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HYPOLIPIDEMIC SCREENING OF *Urena lobata* LEAF METHANOLIC EXTRACT IN LEAD-INDUCED HYPERLIPIDEMIC MALE SWISS WISTAR RATS

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Abstract

Cardiovascular diseases (CVDs) remain a leading cause of morbidity and mortality worldwide, with hyperlipidemia being a major predisposing factor. Exposure to heavy metals, such as lead (Pb), has been implicated in the exacerbation of hyperlipidemia. Despite the ethnopharmacological use of *Urena lobata* in treating various ailments, its potential effects on heavy metal-induced hyperlipidemia have not been thoroughly investigated. This study evaluated the lipid-modulating effects of methanolic leaf extract of *Urena lobata* (ULLME) in lead-induced hyperlipidemic male rats. Leaves of *Urena lobata* were collected, authenticated, processed, extracted with 70% methanol-water mixed solvent, concentrated and re-constituted. Thirty male Wistar rats were divided into five groups (n=6): normal control, lead-induced (60 mg/kg lead acetate, intraperitoneally), and three respective treatment groups that received 100, 300, and 500 mg/kg ULLME orally daily after induction for ten days. The animals were assessed for serum lipid profile on the eleventh day. Data obtained were expressed as Mean ± SEM and analyzed by one-way ANOVA with Tukey's post hoc test ($p < 0.05$). Lead exposure significantly increased triglycerides and total cholesterol (TC) levels and decreased high density lipoprotein cholesterol (HDL-C), indicating hyperlipidemia. Treatment with ULLME at doses of 100, 300, and 500 mg/kg significantly reduced both serum triglycerides (from 185±17.02 mg/dL in untreated to 85.44±17.03, 130.67±11.5, and 135.69±14.07 mg/dL in the groups treated with 100, 300 and 500 mg/kg.bw, respectively) and serum TC levels. Notably, only the 500 mg/kg.bw dose significantly increased HDL-C (from 285±17.07 mg/dL to 400.19±11.81 mg/dL). Low density lipoprotein cholesterol (LDL-C) was significantly lowered with 500 mg/kg.bw dose (102.63±12.75 mg/dL) but showed no significant change at lower doses. *Urena lobata* methanolic leaf extract demonstrated dose-dependent LDL-C-lowering and HDL-raising effects in lead-induced hyperlipidemic rats. The extract is a potential therapeutic agent in managing heavy lead-induced hyperlipidemia. Further studies should elucidate the molecular mechanisms underlying thetherapeutic effects observed.

Keywords: Cardiovascular disease, Heavy metal, High-density lipoprotein cholesterol, Hyperlipidemic, *Urena lobata,* Lipid-lowering

Introduction

Cardiovascular diseases (CVDs) describes many diseases affecting the heart and, or the circulatory vessels and include hypertension, dyslipidemia, atherosclerosis, heart failure, myocardial infarction, and cerebrovascular dysfunction (Flora & Nayak, 2019; Jensen et al., 2024). CVD is a leading cause of morbidity and mortality globally, with 19.8 million death recorded in 2022 (Idowu, 2022), representing 32% total global mortality (World Health Organisation (WHO), 2025). Hyperlipidemia, marked by higher bodily lipid level than optimum, results from elevated blood levels of triglycerides and cholesterols and is a strong predisposing factor to cardiovascular dysfunction (University of Ottawa Health Institute, 2025). Other factors, such as exposures to heavy metals (including lead), poor dietary habits, tobacco use, and increasing rates of obesity have also been observed to exacerbate hyperlipidemia in humans (Bays et al., 2019).

Ethnopharmacologically, organs of various plants are used in different forms to treat myriads of diseases, including malaria, gonorrhea, leucorrhea, hematemesis, carbuncle, trauma, bleeding, cold, fever, pain, and numbness from rheumatism, wounds, toothache, and inflammation (Jia et al., 2010).*Urena lobata*(Caesar's weed), a member of the *Malvaceae* family, is found in Asia, South America, and Africa (Babu et al., 2016). The aerial part of *U. lobata* is used as an anti-inflammatory, anti-pyretic, antalgic, antibacterial, and amoebicidal agent for the treatment of fever, rheumatism, bronchitis, diarrhea, dysentery, edema, gastritis, cough, nephouritis, pneumonia, gingivitis, menorrhagia, and emmenagogue (Jia et al., 2010). The root of *U. lobata* is used as a diuretic and could be applied externally to treat lumbago and rheumatism. A decoction of the stem and root is used to treat windy colic. In dry coughs, the flowers are used as a pectoral and expectorant. Flowers infusion is also used as a gargle for aphthae and sore throat (Islam, 2017).

Heavy metals environmental assaults emanate from industrial effluents, mining, smelting of iron, combustion of fossil fuels, waste and biomass burning, manufacturing, use and disposal of electronic gadgets, and a host of other human initiated processes. Essential heavy metals, such as Fe, Mn, Cu, Zn, Co, Ni, Mo and Se are required in biological systems for fundamental metabolic purposes (Aziet al., 2018). Some of these essential heavy metals serve as cofactors that are functionally and structurally important for biological catalysis. However, high levels of these minerals in biological systems result to unhealthy metabolic disturbances (Anyawu, 2020). Non-essential heavy metals include Pb, Cd, Hg, As, Sn, Al, Ag, Au, Sb, Bi, Pd, Pt, V, Sr, Te, Ti, U, and Cr (particularly Cr (VI)) (Tchounwou *et al.,* 2012). Non-essential heavy metals have no known metabolic benefits to the living systems and could be toxic at low concentrations (Azi et al., 2019). Food and water are the main route through which toxic heavy metals enter into biological systems, including mammalian bodily systems.

Pb has been reported to bioaccumulate in plants and enter into the blood circulations of mammals that feed on the affected plants, where it elicits toxicity (Wegwu & Omeodu, 2010). Pb exerts its toxic effect by mimicking and antagonizingthe native activities of divalent cations such as $Fe^{2+}$and Ca^{2+} (Colin et al., 2022).When Pb^{2+} interacts with biomolecules whose native cofactors or coordinating ions are divalent essential heavy metal ions, it hampers normal metabolism (Rolić et al., 2025). The resultant metabolic disturbance can lead to varied downstream effects, including distortion in central nervous system functioning, vitamin D metabolism,

heme biosynthesis, reproductive health, brain and kidney functioning, and gastro-intestinal integrity (Kennelly et al., 2023; Wani et al., 2015).

Lead poisoning was implicated for the death of 163 people (including 111 children) in Zamfara State in 2010 (Yahaya, 2010) and 42 people (of which 82.3% are children) in Sokoto State in 2024 (Africa Centre for Disease Control and Prevention, 2024), in Nigeria. Unauthorized and illegal mining of gold ores(apparently containing high levels of Pb) caused widespread contamination of soil and drinking water sources with Pb. High concentration of Pb was detected in the blood of Nigerian children, many of whom had suffered from headaches, vomiting, abdominal pains, seizures and death (Anyanwu et al., 2018). Artisanal mining operations, similar to that in Zamfara State have been spreading across the country, and a recent investigation suggests that about two million people in Southwestern Nigeria may be at risk of Pb and Hg poisoning (Vanguard, 2021). Lead toxicity has been linked to hyperlipidemia among others (Pan et al., 2024; University of Ottawa Health Institute, 2025).

Several case management options for hyperlipidemia are in operation (Singh, 2024). However, disparities in access to healthcare, knowledge gap, and funding worsen the outcomes of dyslipidemic case management in a manner that disproportionately affect marginalized populations (WHO, 2025). Comprehensive strategic approach, including the use of medicinal plant and their derivatives, could prove effective in managing CVDs, including hyperlipidemia. Although a lot of studies have been carried out on *U. lobata,* there is paucity of data on the potential of the methanolic leaf extract of *U. lobata* in preventing hyperlipidemia induced by Pb toxicity. Therefore, this study investigated the effects of *Urena lobata* methanolic extract on heavy metal-induced hyperlipidemia in male rat model.

Materials and Methods

Urena lobata plant was collected from a farmland at Omi-Adio area of Ibadan, Ido Local Government, Oyo State, South-Western part of Nigeria. The identification and authentication was carried out at Forestry Research Institute of Nigeria (FRIN), Ibadan, Oyo State, with voucher sample number, FHI-112616.

Leaves of *U. lobata* were rinsed with plentiful tap water, drained and oven-dried at 40°C before being pulverized into fine particulate size. The pulverized samples were macerated in a glass jar containing 70% methanol in water solution for 72 hours with intermittent mechanical agitation. The resultant suspension was filtered through Whatmann No1 filter paper. The filtrate was concentrated at 40°C using a rotary evaporator (Buchi Rotavapor RE-3, BuchiLabortecknic, Switzerland) and stored at 4°C transiently for dyslipidemic study.

Thirty (30) male rats (Wistar strain) weighing 140±20g were obtained from the Animal Facility of Babcock University, were acclimatized for 14 days during which water and feed were provided *ad libitu*. Animal housing, caging and handling during the study followed the National Institute of Health (NIH) guideline for care and use of laboratory animals as regulated by the local research ethics authority.

The animals were randomly assigned five (5) experimental groups of six (6) rats each. Each rat was administered daily with 60 mg/Kg lead acetate intraperitoneally for 10 days. After two (2) hours of induction each day, *Urena lobata* Leaf Methanol Extract (ULLME) was orally given to the animals. The animals were

appropriately tagged for easy identification within each group.

Group 1: received standard chow and distill water orally.

Group 2: received intraperitoneal administration of 60 mg/Kg lead acetate

Group 3: received oral administration of 100 mg/Kg ULLME

Group 4: received oral administration of 300 mg/Kg ULLME

Group 5: received oral administration of 500 mg/Kg ULLME

Animals were sacrificed on the eleventh day after overnight fasting. Blood was collected from the animals by cardiac puncture into lithium heparin tubes and centrifuged at 4,000 rpm at room temperature for 15 minutes to obtain the serum. The sera, which were stored at -10ºC for not more than three days, were used for lipid profiling. The remains of the animals were disposed according to standard regulation.

The sera lipid profiles; high density lipoprotein cholesterol (HDL-C), total cholesterol (TC) and triglycerides (TG), were estimated following procedures from commercially available kits (Randox Laboratories Limited, UK) while low density lipoprotein cholesterol (LDL-C) was calculated following the Friedewald's formula:

$$\text{LDL Cholesterol} = \text{Total Cholesterol} - \frac{Triglycerides}{5} - \text{HDL Cholesterol}$$

Experiments were performed in triplicates and values were expressed as mean ± standard error of mean. One-way analysis of variance (ANOVA) on GraphPad Prism® version 8.0.2 was used to compare the values obtained. Variations in mean values of experimental groups were assessed using Tukey Kramer post-hoc analysis at $p< 0.05$.

Results

Triacyglycerol Concentration

Data in Fig. 1 showed that 100 mg/kg b.w. (85.44±17.03 mg/dL), 300 mg/kg b.w. (130.67±11.5 mg/dL), and 500 mg/kg b.w. (135.69±14.07 mg/dL), ULLME treated animals induced with hyperlipidemia using lead sulfate shows significant ($p<0.05$) decrease in the concentration of triglyceride when compared to untreated control group (185±17.02 mg/dL).

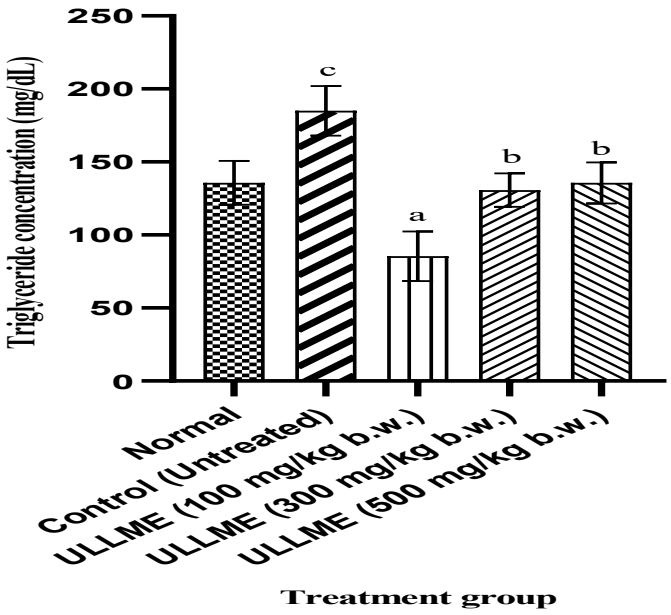

Figure 1: Effect of different doses of *Urena lobata* leaf methanol extract on triacyglycerol (TAG) concentration.

Note**:** Each bar represents Mean ± SD (n=6). Similar letters indicate no significant differences between groups. Different letter shows significant difference at $p<0.05$

Cholesterol Concentration

Data in Fig. 2 showed that 100 mg/kg b.w. (506.92 ± 14.03 mg/dL), 300 mg/kg b.w. (508.23 ± 15.55 mg/dL), and 500 mg/kg b.w. (519.96 ± 12.32 mg/dL), ULLME treated animals induced with hyperlipidemia using lead sulfate shows significant ($p<0.05$) decrease in the concentration of cholesterol when compared to untreated control group (553.08 ± 13.43 mg/dL).

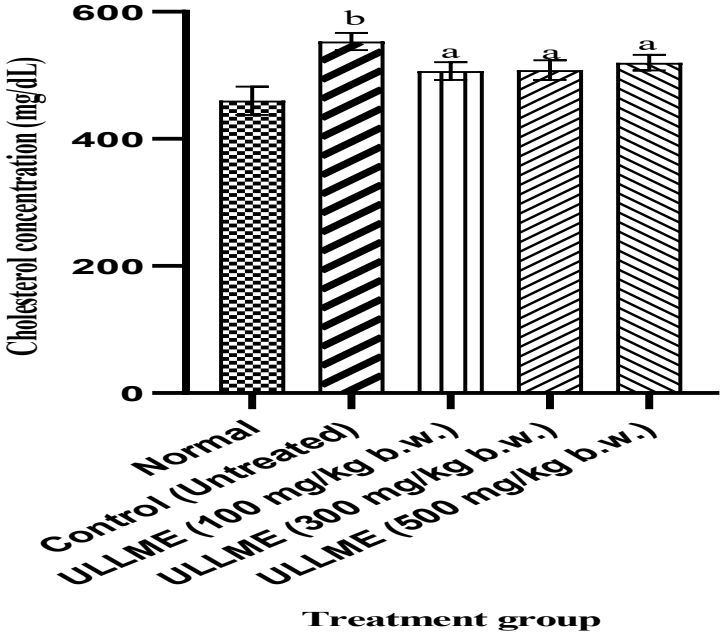

Figure 2: Effect of different doses of *Urena lobata* leaf methanol extract on cholesterol concentration

Note: Each bar represents Mean ± SD (n=6). Similar letters indicate no significant differences between groups. Different letter shows significant difference at $p<0.05$

High Density Lipoprotein (HDL) Cholesterol (HDL-C) Concentration

Data in Fig. 3 showed that 100 mg/kg b.w. (269.43 ± 19.16 mg/dL) and 300 mg/kg b.w. (277.36 ± 19.02 mg/dL), ULLME treated animals induced with hyperlipidemia using lead sulfate showed no significant difference ($p>0.05$) in the concentration of HDL-C when compared to untreated control group (285 ± 17.07 mg/dL) while 500 mg/kg b.w. (400.19 ± 11.81 mg/dL), ULLME treated animals showed a significant ($p<0.05$) increase when compared against the untreated control.

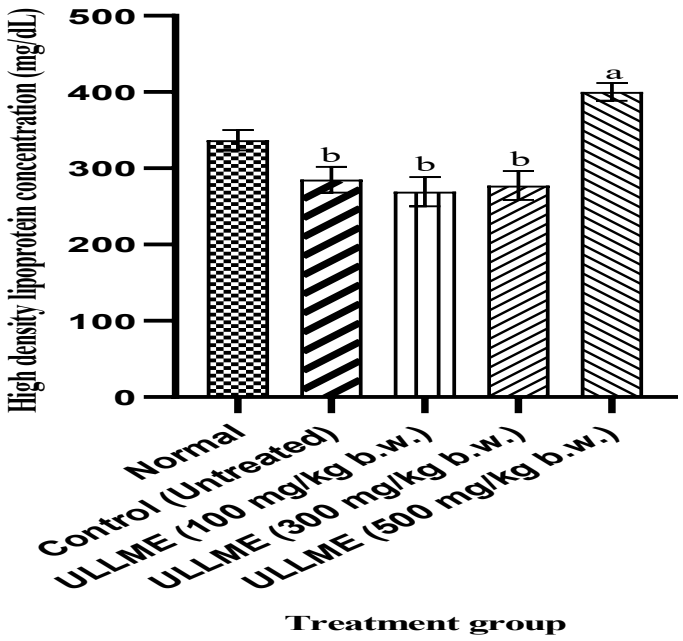

Figure 3: Effect of different doses of *Urena lobata* leaf methanol *extract* on high density lipoprotein cholesterol (HDL-C) concentration

Note: Each bar represents mean ± SD (n=6). Similar letters indicate no significant differences between groups. Different letter shows significant difference at $p<0.05$

Low Density Lipoprotein Cholesterol (LDL-C) Concentration

Data in Fig. 4 showed that 100 mg/kg b.w. (220.43 ± 13.66 mg/dL) and 300 mg/kg b.w. (203.41 ± 11.79 mg/dL), ULLME treated animals induced with hyperlipidemia using lead sulfate showed no significant difference ($p>0.05$) in the concentration of LDL-C when compared to untreated control group (230.53 ± 15.92 mg/dL) while 500 mg/kg b.w. (102.63 ± 12.75 mg/dL), ULLME treated animals showed a significant ($p<0.05$) decrease when compared against the untreated control.

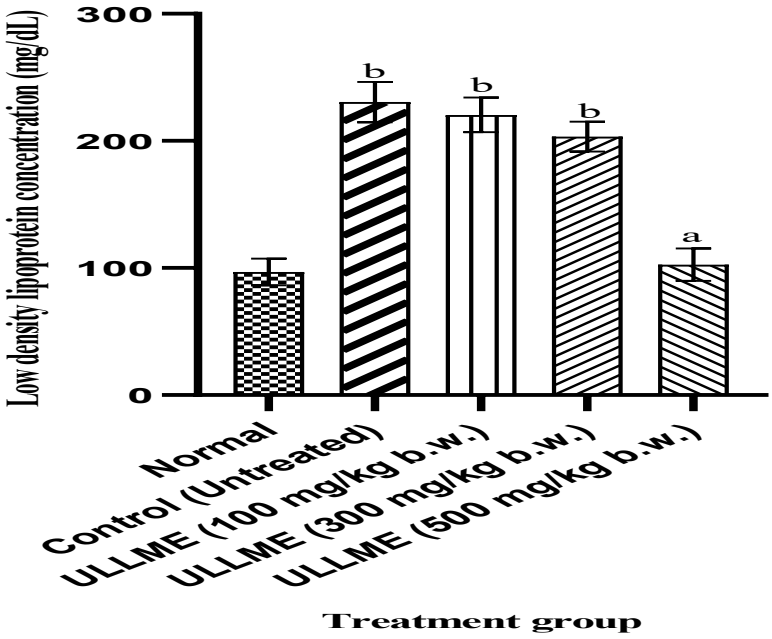

Figure 4: Effect of different doses of *Urena lobata extract* on low density lipoprotein (LDL) concentration

Note: Each bar represents mean ± SD (n=6). Similar letters indicate no significant differences between groups. Different letter shows significant difference at $p<0.05$

Discussion

The present study evaluated the effects of methanol extract of *Urena lobata* leaves (ULLME) on lipid profile parameters in rats subjected to lead sulfate-induced toxicity. Lead exposure is well-documented to disrupt lipid metabolism, resulting in dyslipidemia characterized by elevated triglycerides (TAG), total cholesterol (TC), and low-density lipoprotein cholesterol (LDL-C), accompanied by a reduction in high-density lipoprotein cholesterol (HDL-C), thereby increasing the risk of cardiovascular diseases (Alya et al., 2015). Data obtained from this study confirm these pathophysiological alterations and demonstrate the lipid-modulating potential of ULLME.

Lead exposure significantly elevated serum TAG levels compared to normal control rats, consistent with previous reports of lead-induced hypertriglyceridemia (Ugbaja et al., 2013). Administration of ULLME at 100 mg/kg markedly reduced TAG concentrations, restoring levels toward baseline, whereas higher doses (300 and 500 mg/kg) did not produce comparable effects. This dose-dependent response may be attributed to factors such as phytochemical bioavailability or saturation kinetics..

Total cholesterol levels were significantly increased following lead exposure, corroborating earlier discussions that the development of hypercholesterolemia induced by lead may be attributed to the activation of cholesterol biosynthetic enzymes alongside the simultaneous inhibition of cholesterol catabolic enzymes (Ademuyiwa et al., 2005). Conversely, treatment with all tested ULLME doses significantly decreased these Pb-induced alterations relative to the untreated

lead group. This observation may be explained by ULLME's capacity to lower blood lipid leuvels through enhanced cholesterol absorption, conversion, and accelerated reverse cholesterol transport (Zhang et al., 2017).

Lead intoxication resulted in a significant reduction in HDL-C compared to other treated groups, a concerning finding given HDL's established role in atheroprotection and reverse cholesterol transport (Rosenson et al., 2016). Notably, ULLME administered at 500 mg/kg significantly elevated HDL-C above the levels observed in lead-exposed untreated rats, while lower doses failed to restore HDL-C. This suggests that adequate phytochemical concentrations are required to favorably modulate HDL metabolism, possibly via upregulation of apolipoprotein A1 synthesis or inhibition of lipid peroxidation pathways (Qidwai & Ashfaq, 2013).

Serum LDL-C levels were markedly increased in lead-exposed untreated rats, consistent with lead-mediated oxidative modification of LDL and its atherogenic consequences. Treatment with ULLME at 500 mg/kg normalized LDL-C concentrations, whereas lower doses elicited partial reductions. ULLME may inhibit the oxidative modification of low-density lipoprotein cholesterol (LDL-C), a pivotal process in the pathogenesis of atherosclerosis, by preserving the structural integrity of LDL particles and reducing their uptake by macrophages. This mechanism potentially attenuates plaque development and the ensuing cardiovascular sequelae (Rajpoot & Sharma, 2025). The LDL-lowering effect may also be attributed to bioactive constituents such as sterols or flavonoids that inhibit HMG-CoA reductase activity or enhance LDL receptor expression, as demonstrated in previous phytochemical investigations (Njoku et al., 2021).

The dyslipidemia observed in untreated lead-exposed animals reflects hyperlipidemic conditions predisposing to coronary heart disease (Ige et al., 2019). Elevated triglycerides may result from decreased lipoprotein lipase activity in the vasculature, impairing triglyceride metabolism and clearance (Pan et al., 2024). Collectively, these findings underscore the prophylactic potential of ULLME in ameliorating lead-induced dyslipidemia and its cardiovascular implications.

Conclusion

The data demonstrate that lead exposure induces significant disruptions in lipid profile parameters indicative of dyslipidemia, which can be ameliorated by treatment with *Urena lobata* leaf extract, particularly at 500 mg/kg. The extract's phytochemicals likely exert antioxidative and lipid metabolism regulatory effects that restore lipid homeostasis.

Conflict of Interest

There is no conflicting interest whatsoever that is associated with this study.

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