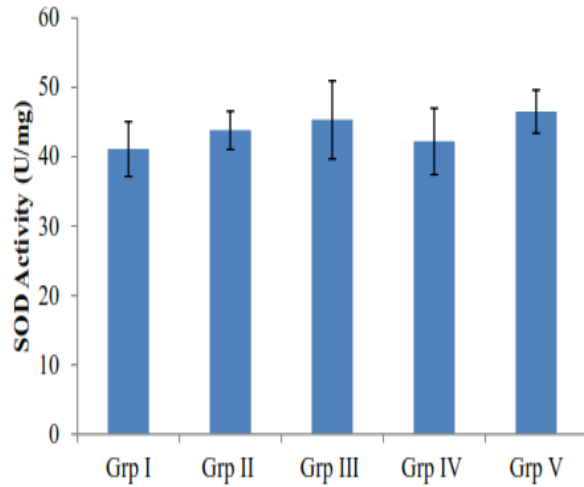


Figure 6: Liver superoxide dismutase activity of rats treated with distilled water, paraquat and selenium for a week

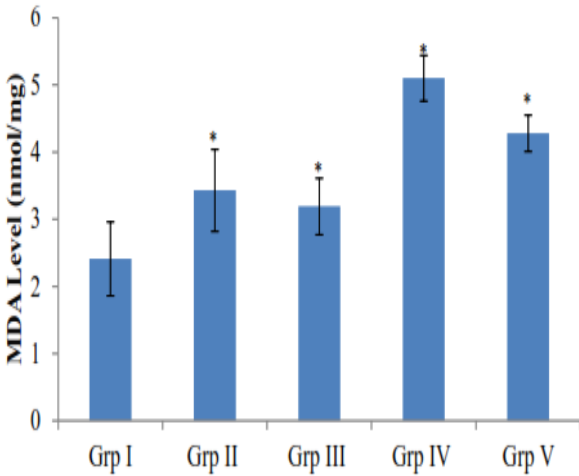


Figure 7: Liver malonaldehyde concentration of rats treated with distilled water, paraquat and selenium for a week.
* Significantly different from control group (Grp I)

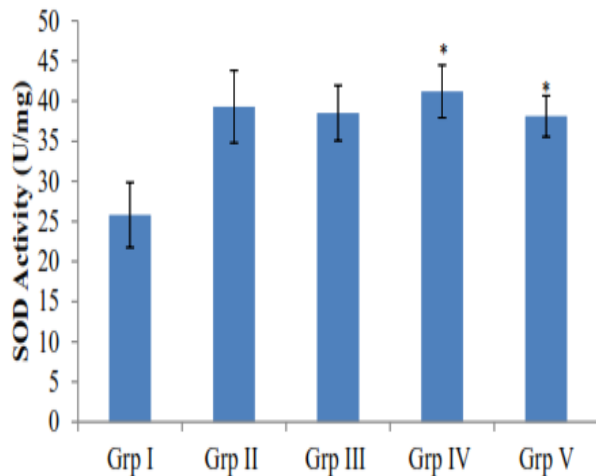


Figure 8: Lungs superoxide dismutase activity of rats treated with distilled water, paraquat and selenium for a week.
* Significantly different from control group (Grp I)

Grossly, no observable pathology was observed in the distilled water-treated group. In addition, none of the treated groups' spleens, kidneys, or hearts had any visible gross abnormalities. However, lungs of rats treated with PQ and supplemented with sodium selenite showed mild to moderate congestion and haemorrhages (Plate IA) when compared to non-supplemented groups which was emphysematous with severe congestion and areas of necrosis (Plate IB). There was also an accidental nodular lesion seen on liver of rat from group III (Plate IC).

Histopathology showed no observable lesions on the liver of control group of rats (Plate II). Sections of liver of PQ treated groups revealed vacuolar degenerative hepatocellular changes, haemorrhages and congestion (Plate III). Sections of lung of treated groups revealed thickened alveolar walls, pinkish

filled oedematous alveolar sacs, haemorrhages and mononuclear cellular infiltrations (Plate IV and V). Section of the kidney showed necrosis of renal tubular epithelium and pinkish oedema fluid within the lumen (Plate VI).

Discussion

Paraquat is highly toxic to animals and humans when exposed via ingestion, inhalation or skin contact. Since its introduction to use in agriculture, it has caused several human deaths from both accidental and deliberate ingestion (Tan *et al.*, 2015), with several countries calling for its ban (Chang & Gunnell, 2019). PQ toxicity is attributable to its induction of ROS during redox cycling (Black *et al.*, 2008) with the lungs being the primary organ affected and no effective therapeutic approach is currently available (Pouokam *et al.*, 2017). In this present study, clinical signs observed were less obvious with lower mortality in sodium selenite supplemented group of rats. This may be hypothesized that the harmful effect of the PQ resulting oxidative stress on the rats can be ameliorated via a synergistic interaction between dietary and endogenous antioxidants. The clinical signs noticed were in tandem with that observed by previous researchers (Lalrautfela *et al.*, 2014; Tan *et al.*, 2015). The serum AST, ALT and ALP activities in the treated groups showed a significant increase when compared to the control animals. These findings were in consistent with studies by Akinloye *et al.* (2011), Lalrautfela *et al.* (2014), Oluwatoyin *et al.* (2017) and Ujowundu *et al.* (2018), suggestive of hepatocellular injury. It can be assumed that elevation of these enzymes may be due to free radical induced

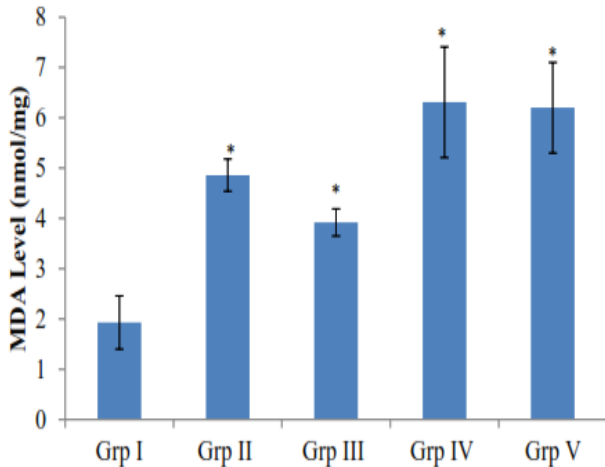


Figure 9: Lungs malondealdehyde concentration of rats treated with distilled water, paraquat and selenium for a week. * Significantly different from control group (Grp I)

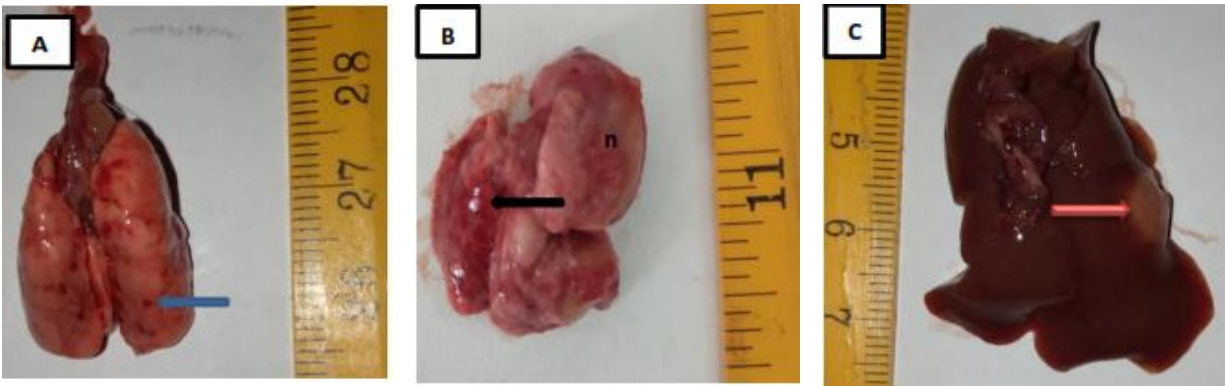


Plate I: A- lung of rat administered PQ at 15 mg/kg and sodium selenite for showing mild to moderate haemorrhagic lesions (blue arrow). B- emphysematous lung of rat administered PQ at 30 mg/kg without supplementation showing severe congestion (black arrow) and necrosis (n). C- liver of rat administered PQ at 15 mg/kg and supplemented with selenium 0.3 mg/kg for 7 days showing nodular lesion (red arrow)

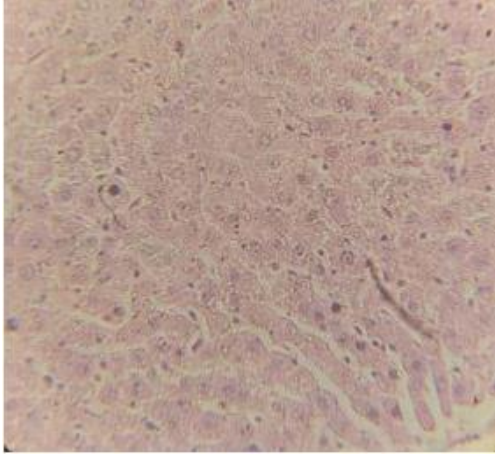


Plate II: Section of liver from group I rats showing no apparent histopathologic changes (x400)

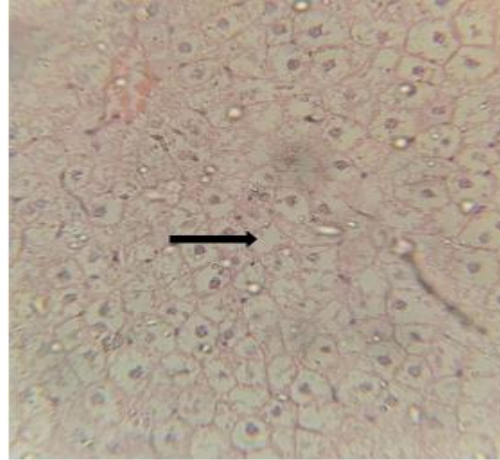


Plate III: Section of liver from group IV rat showing severe vacuolar degenerative hepatocellular changes (H & E x400)

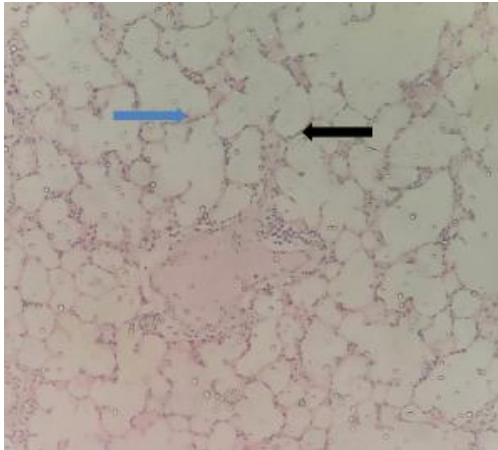


Plate IV: Section of lung from group III rat showing peribronchiolar mononuclear cellular infiltration (black arrow) and pinkish oedema fluid (blue arrow) within the alveolar sac (H & E x200)

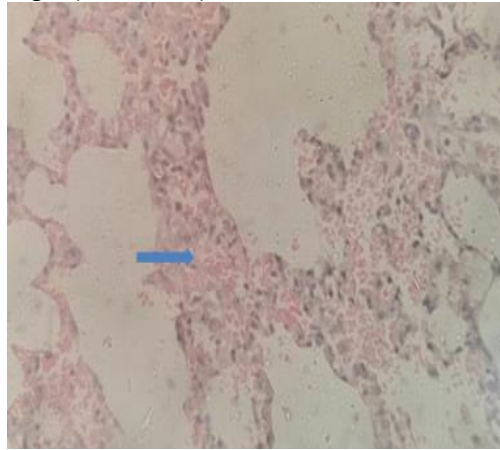


Plate V: Section of lung from group IV rat of showing severe haemorrhages (blue arrow) and thickened alveolar septae (H & E x400)

hepatocellular damage (Anosike *et al.*, 2008; Zeb *et al.*, 2013) since the metabolism of PQ is known to generate free radicals (Ahmad *et al.*, 2008). A relative decrease in liver enzymes activities of rats supplemented with selenium (Group III and V) when compared to PQ treated (Group II and IV) is suggestive of possible hepato-protective role of the antioxidant which is associated with its ability to scavenge ROS (Newairy *et al.*, 2007). BUN and creatinine were significantly higher in treated groups, this findings also concurs with recent report of Ujowundu *et al.* (2020) justifying that PQ induces renal damage in rats. However, reduced concentrations of BUN and creatinine in sodium selenite supplemented rats, although not significant indicated possible protective ability against PQ toxicity to the kidney. The nephroprotective potential of selenium has been earlier proven by Sirota (2010) and Hashish *et al.*

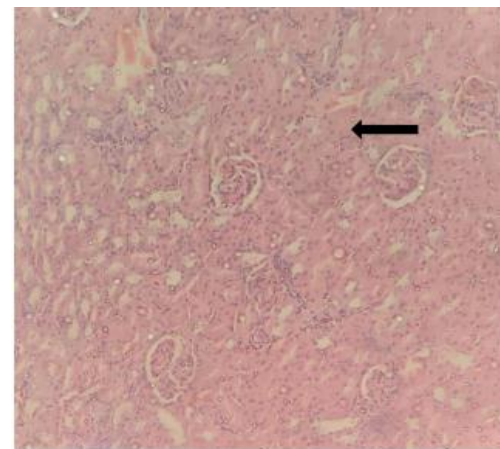


Plate VI: Section of kidney from group IV rat showing necrosis of renal tubular epithelium and pinkish oedema fluid within the lumen (black arrow) (H & E x200)

(2015).

The data of oxidative biomarkers has shown that there was no significant increase in liver SOD rather a significant increase was observed in the lungs. This finding can be corroborated to the fact that despite PQ been metabolized in the liver, the lungs is the primary organ affected and accumulates majority of the toxicant (Tan *et al.*, 2015). The activities of SOD and MDA in this study showed similar changes, increasing with increasing dose of the toxicant. PQ toxicity mechanism involves generation of ROS, resulting in an imbalance between antioxidant scavengers and ROS which reacts with polyunsaturated fatty acids to produce toxic metabolites such as MDA, an end product of lipid peroxidation (Ray *et al.*, 2008). This mechanism explains their possible increases, as SOD, catalase and glutathione peroxidase among various antioxidant constitute primary enzymatic defense system (Suntres, 2002). Rats from the selenium supplemented groups showed non-significantly reduced oxidative stress elicited by PQ, demonstrated by lower SOD activities and MDA levels in both liver and lungs. Gross examination of the lung of the control group (Group I) revealed an apparent normal lung with no visible lesion. However, lungs of PQ-treated groups revealed lesions in a dose-dependent manner from Group II – Group V, with those administered 30 mg/kg of paraquat showing severe congestion, haemorrhages and emphysema. These lesions were similar to that reported by Tamuli *et al.* (2007), Soloukides *et al.* (2007) and Lalrautela *et al.* (2014). Histopathological lesions observed in this study were consistent with previous findings by Akinloye *et al.* (2013) and Lalrautela *et al.* (2014). However, no fibrous tissue proliferations of the liver were noticed in this study which may be attributed to the duration of administration of 14 days by Akinloye *et al.* (2013) as against 7 days in this study. The protective effect of selenium against paraquat toxicity as evident in this study may be attributed to the antioxidant scavenging the superoxide anion generated from redox cycling of PQ, thus reducing lipid peroxidation. In conclusion, these findings demonstrate that selenium supplementation may be a promising therapy and should further be clinically validated.

Conflict of interest

The authors declare that there is no conflict of interest.

References

- Ahmad AK, Shukla S, Pandey HP & Singh C (2008). The involvement of nitric oxide in maneb- and paraquat-induced oxidative stress in rat polymorphonuclear leukocytes. *Free Radical Research*, doi.10.1080/10715760802513733.
- Akinloye OA, Abioye OA, Olaojoyetan OE, Awosika OT & Akinloye DI (2013). Dose-dependent effects of paraquat on c-reactive protein, some lipid profile parameters and histology of tissues in male Albino rats. *Biochemistry and Physiology*, **2**(1): 106-111.
- Akinloye OA, Adamson I, Ademuyiwa O & Arowolo TA (2011). Supplementation of vitamin C, E and its combination on paraquat intoxicated rats: effects of some biochemical and markers of oxidative stress parameters. *Advanced Biomedical Research*, **2**: 92-100.
- Anosike CA, Ugwu UB & Nwakanma O (2008). Effect of ethanol extract of *Pyrenacantha staudtii* leaves on carbontetrachloride induced hepatotoxicity in rats. *Biochemistri*, **20**(1): 17-22.
- Black AT, Gray JP, Shakarjian MP, Laskin DL, Heck DE & Laskin, JD (2008). Increased oxidative stress and antioxidant expression in mouse keratinocytes following exposure to paraquat. *Toxicology and Applied Pharmacology*, doi.10.1016/j.taap.2008.05.014.
- Bus JS & Gibson JE (1984). Paraquat: model for oxidant-initiated toxicity. *Environmental Health Perspectives*, doi.10.1289/ehp.845537.
- Chang SS & Gunnell D (2019). Banning paraquat would prevent nearly 200 deaths from suicide per year in Taiwan. *Taiwan Journal of Psychiatry*, doi.10.4103/TPSY.TPSY_24_19.
- Evans P & Halliwell B (2001). Micronutrients: oxidant/antioxidant status. *British Journal of Nutrition*, **85**(2): 67-74.
- Fridovich I (1989). Superoxide Dismutases. An Adaptation to a Paramagnetic Gas. *The Journal of Biological Chemistry*, **264**(14): 7761-7764.
- Gupta SP, Patel S, Yadav S, Singh AK, Singh S & Singh MP (2010). Involvement of nitric oxide in maneb- and paraquat-induced Parkinson's disease phenotype in mouse: is there any link with lipid peroxidation? *Neurochemical Research*, doi.10.1007/s11064-010-0176-5.

- Hashish EM, Elgaml SA, El-Murr A & Khalil R (2015). Nephroprotective and antioxidant significance of selenium and a-tocopherol on lead acetate-induced toxicity of Nile Tilapia (*Oreochromis niloticus*). *Fish Physiology and Biochemistry*, **41**(3): 651-660.
- Idris SY, Kakkaba HA, Enam SJ, Bello TK, Adekunle LA & Abdullahi I (2020). Ameliorative effect of selenium on haematological changes induced by acute paraquat exposure in male Wistar rats. *Savannah Journal of Veterinary Sciences*, **3**(2): 17-21.
- Lalruatfela PL, Saminathan M, Ingole RS, Dhama K & Joshi MV (2014). Toxicopathology of Herbicide Paraquat in Female Wistar Rats. *Asian Journal of Animal and Veterinary Advances*, **9**(9): 523-542.
- McCormack AL, Atienza JG, Johnston LC, Anderson JK, Vu S & Di Monte DA (2005). Role of oxidative stress in paraquat-induced dopaminergic cell degeneration. *Journal of Neurochemistry*, doi.10.1111/j.1471-4159.2005.03088.x.
- Newairy AA, El-Sharaky AS, Badreldeen MM, Eweda SM & Sheweita SA (2007). The hepatoprotective effects of selenium against cadmium toxicity in rats. *Toxicology*, doi.10.1016/j.tox.2007.09.001.
- Oluwatoyin TA, Donatus CB, Mathew OW & Justice OO (2017). Implication of Acute, Sub-chronic and Chronic Exposure to Different Pesticides via Inhalation on Male Wistar Rats. *Bioengineering and Bioscience*, **5**(4): 74-85.
- Patel S, Singh V, Kumar A, Gupta YK & Singh MP (2006). Status of antioxidant defense system and expression of toxicant responsive genes in striatum of maneb- and paraquat-induced Parkinson's disease phenotype in mouse: mechanism of neurodegeneration. *Brain Research*, doi.10.1016/j.brainres.2006.01.060.
- Pouokam GB, Lemnyuy AW, Ndikontar AS & Sidatt MEH (2017). Pilot study in Cameroon to understand safe uses of pesticides in agriculture, risk factors for farmers' exposure and management of accidental cases. *Toxics*, **5**(4): 30-45.
- Preiser JC (2012). Oxidative stress. *Journal of Parenteral and Enteral Nutrition*, doi.10.1177/0148607111434963.
- Raghu K, Mahesh V, Sasidhar P, Reddy PR, Venkataramaniah V & Agrawal A. (2013). Paraquat poisoning: A case report and review of literature. *Journal of Family and Community Medicine*, doi.10.4103/2230-8229.122023.
- Ray S, Sengupta A & Ray A (2008). Effects of paraquat on anti-oxidant system in rats. *Indian Journal of Experimental Biology*, **45**(5): 432-438.
- Saleem M, Alam A & Sultana S (2000). Attenuation of benzoyl peroxidase-mediated cutaneous oxidative stress and hyperproliferative response by the prophylactic treatment of mice with spearmint (*Mentha spicata*). *Food Chemical Toxicology*, doi.10.1016/s0278-6915(00)00088-0.
- Sekhar P, Prakash DJ & Lessley SSF (2011). Haematological changes in freshwater catfish *Mystus vittatus* exposed to sublethal concentrations of monocrotophos. *International Journal of Pharmaceutical and biological Archives*, **2**(4): 1215-1217.
- Sirota TV (2010). Effect of selenium-containing products on antioxidant enzyme activity in the kidneys, liver, and blood of guinea pigs. *Bulletin of Experimental Biology and Medicine*, doi.10.1007/s10517-010-0958-4.
- Soloukides A, Moutzouris K, Kassimatis T, Metaxatos G & Hadjiconstantinou V (2007). A fatal case of paraquat poisoning following minimal dermal exposure. *Renal Failure*, doi.10.1080/08860220601184134.
- Suntres ZE (2002). Role of antioxidants in paraquat toxicity. *Toxicology*, doi.10.1016/s0300-483x(02)00382-7.
- Tan D, Yiheng W, Bing B, Xuelian Y & Junyan H (2015). Betanin attenuates oxidative stress and inflammatory reaction in kidney of paraquat-treated rat. *Food and Chemical Toxicology*, doi.10.1016/j.fct.2015.01.018.
- Tamuli SM, Baruah GK & Tamuli MK (2007). Pathology of chronic paraquat toxicity in calves. *Indian Journal of Veterinary Pathology*, **31**(2): 130-134.
- Taylor PJ, Salm P & Pillans PI (2001). A detection scheme for paraquat poisoning: validation and a five-year experience in Australia. *Journal of Analytical Toxicology*, doi.10.1093/jat/25.6.456.
- Touat-Hamici Z, Legrain Y, Bulteau AL & Chavatte L (2014). Selective up-regulation of human selenoproteins in response to oxidative stress. *Journal of Biological Chemistry*, doi.10.1074/jbc.M114.551994.
- Ujowundu CO, Linus AN, Favour NU, Nathan NO & Ahmed OO (2018). Hepatotoxicity of Paraquat Dichloride and Ameliorative Effect

- of Nutritional Supplements. *Biochemistry and Molecular Biology Journal*, **4**(3): 1-8.
- Ujowundu CO, Anaba PI, Ulinasombu NB, Ujowundu FN, Igwe KO & Ogbuagu HD (2020). Attenuation of paraquat-induced nephrotoxicity and dysfunction in male wistar albino rats. *Innovative Biosystems and Bioengineering*, **4**(1): 26-35.
- Zeb ST, Ali AB, Ahmad JS & Qazi MH (2013). Effect of Nicotinic Acid (Vitamin B3 or Niacin) on the lipid profile of diabetic and non-diabetic rats. *Pakistan Journal of Medical Science*, doi.10.12669/pjms.295.4193