https://dx.doi.org/10.4314/ijs.v24i2.7

Ife Journal of Science vol. 24, no. 2 (2022)

THE REVERSAL EFFECTS OF *Irvingia gabonensis* SEED EXTRACT ON ETHANOL-INDUCED HYPERTENSION IN MALE WISTAR RATS

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(Received: 2nd February, 2022; Accepted: 14th September, 2022)

ABSTRACT

Irvingia gabonensis (Aubry-Lecomte ex O'Rorke) Baill is a tropical African tree widely used for the treatment of deranged body weight, blood sugar, and blood cholesterol in China, India, and Africa. Despite its medicinal uses, there is no documented report on its role and mechanism of action in the management of hypertension. In this study, we investigated the reversal effects of *n*-hexane extract (oil) of *Irvingia gabonensis* seed on ethanol-induced hypertension in male Wistar rats. Twenty-five (25) male Wistar rats were randomly assigned into five groups. Group A (control) received normal saline (10 mL/kg) orally, while groups B to E received 5% ethanol (10 mL/kg) alone daily for 14 consecutive days to induce hypertension. Thereafter, oral administration of *Irvingia gabonensis* at 250 mg/kg/day, 500 mg/kg/day, and enalapril at 0.1 mg/kg was introduced from day 15 to 35 in groups C to E, respectively. The results showed that ethanol caused a significant increase in diastolic blood pressure (DBP), systolic blood pressure (SBP), mean arterial blood pressure (MABP), heart rate (HR), and a reduction in mean weight gain in normotensive rats. However, treatment with *n*-hexane extract (oil) of the seed of *Irvingia gabonensis* or enalapril showed a significant (P=0.001) reversal in SBP, DBP, MABP, HR, and body weight gain compared to the ethanol-induced hypertensive rats. The study showed that *Irvingia gabonensis seed* oil administered at 250 mg/kg has a potency similar to enalapril in reducing blood pressure and heart rate and reversing weight loss in ethanol-induced hypertension. Also, it reversed the deleterious effects of ethanol on the architecture of the cardiac and renal tissues. The reversal effect of *Irvingia gabonensis* oil on hypertension was attributed to its antihypertensive and cytoprotective effects, resulting from the potent oil fingerprint of the extract.

Keywords: Ethanol, *Irvingia gabonensis*, ogbono, hypertension, kidneys, heart.

INTRODUCTION

Hypertension is a cardiovascular system disease that often impacts many individuals globally (Mills *et al.*, 2016). The condition is known as high blood pressure, characterized by a persistent upsurge in arterial blood pressure over time (Naish and Court, 2014). It affects about 16% to 37% of the world's population (Beaney *et al.,* 2018). Hypertension was thought to be a factor in 18% of all deaths (9.4 million globally) in 2010 and was described as the world's largest preventable risk factor for premature death (Campbell *et al.*, 2015). It increases the risk of strokes, peripheral vascular disease, chronic kidney disease, pulmonary embolism, and atrial fibrillation (Beevers *et al.*, 2001). Given the high rate of morbidity associated with this disease, it is important to explore various means to identify appropriate management for the disorder.

Irvingia gabonensis (Aubry-Lecomte ex O'Rorke) Baill, commonly called Africa mango or ogbono, is a plant that belongs to the *Irvingiaceae* family. It is a non-timber forest tree grown in West African countries, including Nigeria, Southern Cameroon, Ghana, and the Republic of Benin. The tree is made up of a tree trunk (stem), leaves, roots, and fruits. The fruit consists of a fleshy part (exocarp) and a nut. The nut consists of a hard shell and a kernel or seed. The seed has an outer brown testa (hull) and two white cotyledons that are used for cooking in parts of Africa. The seed is very popular and forms part of the regular diet in Nigeria (Ekpe *et al.,* 2007).

Numerous studies have been conducted to ascertain the medicinal, nutritional, and other benefits of *Irvingia gabonensis*. The beneficial effects of *Irvingia gabonensis* fruit and its

metabolites in the prevention and treatment of several human diseases have gained increasing interest. This is because of its diverse pharmacological activities and low toxicological profile. Thus, previous studies agreed that the fruit of *Irvingia gabonensis* is used for treating many diseases, both in modern and conventional medicine (Ude *et al.*, 2006; Olorundare *et al.*, 2020). Ethnomedicinal treatments utilize the plant's bark, kernels, leaves, or roots to manage a variety of ailments (Ainge and Brown, 2001). However, data have shown that *Irvingia gabonensis* has become common as a healthy and necessary portion of our daily meal, based on its beneficial action to slow down the onset and development of many diseases (Ude *et al.,* 2006). Several studies have been carried out to ascertain the medicinal, nutritional, and other benefits of *Irvingia gabonensis* (Ude *et al.*, 2006; Olorundare *et al.*, 2020).

Ngondi *et al.* (2005), who investigated the effects of *Irvingia gabonensis* seed on body weight and blood lipids of obese subjects in Cameroon, reported a significant decrease in blood pressure, total cholesterol, LDL-cholesterol, triglycerides, and an increased HDL-cholesterol. Another study also linked the use of the plant to the treatment of hyperlipidemia and atherosclerosis (Kuyooro *et al.*, 2017). Comprehensive toxicological and various pharmacological reports have shown diverse medicinal values of *Irvingia gabonensis such as* anti-hyperlipidemic (Kuyooro *et al.*, 2017), antioxidant, reno-hepatoprotective (Hubert *et al.*, 2011), antidiabetic, and neuroprotective effects (Adamson *et al.*, 1986; Adamson *et al.*, 1990; Hossain *et al.*, 2012).

Despite the diverse beneficial values of *Irvingia gabonensis* fruits, there is no report on its effects on blood pressure and hypertension. This study was therefore designed to evaluate the reversal effects of *Irvingia gabonensis* seed extract on ethanol-induced hypertension in male Wistar rats.

MATERIALS AND METHODS

Animals

Male Wistar rats 200 - 250 g between 6-8 weeks old used for the experiment were procured from the Animal Housing facility of the University of Medical Sciences, Ondo State, Nigeria, and housed in plastic cages at standard conditions of 12:12 h light/dark cycle. The animals were allowed to acclimatize for 14 days with unrestricted access to food and water (*ad libitum*) before the commencement of the study.

Collection of plant material

The seeds of the *Irvingia gabonensis* were purchased between June and July 2019 from the Laje market, Ondo City, Ondo State, Nigeria, and were authenticated at the Forensic Research Institute, Ibadan, Oyo State, Nigeria. A voucher specimen of the plant has been deposited in the herbarium of the Institute. This was done in line with global practice (Chan *et al.,* 2012). After peeling the fruit, the seeds were dried in an oven at 400 °C for 24 h, crushed with mortar and pestle, and weighed with a digital electronic weighing balance (BXPR106DUHQ, Mettler Toledo, USA).

Preparation of *Irvingia gabonensis* seed extract

The oil used for the study was extracted from the crushed seeds (1.5 kg) of *Irvingia gabonensis* by the solvent extraction method with *n*-hexane as the solvent for extraction according to the method described by Luque-García and Luque de Castro, (2001).

Drugs and chemicals

Enalapril from Dexcel Ltd with NAFDAC No. 046267 used in the study was purchased at the Uche-Care Pharmacy, Ondo while ethanol was obtained from Sigma-Aldrich, St. Louis, USA. The doses of enalapril (0.1 mg/kg) and ethanol (5%, 10 mL/kg) were chosen based on preliminary and previous dose-response effects (Tsuji *et al.*, 1992), while that of *Irvingia gabonensis* was adopted from the outcome of the preliminary study done to establish the effective dose of the oil. However, normal saline (10 mL/kg, p.o.) was administered to the rats in the control group.

Experimental procedures

Twenty-five (25) male Wistar rats weighing between 200-250 g were randomly assigned into five groups (n=5): Rats in group A received normal saline (10 mL/kg) while rats from groups B to E received 5% ethanol (10 mL/kg), once daily for 14 days. From the 15th to the 35th day, group C

was administered with *Irvingia gabonensis* (250 mg/kg, p.o), group D with *Irvingia gabonensis* (500 mg/kg, p.o.), while group E received enalapril (0.1 mg/kg, p.o) once daily, respectively. The treatment which lasted for a total of 5 weeks, was done once daily orally between 8 am and 12 pm by the use of an oro-gastric cannula. Throughout the experiment, the body weight of the animals was taken with the aid of the digital electronic weighing balance (BXPR106DUHQ, Mettler Toledo, USA).

Mortality and signs of toxicity

From a preliminary toxicology investigation done to determine the LD50 using the combined methods of Lorke (1983) and Chinedu *et al.* (2013), the LD50 of the extract was noted to be greater than 5000 mg/kg. In this study, the animals were observed for mortality and gross signs of toxicity twice daily (morning at 7 am and evening at 7 pm) after administration of different doses of the extract. At the end of the preliminary investigation, there was no case of death recorded even at a dose of 5000 mg/kg. This is an indication that the extract is safe for consumption.

Determination of the effective dose of the extract and duration of treatment

The effective dosage of the extract was also determined in a preliminary investigation using graded doses of the extract starting from 50 mg/kg to 1000 mg/kg body weight (b.w). It was also observed that the two dosages of 500 mg/Kg b.w and 250 mg/Kg b.w of the extract were more effective regulators of heart rate and therefore adopted for this main study. The duration of treatment with ethanol was modified from the method described by Vasdev *et al.* (1993).

Measurement of Blood Pressure and Heart rate

At the end of each treatment, the arterial blood pressure and heart rate of all rats were measured using the method of Van Vliet *et al.* (2000). Each rat was sedated with a 1.5 g/kg intraperitoneal urethane injection. To allow for spontaneous breathing, the trachea was exposed and cannulated. To measure arterial blood pressure from the carotid artery, an arterial cannula was connected to a pressure transducer coupled to a hemodynamic recorder (Student Lab MP35, Biopac System Inc., USA) and attached to a computer.

Sample Collection

After the measurement of the blood pressure and heart rate, all the animals were euthanized under thiopentone sodium anesthesia. Thereafter, the animals were dissected by opening the abdomen with a midline incision, and the kidney and heart were harvested for histological processing. After expunging, the samples were washed in heparinized saline to prevent the clotting of the blood and preserved at -20 ^{o}C in plain capped bottles.

Preparation of tissue for microscopic examination

The kidney and heart tissues were prepared for histological examinations following the protocol described by Drury *et al.* (1976) and Adjene *et al.* (2014). Briefly, the harvested kidney and heart tissues were fixed in 10% formalin and dehydrated in 50%–100% ethanol. Xylene was used to rinse the tissues to remove the dehydration, then the tissues were embedded in paraffin for strengthening and easy dissection. Before sectioning, the tissues were rinsed again in xylene to remove the paraffin and washed in a decreasing concentration of ethanol (100%–50%) before rehydrated with water. Tissue sections (6 mm thick) were made and stained with hematoxylin-eosin (H-E) stain to make them visible for photomicroscopic viewing before examination under a light microscope (CB2000C, Celestron Labs, USA) at X400 magnification.

Determination of the Oil fingerprint by Gas chromatography and mass spectrometry

The essential compounds in the oil were detected by their retention times and mass fragmentation patterns of standards using the GC-MS analysis method with the aid of the GC-MS Machine (GC-MS-QP2010 Plus Shimadzu, Japan) with flame ionization and a diethylene glycol succinate capillary column (30m 0.25 0.25 m) according to the method described by Mamoun *et al.* (2020). By comparing the retention times and fragmentation patterns of the components to those of the standard, the components were defined. The peaks of the chromatogram were identified based on MS data analysis to determine the fatty acid

content. The machine determined each fatty acid percentage by the area percentage (%) of each peak. Also, the automated GC-MS machine was able to characterize the various fatty acid composition by comparing detected compounds to the fatty acid methyl ester (FAME) database.

Statistical Analysis

All data were presented as mean ± standard error of the mean (SEM) and analyzed using GraphPad Prism (Version 8) with statistical significance determined by one-way ANOVA (Analysis of Variance) and Bonferroni post hoc test. The mean differences were considered statistically significant at $P<0.05$.

Ethical Clearance

The experimental procedures were approved by the University of Medical Sciences Research and Ethics Committee (UNIMED/RES/2019/2020/02).

RESULTS

Effects of *Irvingia gabonensis* oil and enalapril on systolic blood pressure

Ethanol significantly increased SBP ($P<0.001$) in the treatment groups compared to the control group. Both *Irvingia gabonensis* and enalapril significantly ($P<0.001$) [$F(4, 20) = 12.16$, $P<0.0001$] prevented the effect of ethanol on SPB compared with ethanol-treated groups, respectively (Figure 1).

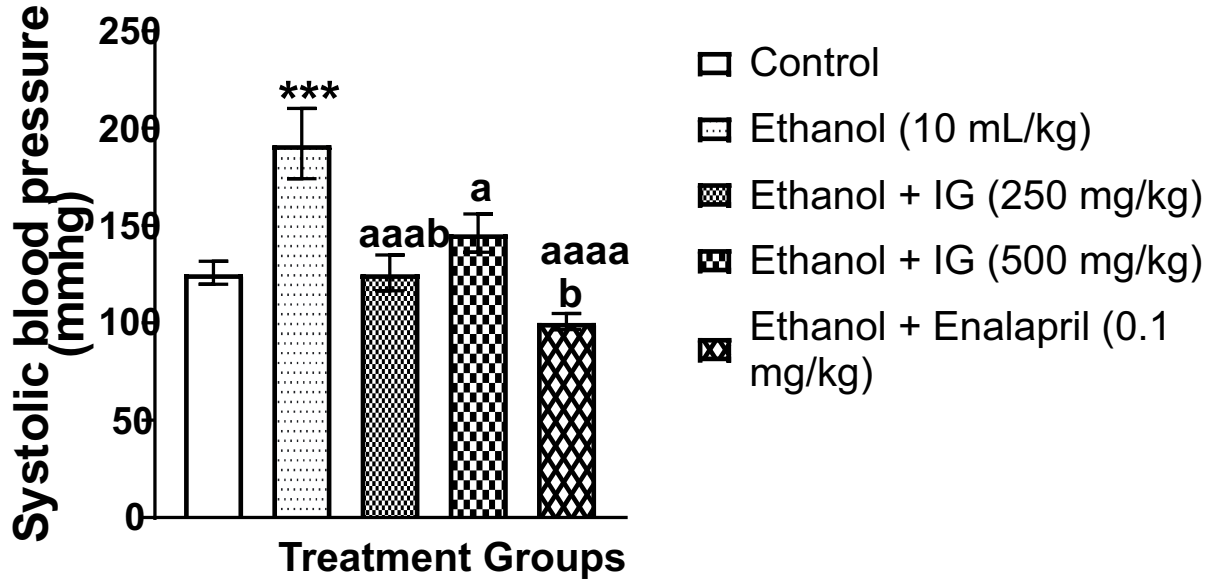

Figure 1: *Irvingia gabonensis* seed extract reversed ethanol-induced alterations in systolic blood pressure in male Wister rats. Bars represent mean ± S.E.M. (n=5) (One-way ANOVA followed by Bonferroni post hoc test). $^{***}P<0.001$ compared with controls; $^{a}P<0.05$, $^{aaa}P<0.001$, $^{aaaa}P<0.0001$ compared with ethanol; $^{b}P<0.05$ compared with IG at 500 mg/kg. IG: *Irvingia gabonensis*.

Effects of *Irvingia gabonensis* oil and enalapril on diastolic blood pressure

Ethanol significantly increased DBP ($P<0.001$) in the treatment group in comparison with the control group. However, *Irvingia gabonensis* at 250 mg/kg and enalapril significantly ($P<0.001$) [$F(4, 20) = 12.32$, $P<0.0001$] prevented the effects of ethanol on DBP compared with ethanol-treated groups, respectively (Figure 2).

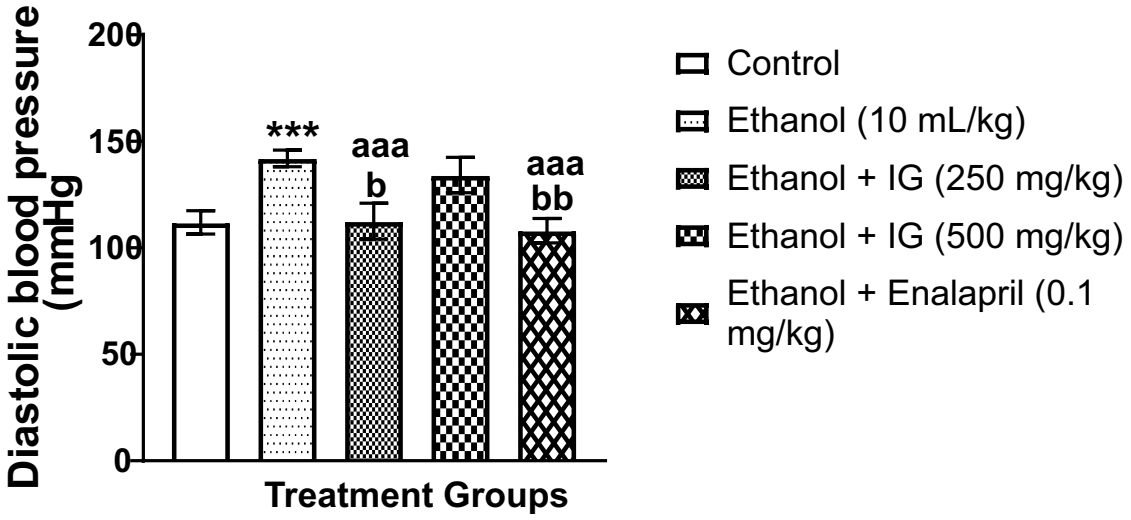

Figure 2: *Irvingia gabonensis* seed extract reversed ethanol-induced alterations in diastolic blood pressure levels in male Wister rats. Bars represent mean ± S.E.M. (n=5) (One-way ANOVA followed by Bonferroni post hoc test). ***P<0.001 Significant compared with the control group; ^{aaa}P<0.001 compared with ethanol; ^{b}P<0.05, ^{bb}P<0.01 compared with IG at 500 mg/kg. IG: *Irvingia gabonensis*.

Effects of *Irvingia gabonensis* seed oil on ethanol-induced alterations in mean arterial blood pressure (MABP)

As presented in Figure 3, ethanol significantly increased MABP (P<0.001) compared to the control group. Both *Irvingia gabonensis* and enalapril significantly (P<0.001) [F (4, 20) = 25.21, P<0.0001] reversed the effects of ethanol on MABP compared with ethanol-treated groups, respectively.

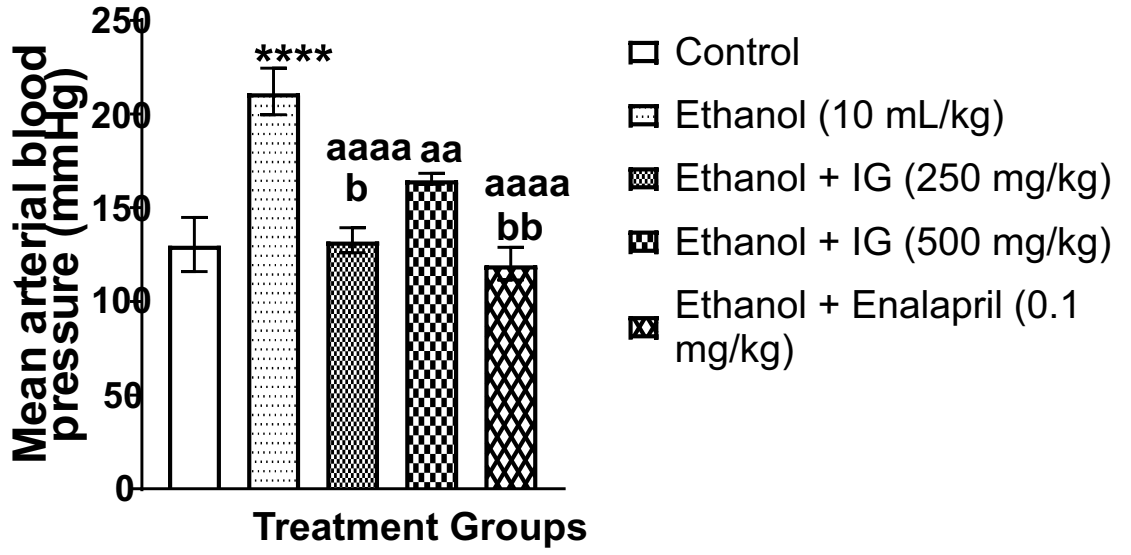

Figure 3: *Irvingia gabonensis* seed extract reversed ethanol-induced alterations in mean arterial blood pressure (MABP) levels in male Wister rats. Bars represent mean ± S.E.M. (n=5) (One-way ANOVA followed by Bonferroni post-hoc test). ***P<0.001 Significant compared with the control group; ^{aaa}P<0.001 compared with the ethanol group; ^{b}P<0.05 compared with IG at 500 mg/kg. IG: *Irvingia gabonensis*.

Effects of *Irvingia gabonensis* seed oil on ethanol-induced alterations in heart rate

There was a significant increase in heart rate (P<0.001) in the ethanol-treated group relative to the control group, and the increase in heart rate was reversed by *Irvingia gabonensis* and enalapril (P<0.001) [F (4, 20) =18.91, P<0.0001] (Figure 4).

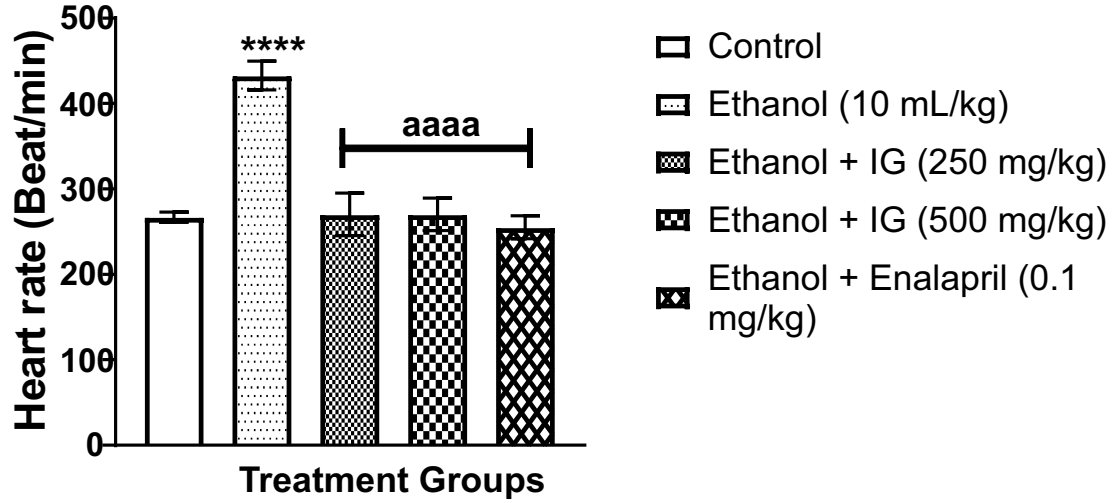

Figure 4: *Irvingia gabonensis* seed extract attenuated ethanol-induced alterations in heart rate in male Wistar rats. Bars represent mean ± S.E.M. (n=5) (One-way ANOVA followed by Bonferroni post-hoc test). ****P<0.0001 compared with the control group; ^{aaaa}P<0.0001 compared with the ethanol group; IG: *Irvingia gabonensis*.

Effects of *Irvingia gabonensis* seed oil on ethanol-induced alterations in body weight

As presented in Figure 5, ethanol significantly caused a net negative body weight gain (P<0.001) in the group treated with ethanol compared to the control group. This effect was significantly [F (4, 20) = 20.26, P<0.0001] reversed in the *Irvingia gabonensis* and enalapril-treated groups.

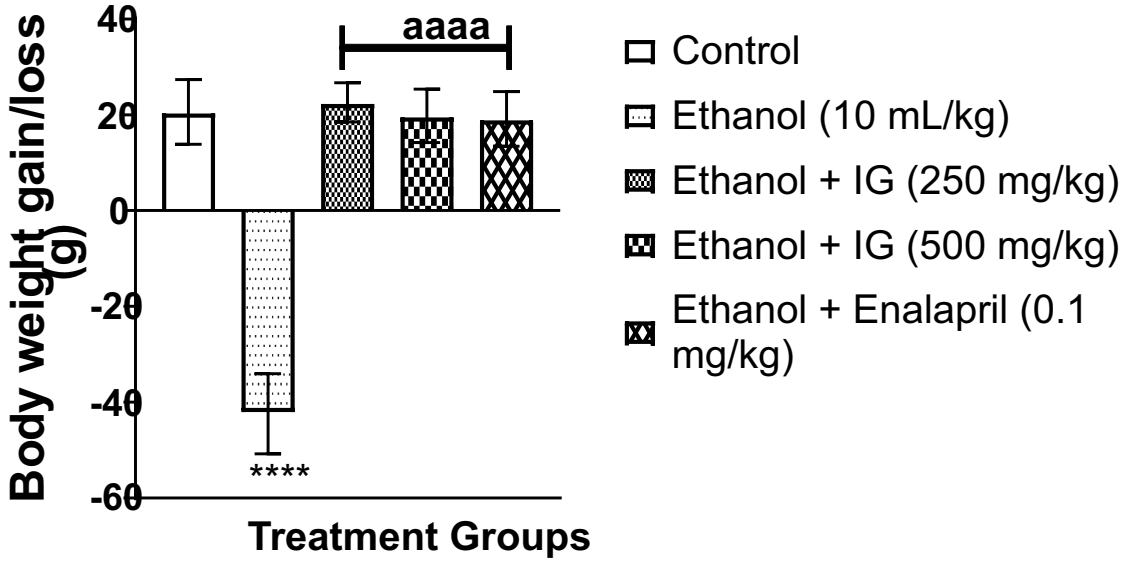

Figure 5: *Irvingia gabonensis* seed extract attenuated ethanol-induced alterations in body weight in male Wistar rats. Bars represent mean ± S.E.M. (n=5) (One-way ANOVA followed by Bonferroni post hoc test). ***P<0.001 compared with controls; ^{aaa}P<0.001 when compared with ethanol. IG: *Irvingia gabonensis*.

The effects of *Irvingia gabonensis* seed extract on histopathological changes in the heart muscle of rats

Irvingia gabonensis at 250 mg/kg and enalapril (0.1 mg/kg) produced no histopathological changes in the heart muscle cells compared to the normal control group (Figure 6). However, the rats treated with ethanol (10 ml/kg/day) had an aggregate of fat cells amidst cardiac myocytes with an indication of fatty infiltration compared with the control group.

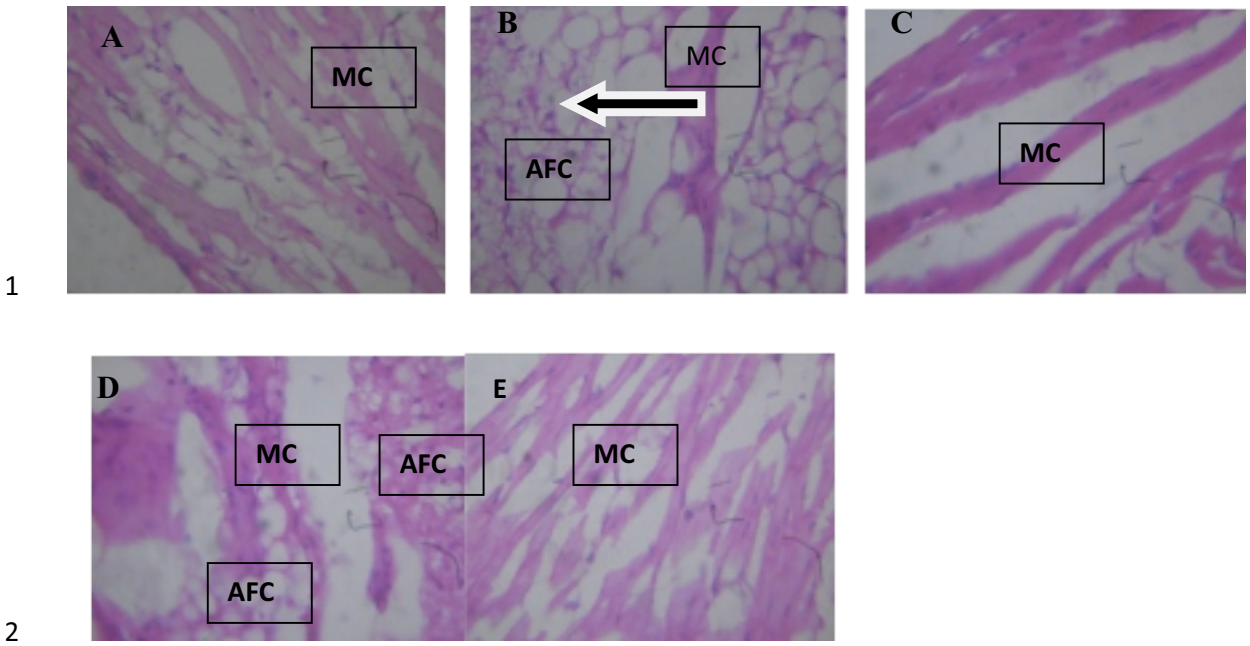

Figure 6: Photomicrographs showing the effects of *Irvingia gabonensis* seed extract on histopathological changes in the heart muscle of rats (X400 magnification) **(**A: Control (normal saline); B: 10 mL/kg of 5% ethanol; C: ethanol + IG (250 mg/kg); D: ethanol + IG (500 mg/kg); E: ethanol + enalapril (0.1 mg/kg). Slides A, C, and E revealed interlacing fascicles of cardiac myocytes/myocardial cells with no abnormalities seen (MC). Slide D revealed interlacing fascicles of cardiac myocytes/myocardial cells (MC) with aggregates of fat cells amidst cardiac myocytes indicating fatty infiltration. Slide B showed interlacing fascicles of cardiac myocytes/ myocardial cells which are aggregates of fat cells amidst cardiac myocytes and indicating fatty infiltration; Black arrow (AFC)- fatty infiltration. Haematoxylin-eosin stain: Original magnification X400, Calibration bar = 0.01 mm (10 μm) for all plates. IG: *Irvingia gabonensis*.

The effects of *Irvingia gabonensis* seed extract on histopathological changes in the kidney of rats

Irvingia gabonensis (250 mg/kg and 500 mg/kg) (C & D) and enalapril (0.1 mg/kg) (E) produced no changes in the kidney architecture compared to the control group, while rats treated with only ethanol were associated with vascular congestion (Figure 7).

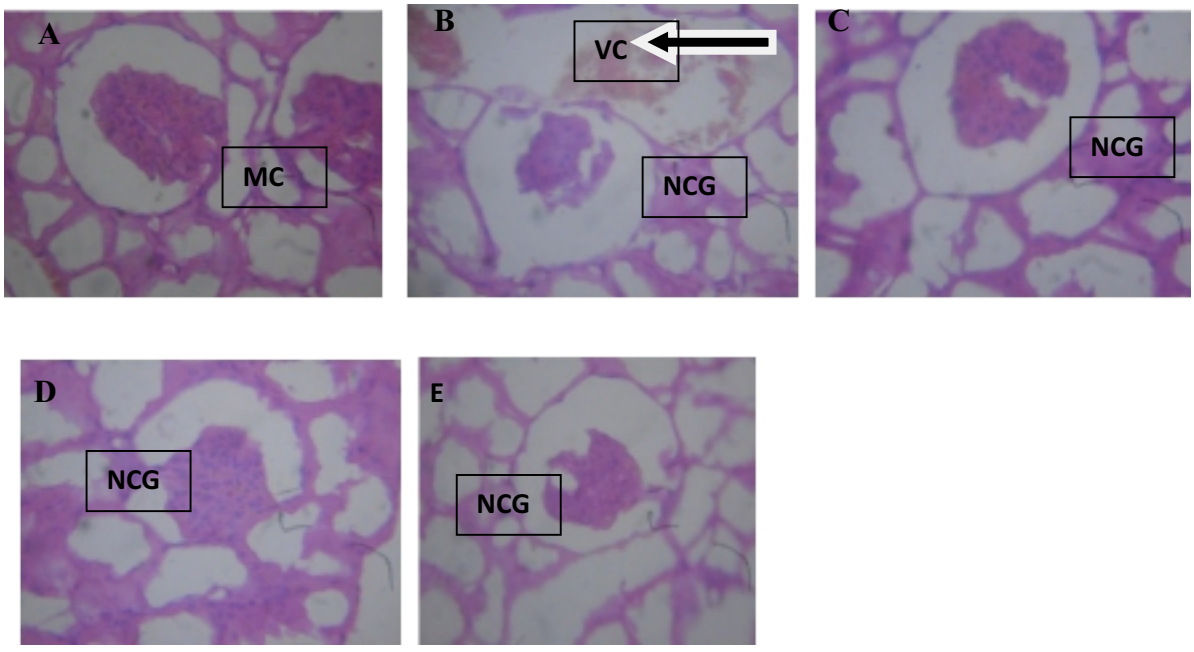

Figure 7: Photomicrographs showing the effects of *Irvingia gabonensis* seed extract on histopathological changes in the kidney of rats (H & E stain, X400 magnification). A: control (normal saline); B: 10 mL/kg of 5% ethanol; C: ethanol + IG (250 mg/kg); D: ethanol + IG (500 mg/kg); E: ethanol + enalapril (0.1 mg/kg). Slides A, C, D, and E revealed normocellular glomerular tufts disposed on a background containing renal tubules (NCG). Slide B: normocellular glomerular tufts disposed on a background containing renal tubules with congestion of blood vessel (VC) (Black arrow). IG: *Irvingia gabonensis*.

Gas chromatography, mass spectrometry analysis report

The extract was characterized by the presence of a fatty acid group and fatty acid methyl ester (FAME). The composition of the oil extract is described in Table 1.

Table 1: Oil Fingerprint of the *Irvingia gabonensis* seed oil.

S/N	Compounds	Concentration
1.	Free fatty acid	4.60 g/100g
2.	peroxide value	2.67 meq/Kg
3.	iodine value	7.40 g/100g
4.	Saponification value	265.50 mg KOH/g
5.	acid value	6.24 mg KOH/g
6.	Colour intensity	3.4 Lovibond units

Percentage composition of oil

Compounds	Percentage	Retention time
Oleic (9Z)-Octadecenoic acid)	0.06	17.168
Lauric (Dodecanoic acid)	7.68	17.369
Myristic (Tetradecanoic acid)	5.23	19.595
Linolenic (9,12 - Octadecadienoic acid)	0.02	20.684
Palmitic (hexadecanoic acid)	11.59	23.048
Stearic (octadecanoic acid)	2.83	23.198
Vitamin E	9.21	27.408

The concentration of fatty acids methyl ester

Class of fatty acids	Percentage
Saturated fatty acids	97.83
Monounsaturated fatty acids	1.96
Polyunsaturated fatty acids	0.21

(Note: Values were extrapolated by summing all fatty acids in the GCMS result sheet and not just compositions in the table above)

The dose-response relationship of *Irvingia gabonensis* seed oil on the heart rate of Wistar rats

Figure 8 showed the dose-response relationship of the oil used in this study. The effective doses were determined to be 250 mg/kg/b.w (ED1) and 500 mg/kg/b.w (ED2) of the *Irvingia gabonensis* seed oil.

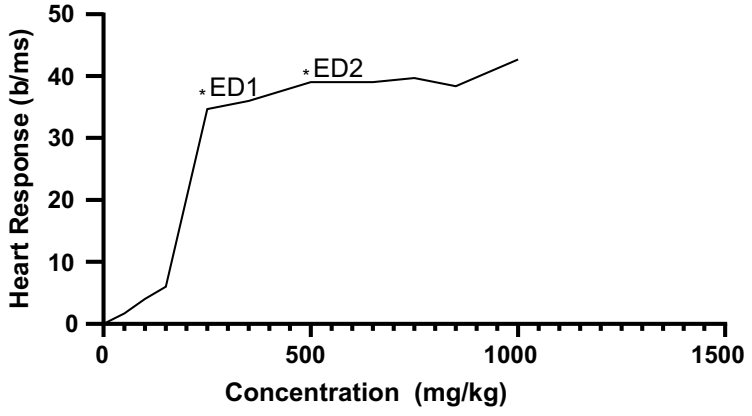

Figure 8: Dose-response graph showing the effective doses of ED1 and ED2. ED- effective dose.

DISCUSSION

The reversal effects of the *n*-hexane extract of *Irvingia gabonensis* were investigated in ethanol-induced hypertensive male rats. Ethanol is known to promote hemodynamic disturbances that cause high blood pressure, and the mechanism by which this is achieved has been well-elucidated (Marchi *et al.,* 2014). In the present study, administration of ethanol (10 mL/kg/day) resulted in a significant increase in systolic, diastolic, mean blood pressure, and heart rate, as well as body weight loss. Chronic consumption of ethanol has been implicated as one of the major contributory factors to hypertension and other cardiovascular anomalies (Halanych *et al*., 2010; Marchi *et al.,* 2014). Previous reports have also shown that ethanol has a complex direct effect on blood vessels, resulting in basal constriction and loss of blood vessel elasticity (Akindele *et al*., 2014; Husain *et al*., 2014). Notably, these blood vessel abnormalities may cause changes in cardiovascular functions, resulting in a decrease in endothelial nitric oxide release. The effects of ethanol may have also caused a spontaneous increase in the activities of baroreceptors, resulting in the sympathetic discharge that eventually caused the increase in blood pressure. A similar report was earlier documented in the findings of Husain *et al.* (2014), which opined that ethanol may induce an increased sympathetic outflow to increase blood pressure.

In this study, the administration of *Irvingia gabonensis* seed oil or enalapril significantly decreased blood pressure in ethanol-induced hypertensive rats. The results suggest that the oil of *Irvingia gabonensis* may have an antihypertensive effect that could be due to its possible action on peripheral resistance. Furthermore, even the lowest dosage of the *Irvingia gabonensis* oil caused a reduction in blood pressure. This could be attributed to the high content of lauric, myristic, and palmitic acids and the high saponification value of the *Irvingia gabonensis* oil extract (Berry and Hirsch, 1986; Grimsgaard *et al*., 1999; Alves *et al.,* 2017; Omoniyi *et al*., 2017). The saponification value of oil has been linked to its health benefits, and it accounts for the amount of short- and medium-chain fatty acids in the oil. The higher the saponification level of the oil, the safer it is for human health and of increased cardiovascular value (Boateng *et al*., 2016). Moreover, the levels of medium-chain fatty acids in the oil are also important. The *Irvingia gabonensis* oil extract used in the present study seems to have a high saponification value, which indicates its level of safety for consumption.

In a previous study, intravenous administration of lauric acid (the most abundant medium-chain fatty acid in plants) was associated with a dose-dependent reduction in blood pressure, induced vasorelaxation effects, and a reduction in oxidative stress in kidney homogenates (Alves *et al*., 2017). In another study, lauric acid was linked with the activation of signaling pathways leading to apoptosis of cancer cells, thereby preventing the proliferation of normal cells (Lappano *et al*., 2017). These could be the major pathway by which the *Irvingia gabonensis* oil normalized the blood pressure and prevented the deleterious effects of ethanol on the cardiac and renal cells. The antihypertensive effects of the oil could also be attributed to its high vitamin E content (9.21%). A previous study (Boshtam *et al*., 2002) found that a vitamin E supplement would increase blood pressure in moderately hypertensive patients over time, owing to nitric oxide. As a result, we hypothesized that this may be one of the active ingredients in the *Irvingia gabonensis* oil that contributes to its anti-hypertensive properties. To the best of our knowledge, this is the first time an *n*-hexane extract of *Irvingia gabonensis* has been linked with antihypertensive properties.

The results of the present study revealed a significant reduction in the body weight of the ethanol-treated group compared with the control group. The weight loss observed in the group treated with ethanol could be due to the deleterious effects caused by ethanol in the cells, thus preventing oxidation and lowering the absorption of nutrients into the cells (Teschke, 2018). In comparison with the ethanol-treated group, there was a significant increase in weight (in the *Irvingia gabonensis* oil and the enalapril-treated groups). However, no significant difference was observed between the control and the *Irvingia gabonensis* oil and the enalapril-treated group. Thus,

it is clear that the dosage of *Irvingia gabonensis* and enalapril used in this study prevented weight loss induced by ethanol consumption. This observation suggests that *Irvingia gabonensis* oil protects the structural integrity of cells against cardiotoxic molecules derived from the metabolism of ethanol. The *Irvingia gabonensis oil* may have worked via a mechanism other than the angiotensin-aldosterone system.

The histopathological examination has been previously used as a reliable tool for the detection of toxic effects (Lanning *et al.*, 2002). We evaluated the effects of ethanol on the heart muscle and the kidney using microscopic and histological examinations. It was revealed that repeated treatment with ethanol caused fatty infiltration in the heart and vascular congestion in the kidney, but histopathological slides of rats treated with *Irvingia gabonensis* oil (250 mg/kg p.o) showed improved and normal architecture of the heart muscle and kidney. This study is comparable to the studies by Emejulu *et al.* (2016), which also demonstrated the reno-protective effects of *Irvingia gabonensis*. This could be due to the cytoprotective and anticancer effects of the *Irvingia gabonensis* oil, initiated by its lauric acid content. Similarly, Lappano *et al.* (2017) linked lauric acid to the activation of signaling pathways, leading to the anticancer effects of the medium-chain fatty acid of coconut oil.

CONCLUSION

The results of this study indicate that *Irvingia gabonensis seed* oil administered at 250 mg/kg has a potency similar to enalapril in reducing blood pressure, and heart rate, and reversing weight loss in ethanol-induced hypertension. Also, it protects the architecture of the cardiac and renal tissues against the deleterious effects of ethanol. The reversal effect of *Irvingia gabonensis* oil on hypertension is due to its antihypertensive and cytoprotective effects, which may justify its empirical use in the treatment of hypertension. These effects of *Irvingia gabonensis* oil are due to its favorable oil fingerprint. Further studies to corroborate the efficacy of the extract in the management of cardiovascular diseases are recommended.

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