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Research Article

Effects of Aqueous Extract of *Piper guineense* and Honey on Lead Induced Changes in The Bone Marrow and Thymus of Adult Wistar Rats

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Abstract: Lead is one of the hazardous heavy metal pollutants of the environment that originates from various sources. This study was carried out to investigate the effect of aqueous extract of *Piper guineense* and honey on lead induced toxicity in the bone marrow and thymus of adult albino Wistar rats. Thirty male Wistar rats were divided into six groups of five rats each. Group A served as the control, Group B as lead untreated group, Group C received 50mg/kg of the extract and 1000mg/kg of honey, Group D received 80 mg/kg of the extract and 1500mg/kg of honey, Group E received 80 mg/kg of the extract and Group F received 1500 mg/kg of honey for 14 days. 110mg/kg of lead was administered to Group B, C, D, E and F for seven days, while group C, D, E and F were treated with *Piper guineense* and honey for 14 days.

At the end of 14 days, the animals were sacrificed by cervical dislocation, blood was collected and the following organ thymus, bone marrow harvested. The tissues were processed using normal histological techniques. Haematological parameters and antioxidant activities were assessed.

The result showed lead distorted the histoarchitecture of both thymus and bone marrow, as shown in group B and haematological and antioxidant status. While the treated group showed regeneration of cells in both bone marrow and thymus, the effect was more pronounced in group treated with combination of extract and honey i.e group C and D and curative effect on haematological parameters.

In conclusion, aqueous extract of *Piper guineense* and honey could have a curative effect on lead acetate induced damage on the bone marrow and thymus.

Keywords: Lead, *Piper guineense*, honey, bone marrow, thymus.

Introduction

Lead is a naturally occurring toxic metal found in the Earth's crust. Its widespread use has resulted in extensive environmental contamination, human exposure and significant public health problems in many parts of the world (WHO, 2019). According to Haleagrahara *et al.,* (2011), toxic effect of lead is closely related to its accumulation in important tissues after its absorption into the blood. There are no known safe levels of lead exposures as even a small intake has an effect on the body particularly the brain and bones, so currently the approved clinical intervention method is to give chelating agents, which binds and removes lead from tissues (White *et al.,* 2007).

Medicinal plants are believed to be a rich source of antioxidants. Besides, they are cost effective and potent alternative with few and transient side effects in the treatment and management of disorders, when compared with the existing conventional therapeutic drugs available in the market (Pandey *et al.,* 2011; Sofowora *et al.,* 2013; Ortega-Ramirez *et al.,* 2014; Guan and He, 2015).

Piper guineense (Piperaceae), widely consumed as a spice in West Africa (commonly called African black pepper; with indigenous names such as Iyere in Yoruba and Uziza in Ibo), contain various biological and pharmacological properties. These properties have therapeutic potential in the prevention and management of hepatotoxicity. *P. guineense* has been recently reported to contain free radical scavengers such as polyphenols, alkaloids, flavonoids, saponins, tannins, and glycosides in appreciable quantities (Nwozo *et al.,* 2012).

Honey, a natural product formed from nectar by honeybees, has been a subject of renewed research interest in the last few years. Evidence indicates that honey can exert several health-beneficial effects such gastroprotective (Gharzouli *et al.,* 2002), hepatoprotective, reproductive (Al-Waili *et al.,* 2006; Mohamed *et al.,* 2012; Zaid *et al.,* 2010), hypoglycemic, antioxidant (Omotayo *et al.,* 2010), antihypertensive (Al-Waili *et al.,* 2003), antibacterial (Tan *et al.,* 2009), anti-fungal (Koc *et al.,* 2011) and anti-inflammatory (Kassim *et al.,* 2010), effects.

Studies have shown that honey, administered alone or in combination with conventional therapy, might be of therapeutic benefits in the management of chronic diseases commonly associated with oxidative stress. This study is aimed at evaluating the effect of aqueous extract of *Piper guineense* and honey on lead acetate induced damage on the bone marrow and thymus and haematological parameters.

Materials and Methods

Honey Purchase

Honey, brand name pure blossom honey, with a net weight 500g was bought from Roban Stores in Abakaliki town, Ebonyi State, and was stored in a cool dry place.

Lead Acetate

Lead acetate was obtained from histology laboratory of Alex Ekwueme Federal University Ndufu Alike, Ikwo (AE-FUNAI).

Ethical Clearance

The ethical clearance was sought from the ethical committee of faculty of Basic Medical Sciences, Alex Ekwueme Federal University Ndufu Alike Ikwo (AE-FUNAI) Ebonyi State.

Collection and Identification

The *Piper guineense* leaves were purchased from Margaret Umahi International market, Abakaliki, Ebonyi state. The leaves were identified at the Department of Plant Sciences and Biotechnology, Faculty of Sciences, University of Nigeria, Nsukka, Enugu state by Onyeukwu C.J., a taxonomist with the Department. The herbarium voucher number is UN12 and this served as the extract.

Preparation and Extraction of *Piper guineense*

Piper guineense leaves were washed and air-dried under room temperature for two weeks. The leaves were grinded into fine powder using an attrition mill (locally fabricated mill). The powder was soaked in water for 72 hours in the ratio of 100g to 50ml of water and the mixture in the container stirred regularly.

The mixture was filtered using a Whatman no. 1 filter paper. The filtrate was evaporated to dryness using water bath at a temperature of 40^{o}C. The powered extract was preserved in freezer until required for use.

Experimental Animals
Thirty male Wistar rats used were adopted from animal house of Alex Ekwueme Federal University Ndufu Alike, Ikwo (AE-FUNAI) and housed in netted cages under standardized condition of light and temperature and allowed access to feed and water during the seven days of acclimatization.

Experimental Protocols
The animals were divided into six groups of five animals

Group A served as control and received rat pellet and water only.

Group B (Lead untreated) received 110mg/kg of lead acetate.

Group C (Medium combined) received 50mg/kg, 1000mg/kg of extract and honey respectively.

Group D (High combined) received 80mg/kg, 1500mg/kg of extract and honey respectively.

Group E (*Piper guineense*) received 50mg/kg of extract.

Group F (honey group) received 1500mg/kg of honey.

Induction
All the groups received 110mg/kg of lead acetate except the control. The dosing was done orally by oral intubation, once daily (mornings) for 21 days based on the weight of the rats in each group. The animals were observed strictly after each administration daily for changes.

Treatment of Animals
The administration of the *Piper guineense extract* and honey was by oral intubation once daily for 14 days.

Animal Sacrifice
The animals were sacrificed by cervical dislocation after 24 hours of fasting and blood samples were collected from the orbital sinus of the rats for biochemical analysis according to the procedure described by Parasuraman *et al.,* (2010). The thymus was harvested, weighed and fixed in 10% formol saline. The tissue was processed using normal histological techniques.

Biochemical Analysis
Blood samples was collected and centrifuged at 4000rmp for 20mins and the serum was collected and used for the assessment of the following biochemical parameters.

Haematological Parameters
The haematological parameters including Haemoglobin (Hb), Packed Cell Volume (PCV), White Blood Cell (WBC) count, Red Blood Cell (RBC) count and platelet count were determined with the aid of an automated haematology analyzer (Mindray Hematology analyzer, BC-2300).

Assay for Anti-Oxidant Activities of the Extract and Honey
The antioxidant status of the animals was evaluated by measuring the concentration of catalase and supraoxide dismutase enzymes.

Statistical Analysis
Results were analyzed using Statistical Package of Social Sciences (SPSS) and results expressed as mean ± S.E and the presence of significant difference between means of groups was determined using one way analysis of variance (ANOVA).

Results

Effect on Body Weight

Table 1. The change in weight of the animals with lead acetate toxicity, treated with *Piper guinennse* extract and honey.

Groups	Initial weight (g)	Final weight (g)	Weight change (g)	Thymus
A	137.78±8.80	186.80±8.59	49.02±0.21	0.18±0.06
B	167.98±13.62	194.98±16.68	27.00±3.06r	0.02±0.02
C	134.64±4.24	173.88±9.28	39.24±5.04*	0.17±0.02
D	141.08±10.92	176.66±11.64	35.58±0.72*	0.15±0.02
E	138.94±4.50	158.38±3.47	19.44±1.03**	0.13±0.01
F	136.32±5.28	183.43±8.06	47.11±2.78*	0.11±0.01
*Significant increase compared to B at P<0.01; ** Significant decrease compared to B at P<0.01; Significant decrease compared to A at P<0.01				

Haematological Parameters

Table 2. The effect of aqueous extract of *Piper guinennse* on the haematological parameters of lead acetate induced toxicity in adult Wistar rats.

GROUP	A	B	C	D	E	F
TWBC	6.30± 0.10	8.25± 0.15*	7.80± 0.10a	10.35± 0.15**	8.65± 0.15	8.65± 0.25
Lymph%	69.15± 0.85	73.50± 0.5*	58.00± 1.0a	55.90± 0.20a	49.30± 0.7a	66.55± 0.45a
Mono%	10.40± 0.10	10.45± 0.15	11.45± 0.0**	17.40± 0.10**	17.85± 0.0**	12.35± 0.15**
Gran%	21.50± 0.10	15.75± 0.0*r	31.45± 0.1**	27.50± 0.50**	33.60± 0.1**	21.80± 0.10**
Lymph#	4.50± 0.15	5.95± 0.05*	4.55± 0.15a	5.65± 0.05**	4.21± 0.11a	5.75± 0.15
Mono#	0.70± 0.10	0.85± 0.05	1.05± 0.15	1.86± 0.06	1.56± 0.06	1.15± 0.15
Gran#	1.65± 0.25	1.55± 0.25	2.55± 0.15	2.65± 0.05	3.00± 0.10**	1.75± 0.05
PDW%	12.40± 0.10	12.65 ±0.10	16.40± 0.3**	10.60± 0.10a	13.85± 0.05a	13.95± 0.15a
PCT%	0.50± 0.10	0.52± 0.02	2.21± 0.11**	0.51± 0.10a	0.51± 0.05a	0.59± 0.02a
Note: TWBC-total white blood cells; LYMPH %- Relative Lymphocytes count; MONO%-Relative Monocyte count; GRAN %- Relative Granulocytes count; MONO#-Absolute Monocyte count; LYMPH#-Absolute Lymphocytes count; GRAN#-Absolute Granulocytes count.						
*Significant increase compared to A at P≤0.01; ** Significant increase compared to B at P≤0.01; *r Significant decrease compared to A at P≤0.01; a Significant decrease compared to B at P≤0.01						

Table 3. The effect of aqueous extract of *Piper guinennse* on the haematological parameters of lead acetate induced toxicity in adult Wistar rats.

GROUP	A	B	C	D	E	F
RBC	7.39± 0.23	8.17± 0.14	0.71± 0.06a	7.50± 0.04	7.11 ± 0.10	7.38 ± 0.15
HGB	15.85± 0.15	17.90± 0.1*	16.50± 0.50	16.85± 0.35	16.80± 0.50	16.00 ± 0.30
PCV%	46.80± 0.20	52.60± 0.4*r	4.25± 0.05a	50.10± 0.10a	48.40± 0.2a	47.45± 0.15a
MCV	66.85± 0.25	65.65± 0.55	66.10± 0.20	67.70± 0.30**	68.40± 0.4**	65.40 ± 0.50
MCH	21.95± 0.05	22.90± 0.05	415.65± 0.5**	22.50± 0.45	23.60± 0.40	21.80 ± 0.10
MCHC	32.95± 0.05	33.90± 0.10	643.15± 0.5**	32.70± 0.10	33.90± 0.10	33.05 ± 0.15
RDW-SD	66.75± 0.45	58.00± 0.3*r	40.95± 0.3a	66.65± 0.35**	60.05± 0.1**	57.90 ± 0.20
RDW-CV	21.50± 0.50	19.10± 0.4*r	13.50± 0.5a	20.90± 0.10**	18.70± 0.3a	18.90± 0.40a
PLT	565.00± 1.00	556.00± 1.00*	1452.50± 1.50**	523.50± 1.50a	537.50± 1.50a	625.00± 1.00a
MPV	9.05 ± 0.25	9.30 ± 0.20	11.30± 0.10**	8.50± 0.50a	9.050± 0.35a	9.55 ± 0.35a
PDW%	12.40± 0.10	12.65± 0.10	16.40± 0.3**	10.60± 0.10a	13.85± 0.05a	13.95± 0.15a
PCT%	0.50 ± 0.10	0.52± 0.02	2.21± 0.11**	0.51± 0.10a	0.51± 0.05a	0.59± 0.02a

Note: RBC-Red blood cells ($x10^{12}$/l); HGB-Haemoglobin (g/dl); PCT-Platelet count (%); PCV-Packed cell volume (%); MCV-Mean cell volume (Fl); MCH-Mean cell haemoglobin (Pg); MCHC-Mean cell haemoglobin concentration (g/dl); RDW-SD-Red cell distribution width-standard deviation (fl); RDW-CV-Red cell distribution width-coefficient variation; PLT-Platelet count ($x10^{9}$/l); MVP-Mean platelet volume (fl) and PWD-Platelet distribution width (%).

*Significant increase compared to A at P≤0.01; **Significant increase compared to B at P≤0.01; *r Significant decrease compared to A at P≤0.01; a Significant decrease compared to B at P≤0.01

Table 4. The effect of aqueous extract of *Piper guineense* on the oxidative stress markers of lead acetate induced toxicity in adult Wistar rats.

GROUP	A	B	C	D	E	F
SOD	18.10± 0.40	16.20± 0.50*	17.39± 0.41	15.95± 0.55**	20.85± 0.25*r	16.75± 0.55
CAT	27.70± 0.30	24.60± 0.40*	26.00± 0.20*r	26.95± 0.35*r	37.10± 0.10*r	28.55± 0.45*r

* Significant decrease compared to A at P≤0.01; ** Significant decrease compared to B at P≤0.01; *r Significant increase compared to B at P≤0.01

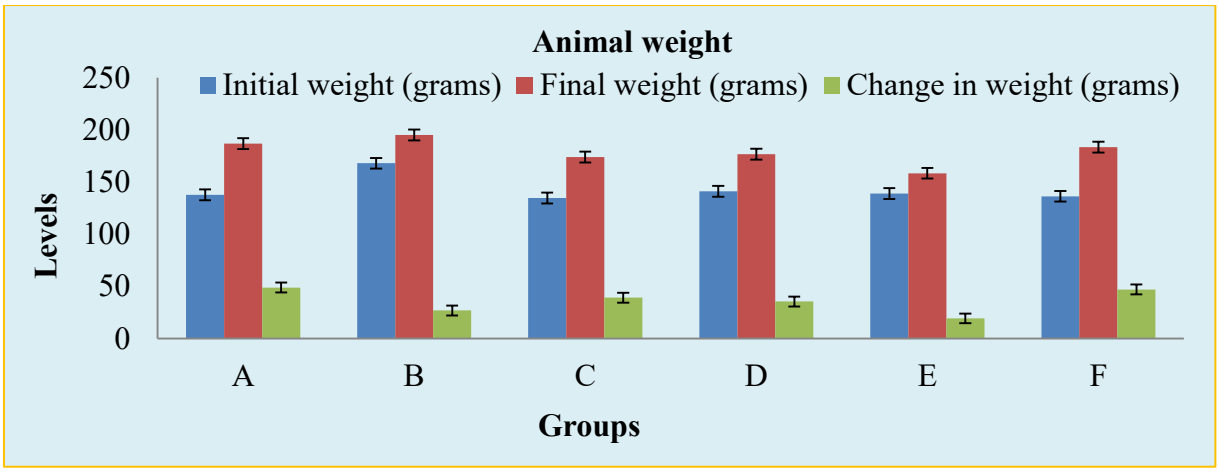

Figure 1. The Chart showing effect on body weight of the animals during lead acetate induction and after treating with *Piper guinennse* and honey.

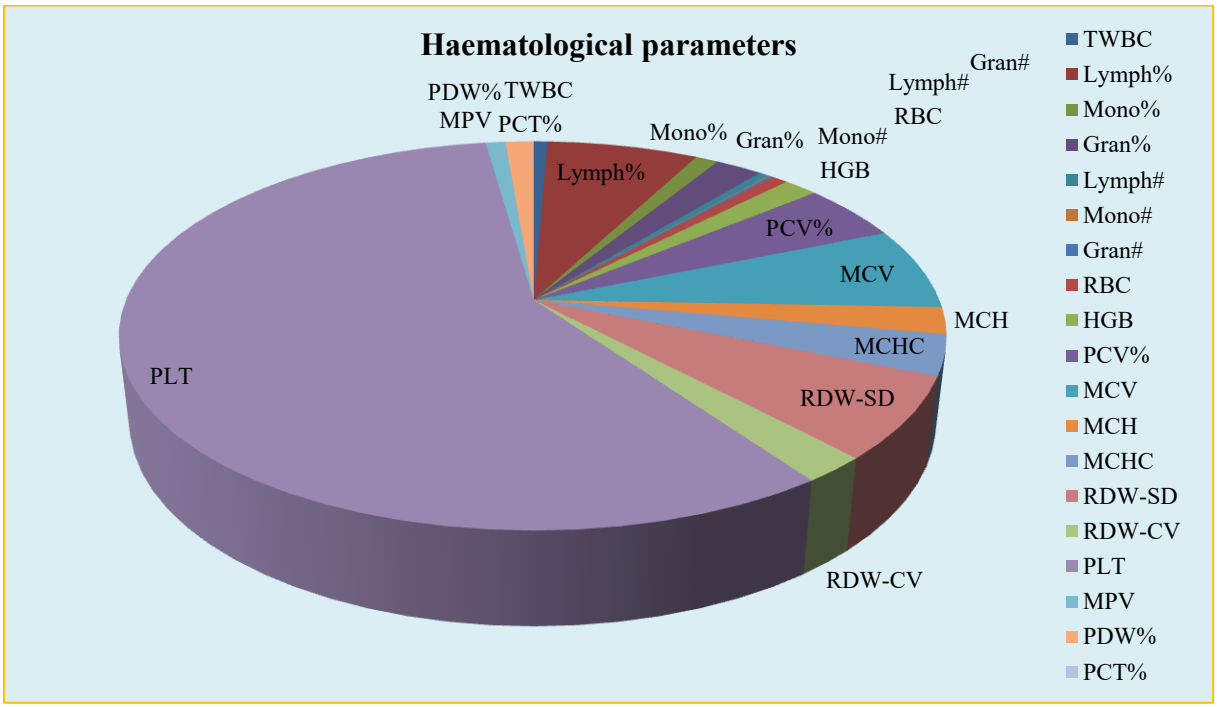

Figure 3. A pie chart showing the effect of aqueous extract of *Piper guinennse* on the haematological parameters of lead acetate induced toxicity in adult Wistar rats.

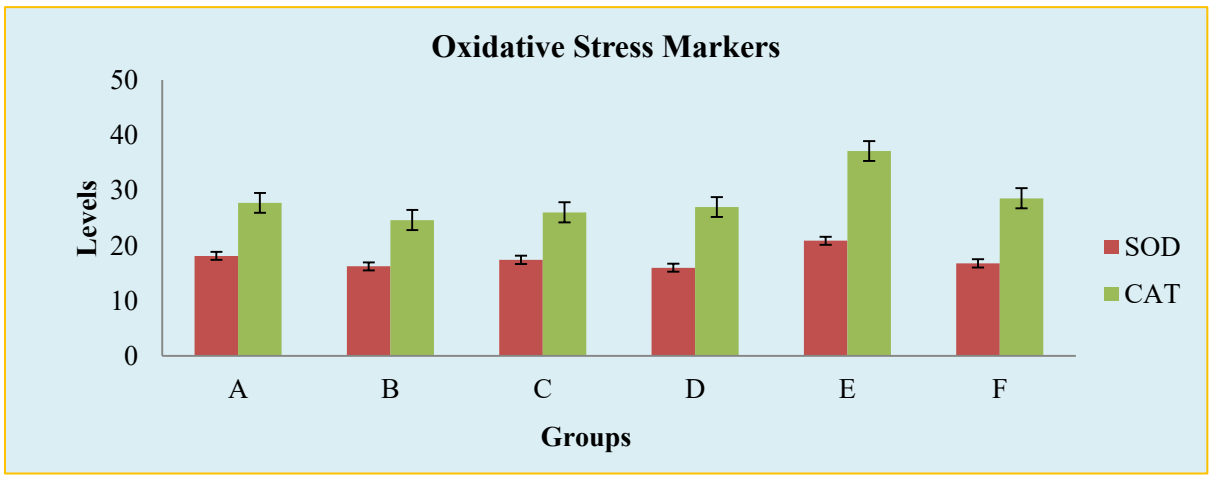

Figure 4. The chart showing the effect of aqueous extract of *Piper guinennse* on the oxidative stress markers of lead acetate induced toxicity in adult Wistar rats.

Histology
Bone marrow cytology

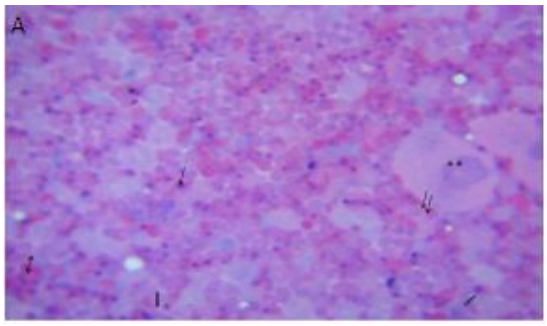

Figure 1. Section of group A bone marrow cytology smear showing many nucleated cells such as Endothelial cells (double arrow), sinusoids (line), megakaryocytes (**), granulocyte (arrow head), orthochromatic erythroblast (double head arrows) (X400) (GIMSA)

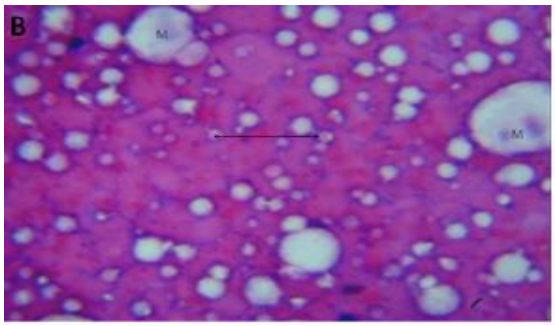

Figure 2. Section of group B bone marrow cytology smear showing significant nuclear abnormalities with severe atrophied granulocytes (double head arrow), megakaryocyte with lost nuclei (M) and all the cells lost their nuclei (X400) (GIMSA)

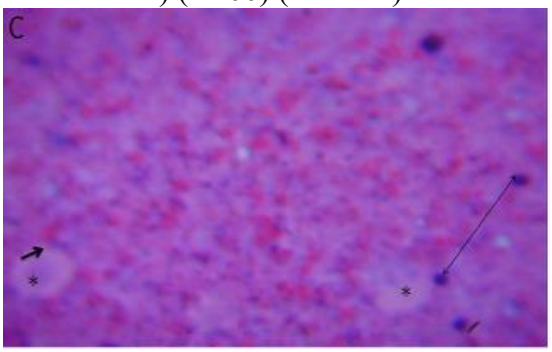

Figure 3. Section of group C bone marrow cytology smear showing regeneration of atrophied granulocytes (double head arrow), megakaryocyte with young nuclei (*), reappearance of endothelial cells (arrow) (X400) (GIMSA)

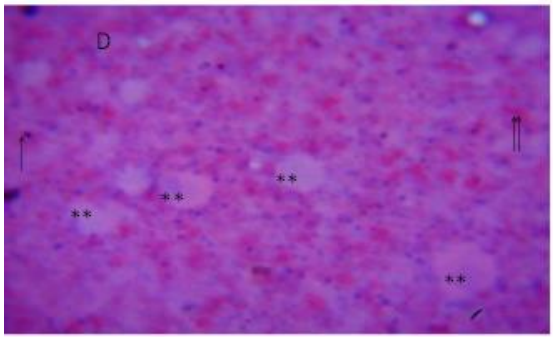

Figure 4. Section of group D bone marrow cytology smear showing increased regeneration of atrophied granulocytes (double head arrow), young megakaryocyte with young nuclei (**), reappearance of eosinophil myelocyte (arrow), orthochromatic erythroblast (double arrows) (X400) (GIMSA)

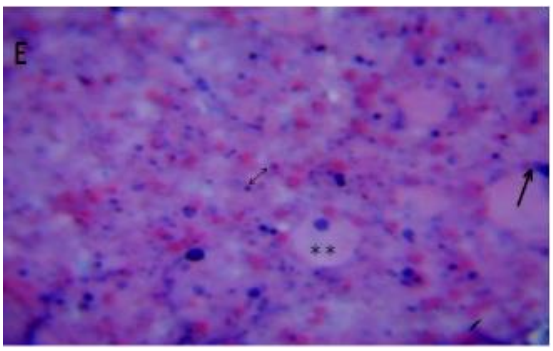

Figure 5. Section of group E bone marrow cytology smear showing regeneration of granulocytes (double head arrow), megakaryocyte with mature nuclei (**), endothelial cells (arrow) (X400) (GIMSA)

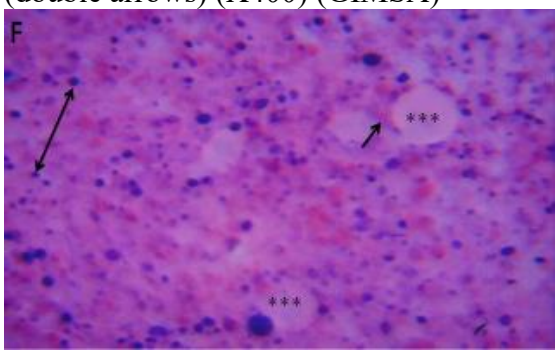

Figure 6. Section of group F bone marrow cytology smear showing granulocytes scattered all over the marrow (double head arrow), megakaryocyte with nuclei (***), reappearance of endothelial cells (arrow) (X400) (GIMSA)

Histology of the thymus

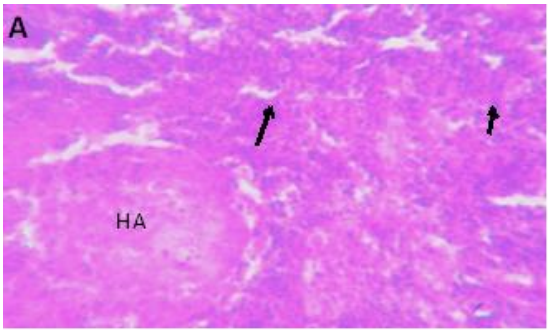

Figure 7. A section of group A (control) thymus showing normal thymus cortex (C), Hassall corpuscle (HA), neutrophils (arrows) X100, H & E

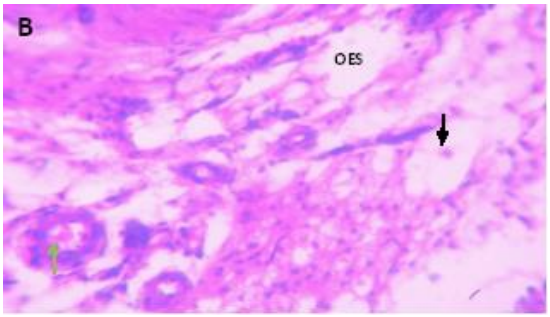

Figure 8. A section of group B thymus showing necrotic cells within the Hassall corpuscle (HA) (green arrow), optical empty spaces within the thymus (OES), cell apoptosis (black arrow), fatty changes within the cortex (circle) X100, H & E

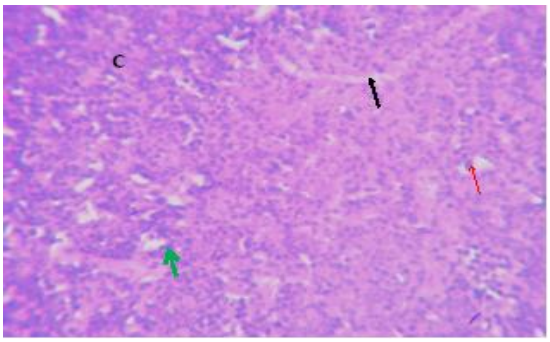

Figure 9. A section of group C thymus showing trabecular (black arrow), macrophage (red arrow), neutrophil (green arrow) X100, H & E

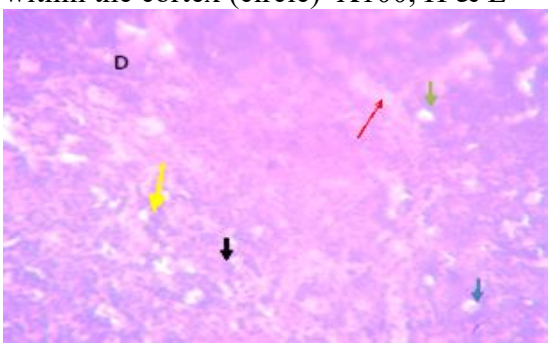

Figure 10. A section of group D thymus showing thymic reticular cell (yellow arrow), neutrophil (black arrow), macrophages (green arrows) scattered in the tissue, trabecular (red arrow) X100, H & E

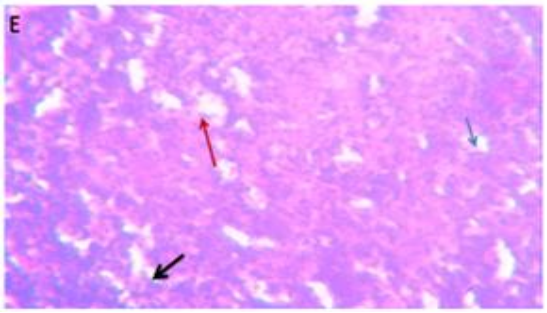

Figure 11. A section of group E thymus showing necrotized cells such as macrophages (blue arrow), neutrophils (black arrow) and reticular cells (red arrow) X100, H & E

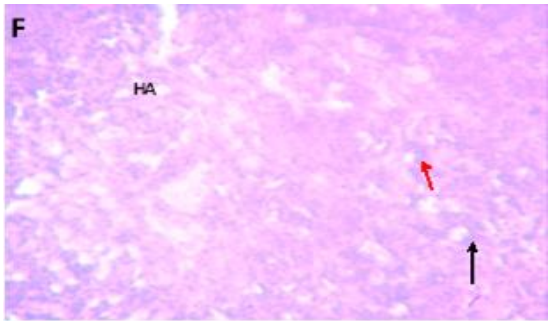

Figure 12. A section of group E thymus showing charred thymic Hassall corpuscle (HA), neutrophil (red arrow), macrophage (black arrow) X100, H & E

Discussion

Lead has been affirmed as a principal lethal metal pollutant to both humans and other living organisms. Occupational and environmental exposures to this toxic metal remain a global health problem (Abdel *et al.,* 2016). Lead-induced oxidative damage has been proposed as one of the important mechanisms of lead-related pathologies (Patrick, 2006). In addition, chelating agents exert detrimental effects and are incapable of alleviating some toxic effects of lead (Ajayi *et al.,* 2009). In

recent times, several studies have been focused on sourcing for alternatives and potentially safe treatments for lead toxicity. Consequently, to mitigate adverse effects of lead toxicity, natural compounds with both chelating and antioxidant activities are considered as good candidates (Bokara *et al.,* 2008). *Piper guineense* and honey seem to be the natural alternative to the chelating agents that we are looking for. The antioxidant activities of both have been reported (Khan *et al.,* 2018). This study showed that there was reduction in mean body weight of the rats in the untreated group (group B) when compared with the rats in the Control group. The weight loss was statistically significant with $p \leq 0.01$ as shown in table 1 above. Loss of appetite, sluggish, lethargic behavior was observed. This agrees to previous study by Ebeye *et al.,* (2007) in which reduction in the mean body weight anorexia is caused by lead acetate exposure.

Mbongue *et al.,* (2005) and Franca and Ibiwari (2019) reported in their work that *P. guineense* and honey increases body weight. The groups which received medium and high dose of *P. guineense* combined with honey showed a significant increase in weight ($p \leq 0.01$) as compared to group B. This agrees with the works of Nwozo *et al.,* (2012), Franca and Ibiwari (2019) which state that sufficient amount of *P. guineense* and honey causes weight gain which may imply that the dose of honey given was high enough to cause body weight increase. In group E which received *P. guineense* alone, it was observed a significant decrease in weight compared to the untreated group which disagrees with previous works done by Ochei *et al.,* (2017); Wassawa *et al.,* (2017), while group F which received honey alone showed a significant increase in body weight in agreement with Atangwho *et al.,* (2020).

It was observed during this study, that the thymus gland in all the groups administered with lead acetate showed a statistically significant ($p \leq 0.01$) decrease in weight in agreement with the study by Okechukwu, *et al.,* (2019). The untreated group showed a significant decrease in weight compared to A as shown in table 2 above. The increment in weight in the treated groups C, D, E and F compared to the lead acetate untreated group indicates a curative effect of both *P. guineense* and honey. The weight of the thymus of the rats in group C which were treated with medium dose of combined *P. guineense* and honey increased significantly ($p \leq 0.01$) closer to the control (group A) which may imply that the medium dose of combined *P. guineense* and honey are effective as curative agents.

The organ weight analysis showed that high doses of *P. guineense* and honey in single states do not make as much difference in its curative properties compared to their combined state. In our study the administration of lead caused a significant increase on total white blood cell (TWBC), when compared to the negative control and decreased in the group treated with the extract and honey when compared to the positive control. There was equally a significant increase in the monocyte count and platelet count in the in the treated groups, compared to negative and positive control. This increase in monocyte count shows that *P. guineense* and honey are an immune-stimulant agent. Previous studies have showed that honey is an immune-stimulant which agrees with our current findings (Fiorani *et al.,* 2006; Goji *et al.,* 2020).

Our study also showed an increase in haemoglobin (Hb), pack cell volume (PCV) increased, in the lead treated group, which decreased in the treated group, when compared to the positive control. This suggests that the extract and honey has a curative effect which could be attributed to the antioxidant properties. Herbal antioxidants have been reported to play a role in ameliorating lead-induced toxicity. They exert their antioxidant properties through the chelating of metal ions, breaking oxidative chain reactions, improving anti oxidative defense enzymes and the scavenging of free radicals (Russo *et al.,* 2003). Aribo *et al.,* (2019) and Goji *et al.,* (2019) in separate studies have report the anti-anaemic properties of *P. guineense* and honey. Aribo *et al.,* (2019) reported an increase in RBC and MCH as a result of the consumption of *P. guineense*, while Goji *et al.,* (2020) reported increase in haemoglobin (Hb), pack cell volume (PCV) and red blood count (RBC). The haemto-curative effect of honey against Cisplatin, Zinc etc has also been reported (Bhalchandra *et*

al., 2018). In our study, mean levels of SOD, and Catalase decreased significantly in the positive control group compared with other groups, while the group treated with honey and *P. guineense* showed a significant increase, these results indicate that the extract of *P. guineense* and honey have free radical scavenging properties, which stabilizes the plasma membrane of blood cells. Moreover, the bioactive components (flavonoids, phenols, etc.) of the *P. guineense* extract possess free radical scavenging properties that help to prevent oxidative damage, cell injury, and cell death.

In previous studies, the extract of *P. guineense* leaves exhibited free radical scavenging properties (Aihiokhai and Okpiabhele, 2022). Honey has been proven to be rich in both enzymatic and nonenzymatic antioxidants such as catalase, flavonoids and other polyphenols, as well as vitamins such as thiamine, riboflavin, pyridoxine, pantothenic acid, ascorbic acid, and nicotinic acid (Gheldof *et al.,* 2002; Kishore *et al.,* 2011; Abubakar *et al.,* 2012). These are responsible for its antioxidant properties. Previous studies have showed that lead poisoning causes a distortion in the histoarchitecture of the bone marrow (Owolabi *et al.,* 2017). The histological examination of sections of the bone marrow in the present study in group A, displayed normal bone marrow histoarchitecture and showing many nucleated cells such as the endothelial cells, sinusoids, megakaryocytes, granulocytes and orthochromatic erythroblast as shown in figure 1.

On the other hand, the untreated lead group portrayed features that could differentiate it from the control such as reduced number of cells, nuclear abnormalities, atrophied granulocytes as well as megakaryocytes without nuclei as shown in figure 2. This agrees with the work of Owolabi *et al.,* (2017) which states that there is less abundant background materials or elements in bone marrow affected by lead toxicity, indicating either a less heamopoietically active marrow or a marrow relatively richer in adipose tissue.

The histological examination of the sections of the bone marrow in medium dose (group C) of combined *P. guineense* and honey as treatment showed a gradual regeneration of the atrophied granulocytes and megakaryocytes as indicated by the presence of young nuclei in figure 3. This is an indication of a high curative effect of *P. guineense* and honey at medium dose. In the high dose of *P. guineense* and honey, it was observed that there an increased regeneration of granulocytes and megakaryocytes compared to the low dose. There was also reappearance of eosinophil myelocyte and orthochromatic erythroblast as shown in figure 4.

The *P. guineense* alone showed a regeneration of granulocytes and presence of mature megakaryocyte with nuclei which may indicate the efficacy of *P. guineense* as an anti-inflammatory agent at high dose (figure 5). The honey group alone shows a section of bone marrow with numerous granulocytes scattered all over it. We also observed the reappearance of endothelial cells and megakatryocytes with nuclei which is an indication of the anti-inflammatory effect of high dose of honey on lead toxicity, see figure 6.

The microscopic examination of the thymic tissue of the control group section (group A) revealed normal histology (figure 7) while that of untreated lead group B showed various distortion of the tissue such as the presence of necrotic cells within the Hassall's corpuscle and optical empty space due to the effects of toxicity on the organs and also cell apoptosis as well as fatty changes within the cortex as shown in figure 8. In group C, it was observed the presence of trabecular, macrophage and neutrophil as shown in figure 9 indicating mild healing of the thymus and the curative effect of *P. guineense* and honey at medium dose.

In the high dose group (D), recorded an increase in the thymic reticular cells, neutrophils, and macrophages scattered within the tissue, see figure 10. This may imply that combine usage of *P. guineense* and honey can useful as an anti-inflammatory agent. In group E, it was observed the presence of necrotized cells such as macrophages, neutrophils and reticular cells as shown in figure 11 indicating little or no curative effect of high dose of *P. guineense*. There were presence of charred

thymic Hassall's corpuscle, neutrophil and macrophage as shown in figure 12 which implies that there is little or no curative effect of high dose of honey.

Conclusion

This present study has shown that lead poison can lead to haemotoxicity and distortion of the histoarchitecture of thymus and bone marrow. This toxicity can be ameliorated by *P. guineense* extract and honey.

Declarations

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