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Evaluation of the Dose Dependent Hepatic, Renal and Lipids Modulatory Effects of Ethanolic Root Extract of *Mezoneuron Benthamianum Baill* in Adult Wistar Rats

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ABSTRACT

The diagnosis and subsequent treatment of diseases involving lipid metabolism and various endocrine disorders such as diabetes mellitus, nephrosis and liver obstruction have been documented to be achieved by lipid levels measurement. The leaves and roots of *Mezoneuron benthamianum Baill* (Caesalpinoideae) have been reported to be useful in the treatment of dermal infection, healing of refractory sore, blood disorders; venereal diseases, e.t.c. This study evaluated the dose dependent effects of ethanolic root extract of *Mezoneuron benthamianum baill* on lipid profile, lipid peroxidation, liver and kidney functions of adult wistar rats. A total of twenty-eight(28) adult male wistar rats weighing between 150g to 180g were used in this study and assigned into four treatment groups of seven (7) rats to each group. Animals in the control group were treated with vehicle (ethanol) while those in the other three groups received mezoneuron 300mg/kg bwt, mezoneuron 500mg/kg bwt and Mezoneuron 750mg/kg bwt respectively. After two weeks of treatment, animals were sacrificed andblood, kidneyand liver samples were collected for analyses. Fasting blood sugar (FBS) level, protein, Lipid profile, electrolyte levels, kidney functional (urea and creatinine), liver functional (AST, ALP and ALT) and lipid peroxidationassays were assessed. Our results revealed that mezoneuron extract at 500 and 750 mg/kg bwt significantly ($p<0.05$ and 0.005 respectively)reduced fasting blood Sugar levels; significantly repressed lipid profile status; activities of liver enzymes (AST and ALT);serum calcium, chloride and bicarbonate levels while increasing serum levels of potassium, sodium, urea and creatininein wistar rats; when compared to the control rats. This study suggests that the extract possesses dose dependent antioxidative, hypoglycemic, hypocholesterolemic and hypolipidemic activities and thus may be useful in the management of lipid and protein associated disorders, wound healing as well as liver and kidney malfunctions.

Keywords: mezoneuron, hypoglycaemia,antioxidants,lipid peroxidation, High density lipoprotein

INTRODUCTION

Medicinal plants possess therapeutic properties and exert beneficial pharmacological effects in humans and animals. They have been used by humans in the treatment of different diseases from the beginning of human history and serve as precursors for synthesis of useful drugs. Their use is increasing worldwide as they are now being recognised as useful tools by researchers in the field of drug discovery and development[1]. Natural products sometimes tend to be more useful and efficient than their synthetic analogues due to the fact that they present less adverse effects, they are economically affordable and have efficacy in multidrug resistant cases[2,3]. Expansion of traditional medicine with subsequent growing interest in herbal medicine has been a major focus in the field of natural products science and consequently promotes the search for several plants that support different pharmacological actions in several diseases. Reduction in the risk of several diseases resulting from antioxidant activities have been attributed to phytochemicals such as flavonoids (present in fruits and vegetables), carotenoids (from carrots), and alkyl sulfide (found in onions and garlic) [4]. Mezoneuron benthamianum Baill is a plant that belongs to the family of Leguminosae-Caesalpinoideae, it is a woody climber with recurred thorn on its black stem and it is also referred to as 'tiger's claw'. It grows extensively in humid and rural localities in dry deciduous woodland and savannah and on roadsides in west tropical Africa[5]. Some Important constituents such as three diterpenes, two flavonoids, resveratrol, garlic acid and its ethyl ester, β-sitosterol glucoside and pheophorbide derivatives have been isolated from the leaves of *Mezoneuron*

benthamianum[6]. The leaves and roots are important medicinal parts in folk medicine and they are being used in many parts of Africa for antimicrobial purposes such as the treatment of dermal infections and wounds in Ghana, as antiseptic in Senegal and for wound treatment in Sierra-Leone[7]. When the leaves are young, they appear bright red in colour while they present dark green colour when old. The plant is native to West Africa and it is known locally as "Jenifiran" in western part of Nigeria[8]. Chloroform, ethanol and petroleum ether extracts of *Mezoneuron benthamianum* have been found to induce antimicrobial activities on a range of organisms[5]. Apart from its antimicrobial properties, *Mezoneuron benthamianum Baill* is also being used locally in Nigeria for the treatment of blood disorders; stomach troubles, pulmonary troubles, treatment of impotence related to venereal diseases, eye treatments, as genital stimulants/depressants, hemorrhoids, pain-killers and as chewing sticks[6, 9-11]. The leaves have also been reported to be used for treating malaria in Guinea[10]. Wound healing is a complex and dynamic process of replacing devitalized and missing cellular structures and tissue layers leading to the reestablishment of tissue integrity and homeostasis[12]. It comprises of inflammation, reepithelization, granulated tissue formation, neovascularization, wound contraction, and remodelling of the extracellular matrix[13]. Impaired wound healing and chronic non- healing wounds resulting in considerable morbidity and mortality has been attributed to hypercholesterolemia. Speeding up resolution of inflammation through enhancement of granulation tissue formation involving increased endothelial progenitor cell (EPC) incorporation and increased paracrine effects of EPCs and consequently accelerating re- epithelialization are major beneficial effects of high density lipoprotein (HDL) in wound healing[14].

Apart from the link between wound healing and HDL, decreased high density lipoprotein (HDL) cholesterol and increased non-HDL cholesterol levels have been reported to be independent risk factors for ischemic cardiovascular diseases[15]. The cardiovascular protective effect of HDLs has been attributed to their capacity to remove excess cholesterol from the peripheral tissues and to transport it back to the liver, for its subsequent elimination in the bile in a process referred to as reverse cholesterol transport (RCT)[16].

Reports have also shown that HDL possesses anti-oxidative, anti-inflammatory, anti-apoptotic, and endothelial protective properties[17,18]. Since there are reports on the correlation between wound healing, cardiovascular diseases and high level of HDL and effects of *mezoneuron benthamianum* on lipid profile, lipid peroxidation, liver and kidney functions have not been fully elucidated, this present study was therefore aimed at evaluating the dose dependent modulatory effects of the ethanolic root extract of this plant on fasting blood sugar level, lipid profile, lipid peroxidation status, protein level, liver and kidney functions of adult male wistar rats. Results from this study may shed more light on the mechanism of antimicrobial properties, antioxidant and free radical scavenging activities reported on the plant and provide information on the effects of *mezoneuron benthamianum* on indices of liver and kidney diseases.

MATERIALS AND METHODS

Plant authentication and extraction

Roots of *Mezoneuron benthamianum baill* were obtained from Ipakodo village along Ishara road, Ogun state, Nigeria. The plant was identified as *Mezoneuron benthamianum* at the Botany department of Olabisi Onabanjo University, Ago-Iwoye, Ogun State, Nigeria after which the plant and its roots specimens were deposited at the herbarium. The roots were then cut into smaller pieces, washed and air dried at room temperature for two weeks. The dried rhizomes were pulverised into coarse powdery form and 300g of it was weighed and used in 1000l of ethanol. Ethanol extraction was done by soaking the sample in 99.7% ethanol for five days. The herbs were decanted and filtered with wool funnel to ensure that the filtrate is used for the extraction. RotoVap 110 was used to evaporate the solvent from herbs, the slurry form was then transferred into a beaker and it was further concentrated using a rotary evaporator at 40°C. The concentrated product was then lyophilised and the dry powder was weighed and stored in a dry container.

Animal Care and Experimental design

The study was conducted in compliance with established protocol of the National Research Council (1999) and was approved by the Animal and Human Health Ethics Committee of Obafemi Awolowo College of Health Sciences, Olabisi Onabanjo University, Ago-Iwoye. Twenty-eight (28) adult male wistar rats weighing between 150g to 180g were obtained from the institute of Advance Medical Research Training (INRAT) Central Animal house, UCH Ibadan, Nigeria and kept in the animal house of physiology department of Olabisi Onabanjo University, Ogun state, Nigeria and acclimatized for a week. All the animals were housed in metallic cages and maintained in well ventilated room provided with 12:12h light and dark cycle for each 24hr period at a temperature of approximately 25°C. They were maintained on standard pelletized rat chow and water ad libitum throughout the period of the study. The animals were assigned into four treatment groups of seven (7) rats to each group namely group CNTL (normal control rats administered with the vehicle); MEZ-3 (rats administered with 300mg/kg bwt ethanolic root extract of *Mezoneuron benthamianum baill)*; MEZ-5 (rats administered with 500mg/kg bwt ethanolic root extract of *Mezoneuron benthamianum baill*) and MEZ-7 (rats administered with 750mg/kg bwt ethanolic root extract of *Mezoneuron benthamianum baill*). All administrations were done as a single dose daily for fourteen (14) days by oral gavage. After fourteen (14) days of administration, rats in all the groups were sacrificed after 12h fasting and after anaesthetising with

diethyl ether. Blood was collected from the inferior vena cava of heart of the animals into plain centrifuge tubes, serum was prepared by centrifugation and rats were evaluated based on the effects of the different concentrations of the extract. The liver and kidney were harvested, washed in ice cold 1.15% KCl solution, dried and weighed. Liver and kidney samples were homogenised in 4 volumes of 5mM phosphate, pH 7.4 buffer and centrifuged at 10,000 x g to obtain post mitochondrial supernatant fraction. Supernatants were stored at -80^{0}C for subsequent analyses.

Biochemical assays

Fasting blood Sugar measurement

Weekly fasting glucose was measured using AccuChek Active© glucometer and glucose strips with blood obtained by tail vein puncture.

Protein Level determination

Serum, liver and kidney protein levels were determined by the method of Lowry et al., (19) using Bovine serum albumin as standard.

Assessment of lipid parameters

Serum total cholesterol (TC), triglyceride (TG) and high-density lipoprotein (HDL) concentrations were estimated following the cholesterol oxidase, glycerol-3-phosphate oxidase and HDL Cholesterol-Direct Clearance methods respectively as described by Abot et al., (1988) (20) while Freidewald formula (21) was used to extrapolate serum low-density lipoprotein (LDL). Commercial kits obtained from Randox Laboratories Ltd. (Crumlin, UK) were used for the assays according to manufacturer's instructions.

Liver and kidney Lipid peroxidation

Liver and kidney lipid peroxidation levels were estimated in liver and kidney homogenate tissues spectrophotometrically by measurement of the thiobarbituric acid- reactive substance (TBARS) as previously described and expressed in terms of malondialdehyde (MDA) formed per mg protein by Khoubnasabjafari et al., 2016 (22).

Electrolyte measurements

To assess possible electrolyte disturbances that arise in normal and mezoneuron treatment, serum levels of calcium (Ca^{2+}), sodium (Na^{+}), chloride (Cl^{-}), potassium (K^{+}) and bicarbonates (HCO^{-}_{3}) and were assayed by ion selective electrode technology with the Roche 9180 electrolyte analyser.

Kidney functional assays

Assay for plasma urea was carried out by the Urease- Berthelot method, Weathewrburn (1967) (23) using the laboratory kit reagents (Randox laboratory Ltd. UK). Colorimetric method as described by Bartels and Bohmer (1972) (24) was used in the assay for plasma creatinine using laboratory kit reagents (Randox laboratory Ltd. UK).

Liver dysfunction marker enzymes activities

Serum Alanine Aminotransferase (ALT) and Aspartate Aminotransferases (AST) were determined using a combination of the methods of Mohun and Cook (1957) (25) and Reitman and Frankel (1957) (26). The estimation of Alkaline Phosphatase (ALP) activities was based on the method of Wiliamson (1972) (27). ALP activity was measured spectrophotometrically by monitoring the concentration of p-nitrophenol formed when ALP reacts with p-nitrophenyl phosphate at 405nm.

Statistical analyses

All data are presented as mean ± SEM indicated by error bars and statistical analyses between treated groups and the control groups were carried out using one-way analysis of variance (ANOVA) followed by Tukey's multiple comparison test. Values for $p<0.05$ are considered to be statistically significant. Graphpad Prism software version 8.231 (Graphpad Software, San Diego, California, USA) was employed for these analyses.

RESULTS

Ethanolic root extract of *mezoneuron benthamianum baill* at 500 and 750mg/kg body weight significantly decreased fasting blood sugar level in wistar rats.

Fasting blood sugar level was significantly reduced by treatment with 500 and 750mg/kg bwt ethanolic root extract of mezoneuron benthamianum baill at $p<0.05$ and $p<0.005$ respectively while no significant difference was observed with the 300mg/kg bwt when compared to the control group (Figure 1).

Ethanolic root extract of *mezoneuron benthamianum baill* at 750mg/kg body weight significantly decreased total serum protein level in wistar rats.

Total serum and tissue protein levels were measured in the serum, liver and kidney. Significant reductions were observed with 500 and 750mg/kg bwt at $p<0.05$ when compared to the control group while no statistical difference was observed with 300mg/kg bwt and at all concentrations in tissue protein levels (Figure 2).

The response of lipid profile status to ethanolic root extract of *mezoneuron benthamianum baill* in Wistar rats.

Total cholesterol level was significantly reduced by 300, 500 and 750mg/kg bwt ethanolic root extract of *mezoneuron benthamianum baill*; low density lipoprotein level was significantly reduced by 300 and 750mg/kg bwt ethanolic root extract of *mezoneuron benthamianum baill* while High density Lipoprotein level was significantly increased in by 750mg/kg bwt ethanolic root extract of *mezoneuron benthamianum baill* when compared to the control group (Figure 3).

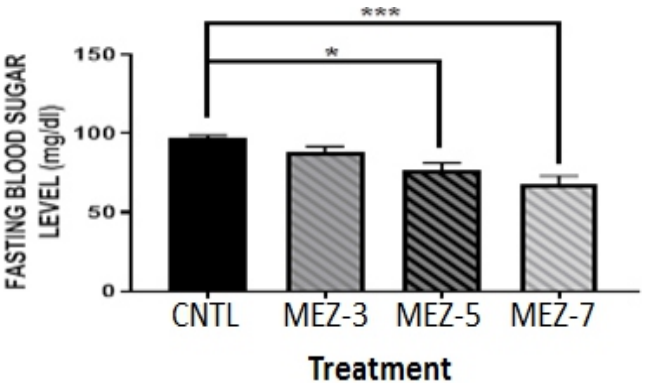

Figure 1: Effects of *mezoneuron benthamianum baill* on fasting blood sugar (FBS) of Wistar rats. Bar charts showing the levels of serum Fasting Blood Sugar (FBS) in control, 300mg/kg bwt, 500mg/kg bwt and 750mg/kg bwt treated rats. Three asterisks indicate p<0.005 and one asterisk indicates p<0.05.

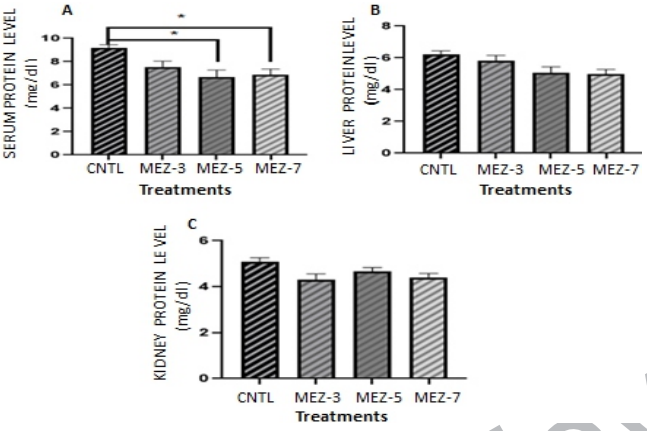

Figure 2: Effects of *mezoneuron benthamianum baill* root extract on Total Serum, liver and kidney protein of wistar rats.
Bar charts showing the levels of Serum total protein (A), Liver total protein (B) and Kidney total protein (C) in control, 300mg/kg bwt, 500mg/kg bwt and 750mg/kg bwt treated rats.One asterisk indicates p<0.05

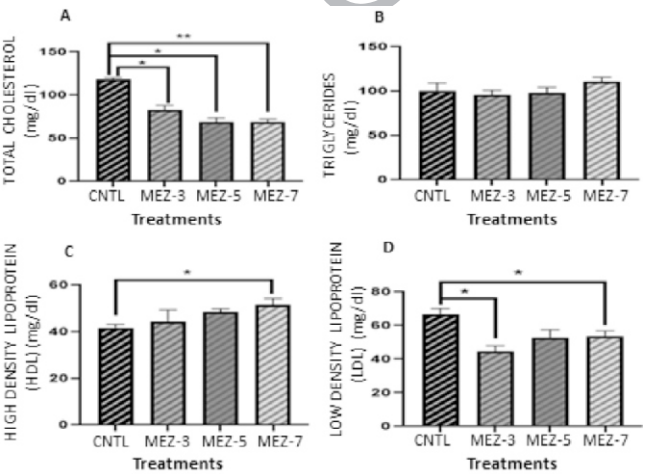

Figure 3: Effects of ethanolic root extract of *mezoneuron benthamianum baill* on lipid profile status of Wistar rats.
Bar charts representations of the levels of total cholesterol (A)Ttriglycerides (B) HDL (C) and LDL (D) in control, 300mg/kg bwt, 500mg/kg bwt and 750mg/kg bwt treated rats. Two asterisks indicate p<0.01 and one asterisk indicates p<0.05.

The effect of ethanolic root extract of mezoneuron benthamianum baill on kidney and liver lipid peroxidation in Wistar rats

Ethanolic root extract of *mezoneuron benthamianum baill* at 300, 500 and 750mg/kg body weight significantly decreased liver MDA level at p<0.05, 0.05 and 0.005 respectively while kidney MDA level was significantly reduced by 300mg/kg bwt of the extract at p<0.05 when compared to the control group (Figure 4).

The response of ion homeostasis to ethanolic root extract of mezoneuron benthamianum baill in Wistar rats

Ethanolic root extract of *mezoneuron benthamianum baill* at 500 and 750mg/kg body weight significantly decreased serum calcium, serum chloride and serum bicarbonate levels while serum sodium and potassium levels were significantly increased at p<0.01 by 750mg/kg bwt of the extract (Figure 5).

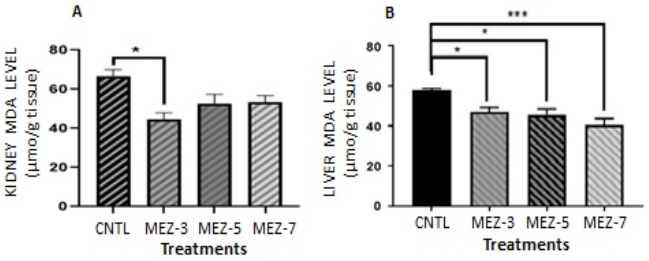

Figure 4: The effects of ethanolic root extract of *mezoneuron benthamianum baill* on both liver and kidney peroxidation in Wistar rats.
Bar charts showing the levels of kidney MDA level (A) and liver MDA level (B) in control, 300mg/kg bwt, 500mg/kg bwt and 750mg/kg bwt treated rats. Three asterisks indicate p<0.005 and one asterisk indicates p<0.05.

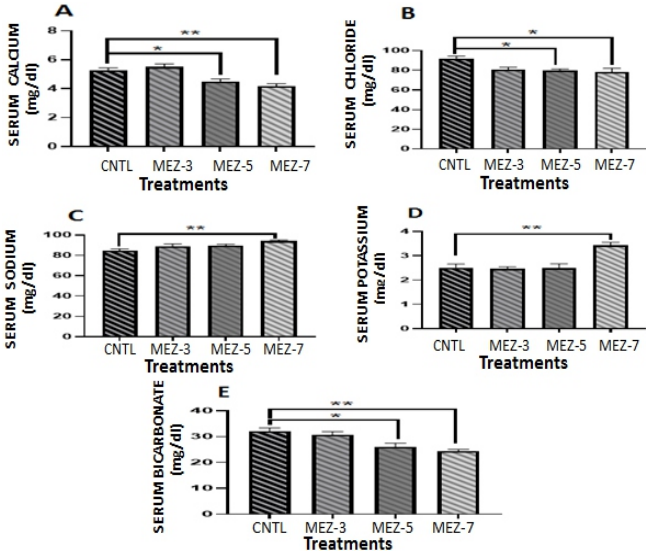

Figure 5: The effects of ethanolic root extract of *mezoneuron benthamianum baill* on ion homeostasis.
Bar charts showing the levels of serum Calcium (A), Chloride (B), Sodium (C), Potassium (D) and Bicarbonate (E) in control, 300mg/kg bwt, 500mg/kg bwt and 50mg/kg bwt treated rats. Two asterisks indicate p<0.01 and one asterisk indicates p<0.05.

The response of kidney function markers (urea and creatinine) to ethanolic root extract of *mezoneuron benthamianum baill* in wistar rats.

Serum levels of urea and creatinine were significantly reduced by treatment with 500mg/kg bwt ethanolic root extract of *mezoneuron benthamianum baill* at p<0.05 while significant increases in urea and creatinine levels were observed by treatment with 750mg/kg bwt at p<0.01 and p <0.005 respectively when compared to the control group (Figure 6).

Ethanolic root extract of *mezoneuron benthamianum baill* exerted statistically significant reductions in the activities of liver enzymes (AST and ALT) of Wistar rats at 750mg/kg bwt.

The activities of AST and ALT were statistically reduced at p<0.05 by treatment with 750mg/kg bwt ethanolic root extract of *mezoneuron benthamianum baill* when compared to the control group while activity of ALP was not affected significantly (Figure 7).

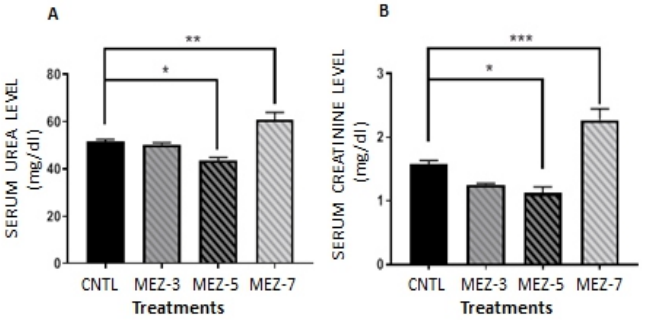

Figure 6: The response of kidney functions markers to ethanolic root extract of *mezoneuron benthamianum baill*. Bar charts showing the levels of serum Urea(A) and Creatinine (B) in control, 300mg/kg bwt, 500mg/kg bwt and 750mg/kg bwt treated rats. Three asterisks indicate p<0.005, two asterisks indicate p<0.01 and one asterisk indicates p<0.05.

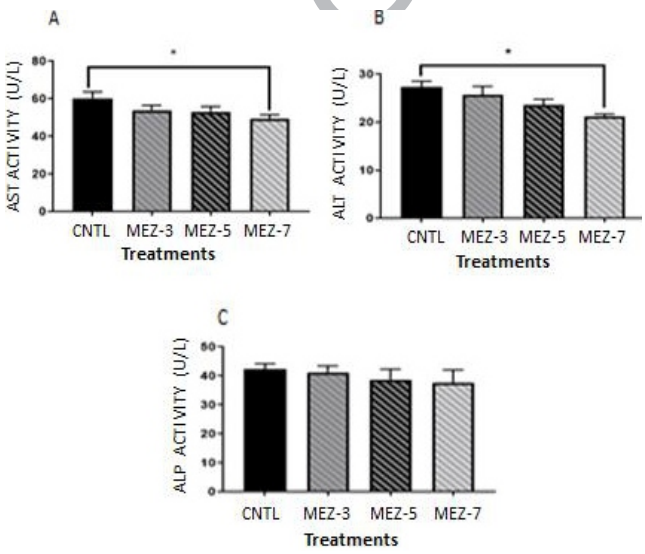

Figure 7: Effects of ethanolic root extract of *mezoneuron benthamianum bail* lon liver enzymes in wistar rats.
Bar charts showing the levels of AST (A) ALT (B) ALP (C) in control, 300mg/kg bwt, 500mg/kg bwt and 750mg/kg bwt treated rats. One asterisk indicates p<0.05.

DISCUSSION

The hypoglycaemic properties of several medicinal plants have been reported[28-32] and *mezoneuron benthamianum baill* was also investigated for its effects on serum fasting blood sugar in male wistar rats. Our results show that fasting blood sugar level was significantly reduced by separate treatments with 500 and 750mg/kg bwt ethanolic root extract of *mezoneuron benthamianum baill* at p<0.05 and p<0.005 respectively while no significant difference was observed with the 300mg/kg bwt when compared to the control group (Figure 1). This result suggests that ethanolic root extract of *mezoneuron benthamianum baill* possesses hypoglycemic property and thus can help in the management of diabetes. The reduction in the level of fasting blood sugar by this plant may be attributed to the fact that most medicinal plants involved in management of diabetes do so by their ability to increase insulin secretion and enhance glucose utilization by adipose or muscle tissues while inhibiting glucose absorption from intestine and glucose production from the liver [33, 34].

Our results on the effects of ethanolic root extract of mezoneuron benthamianum baill on serum protein (Fig 2) revealed significant (p<0.05) reductions in the level of serum protein following the administration of 500 and 750mg/kg bwt of the extract. This result conforms to the one observed by Mbagwu and Adeyemi, 2007[35] using aqueous extract at 250–2000mg/kg bwt. This thus suggests that the extract possesses protein lowering property.

Administration of ethanolic root extract of *mezoneuron benthamianum baill* at 750mg/kg bwt in wistar rats resulted in significant (p<0.05) increase in the level of HDL when compared to the untreated control group (Fig 3C). Since HDL is involved in acceleration of re-epithelialization and the entire process of wound healing (14) thus our results on increase in the level of HDL by treatment with ethanolic root extract of *mezoneuron benthamianum baill* conform to the work of Gordts et al., 2014[14] on effect of HDL treatment in wound healing and consequently suggest beneficial effects of the extract in its ability to raise HDL level and lowering of non-HDL cholesterol. Also, all the three doses (300, 500and 750mg/kg bwt) of the extract significantly (at p<0.05, p<0.05and p<0.01 respectively) reduced the level of total cholesterol (Fig 3A) while 300 and 750mg/kg bwt of the extract significantly (at p<0.05) reduced LDL levels when compared to the control group (Fig 3D). Since decreased high density lipoprotein (HDL) cholesterol and increased non-HDL cholesterol levels have been reported to be independent risk factors for ischemic cardiovascular diseases (15) thus, our results also suggest the beneficial effects of ethanolic root extract of *mezoneuron benthamianum baill* in alleviating and treatment of ischemic cardiovascular diseases due to its ability to raise HDL level while lowering the levels of non- HDL cholesterol.

Lipid peroxidation assessment in both the liver and kidney samples (Fig 4) showed significant reductions in the levels of MDA when compared to the control group. The three doses of the extract (300, 500

and 750mg/kg bwt) in the liver (Fig 4B) reduced MDA levels significantly at $p<0.05$, $p<0.05$ and $p<0.005$ respectively while only 300mg/kg bwt dose significantly reduced lipid peroxidation in the kidney (Fig 4A) when compared to the control group. These observed reductions in lipid peroxidation conform to the work of Dickson et al., 2006 who also reported inhibition of lipid peroxidation by ethanolic extract of *mezoneuron benthamianum baill* [36]. These results confirm that *mezoneuron benthamianum baill* possess antioxidant and ROS scavenging activities which has been reported by many researchers[36-38].

Our results on the response of ion homeostasis to ethanolic root extract of *mezoneuron benthamianum baill* (Fig 5) reflect significant reductions in the levels of serum calcium (Fig 5A), serum chloride (Fig 5B), and serum bicarbonate (Fig 5E), with 500 and 750mg/kg body weight while serum sodium (Fig 5C), and potassium (Fig 5D), levels were significantly increased at $p<0.01$ by 750mg/kg bwt of the extract when compared to the control group. These results show that the ions respond differently to the administration of ethanolic root extract of mezoneuron benthamianum baill. Since hyperglycaemia and hyperproteinamia are well known for their lowering effects on serum sodium levels and vice versa[39-43], these thus explain the link between the observed glucose and protein lowering effect of ethanolic root extract of *mezoneuron benthamianum baill* giving rise to significant increase in the level of sodium observed in this study by treatment with ethanolic root extract of *mezoneuron benthamianum baill*. Hypoproteinemia has been found to be associated with hypocalcaemia[44] and this corroborates our findings in this work on protein and calcium lowering effects of the extract.

Assessment of kidney parameters, serum urea and creatinine levels (Fig 6A and 6B) reflect significant ($p<0.05$) reductions in the levels of urea and creatinine with 500mg/kg bwt dosage of ethanolic root extract of mezoneuron benthamianum baill when compared to the control group.

This result suggests that the plant is a potential source of nephroprotective phytochemical activity, with flavonoids and polyphenols as the major components and natural antioxidants which are also well known for their ability to defend cells and the organism from damage caused by oxidative stress. On the other hand, there were significant increases observed in the levels of these two indices of kidney function (urea and creatinine) at $p<0.01$ and $p<0.005$ respectively with 750mg/kg bwt. This suggests that ethanolic root extract of *mezoneuron benthamianum baill* at 750mg/kg bwt may be toxic to the kidney.

Our results on the effect of ethanolic root extract of *mezoneuron benthamianum baill* on liver enzymes (Fig 7) showed significant ($p<0.05$) decreases in the activities of liver enzymes AST (Fig 7A) and ALT (Fig 7B) at 750mg/kg bwt dose of the extract when compared to the control group. Insignificant reductions were observed in the activities of these two liver enzymes (AST and ALT) with 300 and 500mg/kg bwt of the extract. Since serum metabolic activities of alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP) are considered as indicators of hepatocellular health (45-47), thus the observed reductions in the activities of these liver enzymes suggest that ethanolic root extract of mezoneuron benthamianum baill possesses hepatoprotective property and may be useful in prevention of liver damages.

Conclusively, our results confirmed that *mezoneuron benthamianum baill* possesses antioxidant properties by scavenging free radicals and decreasing lipid peroxidation, it positively modulates HDL level and consequently helps in wound healing. The extract may also be useful in the treatment and management of hyperglycaemia, hyperproteinamia, liver and kidney malfunctions which may also be attributed to its antioxidant property. This work provides reasons for further research to answer important questions regarding the molecular mechanisms underlying the interactions and modulations of metabolic processes by compounds contained in *Mezoneuron benthamianum* root extract.

DECLARATION OF COMPETING INTEREST

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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REFERENCES

1. Fransworth N. The Role of Ethanopharmacology in Drug Development. Bioactive Compounds from Plant. John Wiley & Sons; 2008.
2. Uddin MN, Afrin R, Uddin MJ, Uddin MJ, Alam A, Rahman AA, et al. Vanda roxburghii chloroform extract as a potential source of polyphenols with antioxidant and cholinesterase inhibitory activities: identification of a strong phenolic antioxidant. BMC Complementary and Alternative Medicine. 2015;15(1):1-9.
3. Ye M, Moon J, Yang J, Lim HH, Hong SB, Shim I, et al. The standardized Lycium chinense fruit extract protects against Alzheimer′ s disease in 3xTg-AD mice. Journal of ethnopharmacology. 2015;172:85-90.
4. Craig WJ. Health-promoting properties of common herbs. The American journal of clinical nutrition. 1999;70(3):491s-9s.
5. Koroma L, Yormah T, Kamara L, Robert G. Pharmacognostic Investigation and Mineral Analysis of Dried Powdered Young Leaves of Traditional Medicinal Plant Mezoneurum benthamianum Used for the Treatment of Heartburns/Pyrosis in Sierra Leone.
6. Tchinda A, Loua J, Esters V, Cieckiewicz E, Ledoux A, Angenot L, et al. Study of Mezoneuron

benthamianum, a plant traditionally used against malaria in Guinea. Planta Medica. 2016;82(S 01):P406.
7. Fayemi Scott O, Osho A. Comparison of Antimicrobial Effects of Mezoneuron benthamianum, Heliotropium indicum and Flabellaria paniculata on Candida species. Journal of Microbiology Research. 2012;2(1):18-23.
8. Verger P. Awon ewé Osanyin: Yoruba medicinal leaves: University of Ife, Institute of African Studies; 1967.
9. Burkill HM. The useful plants of west tropical Africa, Vols. 1-3. The useful plants of west tropical Africa, Vols 1-3. 1995(2. ed.).
10. Traore M, Baldé M, Diallo M, Baldé E, Diané S, Camara A, et al. Ethnobotanical survey on medicinal plants used by Guinean traditional healers in the treatment of malaria. Journal of ethnopharmacology. 2013;150(3):1145-53.
11. Traore MS, Diane S, Diallo MST, Balde ES, Balde MA, Camara A, et al. In vitro antiprotozoal and cytotoxic activity of ethnopharmacologically selected guinean plants. Planta medica. 2014; 80(15):1340-4.
12. Eming SA, Krieg T, Davidson JM. Inflammation in wound repair: molecular and cellular mechanisms. Journal of Investigative Dermatology. 2007;127(3):514-25.
13. Singer AJ, Clark RA. Cutaneous wound healing. New England journal of medicine. 1999;341(10): 738-46.
14. Gordts SC, Muthuramu I, Amin R, Jacobs F, De Geest B. The impact of lipoproteins on wound healing: topical HDL therapy corrects delayed wound healing in apolipoprotein E deficient mice. Pharmaceuticals. 2014;7(4):419-32.
15. Assessment R. Major lipids, apolipoproteins, and risk of vascular disease. Jama. 2009;302(18): 1993-2000.
16. Tran-Dinh A, Diallo D, Delbosc S, Varela-Perez LM, Dang Q, Lapergue B, et al. HDL and endothelial protection. British journal of pharmacology. 2013;169(3):493-511.
17. Duffy D, Rader DJ. Update on strategies to increase HDL quantity and function. Nature Reviews Cardiology. 2009;6(7):455.
18. Van Craeyveld E, Gordts S, Jacobs F, De Geest B. Gene therapy to improve high-density lipoprotein metabolism and function. Current pharmaceutical design. 2010;16(13):1531-44.
19. Lowry OH, Rosebrough NJ, Farr AL, Randall RJ. Protein measurement with the Folin phenol reagent. Journal of biological chemistry. 1951;193:265-75.
20. Abot R, Wilson P, Castelli W. HDL-cholesterol, total cholesterol screening and myocardial infarction. Arteriosclerosis. 1988;8:207-11.
21. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clinical chemistry. 1972;18(6):499-502.
22. Khoubnasabjafari M, Ansarin K, Jouyban A. Critical review of malondialdehyde analysis in biological samples. Current Pharmaceutical Analysis. 2016;12(1):4-17.
23. Weatherburn M. Colorimetric Urease-Berthelot method of urea estimation. Anal Chem. 1967;39:971.
24. Bartels H, Böhmer M, Heierli C. Serum creatinine determination without protein precipitation. Clinica chimica acta; international journal of clinical chemistry. 1972;37:193.
25. Mohun A, Cook I. Simple methods for measuring serum levels of the glutamic-oxalacetic and glutamic-pyruvic transaminases in routine laboratories. Journal of clinical pathology. 1957;10(4):394.
26. Reitman S, Frankel S. A colorimetric method for the determination of serum glutamic oxalacetic and glutamic pyruvic transaminases. American journal of clinical pathology. 1957;28(1):56-63.
27. Williamson T. A comparison between the phosphastrate and phenyl phosphate methods of alkaline phosphatase assay. Medical laboratory technology. 1972;29(2):182-7.
28. Ivorra M, Paya M, Villar A. A review of natural products and plants as potential antidiabetic drugs. Journal of ethnopharmacology. 1989;27(3):243-75.
29. Rao BK, Rao CA. Hypoglycemic and antihyperglycemic activity of Syzygium alternifolium (Wt.) Walp. seed extracts in normal and diabetic rats. Phytomedicine. 2001;8(2):88-93.
30. Zaman K. Medicinal plants with hypoglycemic activity. Journal of Ethnopharmacology. 1989; 26(1):1-55.
31. Rajasekaran S, Sivagnanam K, Ravi K, Subramanian S. Hypoglycemic effect of Aloe vera gel on streptozotocin-induced diabetes in experimental rats. Journal of Medicinal food. 2004;7(1):61-6.
32. Mukherjee PK, Maiti K, Mukherjee K, Houghton PJ. Leads from Indian medicinal plants with hypoglycemic potentials. Journal of ethnopharmacology. 2006;106(1):1-28.
33. Tailang M, Gupta BK, Sharma A. Antidiabetic activity of alcoholic extract of Cinnamomum zeylanicum leaves in alloxon induced diabetic rats. People's J Sci Res. 2008;1:9-11.
34. Bathaie S, Mokarizade N, Shirali S. An overview of the mechanisms of plant ingredients in the treatment of diabetes mellitus. Journal of Medicinal Plants. 2012;4(44):1-24.
35. Mbagwu HO, Adeyemi OO, Offor SJ. Acute and Subchronic Toxicity Studies of the Aqueous Extract of MezoneuronbenthamianumBaill (Caesalpiniaceae). 2007.
36. Dickson RA, Houghton P, Hylands P, Gibbons S. Antimicrobial, resistance-modifying effects,

antioxidant and free radical scavenging activities of Mezoneuron benthamianum Baill., Securinega virosa Roxb. & Wlld. and Microglossa pyrifolia Lam. Phytotherapy Research: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives. 2006;20(1):41-5.
37. Fayemi SO, Osho A, Atolani O. In vitro anticandidal and antioxidant potential of Mezoneuron benthamianum. Journal of Acute Disease. 2012;1(2):120-5.
38. Ademoye MA, Lajide L, Owolabi BJ. Phytochemical and Antioxidants Screening of Chrysophyllum albidum, Mezoneuron benthamianum, Phyllanthus muellerianus and Acalypha fimbriata. International Journal of Sciences. 2018;7(11):8-18.
39. Manning Jr R, Guyton A. Effects of hypoproteinemia on fluid volumes and arterial pressure. American Journal of Physiology-Heart and Circulatory Physiology. 1983;245(2):H284-H93.
40. Huffman G. Adjusting Sodium Levels in Patients with Hyperglacemia. American Family Physician. 1999;60(6):1821-.
41. Roscoe J, Halperin M, Rolleston F, Goldstein M. Hyperglycemia-induced hyponatremia: metabolic considerations in calculation of serum sodium depression. Canadian Medical Association Journal. 1975;112(4):452.
42. Liamis G, Liberopoulos E, Barkas F, Elisaf M. Diabetes mellitus and electrolyte disorders. World Journal of Clinical Cases: WJCC. 2014;2(10):488.
43. Butt HS, Mahmood L, Herrera A. P66 A case of pseudohyponatremia due to hyper-cholesterolaemia in a patient with cholestasis. Archives of Disease in Childhood. 2019; 104(Suppl 3):A182.
44. Galvão J, Simpson K, Birnbaum N. Fluid and electrolyte disturbances in gastrointestinal and pancreatic disease. Fluid, electrolyte, and acid–base disorders in small animal practice 4th ed St Louis, MO: Elsevier Saunders. 2012:443-62.
45. Amacher DE. Serum transaminase elevations as indicators of hepatic injury following the administration of drugs. Regulatory toxicology and pharmacology. 1998;27(2):119-30.
46. Gwaltney-Brant SM. Nutraceuticals in hepatic diseases. Nutraceuticals: Elsevier; 2016. p. 87-99.
47. Whitehead M, Hawkes N, Hainsworth I, Kingham J. A prospective study of the causes of notably raised aspartate aminotransferase of liver origin. Gut. 1999;45(1):129-33.