Protective Effect of *Carica Papaya* leaves and seeds against Electrolyte and Hematological Alterations in Albino Wistar Rats Exposed to Lead Nitrate

Abstract

Background: Exposure to lead produces a variety of adverse health effects. This study evaluated the protective effect of aqueous extracts of *Carica papaya* leaves and seeds against electrolyte and hematological alterations in albino Wistar rats exposed to lead nitrate. **Methods:** Thirty male albino Wistar rats weighing between 174- 196g were assigned to six groups of five animals. Group 1 served as control, group 2 received 50mg/kg body weight lead nitrate ($PbNO_3$), groups 3 and 4 received 500 mg/kg body weight aqueous extract of *Carica papaya* leaves (CPL) and *Carica papaya* seed (CPS) respectively, groups 5 and 6 received 50mg/kg body weight $PbNO_3$ + 500mg/kg body weight CPL and CPS respectively for 31 days by oral gavaging. Animals were sacrificed and blood collected for various assay using standard methods. ANOVA on SPSS version 25 was used to determine variations within and between groups. **Results:** Increases in sodium and potassium, and decreases in chloride, calcium and bicarbonate levels were observed in the lead intoxicated group. Treatment with CPL and CPS reversed the alterations in electrolytes. Levels of RBC, PCV, Hb, MCH, MCHC and lymphocytes were lower in the lead intoxicated group relative to the lead intoxicated groups complemented with CPL and CPS, while WBC, MCV and platelet counts were higher in the lead intoxicated group when compared to the group complemented with CPL and CPS. **Conclusion:** This finding suggests that CPL and CPS could be protective against lead induced alterations in electrolytes and hematological parameters and could be harnessed for these potentials.

Keywords: *Carica papaya* leaf and seed; lead nitrate; electrolyte; haematology

Introduction

Heavy metals are environmental pollutants owing to their toxicity, longevity in the atmosphere, and ability to bio-accumulate in the human body. Most heavy metals occur naturally, but their increased atmospheric and environmental levels are as a result of anthropogenic activities [1]. Heavy metals have harmful effects on human health, and exposure to these metals has been increased by industrial and Contamination of water, air and even food by toxic metals is a public health concern [2]. Heavy metals are characterized by their high atomic mass and toxicity to living organisms. Most heavy metals may be lethal to humans [1]. Exposure to heavy metals can occur through ingestion, absorption or inhalation. Exposure to heavy metals result in bioaccumulation in biological systems [3]. Metals may frequently react with biological systems by losing one or more electrons and forming metal cations which have affinity to the nucleophilic sites of vital macromolecules. Simultaneous exposure to two or more metals may have cumulative effects [4,5,6,7]. Low level exposure to lead has been linked with functional and structural impairments in both human and experimental animals [8]. The hematopoietic, nervous and renal tissues are the main targets of lead. Moreover, it hinders the efficiency of the hepatic, reproductive and immune function [9,10]. Approximately 90% of absorbed lead is reported to be stored in the bone with a half-life of 600 - 3000 days. The remaining 10% is stored in soft tissues like kidney, liver and brain. The half-life of lead in these tissues ranges from 40 - 50 days [11]. Lead is conjugated in the liver and passed to the kidney, where a small quantity is excreted in urine and the rest accumulates in various body organs, affecting many biological activities at the molecular, cellular and intercellular levels, which may result in morphological alterations that can remain even after lead levels have fallen [13,14,15].

Lead toxicity is closely related to its accumulation in various tissues and its interference with the electrolytes that hamper several physiological processes [16]. Electrolytes are structural components of body soft tissues like liver, muscle and also participate in acid-base balance and are components of blood buffers. Electrolytes play significant role in several body processes, such as controlling fluid levels, acid-base balance (PH), nerve conduction, coagulation and muscle contraction [12,17]. Fluid and electrolytes homeostasis is usually maintained within narrow limits [18] and therefore, it must be kept at a level that is suitable for normal biochemical and physiological functions [19]. Therefore, imbalance in serum electrolytes is an important indicator of toxicity in identifying target organs and general health status of animals. Lead is known to substitute for zinc in a number of enzymes in heme biosynthetic pathway and pyrimidine, 5- nucleotidasec, important for the correct metabolism of deoxyribonucleic acid (DNA) and can therefore cause fetal damage [20].

About 99% of the lead present in the blood is bound to erythrocytes. They have a high affinity for lead and contain the majority of the lead found in the blood stream, which makes them more vulnerable to oxidative damage than many other cells. Erythrocytes can spread lead to different organs of the body [21]. The alteration in hematological parameters serves as the earliest indicators of the effect of toxins in tissues. Therefore, abnormal alteration in blood parameters is one of the reliable indicators of toxic effects of drugs, chemicals and diseases in the body system [22]. Hematological effects of chronic toxicity of the Pb acetate (0.4%) in drinking water for 12 weeks in adult male rats showed significantly decreased red blood cell (RBC) count, while increasing total and differential WBC counts [23]. In humans, anemia may develop with Pb poisoning via the inhibition of ferrochelatase and δ-aminolevulinic acid dehydratase (ALAD), the two of many enzymes involved in heme biosynthesis. The inhibition of ferrochelatase and ALAD by lead decreases heme synthesis which leads to anemia [24].

The leaves of *C. papaya* have been shown to contain many active components that can increase the total antioxidant power in blood and reduce lipid peroxidation level, such as papain, chymopapain, cystatin, tocopherol, ascorbic acid, flavonoids, cyanogenic glucosides and glucosinolates. *C. papaya* leaf tea or extract also has a reputation as a tumor-destroying agent Kadiri et al. [25], in their study on 'chemical composition, functional and antioxidant properties of *Carica papaya* seed flour, protein concentrate and protein isolate', found the plant to possess metal chelating ability which increased as the concentration of the samples increased. The present study, investigated the protective effect of aqueous extracts of *Carica papaya* leaves and seeds against electrolyte and hematological alterations in albino Wistar rats exposed to lead nitrate.

Materials and Methods

Preparation of plant sample

The leaves of *Carica papaya* were plucked and washed with distilled water to be free from dirt or debris and other contaminants while the seeds were gotten from ripe *C. papaya* fruits which were cut into two halves so as to obtain the seeds easily. The leaves and seeds were air-dried separately for 2 weeks and blended into powdered form respectively. The blended leaves and seeds weighed 2492g and 1005g respectively. The blended leaves and seeds of *C. papaya* were soaked in 1500ml of distilled water for 24hours in an air-tight container and were kept in a room temperature (25^0C). The extracts were filtered, separating the residue from the solvent using a funnel and whatman No. 1 filter paper into separate well-labeled beakers. The solvents from both the leaves and seeds were concentrated in a water bath at 50^0 C for three consecutive days and slurry formed from the leaves and seeds samples were obtained and were preserved in a refrigerator at 4^0c to avoid spoilage until use.

Experimental design and animal grouping

Male albino rats weighing between 174g to 196g were obtained from the animal house of the Department of Science Technology, Biochemistry unit, Akwa Ibom State Polytechnic, Ikot Osurua. Animals were housed and maintained in wooden cages (47 by 35.5 by 33cm) with wire mesh covers on the cages at 25ºC under a 12:12 light/dark cycle, with free access to food and water. Experiments were carried out during the normal light/dark cycle and always started at the same hour (10 am). The animal study was conducted in accordance with the Ethical Guidelines for the Use of Animals in Research National Committee for Research Ethics in Science and Technology (NENT) [26].

Thirty adult male albino rats were randomly allocated to six groups of five rats each: **Group 1 (control):** Animals in this group served as control and received only 0.2ml of distilled water.

Group 2 ($Pb(NO_3)_2$): Animals in this group received 0.2ml lead nitrate at a dose of 50mg/kg body weight for 31 days by oral gavaging. The chosen dose fell within the ranges of doses applied in previous studies [27, 28].
Group 3 (CPL): Animals in this group received 0.2ml aqueous extract of *C. papaya* leaves at a dose of 500mg/kg body weight for 21 days by oral gavaging.
Group 4 (CPS) : Animals in this group received 0.2ml aqueous extract of *C. papaya* seeds at a dose of 500mg/kg body weight for 21 days by oral gavaging.
Group 5 (CPL + $Pb(NO_3)_2$): This group of animals received 0.2ml aqueous extract of *C. papaya* leaves (500mg/kg body weight) beginning eleven (11) days after the start of lead nitrate treatment [29]. An hour after the treatment with *C. papaya* leaves, the animals receive 0.2ml of lead nitrate (50mg/kg) [30].
Group 6 (CPS + $Pb(NO_3)_2$): This group of animals received 0.2ml aqueous extract of *C. papaya* seeds (500mg/kg body weight) beginning eleven (11) days after the start of lead nitrate treatment. An hour after the treatment with *C. papaya* seeds, the animals receive 0.2ml of lead nitrate (50mg/kg).
All experimental groups received treatment once daily for 3 weeks following 1 week treatment with lead nitrate for the lead treated groups. No group received above 1ml of extract or lead nitrate.

Collection of blood sample

After 24hours fast, the animals were anesthesized with chloroform on the morning of the 4th week. The unconscious animal was pinned down on the dissecting board with the help of a tag pin and was dissected medioventially and whole blood was collected from the aorta with the use of a syringe and needle using cardiac puncture method. The blood was immediately transferred into an EDTA bottle which contained anticoagulant to prevent blood clotting.

Determination of electrolytes

Serum sodium, potassium, and bicarbonate concentrations were determined using a spectrophotometer according to the method of Henry et al. [31] while chloride and calcium concentrations were determined according to the methods of Tietz [32] and Raysarkar [33] respectively.

Determination of hematological parameters

White blood cell, granulocytes, lymphocytes, monocytes, red blood cell, packed cell volume, hemoglobin, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, mean corpuscular volume and blood platelets were determined digitally with the help of Mythic 18 analyzer**.** Mythic 18 analyzer is used for assessment of full blood count using whole blood. The Mythic 18 is a fully automated in-house hematology analyzer performing hematological analyses on EDTA anticoagulated blood. For counting the cellular blood components, the Mythic 18 uses the impedance technique. A cyanide-free spectrophotometry method is used to measure hemoglobin by formation of oxyhemoglobin at 555 nm. Hematocrit is measured by volume integration. The sample volume is 10 µl. The instrument can determine 16 parameters in the normal mode and 18 in the research mode: white blood cell count (WBC) with absolute number and percentage of lymphocytes (LYM), monocytes (MONO), and granulocytes (GRAN), red blood cell count (RBC), hemoglobin concentration (HGB), packed cell volume (PCV), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC). For platelet counting, a floating threshold is used whereas for RBC and WBC counts, the thresholds are predefined. Results are provided within 1 min on the liquid crystal display (LCD) which is printed out on a printer and stored in the resident memory or in a USB key.

Statistical analysis

Results were analyzed using the IBM Statistical Product and Service Solutions (SPSS) version 25 and expressed as mean and Standard Error of Mean (SEM). Multiple Comparisons was made between control and experimental groups and among experimental groups using ANOVA. Significant differences among treatments were detected using LSD and values of $P < 0.05$ were considered statistically significant.

Results

Body weight of the experimental animals

Table 1 presents the body weight of experimental animals after treatment with lead and either *Carica papaya* leaves or seeds. Non- significant body weight gain was observed in all experimental groups except groups treated with *Carica papaya* seeds only and the lead treated group complemented with *Carica papaya* seeds which experienced weight loss.

Table 1

Body weight of the experimental animals

Group	Treatment	Initial weight (g)	Final weight (g)	Change in body weight (g)
1	Control	192.00±21.71	192.80±24.23	0.80±5.41
2	$Pb(NO_3)_2$	178.60±21.88	183.40±21.39	4.80±24.05
3	CPL	196.00±29.59	219.20±32.66	23.20±33.52
4	CPS	185.80±17.32	176.20±13.51	-9.60±6.84
5	$Pb(NO_3)_2$ + CPL	173.20±30.63	184.00±30.15	20.80±7.88
6	$Pb(NO_3)_2$ + CPS	192.80±29.68	182.60±28.67	-10.20±40.43

Pb(NO3)2 - Lead nitrate
CPL - *Carica papaya* leaves
CPS - *Carica papaya* seeds

Organ weight of experimental animals

Table 2 indicates that the liver weight of animals in all lead treated groups were non-significantly lower (P> 0.05) than the control and other groups, while the kidney weight was higher compared to all other treatment groups. There were however no significant changes in organ weights on complementing lead treatment with *Carica papaya* leaves and seeds. The heart and spleen of the groups treated with *Carica papaya* seed were however significantly reduced (P< 0.05) compared to the control.

Table 2: Organ weight of the experimental animals

Group	Treatment	Heart (g)	Liver (g)	Spleen (g)	Lung (g)	Kidney (g)
1	Control	0.82± 0.77	6.15 ±0.77	0.88±0.08	1.47±0.14	1.25±0.13
2	$Pb(NO_3)_2$	0.69± 0.05	5.52± 0.48	0.74±0.06	1.31±0.20	1.22±0.07
3	CPL	0.65± 0.72	6.79± 0.92	0.67±0.08	1.33±0.15	1.10±0.16
4	CPS	0.55± 0.47*	6.10±0.73	0.60±0.04*	1.57±0.23	0.99±0.09
5	$Pb(NO_3)_2$ + CPL	0.63± 0.09	5.66±0.75	0.64±0.12	1.36±0.12	1.05±0.15
6	$Pb(NO_3)_2$ + CPS	0.66± 0.03*	6.26±0.72	0.67±0.10	1.65±0.15	0.91±0.13

Values with * are significant compared to control (P< 0.05)
Pb(NO3)2 - Lead nitrate

CPL - *Carica papaya* leaves
CPS - *Carica papaya* seeds

The effect of aqueous extract of *C. papaya* leaves and seeds on Electrolyte concentration in albino Wistar rats exposed to lead nitrate

Table 3 shows a non- significant increase in serum sodium concentration of all the test groups when compared to control except for the group administered 500mg/kg of *C. papaya* leaf extract which was significantly higher when compared to control. Sodium levels were however non-significantly decreased in groups 5 and 6 when compared to group 2. A non-significant decrease ($P>0.05$) in the chloride levels were observed in all experimental groups when compared to control. A non-significant increase was however recorded in groups 5 and 6 when compared to group 2. Calcium levels were non-significantly increased ($P>0.05$) in groups 2, 4, and 5 when compared to control and non-significantly decreased ($P>0.05$) in group 6 when compared to group 2. Potassium levels recorded significant increase ($P<0.05$) in group 3 when compared to control and other test groups except for group 5. Groups 4, 5 and 6 were non-significantly decreased ($P>0.05$) when compared to control. Bicarbonate levels were non- significantly increased ($P>0.05$) in all test groups except group 3 when compared to control. The increases were higher in groups 5 and 6. The level of bicarbonate was decreased in group 2. when compared to all other groups.

Table 3
The effect of aqueous extract of *C. papaya* leaves and seeds on Electrolyte concentration in albino Wistar rats exposed to lead nitrate

Experimental groups	Treatment	Electrolyte Sodium Na^+	Concentration Chloride Cl^-	(mmol/l) Calcium Ca	Potassium K^+	Bicarbonate HCO_3^-
1	Control	146.0 ± 12.37[ab]	111.20 ± 3.12[a]	1.19 ± 0.04[a]	5.10 ± 0.21[a]	22.16 ± 1.40[a]
2	$Pb(NO_3)_2$	158.60 ± 3.14[a]	106.4 ± 2.06[a]	1.22 ± 0.2[a]	5.35 ± 0.08[a]	21.84 ± 0.74[a]
3	CPL	177.00±10.17[ac]	107.20 ± 2.57[a]	1.28 ± 0.10[a]	4.61 ± 0.09[b]	22.08 ±0.77[a]
4	CPS	162.00 ± 1.02[a]	106.80 ± 407[a]	1.20 ± 0.01[a]	5.20 ± 0.25[a]	22.19 ± 0.96[a]
5	$Pb(NO_3)_2$ + CPL	152.80 ± 9.7[a]	109.60 ± 3.58[a]	1.23 ± 0.1[a]	4.94 ± 0.50[ab]	22.72 ± 0.92[a]
6	$Pb(NO_3)_2$ + CPS	150.80 ± 4.73[a]	108.80 ± 2.17[a]	1.18 ± 0.1[a]	5.09± 0.16[a]	22.94 ± 0.84[a]

Result are expressed as mean ± standard error

Values in the same column with different superscript are significantly different.

Effect of aqueous extracts of *Carica papaya* leaves and seeds on hematological parameters in albino Wistar rats.

The result as presented in table 4, showed that all hematological parameters except MCV, and lymphocytes increased in the lead treated groups when compared to the control. A decrease in WBC, lymphocytes, RBC, PCV, Hb, MCH and MCHC and an increase in MCV and platelet count in the non-complemented lead group- 2, was observed when compared to the complemented lead treated group. The lead treated groups complemented with both *C. papaya* leaves and seeds (Groups 5 and 6) showed increases in WBC, lymphocytes, RBC, PCV, Hb, MCH and MCHC and a decrease MCV and platelet count when compared to the non-complemented lead treated group- 2

Table 4

The effect of aqueous extract of *C. papaya* leaves and seeds on hematological parameters in albino Wistar rats exposed to lead nitrate

Group	Treatment	WBC ($\times 10^3$)	Lymphocytes (%)	RBC ($\times 10^6$)	PCV (%)	Hb (%)	MCH (pg)	MCHC (g/dl)	MCV (fl)	Platelets ($\times 10^3$)
1	Control	7.00 ± 1.51^a	57.82 ± 7.52^b	6.18 ± 0.73^a	33.26 ± 3.80^a	12.52 ± 1.53^a	20.26 ± 0.39^a	37.50 ± 0.44^a	54.04 ± 0.89^a	448.40 ± 210.63^a
2	$Pb(NO_3)_2$	12.28 ± 1.86^a	68.48 ± 5.70^a	8.12 ± 0.48^{bd}	43.18 ± 0.94^b	16.48 ± 0.54^b	19.54 ± 0.29^a	37.54 ± 0.44^a	54.46 ± 0.90^a	999.20 ± 110.03^b
3	CPL	7.42 ± 1.57^a	58.96 ± 2.57^a	7.70 ± 0.21^b	40.38 ± 1.14^b	15.34 ± 0.51^b	19.88 ± 0.13^a	37.96 ± 0.34^a	52.30 ± 0.25^a	1012.80 ± 98.86^b
4	CPS	7.50 ± 1.97^a	65.52 ± 4.19^a	9.64 ± 0.66^{bc}	46.32 ± 1.22^b	17.64 ± 0.44^b	19.96 ± 0.29^a	38.10 ± 0.32^a	52.12 ± 0.78^a	997.20 ± 111.74^b
5	$Pb(NO_3)_2$ + CPL	10.08 ± 0.88^a	72.78 ± 2.54^a	8.45 ± 0.33^b	43.94 ± 1.46^b	16.64 ± 1.06^b	20.46 ± 0.30^{ac}	38.34 ± 0.36^a	53.42 ± 1.05^a	607.60 ± 109.26^{ac}
6	$Pb(NO_3)_2$ + CPS	11.96 ± 3.47^a	71.00 ± 3.99^a	8.16 ± 0.22^{bd}	43.46 ± 03.02^b	16.68 ± 0.45^b	20.44 ± 0.18^{ac}	38.60 ± 0.47^a	53.38 ± 1.01^a	920.00 ± 42.94^b

Values are expressed as mean ± SEM. Values in the same column with different superscript are significantly different.

KEY:

$Pb(NO_3)_2$	-	Lead nitrate
CPL	-	*Carica papaya* leaves
CPS	-	*Carica papaya* seeds
WBC	-	White Blood Cell
RBC	-	Red Blood Cell
PCV	-	Packed Cell Volume
Hb	-	Hemoglobin
MCHC	-	Mean Corpuscular Hemoglobin Concentration
MCV	-	Mean Corpuscular Volume
MCH	-	Mean Corpuscular Hemoglobin

Discussion

Exposure to lead produces a variety of adverse health effects including disorders of the central nervous, hematopoietic, hepatic and renal systems, especially in sensitive populations. This study evaluated the protective effect of aqueous extracts of *Carica papaya* leaves and seeds against electrolyte and hematological alterations in albino Wistar rats exposed to lead nitrate. Electrolytes play significant role in several body processes, such as controlling fluid levels, acid-base balance (PH), nerve conduction, coagulation and muscle contraction [12, 17]. Fluid and electrolytes homeostasis is usually maintained within narrow limits [18] and therefore, it must be kept at a level that is suitable for normal biochemical and physiological functions [19]. Therefore, imbalance in serum electrolytes is an important indicator of toxicity in identifying target organs and general health status of animals. Decrease in serum electrolytes concentrations of chloride, calcium and bicarbonate was observed in the group administered lead alone. This supports the findings of Okediran et al. [12]. Decreased plasma electrolyte levels is an indication in perturbation of electrolytes metabolism due to exposure to lead thus leading to alterations in cellular functions in which these electrolytes are involved. Studies have shown that lead can replace calcium, thereby affecting key neurotransmitters like protein kinase C, which regulates long term neural excitation and memory storage, it can also affect sodium ion concentration which is responsible for numerous vital biological activities like for the purpose of cell to cell communication, uptake of neurotransmitters and regulation of uptake and retention of calcium by synaptosomes [34, 53, 36, 37]. The ionic mechanism of action for lead mainly arises due to its ability to substitute other bivalent cations such calcium, magnesium, iron and monovalent cations like sodium ions, thus affecting various fundamental biological processes of the body by damaging cellular components [35, 36]. However, complementing lead with C. papaya leaves and seeds increased the levels of these electrolytes. This increase could be due to the rich array of phyto-nutrients and healing property *C. papaya* leaves on many chronic diseases [38, 25]. Sodium levels were however non-significantly decreased in the groups administered lead complemented with *C. papaya* leaves and; seeds when compared to lead alone group. The decrease observed in sodium and potassium levels of the lead groups complemented with *C. papaya* leaves and seeds was also reported by Eze [39] in albino wistar rats when administered with *C. papaya* seeds in a carbontetrachloride induced renal toxicity experiment. The elevated level of potassium in the lead treated group suggests that lead nitrate could have produced hyperkalemic effect, or excess potassium in the blood. This condition occurs in cases of renal failure because the kidney loses the ability to excrete the mineral. Severe dehydration could also produce hyperkalemia. This could also lead to alteration of the osmotic pressure of body fluids. Potassium levels however decreased in the group complemented with *C. papaya* leaves and seeds. The decrease in these two groups compared to the lead alone group indicates that *C. papaya* leaf and seed extracts could be used to modulate the alterations in renal function markers. *C. papaya* leaves and seeds may have protective effects against acute kidney damage especially if the damage is caused by accumulation of heavy metals [40].

All hematological parameters except MCV increased in the lead treated groups when compared to the control. Terayama [41] conducted a study that showed an increase in the levels of WBC when administered with lead. Jassim and Hassan [42], also reported that lead acetate when given orally to female rats at a dose of 10 mg/kg produced significant increase in percentage of WBC count and MCV. In contrast, a research conducted by Enagbonma et al. [43] revealed that when 0.10mg/kg of lead was administered to albino rats, the RBC levels reduced when compared to the control. This could be due to the difference in dosage of lead administered. In the present study, levels of RBC, PCV, Hb, MCH, MCHC and lymphocytes were lower in the non-complemented lead treated group when compared to the complemented lead treated groups, while WBC, MCV and platelet counts were higher in the lead intoxicated group when compared to the lead group complemented with C. papaya leaves and seeds. A study conducted by *Orji* et al. [44] also showed significant reduction ($P<0.05$) in the red blood cell count following treatment albino of rats with 75mg/kg lead. Okediran et al. [14], also reported inhibition of haem synthesis and reduction of packed cell volume following exposure to lead. In humans, anemia may develop with Pb poisoning via the inhibition of ferrochelatase and δ-aminolevulinic acid dehydratase (ALAD), the two of many enzymes involved in heme biosynthesis. The inhibition of ferrochelatase and ALAD by lead decreases heme synthesis which leads to anemia [24].
Treatment of lead intoxicated groups in the present study with both *C. papaya* leaves and seeds showed increases in RBC, PCV, Hb, MCH, MCHC and lymphocytes, and decreases in WBC, MCV and platelet count when compared to the lead intoxicated group. Sule et al. [45] and Oduola *et al*. [46] also reported similar trend as the plant *Carica papaya L* produced significant increases in PCV, Hb, RBC, MCV, MCH and lymphocytes. This suggests that the leaves and seeds of *C. papaya* could minimize the alterations of hematological parameters induced by lead intoxication in the albino rats. Consistent with the findings of this study are the reports of Oduola

et al. [46] and Sule et al. [45], that WBC levels were decreased in rats further treated with *C. papaya* seeds and leaves respectively.
Terayama [41], Al-Saleh [47], Enagbonma et al. [43], *Orji* et al. [44] and Savithri et al. [48] all reported that exposure to lead significantly decreased RBC counts values and Hb in rats but when *C. papaya* leaf extract was administered to albino wistar rats, there was a significant increase in the RBC and Hb levels. The decreased RBC in the lead treated group could be as a result of iron deficiency anemia, bone marrow disorder and chronic inflammatory diseases. According to Oduola *et al*. [46], MCV levels were decreased in rats also treated with 100mg/kg *C. papaya* leaves. The findings of this study corroborates that of Savithri *et al*. [48], where platelets count revealed a significant increase in intoxicated animals following treatment of albino rat with lead acetate. Platelet level was decreased in rats treated with *C. papaya* leaves [46]. This finding however contrasts a research conducted by Enagbonma et al. [43] who reported that following the administration of 0.10mg/kg of lead to albino rats, the platelet levels reduced when compared to the control. Sule et al. [45], reported that the levels of lymphocytes increased in rats pretreated with *Carica papaya* when compared with rats administered with CCl4 only. The increases in WBC observed in the lead intoxicated group in present study may be considered a defensive mechanism by the immune system in response to the antigen. However, treatment with *C. papaya* leaves and seeds tended to ameliorate this effect.
This may go a long way to suggesting that this plant may have influenced the defense mechanism of the test rats. So, the continuous exposure of the body systems of animals to *C. papaya* may cause lymphocytosis, which may then account for the use of these plants for medicinal purposes [49]. Earlier report made by Oladunmoye and Osho [50] revealed that the higher values of some haematological indices in rats pretreated with *Carica papaya* may be due to the inability of the toxicant to cause haemolysis resulting from the anti-inflammatory potentials inherent in the herb.

Xenobiotics can cause haemolytic anaemia when sulphydryl groups of the erythrocyte membrane is oxidized which inflicts injury to the erythrocyte membrane [45]. *Carica papaya* was reported to rank among the first fruits for vitamin C, vitamin A, riboflavin, foliate, calcium, thiamine, iron, niacin, potassium and fibre and may probably be responsible for *Carica papaya* conferring erythropoietic properties on the pretreated rats [51]. The haematological alterations were minimized by the administration of *Carica papaya* leaves and seeds. Flavonoids, reported to be present among other active components are known to be vasculo protector and a powerful antioxidant [51].

Conclusion
The study evaluated the protective effect of aqueous extracts of *Carica papaya* leaves and seeds against electrolyte and hematological alterations in albino Wistar rats exposed to lead nitrate Increases in sodium and potassium levels, and decreases in chloride, calcium and bicarbonate levels were observed in the lead intoxicated group. Treatment of lead intoxicated groups with CPL and CPS reversed the levels of the altered electrolytes. The hematological analysis revealed an increase in all hematological parameters except MCV when compared to the control. Levels of RBC, PCV, Hb, MCH, MCHC and lymphocytes were lower in the non-complemented lead intoxicated group when compared to the lead intoxicated groups complemented with CPL and CPS, while WBC, MCV and platelet counts were higher in the lead intoxicated group when compared to the lead intoxicated group complemented with CPL and CPS. This finding suggests

that *C. papaya* leaves and seeds could be protective against alterations in electrolytes and hematological parameters induced by lead toxicity and could be harnessed for these potentials.

Declarations:

Ethical Approval

The animal study was conducted in accordance with the Ethical Guidelines for the Use of Animals in Research National Committee for Research Ethics in Science and Technology (NENT) (2018).

Consent for publication
All authors have approved this manuscript for publication

Data Availability:
All datasets are available on the manuscript

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