JASEM ISSN 1119-8362

Full-text Available Online at
https://www.ajol.info/index.php/jasem
and www.bioline.org.br/ja

J. Appl. Sci. Environ. Manage. *Dec,* 2017
Vol. 21 (7) 1286-1290

Effect of Aqueous *Allium Cepa* Extract from Red Onion on Aluminum Chloride-Induced Anemia in Female Rats

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ABSTRACT: This study examined the protective effect of *Allium cepa* extract from red onion on aluminum – induced anemia in female wistar rats. Twenty-four animals (six rats per group) were used for this study. They were divided into four groups: group one served as control, group two animals were treated with 100mg/kg BW of aluminum chloride and served as Aluminum chloride ($AlCl_3$) group, group three, *Allium cepa* alone group were treated with 1mL/100g BW of *Allium cepa* while group four was simultaneously treated with 1mL/100g BW of *Allium cepa* and 100mg/kg BW $AlCl_3$. Treatments lasted for 4 weeks. Red blood cells (RBC), packed cell volume (PCV), Hemoglobin concentration (Hb) were measured from blood sample collected from each rat. Serum urea, serum and kidney malondialdehyde (index of lipid peroxidation) and kidney catalase and superoxide dismutase (SOD) activities were measured spectrophotometrically. Significant decrease in RBC, PCV, Hb, catalase, SOD and significant increase in serum urea and malondialdehyde were observed in aluminum treated animals when compared with control. Animals treated with *Allium cepa* alone had significant increase in PCV, Hb, SOD and significant decrease in malondialdehyde and serum urea while there was no significant different in RBC and catalase when compared with control. Simultaneous treatment of the animals with *Allium cepa* and aluminum chloride resulted in significant increase in PCV while there was no significant different in RBC, Hb, catalase, malondialdehyde when compared with control.This study reveals that *Allium cepa* extract treatment ameliorate aluminum-induced anemia through antioxidant system.

DOI: **https://dx.doi.org/10.4314/jasem.v21i7.11**

Received 16 October 2017; received in revised form 11 November 2017; accepted 14 December 2017

Keywords: Anemia, *Allium cepa,* Aluminum chloride, lipid peroxidation.

Anemia, one of blood disorders, is a fall in the total amount of red blood cell and hemoglobin in the blood, characterize with decrease oxygen carrying ability of blood (Rodak, 2007). Anemia being the most common blood disorder affecting large number of world population (Janz *et al*., 2013), resulted in death in not less than 183,000 in 2013 (Global Burden of Disease Study, 2013) with highest prevalence rate in women (Vos *et al*., 2012). Anemia occurs when the rate of production of mature red blood cells does not keep pace with rate of its destruction. Decrease/impair red blood cell production is one of the main causes of anemia.

Aluminum (Al) is one of the toxic trace elements, to both humans and animals. Humans are exposed to aluminum through diet (salt, herbs, spices, corn *etc.*) (Yousef, 2004), drinking water, cosmetics, cookware utensils, containers, antacids, vaccines and tooth paste (Abbasali *et al*., 2005). There is no known physiological role of aluminum in the living tissues; however, exposure to excess aluminum produces adverse physiological effects. Aluminum is a known environmental toxicant that can cause neurological diseases (Yousef, 2004), reproductive dysfunctions such as, damage of the ovarian structure, ovulation inhibition and testicular dysfunction (Wang *et al.*, 2012; Fu *et al.*, 2014; Ighodaro *et al.*, 2012). It is also known to induce anemia (Mahieu *et al.,* 2000). Reduction in erythropoietin synthesis and secretion, and inhibition of intestinal absorption of iron has been proposed as mechanisms of aluminum-induced anemia (Kalaiselvi *et al*., 2015) with increase hemolysis and reduce heme and globulin syntheses reported due to aluminum toxicity. Uremia is usually seen with aluminum-hematotoxicity (Mahieu *et al.,* 2000). Likewise, cardiovascular diseases, cognitive impairment and reduction in quality of life are associated with anemia in kidney diseases (Wang *et al.*, 2012). Erythropoietin deficiency is the predominant cause of anemia in kidney diseases (Babitt and Lin, 2012) due to the fact that kidney is the main source of erythropoietin. So also, oxidative stress has been implicated in the genesis and progression of kidney diseases (Jha *et al*., 2016), long-chain polyunsaturated fatty acids present in the kidney enhance the oxidative stress-induced kidney disease.

Allium cepa is a potent antioxidant (Ige *et al*., 2017), reported to protect against aluminum-induced reproductive dysfunction (Ige and Akhigbe, 2012) and cadmium-induced nephrotoxicity (Ige *et al.,* 2011). Many studies have been carried out on the effects of *Allium cepa* on blood parameters (Enitan *et al*., 2012; Nwaehujo *et al*., 2014; Jaiswal *et al*.,

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2013). Enitan *et al*., reported significant increase in packed cell volume, red blood cell count and hemoglobin concentration (Enitan *et al*., 2012). Increase red blood cells membrane stability and attenuation of $HgCl_2$-induced oxidative stress in rats erythrocytes was also reported (Nwaehujo *et al*., 2014; Jaiswal *et al*., 2013). In view of all these findings, there is a dearth of information on the effect of *Allium cepa* on the aluminum-induced anemia. Therefore, this study was carried out to examine the effect of *Allium cepa* extract on aluminum chloride - induced anemia.

MATERIALS AND METHODS

Animals: Twenty four adult female wistar rats weighing 150-200g were used for this study. Animals were kept in research section of the animal house of Department of Physiology, Ladoke Akintola University of Technology, Ogbomoso, Nigeria. They were fed with standard diet *ad libitum* and divided into four groups of six rats each: group one served as control, group two animals were treated with 100mg/kg BW of aluminum chloride and served as Aluminum chloride ($AlCl_3$) group, group three, *Allium cepa* alone group were treated with 1mL/100g BW of *Allium cepa* while group four was simultaneously treated with 1mL/100g BW of *Allium cepa* and 100mg/kg BW $AlCl_3$. The treatments were given daily, orally for 28 days. Animals were cared for according to United States National Institute of Health Guidelines for the Care and Use of Laboratory Animals (NIH publication No 85-23).

Allium cepa extract preparation: *Allium cepa* was prepared following previous study procedure (Ige and Akhigbe, 2013). *Allium cepa* (red onion) bulbs purchased from local market in Ogbomoso, Oyo state, Nigeria, were rinsed thoroughly in distilled water, air dried, and 200 g was then blended. The resulting paste was allowed to stand for 24 h. Juice was then filtrated and squeezed out of it using a tight sieve. The filtrate/juice was prepared on weekly basis following the same procedure and kept at 4°C to prevent it from losing its potency.

Hematological parameters measurements: Blood samples were collected by cardiac puncture and divided into two; one half in plain bottles and the other in ethylene diamine tetra-acetic acid (EDTA) bottles, plasma and serum were obtained by centrifuge at 3000 rpm for 20 minutes.

PCV was determined using microhaematocrite method, RBC counts were determined using haemocytometer method, haemoglobin determination was by cyanmethaemoglobin method. Serum urea and malondialdehyde concentration were determined spectrophotometrically using Berthelot enzymatic colorimetric method (Kaplan, 1984) and Varshney and Kale, (1990) method, respectively.

Determination of kidney antioxidant and lipid peroxidation status: After animals were sacrificed at end of the experimental period, kidney of each rat was dissected and homogenized in phosphate buffer, centrifuge at 4000 rpm for 10 minutes. The supernatants collected were used for the biochemical analyses. Malondialdehyde concentration, catalase and superoxide dismutase activities were determined as described in previous studies (Varshney and Kale, (1990); Sinha, (1972); Fridovich, (1986) respectively.

Statistical analysis: All values were reported as mean ± S.E.M. One-way analysis of variance (ANOVA) was used to analyze for the significance of differences between means followed by unpaired Student's *t*-test using Microsoft excel. Values of $P < 0.05$ were considered statistically significant.

RESULTS AND DISCUSION

Red blood cells counting (RBC), hemoglobin concentration (Hb) and packed cell volume (PCV) are part of hematological parameters usually employed to diagnose effects of toxic substances exposure. RBC, hematocrit and Hb are use to determine anemia while low Hb has been linked with increase mortality and morbidity rate (Aletan, 2014). In the present study, treatment of animals with aluminum chloride significantly decreased the blood parameters: RBC, PCV and Hb. Animals treated with *Allium cepa* alone had significant increase in PCV and Hemoglobin concentration when compared with control. Simultaneous treatment of the animals with *Allium cepa* and aluminum chloride resulted in significant increase in PCV when compared with control, while there was no significant different in RBC and Hb, (Table 1).

Table 1: Effect of *Allium cepa* on some blood parameters of aluminum treated rats

Parameters	Control	Al	*Allium cepa*	Al + *Allium cepa*
RBC (mL/mm^3)	6.96 ± 0.66	5.18 ±0.184*	8.37 ± 0.129	7.78± 0.20
Hb (g%)	12.7 ± 0.73	10.64 ± 0.50*	17.28 ± 0.64*	13.76 ± 0.48
PCV (%)	44 .4 ± 1.33	40.0 ± 0.71*	53.4 ± 1.12*	49.0± 1.41*

*p<0.05 vs control

The reduction in red blood cells count, hemoglobin concentration and packed cell volume in animals treated with aluminum chloride observed in this study is in agreement with previous studies (Mahieu *et al*., 2000; Kalaiselvi *et al*., 2015). They reported that reduction in hemoglobin concentration and red blood cells count as a result of exposure to aluminum are a reflection of disrupt red blood cell synthesis. The study of Kalaiselvi *et al*., has also suggested that reduction in RBC and Hb due to aluminum exposure might be the result of erythropoiesis inhibition couple with increase hemolysis (Kalaiselvi *et al.*, 2015). In our study, the reduction in RBC, PCV and Hb was ameliorated by treatment of the aluminum exposed rats with *Allium cepa.*

Anemia is one of the major health problems, with about 30% world populations suffer from it (Iuchi, 2012). One of the causative factors of anemia is reactive oxygen species of erythrocyte, though iron deficiency is the most common causative factor (Iuchi, 2012). Alteration in trace elements especially zinc, copper and iron and lipid peroxidation in plasma and erythrocytes have also been suggested as mechanism of aluminum-induced anemia (Guo *et al*., 2004). Accumulation of aluminum can affect the iron and zinc concentration of a tissue (Domingo, *et al*. 1993; Jia *et al*, 2001) thereby decreases the antioxidant activities while lipid peroxidation increases. Iron and aluminum may also compete for absorption because both are transported by transferrin. Deloncle *et al,* (2001) study has demonstrated this where radio labeled iron absorption was inhibited by aluminum.

The study of Yousef, (2004) has also shown that aluminum chloride induces oxidative stress in rabbit organs with kidney inclusive. Oxidative stress has also been implicated in aluminum-induced organs/ tissues dysfunction and toxicity such as hepatotoxicity (Al-Qayim and Saadoon, 2013), reproductive toxicity (Ige *et al*., 2012; Kalaiselvi *et al*. 2014) and nephrotoxicity (Oda, 2016).

The present study reveals significant increase in serum and kidney malondialdehyde (an index of lipid peroxidation) and significant decrease in kidney catalase and SOD activities in aluminum alone treated rats, (Table 2 and Figure 1). The significant increase in malondialdehyde observed in the present study is in agreement with previous study of Oda, (2016) where administration of aluminum chloride resulted in increased serum malondialdehyde. Significant decrease in malondialdehyde and increase in kidney catalase and superoxide dismutase activities were observed in *Allium cepa* treated animals. Insignificant difference (compared to control) in malondialdehyde, catalase and superoxide dismutase activities of animals treated with aluminum and *Allium cepa* confirms the antioxidant effect of *Allium cepa* against aluminum chloride induced-nephrotoxicity in this study. The present study also corroborates our previous studies where antioxidant property of *Allium cepa* against various organs toxicity induced by toxic substances (Ige *et al*, 2012; Ige *et al* 2017) which include kidney toxicity (Ige *et al.*, 2011) were confirmed.

Table 2: Effect of *Allium cepa* on kidney antioxidant activities and lipid peroxidation status of aluminum treated rats

Parameters	Control	Al	*Allium cepa*	Al + *Allium cepa*
SOD (U/g tissue)	0.31 ± 0.02	0.19 ± 0.01*	0.54 ± 0.02*	0.24 ± 0.01*+
Catalase (IU/g tissue)	0.0089 ± 0.0012	0.0051 ± 0.0006*	0.014 ± 0.002	0.0080 ± 0.001
MDA (U/g tissue)	2.6 ±0.14	3.4 ± 0.18*	1.23 ± 0.27*	2.13 ± 0.31

*p<0.05 vs control, +p<0.05 vs Al

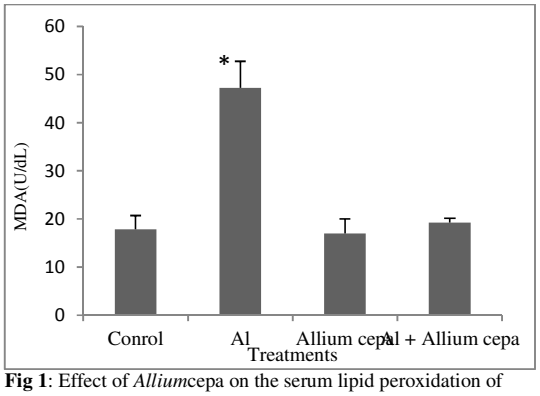
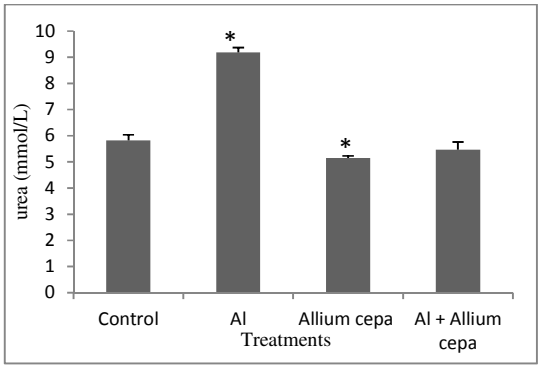


Fig 1: Effect of *Allium*cepa on the serum lipid peroxidation of aluminum treated rats. *p<0.05 vs control

Anemia can also be caused by diseases especially kidney diseases, some patients with kidney disease have been reported to develop anemia (Brugnara and Eckardt, 2011). Diseased or damaged kidneys don't produce sufficient erythropoietin which stimulates bone marrow to produce red blood cells (Winearls *et al*., 1986). Hematotoxic effect of aluminum has been observed to occur with renal damage manifested with uremia (Mahieu *et al*., 2000). In the present study serum urea was studied and it was found that aluminum exposure significantly increased serum urea (Figure 2). This is in consonance with Mahieu *et al*., (2000) study. The simultaneous treatment of aluminum exposed rats with *Allium cepa* mitigates the significant increase in serum urea (Figure 2).



*p<0.05 vs control

Fig 2: Effect of *Allium*cepa on the serum Urea of aluminum treated rats.

In conclusion, this study gives a vivid clarity that *Allium cepa* ameliorates aluminum-induced anemia and uremia associated with kidney damage from oxidative effect of aluminum.

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