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Tomato Pomace Alleviated Motor Abnormality, Oxidative Impairments and Neurotoxicity Induced by Lead Acetate in Male Rats

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ABSTRACT

The brain is highly sensitive to lead intoxication. Plant-derived products with antioxidant activity have been useful in reducing lead-induced neurotoxicity. The present study investigated the possible protective effect of tomato pomace powder (TPP) on brain damage induced by lead acetate (LAc) in rats. Thirty rats were divided equally into five groups: control; propylene glycol; TPP (50 mg/kg), LAc (50 mg/kg), and LAc+ TPP. All treatments were administered orally by gavage for 42 days. Rats were euthanized on day 43 of experiment. Behavioural tests, oxidative and blood parameters were done and brain tissue was examined with regard to histological parameters. Results indicated that LAc significantly ($p<0.05$) induced increased levels of lipid peroxidation and activity of SOD, but reduced GSH level. Similarly LAc caused alteration in the haematological and behavioural parameters, and microscopic anatomy of the cerebellum, dentate gyrus, and Cornu Ammonis3 of rats. These alterations were significantly ($p<0.05$) reversed by 50 mg/kg co-treatment of TPP with LAc when compared with the LAc group. In conclusion, co-treatment with TPP offered relative protection from LAc-induced neuropathy, motor abnormality and oxidative impairment. Our data suggest that TPP may be useful in the modulation of lead acetate-induced intoxication in rat.

Key words: Lead acetate, tomato pomace, neurotoxicity, oxidative damage, rat brain

INTRODUCTION

Lead poisoning is a recognized major public health risk especially in developing countries. The unique properties of lead like softness, high malleability, ductility, low melting point and resistance to corrosion, have enhanced its widespread use in different industries like automobiles, paint, ceramics, and plastics. Lead may be present in the environment water, in brass plumbing fixtures, paints, soil, dust and other products manufactured with lead (Garaza *et al*, 2006; Flora *et al*, 2012). Lead as a metal exists chemically in both organic (tetraethyl lead) and in the inorganic (lead acetate, lead chloride) forms in the environment (Shalan *et al*, 2005).

Exposure to lead mainly occurs through the respiratory and gastrointestinal systems. Whether inhaled or ingested, absorbed lead is stored in soft tissues before its conjugation in the liver, then passed to the kidney where a small quantity is excreted in urine while the remaining accumulates in various body organs,

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affecting many biological activities at the molecular, cellular and intercellular levels, which may result in morphological alterations (Nehru and Sidhu, 2004; Flora *et al*, 2012). It is the absorbed lead that accumulates in various tissues, and then interferes with several physiological processes which precipitates various deleterious effects on the central nervous system, haematopoietic, renal and reproductive systems (Kalia & Flora, 2005; Berrahal *et al*, 2007). Compared to other organ systems, the nervous system appears to be the most sensitive and chief target for lead induced toxicity (Kiran *et al*, 2009; Hassan & Jassim, 2010). At higher levels, lead toxicity can cause permanent brain damage and even death (Cleveland *et al*, 2008). Oxidative stress has been reported to be one of the mechanisms involved in brain neurotoxicity induced by lead exposure (Wang *et al*, 2006). This finding has been supported by numerous reports that have documented increased lipid peroxidation (LPO), decreased glutathione (GSH), and superoxide dismutase (SOD) activity in the brain homogenates of lead treated rats (El-sokkary *et al*, 2003; El-Masry *et al*, 2011).

Natural substances with antioxidant activity have been reported to significantly reduce lead-induced neurotoxicity, example of which are: curcumin (Shukla *et al*, 2003), *Zingibe officinale* (Attia *et al*, 2013), and propolis, (El-Masry *et al*, 2011). These reports stimulated interest in tomato or *Lycopersicon esculentum* Mill, a plant in the family of Solanaceae, reported to possess phytochemicals and exhibit antioxidant activity (Wattanathorn *et al*, 2012; Khalaf *et al*, 2014). Antioxidant nutrients in the tomato fruit include carotenoids such as lycopene, B-carotene, phytofluene, vitamin C and vitamin E (Kanabur and Reddy, 2014). Tomato pomace powder (TPP) made from tomato has been beneficial in protecting against cognitive deficit and experimental stroke (Wattanathorn *et al*, 2012; Thukhammaee *et al*, 2012).

In mammals, the hippocampus is intimately involved in memory, learning and spatial cognition (Alexandrov *et al*, 2013). Similarly, the cerebellum regulates motor coordination, equilibrium, both saccadic and smooth eye movements and maintains muscle tone (Affi and Bergman, 2005). Lead toxicity of these neural components will affect both the structure, form and function of the affected parts.

Although Nwokocha *et al*. (2011) had investigated the effect of tomato concentrate on effect of lead in the liver of rats, literature is scanty on its potential value in improving the lead-induced alteration of the microanatomy of rat brain. Therefore, the present study was designed to investigate the protective role in this regard utilizing tomato's known antioxidant property. This study therefore aimed to answer the question: 'Can *Lycopersicon esculentum* as tomato pomace powder treatment exhibit a protective role on lead-induced neurotoxicity in rats?'

MATERIALS AND METHODS

Experimental animals

This study was carried out using thirty male Wistar rats with initial weight 104 ± 11 g, which were housed in the Animal House, of the Department of Veterinary Physiology, Biochemistry and Pharmacology, University of Ibadan, Nigeria. They were acclimatized to laboratory room conditions (12 hours dark – light period) for a week before the onset of experiment. The rats were fed with rat chow from Ladokun Feeds, Ibadan, Nigeria and water *ad libitum.* The experimental protocols were carried out according to the approval and guidelines given by the University of Ibadan Ethical Committee No: UI-ACUREC/App/2015/022, which conformed to the acceptable guidelines on the ethical use of animals in research (Public Health Service, 1996).

Tomato Pomace Powder (TPP) Preparation and Administration

Fresh tomato fruits *(Lycopersicum esculentum)* were purchased from Bodija market, Ibadan, Nigeria. TPP was prepared according to the published method of Thukhammee *et al*. (2012). Briefly, the fresh tomatoes were washed and cut into small pieces after which the tomato juice was extracted to retain the skin, pulp and seeds which were then dried in an oven at 50°C for two hours. The dried parts were weighed and grinded in a blender and the resulting powder termed *Tomato Pomace Powder (TPP)* was kept in a clean airtight plastic container at room temperature till ready for use. The administration of TPP was performed by using propylene glycol as vehicle.

Chemicals

Propylene glycol was obtained from Guangdong Guanghua Science Tech. Co Ltd. (China). Ketamine was manufactured by Rotex Medica, Trittau, Germany. Lead acetate purchased from Femolak Chemical, Yemetu, Ibadan was manufactured by May & Baker Ltd, Dagenham England, Batch number L54/18/90. All other reagents were of analytical grade and were obtained from the British Drug Houses (Poole, Dorset, UK).

Administration of propylene glycol/ Lead acetate

Oral administration of propylene glycol (PG) was at a dose of 0.2 mL/rat/day using gavage. Lead acetate (LAc)

was prepared diluted with distilled water as stock solution from which the measured dose of 50 mg/kg body weight of rats was administered orally using gavage.

Experimental design: After the period of acclimatization, the thirty male rats were randomised into 5 groups of 6 rats each (Table 1). All treatments were given orally via gavage. The dose of TPP was based on the method of Thukhammee *et al*. (2012) while that of LAc was based on the method Shukla *et al*. (2003).

Table 1:
Research design

Grouping	Treatment
Group I	Control, 0.5 mL tap water daily.
Group II	Propylene glycol, PG, 0.2 mL daily for 42 days.
Group III	TPP, 50 mg/kg bwt daily for 42 days.
Group IV	Lead acetate, LAc, (75 mg/bwt) daily for 42 days.
Group V	TPP+LAc, (TPP, 50mg/kg bwt)+Lac (75 mg/kg bwt) for 42 days. These two doses were given at two hours interval.

PG, propylene glycol as vehicle; TPP, tomato pomace powder

Behavioural tests
On day 43 of the experiment (24 hours after the last dose of treatment), animals of all groups were weighed before they were subjected to behavioural assessment paradigm, namely: (1) Forelimb grip test, (2) negative geotaxis, and (3) open field test.

Forelimb grip test
A modification of the method of VanWijk *et al*. (2008) in which each rat was suspended with both forepaws on a horizontal steel wire (1 meter long, diameter 7 mm) was employed. Each rat was held in a vertical position when its front paws were placed in contact with the wire. When the rat grasped the wire, it was released, and the latency to fall was recorded with a stopwatch. Rats were randomly tested and each animal was given two trials with a 30 min inter-trial rest interval thus enabling muscle strength and balance to be assessed.

Negative geotaxis
Negative geotaxis was tested by placing rats head-down on an inclined plane and then watching the rat orient in a head-up direction (Kreider and Blumberg, 1999). The time it took for the rat to orient in a head-up direction was recorded with a stopwatch. The average of two trials was obtained.

Open field test
The method of Mohammad *et al*. (2010) was employed with slight modification. The apparatus consisted of a square arena (56×56×20 cm) made of white wood with its floor divided by lines into 16 squares that allowed the definition of central and peripheral parts. At the beginning of the session, each rat was individually placed in the centre of the arena and its activity was recorded for 5 min. The number of squares crossed with all paws (crossing) and standing on legs (rearing) were evaluated during 5 minute sessions. The crossing numbers were indicators of locomotor while the rearing numbers indicated vertical and exploratory activities. At the end of each session, each rat was removed from the open field and the experimental chamber was thoroughly cleaned with a damp cloth and dried.

Sample collection and histological preparation
On day 43 of the experiment, all animals in both control and experimental groups were weighed. Blood was collected via the retro-orbital venous sinus into heparinized bottles for haematological parameters. Rats were thereafter euthanized by ketamine (100 mg/kg) i.p. followed by cervical dislocation. Each rat was decapitated at the cervico-medullary junction for uniformity and the skulls opened after which the brains were quickly extracted and weighed. We adopted the method of Igado *et al*. (2012) wherein the right hemisphere, was preserved for histology and fixed in 10% neutral buffered saline for three days. The other half of the brain preserved for biochemical assays was rapidly rinsed, mopped with filter paper, weighed and kept in freshly prepared cold phosphate buffered solution (PBS) and then kept in the freezer till processed. The cerebellum and cerebrum of each animal were dissected and then preserved in 10% formalin and later processed for histology by paraffin embedment technique.

Determination of haematological values
K2 EDTA-added whole blood samples were used for hematological analyses immediately after collection with the aid of Sysmex Automated Hematology (KX-21, Kobe, Japan) Analyzer. The haematocrit or packed cell volume (PCV), haemoglobin (Hb), red blood cell count (RBC), mean cell volume (MCV), mean cell haemoglobin (MCH), and mean cell haemoglobin concentration (MCHC) and white blood cell count (WBC), were obtained.

Biochemical Assays
The left hemisphere of the brain samples was homogenized in 50 mM Tris–HCl buffer (pH 7.4)

containing 1.15% potassium chloride, and the homogenate centrifuged at 10,000 g for 15 minutes at 4 °C. The supernatant was collected for the estimation of the various biochemical bioassays. Lipid peroxidation was quantified as malondialdehyde (MDA) according to the method described by Farombi *et al*. (2000) and expressed as micromoles of MDA per milligram protein. Protein concentration was determined by the method of Lowry *et al*. (1951). Reduced glutathione (GSH) was determined at 412 nm using the method described by Jollow *et al*. (1974). Superoxide dismutase (SOD) was assayed by the method described by Misra and Fridovich (1972).

Histology

The cerebellum from each group was obtained and homologous sampling was assured by obtaining transverse sections of the right cerebellar hemisphere from each specimen from the lateral zone portions of the cerebella hemisphere (vermal, paravermal and flocullus portions were not utilized) for uniformity. Coronal sections of the right half of each brain were made to obtain samples of the cerebral cortex and hippocampal tissue. The brain was sectioned at 5-6 µm thickness and then stained with Haematoxylin and Eosin according to the method of Bancroft and Gamble, (2008). Thereafter, slides were examined on an Olympus CH (Japan) light microscope looking for possible neuronal damage or alterations of the histologic features of the cerebellum and hippocampus. Photomicrographs were acquired with a Sony DSC-W 3 digital camera (Japan) while photomicrograph calibration was done with Image J (Abramoff *et al*, 2004).

Statistical analysis

All data were expressed as means ± standard deviation. Data were analyzed using one-way analysis of variance (ANOVA) using GraphPad Prism 4.0 version software, San Diego, CA, USA. Post hoc comparisons were performed using Dunnett's test. Statistical significance was set at $p<0.05$.

RESULTS

Blood cells

Table 2 shows the alterations in the erythrocyte parameters i.e. packed cell volume (PCV), haemoglobin level (HgB), red blood cell count (RBC), mean corpuscular volume (MCV), and mean corpuscular haemoglobin concentration (MCHC) of the rats were not statistically significant ($p>0.05$) in the LAc group when compared with the control group. So also the TPP+LAc treatment did not elicit significant changes when compared with the LAc group. Table 3 shows that LAc treatment induced a 55% significant reduction ($p<0.05$) in the values of the neutrophils whereas the reduction of the WBC, lymphocytes and monocytes were insignificant when compared with the control. Pretreatment with TPP before LAc showed significant increase of the neutrophils whereas the increases in the WBC, lymphocytes and monocytes were not significant when compared with LAc group.

Concentration of Lipid Peroxidation and reduced glutathione (GSH)

In Table 4, LAc induced a significant increase in brain MDA level (72%) as compared with control group ($p<0.05$), administration with TPP+LAc recorded significant decrease in brain MDA content (47%) as compared with LAc group. Also LAc treatment elicited a significant reduction of GSH by (47%) when compared with the control, whereas TPP+LAc treatment produced a significant 1.8 fold increase in the level of GSH relative to the LAc as shown in the table.

Table 2:
Effect of Lead acetate and tomato pomace powder on Erythrocyte indices of male Wistar rats.

Groups	PCV (%)	HB (g/dL)	RBC ($x10^6$/µL)	MCV (fL)	MCHC (g/dL)
Control	44.0±2.5	15.1±0.3	7.26±0.3	60.0±1.6	33.33±0.5
PG	44.0±4.6	15.1±2.0	7.50±1.2	56.0±2.2	33.00±0.0
TPP	44.0±1.2	15.0±0.5	7.63±0.1	57.40±0.8	34.00±0.0
LAc	43.0±1.2	14.4±0.4	7.14±0.3	57.70±0.9	33.00±0.8
LAc+TPP	45.0±2.1	15.5±0.7	7.44±0.4	59.8±1.7	34.33±0.5

Data are expressed as Mean ± Standard Deviation of 6 rats in each group. PG, propylene glycol; TPP, tomato pomace powder. LAc, lead acetate.

Table 3:
Effect of Lead acetate and tomato pomace powder on the Leukocyte indices of male Wistar rats

Groups	WBC ($x10^3/\mu L$)	Cells ($x10^3/\mu L$)		
		L	N	M
Control	5.9±0.5	2.0±0.2	3.8±0.7	1.4±0.3
PG	5.5±0.3	2.0±0.9	2.7±0.7	1.2±0.1
TPP	5.9±0.4	1.9±0.4	2.8±1.8	2.1±0.1
LAc	4.7±0.3	1.7±0.2	1.7±0.5*	1.0±0.2
LAc +TPP	5.9±0.7	2.1±0.7	3.9±1.02**	1.5±0.1

L = lymphocytes; N = Neutrophil; M=monocyte
*Data are expressed as mean ± standard deviation of 6 rats in each group. PG, propylene glycol; TPP, tomato pomace powder. LAc, lead acetate. * P< 0.05 versus Control group; ** P< 0.05 versus LAc group.*

Table 4:
Effect of TPP on LAc-induced alterations in brain lipid peroxides (measured as MDA), GSH and SOD levels.

Groups	MDA Level (u moles/mg protein))	GSH Level (ug/ml/mg protein)	SOD/ Unit mg protein
Control	1.67±0.12	9.29±1.05	0.40±0.042
PG	1.15±0.07	3.69±0.04	0.29±0.02
TPP	1.03±0.19	3.13±0.94	0.22±0.13
LAc	2.88±0.96*	5.06±1.29*	0.63±0.17*
LAc+TPP	1.52±0.31**	11.59±3.71**	0.51±0.03

Data are expressed as mean ± standard deviation of 6 rats in each group. PG, propylene glycol; TPP, tomato pomace powder. LAc, lead acetate.
* P< 0.05 versus Control group; ** P< 0.05 versus LAc group.

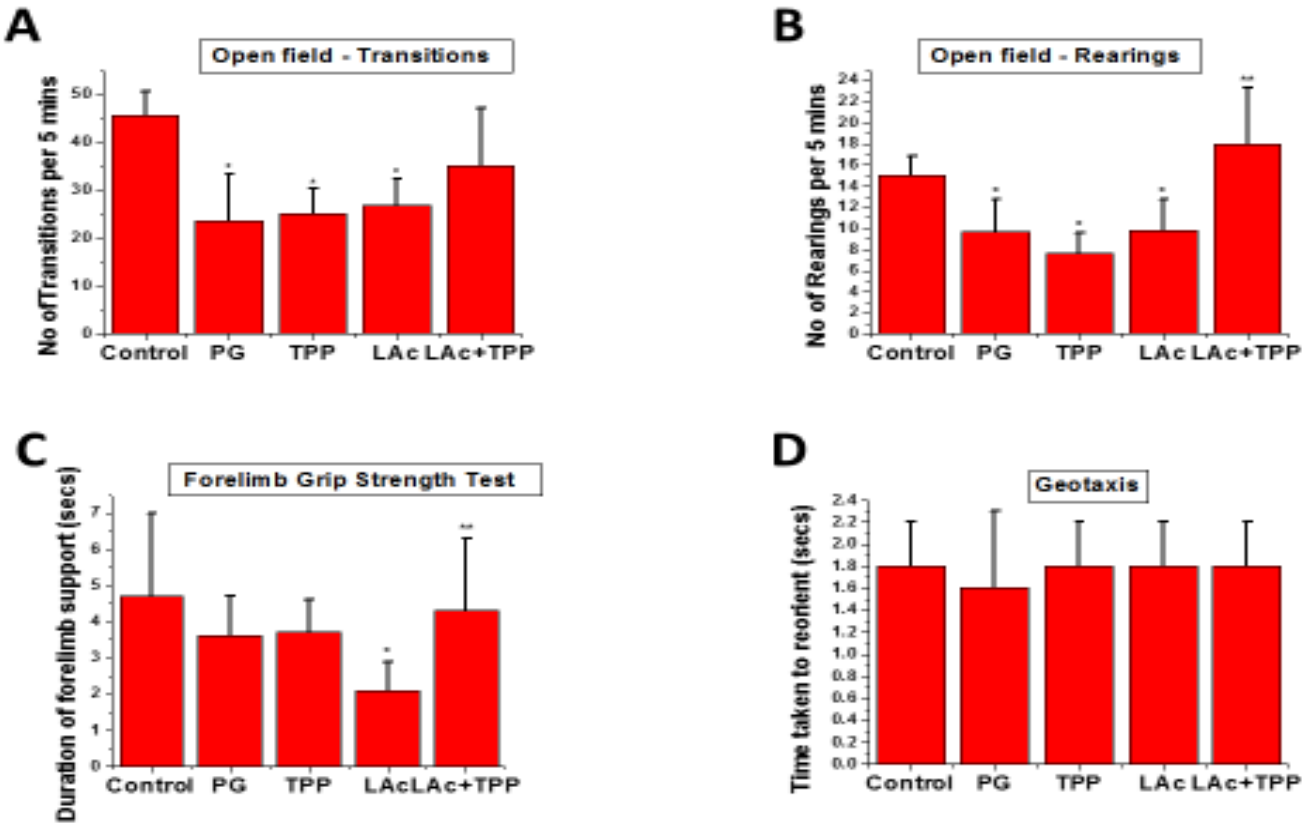

Figure 1: Histogram of behavioural tests in the control and treated groups. A: Horizontal movements (transitions), B: Vertical movements (rearings), C: forelimb muscular strength, D: negative geotaxis. Movements and forelimb strength were significantly reduced by LAc treatment. Pre-treatment with TPP ameliorated transition, rearing movements and forelimb strength significantly ($p<0.05$) while geotaxis was unaffected. TPP, tomato pomace powder; PG, propylene glycol; LAc, lead acetate. Values are expressed as mean ± S.D. of 6 rats in each group. * P< 0.05 versus Control group; **= P< 0.05 versus LAc group.

Activity of Antioxidant Enzyme SOD

Administration of LAc alone caused a significant rise ($p<0.05$) in the levels of antioxidant enzyme SOD (58%) when compared with control (Table 4). Rats treated concomitantly with TPP and LAc showed a non-significant rise in the level of SOD when compared with LAc alone.

Behavioural observations

The summary of the effect of LAc treatment on behavioural and locomotor activities of the rats is presented in Figure 1. The number of lines crossed, rearing, and forelimb grip were significantly reduced ($p<0.05$) by LAc treatment relative to control. There was however, significant increases in the TPP+LAc group of the rearing and forelimb grip when compared with the LAc alone group ($p<0.05$). There was no observable differences on the effect on geotaxis between the groups.

Histological parameters

Cerebellum : The normal histological layers of an adult rat cerebellum, namely: granular, molecular, and Purkinje are observed in Plates 1A, 1B, and 1C. LAc's effect on the Purkinje cells of the cerebellum is shown by the eosinophilic staining (Plate 1D) relative to the control. Observe in Figure 2E, that Purkinje cells exhibit the usual basophilic staining when compared with the LAc group.

Dentate gyrus: The histological features of dentate gyrus showing molecular layer, granule cell layer and the polymorphic layer are shown in Plate 2A, 2B, and 2C. The effect of LAc is shown in Plate 3D with some of the granule cell neurons undergoing pyknotic changes (arrowheads). Plate 2E shows some partial ameliorative effect of co-treatment of TPP with LAc when compared with Figure 3D.

Cornu ammonis3: (CA3): The CA3 subfield of the hippocampal formation of the control rats showed portions of the normal histological features of the stratum oriens, pyramidal cell layer, stratum radiatum, all of which show normal cytoarchitecture as shown in Plate 3A, 3B, and 3C. In Plate 3D, lead toxicity on the pyramidal neurons was exhibited by pyknotic neurons (arrowheads) among the few healthy neurons (arrows). Plate 3E shows the effect of co-treatment of TPP with LAc showing less pyknotic neurons (arrowheads) interspaced by relatively numerous healthy pyramidal neurons (arrows) compared with Plate 3D.

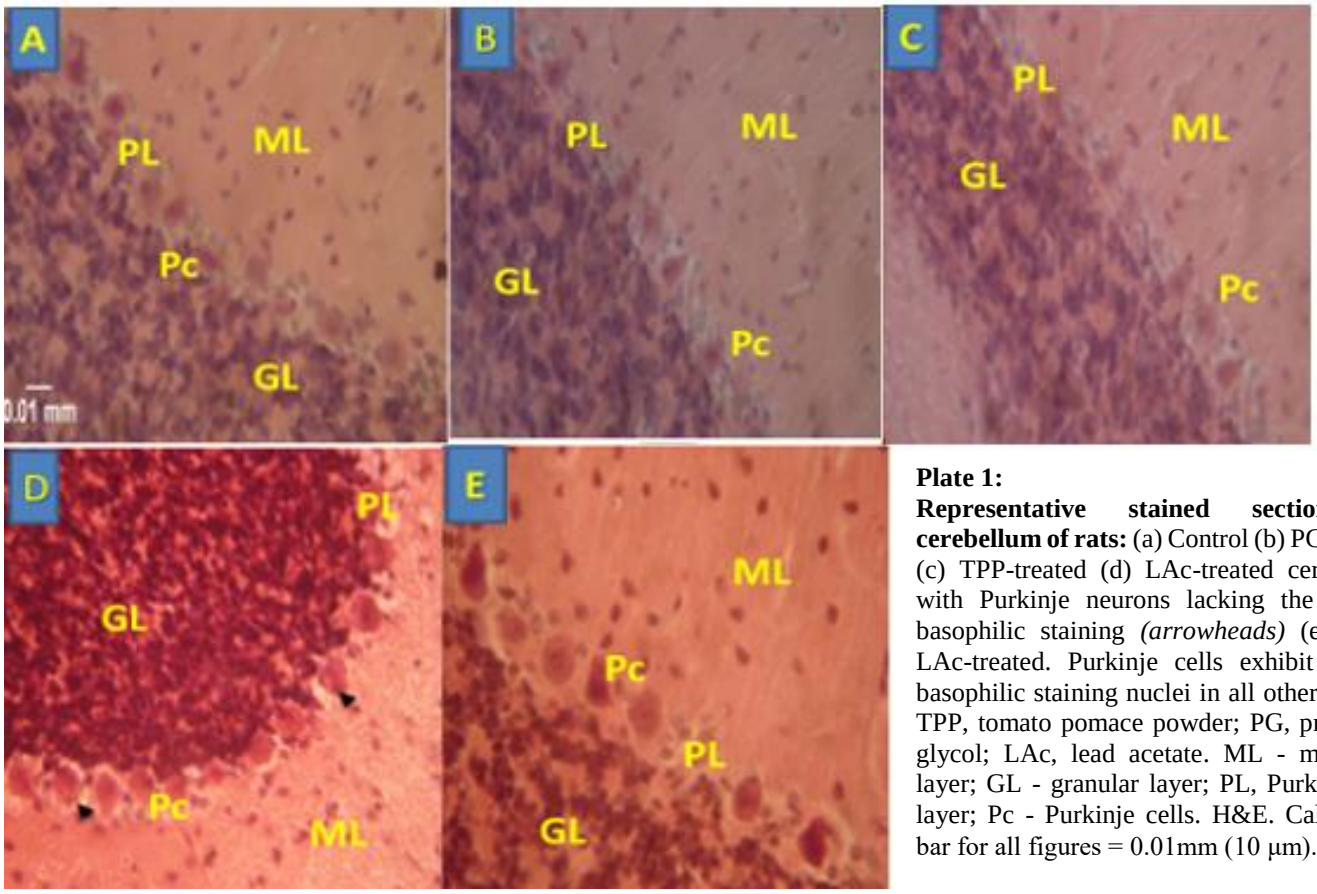

Plate 1:
Representative stained sections of cerebellum of rats: (a) Control (b) PG-treated (c) TPP-treated (d) LAc-treated cerebellum with Purkinje neurons lacking the normal basophilic staining *(arrowheads)* (e) TPP+ LAc-treated. Purkinje cells exhibit normal basophilic staining nuclei in all other groups. TPP, tomato pomace powder; PG, propylene glycol; LAc, lead acetate. ML - molecular layer; GL - granular layer; PL, Purkinje cell layer; Pc - Purkinje cells. H&E. Calibration bar for all figures = 0.01mm (10 μm).

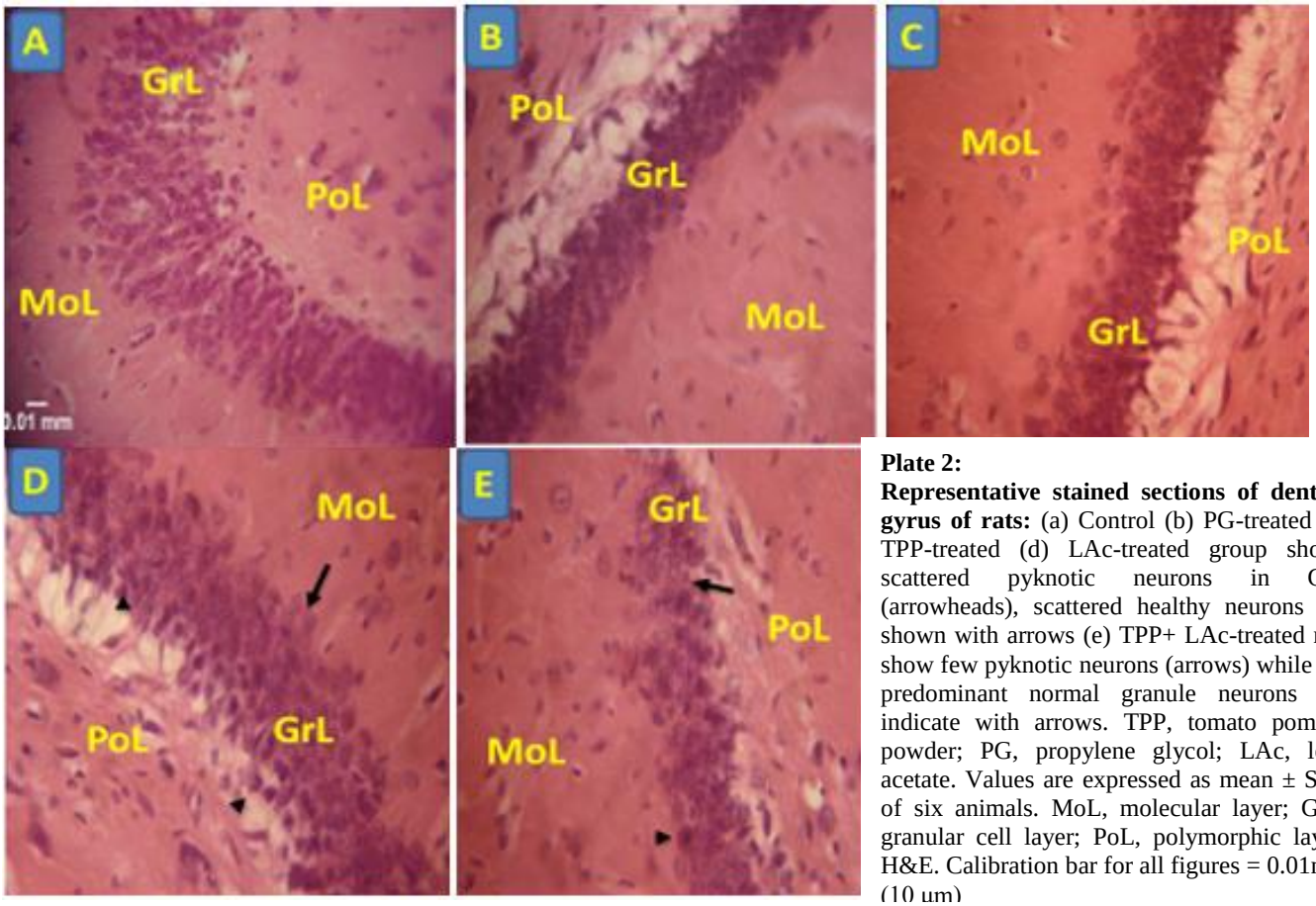

Plate 2:
Representative stained sections of dentate gyrus of rats: (a) Control (b) PG-treated (c) TPP-treated (d) LAc-treated group shows scattered pyknotic neurons in GrL (arrowheads), scattered healthy neurons are shown with arrows (e) TPP+ LAc-treated rats show few pyknotic neurons (arrows) while the predominant normal granule neurons are indicate with arrows. TPP, tomato pomace powder; PG, propylene glycol; LAc, lead acetate. Values are expressed as mean ± S.D. of six animals. MoL, molecular layer; GrL, granular cell layer; PoL, polymorphic layer. H&E. Calibration bar for all figures = 0.01mm (10 µm)

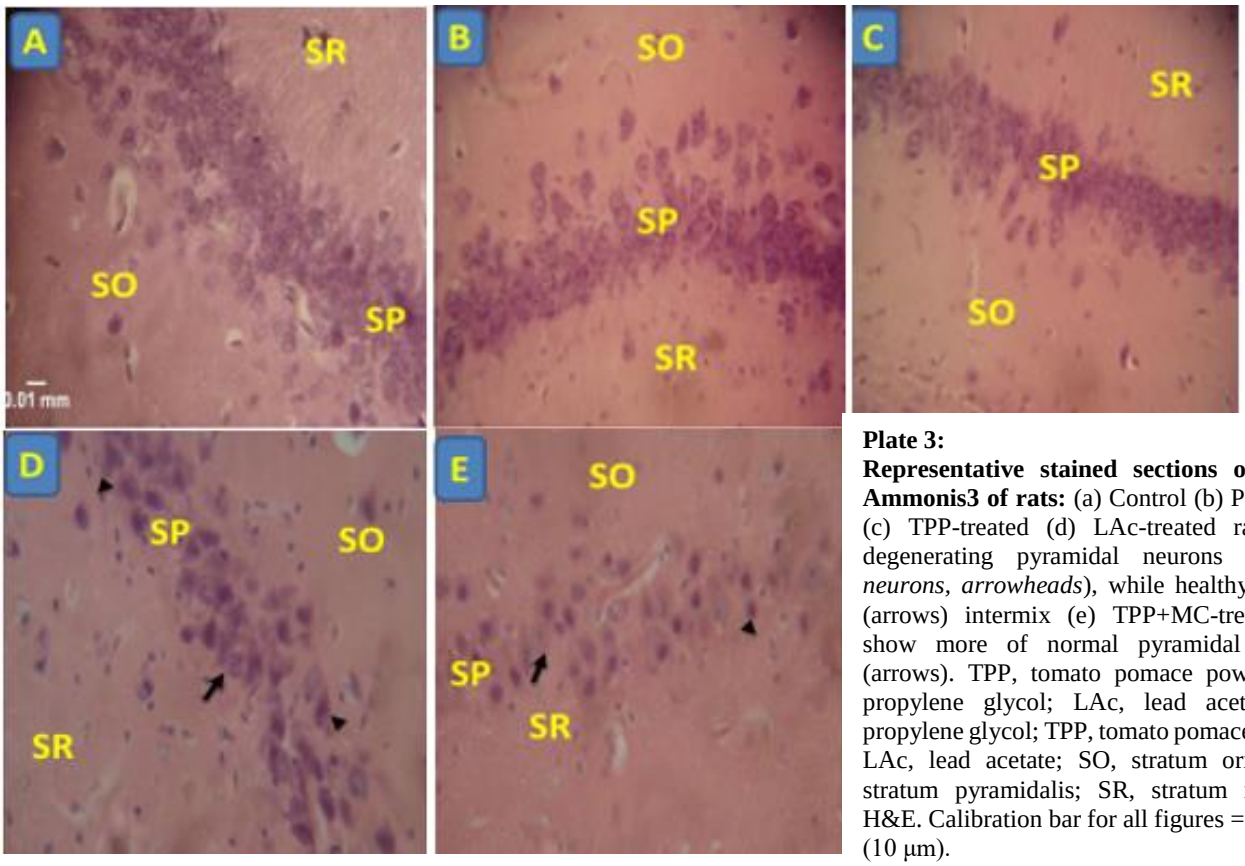

Plate 3:
Representative stained sections of Cornu Ammonis3 of rats: (a) Control (b) PG-treated (c) TPP-treated (d) LAc-treated rats show degenerating pyramidal neurons (*pyknotic neurons*, *arrowheads*), while healthy neurons (arrows) intermix (e) TPP+MC-treated rats show more of normal pyramidal neurons (arrows). TPP, tomato pomace powder; PG, propylene glycol; LAc, lead acetate. PG, propylene glycol; TPP, tomato pomace powder; LAc, lead acetate; SO, stratum oriens; SP, stratum pyramidalis; SR, stratum radiatum. H&E. Calibration bar for all figures = 0.01 mm (10 µm).

DISCUSSION

In this present study, our data demonstrated the ability of tomato pomace powder (TPP) obtained from *Lycopersicon esculentum*, in ameliorating some of the oxidative parameters, histological, haematological, behavioural alterations induced by lead acetate (LAc) treatment in male rats.

Our observation of increased aldehydic by-products like malondialdehyde (MDA) by lead treatment in rat brain is supported by previous reports (Bennet *et al*, 2007; El-Masry *et al*, 2004) and is an evidence of generation of free radicals which initiated lipid peroxidation which the MDA reflected. The reduction of GSH level reflects the consumption of tissue thiols in lead treated group which is in agreement with previous reports (El-sokkary *et al*, 2003; Sharma *et al*, 2010). The report of Wang *et al*. (2006) that decreased antioxidant function as part of oxidative stress being involved in lead-induced brain toxicity also explains this finding. Our report of an increase in SOD activity in the brain homogenates contrasts with that of El-sokkary *et al*. (2003) who observed a decrease. This difference might be due to an adaptive process leading to synthesis of more SOD to neutralize excess superoxide radicals generated in the course of this chronic study that spanned forty two days. However, the findings that co-treatment of TPP with LAc elicited reduction of the MDA level and the increase in the level of GSH and activity of the antioxidant enzyme SOD confirmed the reported antioxidant capability of tomato in neutralizing oxidative changes.

The findings that the haematological cells were not very sensitive to lead-exposure was a contrast to the reports of Kalia & Flora, (2005) and Flora *et al*. (2012). The erythrocytes parameters were unaltered while only the neutrophils were reduced by the lead exposure which was returned to normal by TPP co-treatment. Our findings in the behavioural tests showed the diminution of motor, exploratory skill, and reduction in forelimb muscular strength by LAc treatment which agrees with the report of Nehru and Sidhu, (2001) who used the same dose of 50 mg/kg for 8 weeks and obtained similar results. Co-treatment of LAc with TPP, ameliorated these parameters.

The observation of degeneration of Purkinje neurons in the cerebellum of LAc-treated brain of rats suggested that the prolonged exposure to lead treatment for 42 days induced toxicity in these neurons. This toxicity must have caused complete dissolution of the basophilic nucleic materials of Purkinje cells of the cerebellum of the rats showing eosinophilia, suggesting damage to neuron. Similarly, the degeneration of the granule cells of the dentate gyrus of rats with evidence of cell death in the LAc-treated group is evidence of lead-induced injury in the neurons. Co-treatment with TPP ameliorated this cell death partially. So also was the damage observed in the pyramidal neurons of the LAc treated Cornu Ammonis3 (CA3) of rats shown by the degenerating pyramidal neurons which was evidence of exposure to LAc treatment. However, co-treatment with TPP partially protected these neurons as shown by the reduction of degenerated neurons.

Compared to other organ systems, the nervous system is regarded to be the most sensitive for lead induced toxicity (Cory-Slechta, 1996; Hassan & Jassim, 2010). At higher levels, lead has been reported to cause permanent brain damage and even death (Cleveland *et al.,* 2008). The high level of malondialdehyde in the brain of lead-exposed rats suggested the potential for neuronal membrane damage and hence neurotoxicity which we reported. Increased reactive oxygen species leads not only to lipid peroxidation but may lead to enzyme inactivation, DNA damage and even cell death due to oxidative stress (Wu *et al*, 2003). This might explain the neuronal damage as shown in the Purkinje cells where the LAc-treated neurons lacked basophilic stain due to possible RNA and DNA damage, as well as the cell death demonstrated in the granule cell neuron of the dentate gyrus, as well as the pyramidal neurons of the CA3.

The lead-induced Purkinje cell damage may cause cerebellar injury leading gait, movement and posture impairments (Pisu *et al*, 2004). Similarly, the histological alterations caused by neuronal death observed in the dentate gyrus granule cells and those of the pyramidal cells of CA3 might disrupt the smooth flow of neural information from the entorhinal cortex to the granule cell neurons of dentate gyrus via the perforant path. This may in addition affect the onward projection of mossy fibres from granule neurons to the CA3 and CA1 subzones of the hippocampus as reported (Scharfman, 2007). With evidence of death of pyramidal neurons of CA3, the subsequent projection of impulses from CA3 via the Schaffer's fibres to CA1 may be affected further altering the flow of neural information. In essence, this suggests that memory and other hippocampal functions might potentially be affected in such rats (Scharfman, 2007).

Since antioxidants are known to ameliorate the effect of oxidative stress, our study has demonstrated the ability of tomato in protecting the brain components

studied from LAc-induced injury possibly via its antioxidant property. Its ability to provide protection from focal ischaemic cerebral injuries had been reported (Hsiao *et al*, 2007; Kanabur and Reddy, 2014). TPP was also reported to be beneficial in protecting against experimental stroke and improvement of cognition (Wattanathorn *et al*., 2012; Thukhammaee, *et al*., 2012).

Co-treatment of LAc with TPP demonstrated neuroprotection of the Purkinje neurons of the cerebellum, and partial histomorphological protection for the dentate granule cells of dentate gyrus and the pyramidal neurons of the CA3 of the hippocampus as demonstrated in the improvement in the histological features observed in the treated brains. The neurobehavioural test results and antioxidant activity of TPP suggested that TPP ameliorated these parameters thus contributed at least in part to the neuroprotection observed against LAc-induced neurotoxicity.

In conclusion, oral co-administration of *Lycopersicon esculentum as* TPP co-treatment offers relative protection from LAc-induced neuropathy, motor abnormality and oxidative impairment. Our data suggest that TPP may be useful in the modulation of lead acetate-induced intoxication in rat.

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