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Allium Cepa Juice Prevented Oxidative Stress-Mediated Metabolic Disorder Following Chronic Lead Acetate Exposure in Male Rats

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Abstract

Background: The deleterious effects of chemical toxins on human health have been documented. Studies have also shown the health benefits of plant extracts.

Aims: We hypothesized that administration of *Allium cepa* (common onion) juice has no significant effect on metabolic indices and markers of oxidative stress in male Wistar rats exposed to lead acetate.

Study Design: 28 adult male Wistar rats weighing 150-160g were randomly divided into vehicle, lead acetate (LA), *Allium cepa* juice (ACJ), and LA+ACJ groups for four weeks.

Methods: The animals were housed in plastic cages and maintained under standard laboratory conditions. They were simultaneously administered 75mg/kg (P.O.) of LA and 1ml/200g body weight of ACJ (P.O.) using oral gavage.

Results: Exposure to LA caused significant reduction in high density lipoprotein (HDL), calcium, superoxide dismutase (SOD), catalase and glutathione (GSH) and also resulted to a significant increase in total cholesterol (TC), low density lipoprotein (LDL), triglyceride (TG), very low density lipoprotein (VLDL), lipid profile ratios, atherogenic index of plasma (AIP), sodium ions, potassium ions, chloride ions and malondialdehyde (MDA). ACJ treated rats showed a significantly reduced TC, TC/HDL, LDL/HDL and potassium and a significant increase in SOD, catalase and GSH. LA+ACJ group exhibited significantly low LDL/HDL ratio and a significantly high SOD but there was no significant change in TC, LDL, TG, VLDL, AIP, sodium, potassium, chloride, MDA, catalase and GSH.

Conclusions: *Allium cepa* juice prevented oxidative stress-mediated metabolic dysfunction following chronic lead acetate exposure in male rats.

Key words: *Allium cepa* juice, lead acetate, superoxide, atherogenic index of plasma, malondialdehyde

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INTRODUCTION

Metabolic disorders are medical conditions orchestrated by impairments in normal metabolic processes (1). Over the years, metabolic disorders, particularly metabolic syndrome has been associated with genetics (2), stress (3) and alterations in diet (4), exercise (5, 6), lifestyle (7) and age (8). Evidence abounds to indicate that exposure to exogenous factors most especially chemicals contributes to the etiology of metabolic disorders (9, 10, 11).

Lead is a chemical substance and it is used in battery manufacturing, soldering, painting, refining and electric wiring (12). Due to its non-degradability, it accumulates in soft tissues and induces a spectrum of adversities on physiological functions (13). Many studies have reported the adverse metabolic effects of lead exposure. For example, Ugbaja *et al.*,(14) showed that exposure of rats to lead resulted in hypercholesterolemia, hypertriglyceridemia and hyperphosphatemia.

In battery workers, Shyam *et al.*,(15) reported a high level of total cholesterol, low density lipoprotein and a decreased level of high density lipoprotein. Lead intoxication also led to a decrease in bone calcium density in rats (16) and caused disrupted electrolyte balance through its interference with sodium-potassium ATPase (17). Lead induced dysfunctions are also characterized by increase in production of reactive oxygen species, decrease in antioxidant capacity and derangement in oxidant/antioxidant balance (18, 19).

Besides chemicals, edible plants are other examples of exogenous factors. Investigators have documented the immense benefits of edible plants on health. Garlic for instance has been shown to prevent decline in reproductive hormones in lead intoxicated mice (20). In our previous studies, we reported that common onion (*Allium cepa*) extract mitigated aluminum chloride-induced hepatotoxicity (21), antagonized toxic effects of aluminum chloride on male reproductive function (22), ameliorated ethanol-induced gastric injury (23) and prevented cadmium-induced renal derangements (24, 25). The present study is designed to investigate the effect of *Allium cepa* juice on metabolic indices and markers of oxidative stress in male rats exposed to lead acetate.

ANIMALS, MATERIALS AND METHODS

Animal care and management

Twenty-eight male Wistar rats weighing between 150g-160g were used in this study. They were obtained from the Animal house of the Department of Physiology, Ladoke Akintola University of Technology Ogbomoso, Oyo State, Nigeria. They were housed in standard cages at room temperature and 12hr light/12hr dark cycle. The animals were acclimatized for 1 week. All rats were fed pelletized grower mash (standard chow) and distilled water *ad libitum.*

Ethical consideration

The study was conducted in line with the guidelines of National Institute of Health (NIH) for the use of laboratory rats.

Preparation of *Allium cepa* juice

Fresh red onions (*Allium cepa*) were gotten from Arada market Ogbomoso, Oyo State, Nigeria. The onions were rinsed with distilled water and dried for 24 hours. The onions were crushed properly using a grating machine. The crushed onion was then poured into a clean sieve and the juice was squeezed out. The *Allium cepa* juice was freshly prepared for each day of the administration following the same procedure.

Preparation of lead acetate

500 mg of Lead acetate was dissolved in 100 mL of water (H_2O) to prepare a stock solution. The solution was prepared weekly and kept in a bottle at room temperature.

Study design

Experimental animals were randomly divided into four groups of seven rats each as follows:

Group A: received standard chow and distill water orally and was designated as vehicle-treated group (VEHICLE).

Group B: received oral administration of 75mg/kg of lead acetate (LA).

Group C: received oral administration of 1ml/200g of *Allium cepa juice* (ACJ).

Group D: received oral administrations of 75mg/kg of lead acetate and 1ml/200g of *Allium cepa juice*.

Lead acetate and *Allium cepa juice* spanned for four weeks were simultaneously administered.

Determination of Glutathione (GSH)

Glutathione (GSH) was determined using the method of Beutler *et al.*,1963 (26) reported by Banerjee *et al.*,(27).

Determination of Malondialdehyde (MDA)

Malondialdehyde (MDA) was determined using the method described by Buege and Aust, (1978) (28) reported by Yadegari *et al.*,(2007) (29).

Estimation of Catalase activity

This was done using the method described by Aebi, 1974 (30) reported by Zhang *et al.*,(2002) (31).

Estimation of serum electrolyte

Estimation of serum electrolytes Sodium (Na^+), Potassium (K^+), Calcium (Ca^{2+}) and Chloride (Cl^-) was done using automated Ion Selective Electrodes-analyzer (SFRI, France).

Determination of lipid profile, lipid profile ratios and atherogenic index of plasma

Plasma total cholesterol (TC), high density lipoprotein (HDL), low density lipoprotein (LDL) and triglyceride were estimated using enzyme linked immunosorbent assay (ELISA).

Very low density lipoprotein (VLDL) was obtained using the formula:

VLDL= Triglyceride (mg/dl)/5 (32)

LDL/HDL, TC/HDL, Triglyceride/HDL ratios were mathematically calculated.

Atherogenic index of plasma (AIP) was calculated using the formula:

AIP= log (triglyceride/HDL) (33, 34).

Statistical analysis

The results obtained were expressed as mean ± standard error of mean (Mean ± SEM). Statistical analysis was done using SPSS 21. Pairwise comparison was done using least square difference. Values with $p<0.05$ were regarded as being significant.

RESULTS

Table 1 show that there was a significant increase in total cholesterol, low density lipoprotein, triglyceride and very low density lipoprotein in lead acetate exposed rats when compared with vehicle-treated group. There was a significant decrease in high density lipoprotein of lead acetate exposed rats when compared with vehicle-treated group. There was a significant decrease in total cholesterol of *Allium cepa* juice treated rats when compared with vehicle-treated group.

Table 2 shows that there was a significant increase in TC/HDL, LDL/HDL, TG/HDL and AIP of lead acetate exposed rats when compared with vehicle-treated group.

Table 1 Effect of Allium cepa juice and lead acetate on plasma lipid profile

Groups	Total cholesterol (TC) (mg/dl)	High density lipoprotein (HDL) (mg/dl)	Low density lipoprotein (LDL) (mg/dl)	Triglyceride (TG) (mg/dl)	Very low density lipoprotein (VLDL) (mg/dl)
Vehicle	90.5±0.474	29.33±0.183	47.33±1.56	82±0.633	16.4±0.1265
Lead acetate	130.5±2.056*	21.75±1.018*	65.66±3.17*	118±0.949*	23.6±0.1897*
Lead acetate + *Allium cepa* juice	91±0.3162 [a]	30±1.265 [a]	45.67±0.18 [a]	84.5±1.11 [a]	16.9±0.2214 [a]
Allium cepa juice	68.32±1.495* [a]	28.4±0.6 [a]	49.5±3.64 [a]	78±2.53 [a]	15.6±0.60596 [a]

* represents significant difference (P<0.05) from vehicle

Table 2 Effect of Allium cepa juice and lead acetate on lipid profile ratios and atherogenic index of plasma (AIP)

Groups	TC/HDL	LDL/HDL	TG/HDL	Atherogenic index of plasma (AIP)
Vehicle	3.282±0.051	1.613±0.043	2.796±0.2778	0.4465±0.00428
Lead acetate	6.054±0.2996*	3.303±0.122*	5.474±0.2626*	0.7363±0.02083*
Lead acetate+ *Allium cepa* juice	3.26±0.0928 [a]	1.23±0.049* [a]	2.8434±0.159 [a]	0.4511±0.02413 [a]
Allium cepa juice	2.64±0.13* [a]	1.31±0.0512* [a]	2.752±0.107 [a]	0.4383±0.1716 [a]

* represents significant difference (P<0.05) from vehicle

Table 3 shows that there was a significant increase in plasma levels of sodium ion, potassium ion and chloride ions in lead acetate exposed rats when compared with vehicle treated group. There was a significant decrease in plasma calcium ions in lead acetate exposed rats when compared with vehicle treated group. Administration of *Allium cepa* juice decreased plasma potassium level.

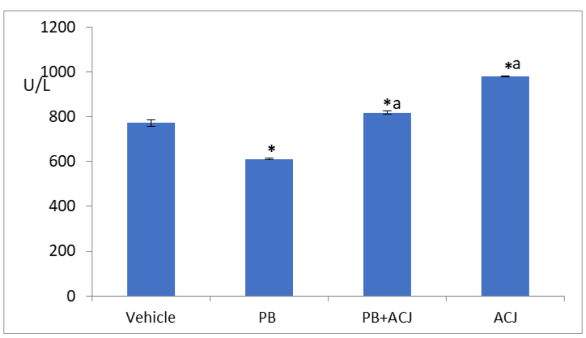
Table 3 Effect of Allium cepa juice and lead acetate on plasma electrolyte profile

Groups	Sodium ion (mmol/l)	Potassium ion (mmol/l)	Chloride ion (mmol/l)	Calcium ion (mg/dl)
Vehicle	137.67±0.483	3.79±0.01	95±0.9487	9.2±0.063
Lead acetate	145.33±0.7303*	4.45±0.098*	108±0.6325*	7.5±0.032*
Lead acetate+ *Allium cepa* juice	139±0.3100 [a]	3.93±0.008 [a]	95.5±1.11 [a]	9.19±0.014 [a]
Allium cepa juice	139±0.3162 [a]	3.55±0.0158* [a]	95.3±0.966 [a]	9.2±0.037 [a]

* represents significant difference (P<0.05) from vehicle

Figure 1 shows the effect of *Allium cepa* juice and lead acetate on superoxide dismutase.

Figure 1 Superoxide dismutase



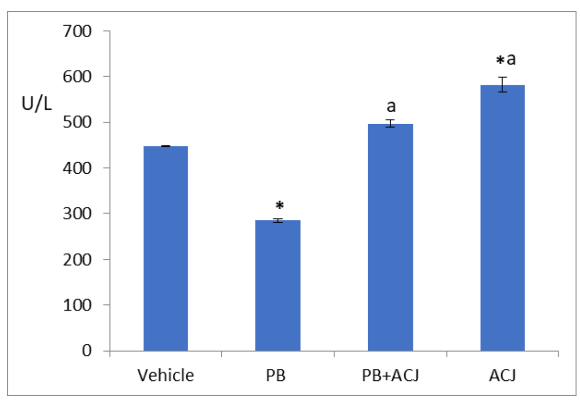
* represents significant difference (P<0.05) from vehicle

There was a significant decrease in superoxide dismutase activity of lead acetate exposed rats when compared with vehicle treated group. There was a significant increase in superoxide dismutase activity of *Allium cepa* juice treated rats when compared with vehicle treated group.

There was also a significant increase in superoxide dismutase activity in lead acetate exposed rats treated with *Allium cepa* juice when compared with the vehicle treated.

Figure 2 shows the effect of *Allium cepa* juice and lead acetate on catalase.

Figure 2 Catalase

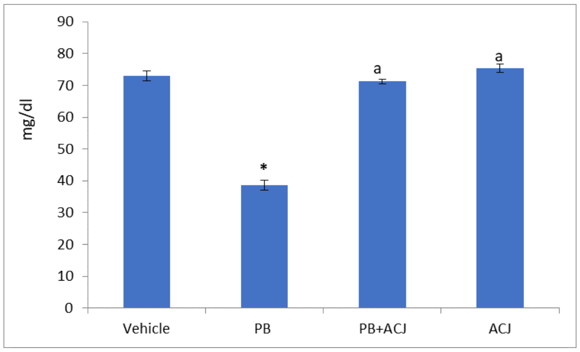


*Significant difference (P<0.05) from vehicle.

There was a significant decrease in catalase activity of lead acetate exposed group when compared with vehicle treated group. There was a significant increase in catalase activity in *Allium* *cepa* juice treated group when compared with vehicle treated group

Figure 3 shows the **e**ffect of *Allium cepa* juice and lead acetate on glutathione.

Figure 3 Effect of Allium cepa juice and lead acetate on glutathione

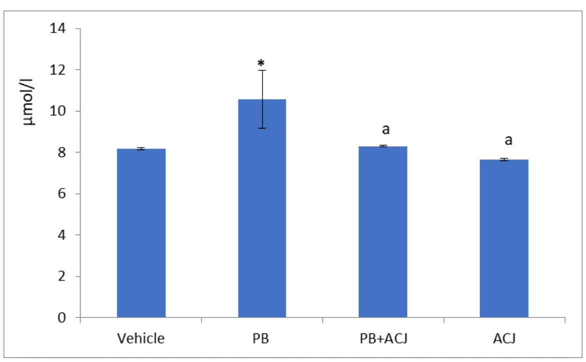


*Significant difference (P<0.05) from vehicle.

There was a significant decrease in glutathione level of lead acetate exposed group when compared with vehicle treated group.

Figure 4 shows the effect of *Allium cepa* juice and lead acetate on malondialdehyde.

Figure 4 Effect of Allium cepa juice and lead acetate on malondialdehyde



* represents significant difference (P<0.05) from vehicle

There was a significant decrease in malondialdehyde level of lead acetate exposed group when compared with vehicle treated group.

DISCUSSION AND CONCLUSION

Studies have shown the therapeutic potentials of plant extracts on heavy metal induced toxicity. We investigated the effect of *Allium cepa* juice on lead acetate induced metabolic disorder in male rats. The results of the lipid profile, lipid profile ratio, atherogenic index of plasma and electrolyte profile clearly indicated that chronic exposure to lead caused metabolic dysfunction.

The low high density lipoprotein and high levels of total cholesterol, low density lipoprotein, triglyceride and very low density lipoprotein observed in rats exposed to lead acetate concurred with the findings of Rubin and Soto (2009) (9), Ige and Akhigbe, (2013) (10) and Heindel *et al.*,(2017) (11). In scientific consensus, Low high density lipoprotein and high levels of total cholesterol, low density lipoprotein, triglyceride and very low density lipoprotein increase the risk of atherosclerosis and cardiovascular diseases (35, 36). We suggest that the abnormal lipid profile observed in rats that were exposed to lead acetate may be due to alteration in the activity of 3-hydroxy, 3- methylglutarylcoA reductase (HMGCoA reductase), an enzyme responsible for endogenous synthesis of cholesterol (37). Conversely, the insignificant change in lipid profile in lead acetate exposed rats treated with *Allium cepa* juice was corroborated by our earlier report (10). We also noticed a high HDL and low values of total cholesterol, LDL and triglyceride were observed in lead acetate exposed rats treated with *Allium cepa* juice when compared with rats that were exposed to lead acetate

In addition to lipid profile, lipid profile ratios (LDL/HDL, Total cholesterol/HDL and triglyceride/HDL) and atherogenic index of plasma are also important predictors of cardiovascular diseases (33, 38, 34). We observed that rats exposed to lead acetate exhibited higher atherogenic index of plasma and LDL/HDL, Total cholesterol/HDL and triglyceride/HDL ratios. This may be consequent to higher values of total cholesterol, low density lipoprotein and triglyceride and lower value of high density lipoprotein. Heavy metal intoxication is known to cause abnormal lipid profile ratios (11).

We showed that administration of *Allium cepa* juice decreased LDL/HDL significantly but had no effect on atherogenic index of plasma, total cholesterol/HDL and triglyceride/HDL. However, there was a reduction in LDL/HDL, TC/HDL, triglyceride/HDL and atherogenic index of plasma in lead acetate exposed rats treated with *Allium cepa* juice when compared with rats that were exposed to lead acetate .This suggests a plausible role of *Allium cepa* juice in lipid homeostasis and an additional evidence on the anti-atherogenic potentials of plants and plant extracts (39).

Furthermore, we observed that lead acetate exposed rats had a lower level of plasma calcium and higher plasma levels of sodium, potassium and chloride. This indicated that lead acetate inflicted disruptions on homeostatic mechanisms controlling these electrolytes. For example, the increases in sodium, potassium and chloride ions may be due to inhibition of sodium-potassium ATPase by lead (17). Lead acetate may also interfere with urinary excretion of calcium culminating in low plasma calcium level (12). However, we noticed that in rats exposed to lead acetate, *Allium cepa* juice administration elicited no significant change in sodium, potassium, chloride and calcium. In lead acetate exposed rats treated with *Allium cepa* juice, we observed that while sodium and calcium ions increased, potassium and chloride ions decreased.

As far as this study is concerned, lead acetate induced abnormalities in lipid and electrolyte profiles may be due to oxidative stress. Our study shows that exposure of rats to lead acetate resulted to an increase in malondialdehyde and a decreased level of superoxide dismutase, catalase and glutathione. Increase in malondialdehyde and decrease in superoxide dismutase, catalase and glutathione represent antioxidant dishomeostasis (40, 41) and increased tendency of metabolic derangements (42). Apart from the insignificant change in superoxide dismutase, catalase, malondialdehyde and glutathione in lead acetate exposed rats treated with *Allium cepa* juice, the significant increase in superoxide dismutase, catalase and glutathione in lead acetate exposed rats treated with *Allium cepa* juice showed the tendency of our treatment to mitigate oxidative stress characterizing lead acetate toxicity.

In conclusion, the results of our study indicate that *Allium cepa* juice exhibits potential of remediating lead acetate induced metabolic derangement.

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Conflict of Interest Disclosure: None declared.

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