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Biology

Preventive Effects of the Aqueous Extract Of Aerial Part of Leersia Hexandra Swartz (Poaceae) In Ethanol-Induced Hypertensive Rats

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Abstract | **Original Research Article**

Background: *Leersia hexandra* is an herbaceous plant used in traditional Cameroonian medicine to treat hypertension. The aim of this study was to evaluate the preventive effects of the aqueous extract of *Leersia hexandra* in alcohol-induced hypertension in rat. ***Method****:* Animals were divided into 5 groups of 6 animals each and treated during 35 days as followed: One group received distilled water (10 mg/kg), the other 4 groups received each in addition to 40° ethanol (5 g/kg), distilled water, the plant extract (100 and 200 mg/kg respectively) and nifedipine (10 mg/kg). At the end of the treatment, hemodynamic parameters were recorded by direct method. The heart and left ventricle were weighed and the ventricular hypertrophy index was calculated. Serum and tissue parameters were evaluated by the colorimetric method. ***Results:*** *Leersia hexandra* significantly prevented the increase of mean blood pressure ($p < 0.001$), heart rate ($p < 0.05$), creatinin, total cholesterol, triglycerides, LDL-cholesterol and transaminase activities caused by ethanol compared to hypertensive rats. The extract also prevented the decrease ($p < 0.001$) of HDL-cholesterol levels. At the dose of 200 mg/kg, the extract prevented ($p < 0.01$) the significant increase of left ventricle hypertrophic index. The extract also prevented the decrease in reduced glutathione level, superoxide dismutase activity and the increase in malondialdehyde in investigated organs. ***Conclusion:*** These results suggest that *Leersia hexandra* aqueous extract may act on vascular resistance and possess lipid lowering and antioxidant activities which may justify its traditional use in the management of hypertension.

Keywords: Hypertension; *Leersia hexandra*; ethanol; antioxidant; rat.

INTRODUCTION

Hypertension is a chronic medical condition which is most of the time asymptomatic in the early stages and many people go therefore undiagnosed. Those who are diagnosed may not have access to treatment and may not be able to successfully control their illness over the long term [1]. It is then advisable to prevent hypertension by having the habit of controlling our blood pressure and adopting appropriate behaviors [1]. Chronic and heavy alcohol intake usually causes cardiovascular injuries leading to physiological dysfunctions and their complications [2]. Alcohol can directly or indirectly induce blood pressure raise through several possible mechanisms [3]. Some of them passed through the increase of vascular sensitivity to vasocontrictor due to the shifts of the extracellular calcium to intracellular space [3]. Ethanol consumption is able to induce oxidative stress which is responsible at least in part of its injuries on different organs [2]. There are many traditional medicinal plants used in the treatment of hypertension and its complications, mainly due to their important contain of antioxidant compounds [4] *Leersia hexandra* is a medicinal plant, widely used in Africa to manage cough and its complications [5]. The plant is also known for its anti-proliferative and anti-invasive effects [6]. In Cameroon, the plant is used to manage high blood pressure by the population. Since some plants with anticancer activity are also known to possess anti-hypertensive activity due to their calcium blocker properties [4], it was then suggested that the benefic effects of *L. hexandra* on hypertensive patients were linked to its anticancer activity. In order to verify this hypothesis, the present study was designed to evaluate the protective effect of *L. hexandra* aqueous extract on alcohol-induced hypertension and oxidative stress in rat.

MATERIAL AND METHODS

Preparation of plant extract and phytochemical screening

The external parts of *Leersia hexandra* Swartz were collected in February at Bamendou in the west

region of Cameroon. The plant was authenticated at the National Herbarium by comparison with the existing voucher specimen N° 6850/HNC. The plant was dried at room temperature and reduced to a powder. The material was added to six liters of hot water (100 ºC) and allowed to macerate until cooling down and then filtered. The solution obtained after filtration was lyophilized and gave 19 g (3.9 % yield) of a green powder. Phytochemical investigations of alkaloids, flavonoids, saponins, Polyphenols, gallic tannins, catechic tannins Anthocyanes, anthraquinones, glycosides, triterpenes and steroid were done according to the procedure described by Odebiyi and Sofowora [7] and Mujeeb*etal* [8].

Drugs and chemicals

All the drugs and chemicals used in this experiment were purchased from Sigma Chemical Company (St. Louis, MO, USA). The chemicals were of analytic grade.

Animals

The antihypertensive activity of the extract was carried out on 30 male albino Wistar rats aged 6-8 weeks and weighting 150-160 g prior to the experiment. Animals were housed in standard environmental conditions under a 12/12 h light/dark natural cycle in the animal house of the Laboratory of Animal Physiology of the University of Yaoundé I. All animals had free access to standard diet and tap water *ad libitum*. All animal treatment procedures used in the present study were approved by the Cameroon National Ethical Committee (Ref. N° FWIRB 00001954).

Experimental design

The antihypertensive activity of the aqueous extract of *L. hexandra* was evaluated by using ethanol induced hypertension in rats. Rats were randomly divided into five groups of six rats each and received concomitantly orally daily in addition to ethanol 40° (5 g/kg), different treatments as followed: Water (1 mL/ 100 g) group 2, plant extract (100 and 200 mg/kg) group 3 and 4 respectively, nifedipine (10 mg/kg) group five. A last group of six normotensive rats was receiving water (1 mL/ 100 g) 2 times group 1. During the experimental period, body weight as well as food intake were assessed. At the end of the treatment period, hemodynamic parameters (blood pressure and heart rate) of all rats were recorded according to the method previously described [9]. Briefly, each rat was anesthetized using an intraperitoneal injection of urethane (1.5 g/kg). The trachea was exposed and cannulated to facilitate spontaneous breathing. The arterial blood pressure and heart rate were measured from right carotid artery via an arterial cannula connected to a pressure transducer coupled with a hemodynamic recorder Biopac Student Lab. (MP35) and visualized with a computer.

Biochemical and histological analysis

After hemodynamic parameters recording, rats were sacrificed; blood was collected and centrifuged at 3000 rpm for 15 minutes. The serum obtained was stored at -20°C for biochemical analysis. Serum samples were assayed for triglycerides, total cholesterol, HDL-cholesterol, LDL-cholesterol, creatinin, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) using commercial diagnostic kits Fortress. The atherogenic index (AI) was calculated by the following formula: AI = ([total cholesterol] – [HDLcholesterol)])/[HDL-cholesterol)] [10]. After blood collection, the heart, aorta, liver and kidneys were dissected out and weighed. The left ventricle was also separated from the heart and weighed. Those organs were homogenized in Mc Even solution for aorta and heart, or in Tris-HCl 50 mM buffer solution for liver and kidneys to make a 20% homogenate. Each homogenate was centrifuged at 10000 g for 30 minutes at 4 ºC and stored at -20 ºC. Tissue protein concentration was assayed according to Gornall*et al* [11] using the Biuret reagent and bovine serum albumin as a standard. Reduced glutathione (GSH) and superoxide dismutase (SOD) were determined using the method of Ellman [12] and Misra and Fridovish [13] respectively. Malondialdehyde (MDA), the end-product of lipid peroxidation was determined using the procedure of Wilbur *et al* [14].

For microscopic evaluation, part of investigated aorta was fixed in 10% formalin for 7 days and embedded in paraffin for microscopical examination in accordance with routine laboratory procedure. Paraffin sections of 4 µm were prepared and stained with haematoxylin and eosin (H&E) for histological examination.

STATISTICAL ANALYSIS

Results are expressed as the mean ± SEM. The difference between treated groups was compared using one-way analysis of variance (ANOVA) followed by Tukey posttest, using Graphpad Prism version 5.03 software. The value of $p < 0.05$ was considered statistically significant.

RESULTS

Phytochemistry

The phytochemical screening of *Leersia hexandra* aqueous extract revealed the presence of alkaloids, saponines, flavonoids, phenols, glycosides, anthraquinones, tannins, terpenes and steroid. gallic tannins and anthocyanes were absent.

Effects of *L. hexandra* on body weight gain and food intake

The effects of *L. hexandra* on the evolution of the body weight as well as the food intake during the treatment period were assessed. As shown on figure 1, during the treatment period, weight in all the groups did not increase significantly. Nonetheless, at week 5, the

body weight of the animals in the group receiving alcohol and distilled water was significantly low (34.93%; $p < 0.01$) as compare to the normal control group. Nifedipine as well as plant extract prevented that light decrease.

As shown in figure 1, after 5 weeks of treatment, ethanol significantly reduced the food intake by 21.59% ($P < 0.05$), 14.99% ($P < 0.05$), 20.73% ($P < 0.01$), 37.28% ($P < 0.001$), 52.75% ($P < 0.001$) for week 1, 2, 3, 4 and 5 respectively as compared to normotensive group. *L. hexanda* aqueous extract (100 mg/kg) has prevented that decrease by 19.80% ($p < 0.05$), 45.55% ($p < 0.001$) and 88.88% ($p < 0.001$) respectively on week 3, 4 and 5. At the dose 200 mg/kg, the prevention by the extract was of 24.89% ($p < 0.05$), 23.29% ($p < 0.05$), 35.62% ($p < 0.01$), 74.32% ($p < 0.001$) and 115,78% ($p < 0.001$) respectively on week 1, 2, 3, 4 and 5. In the same conditions, nifedipine (10 mg/kg) also prevented the decrease on food intake by 16.96% ($p < 0.05$), 29.80% ($p < 0.001$), 68.94% ($p < 0.001$) and 115.78% ($p < 0.001$) respectively on week 2, 3, 4 and 5 as compared to alcohol hypertensive rats.

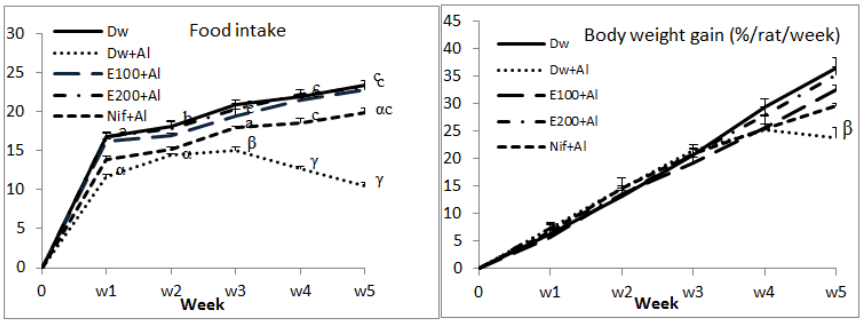

Fig-1: Effects of *L. hexandra* on body weight gain and food intake

Each point represents means of percentage ± S.E.M. n = 6. $^{\alpha}p< 0.05$, $^{\beta}p< 0.01$ and $^{\gamma}p< 0.001$: significantly different compared to normotensive rats .$^{a}p< 0.05$, $^{b}p< 0.01$ and $^{c}p< 0.001$: significantly different compared to hypertensive rats. Dw: distilled water 10mL/kg, Dw+Al: distilled water and alcohol 5g/kg, E100+Al: Extract100mg/kg and alcohol, E200+Al:Extract 200mg/kg and alcohol, Nif+Al: Nifedipine 10mg/kg and alcohol, W: week.

Effects of *L. hexandra* on heart and left ventricle weight

Table 1 shows that the administration of ethanol (5 g/kg) during 5 weeks increased significantly the heart weight 15.65% ($p < 0.001$) and the left ventricle weight 44.73% ($p < 0.001$) respectively as compared to distilled water (normotensive group). Aqueous extract of *L. hexandra* significantly prevented the increase of heart weight by 11.32% ($p < 0.01$) and left ventricle weight by 29.09% ($p < 0.001$) at the dose of 200 mg/kg respectively as compared to ethanol hypertensive rats. At the dose of 100 mg/kg, the plant extract prevented only the increase of left ventricle weight (15.15%; $p < 0.01$) as compared to ethanol hypertensive rats. Nifedipine administered in the same condition significantly prevented the rise in heart (13.25%; $p < 0.01$) and left ventricle (31.51%; $p < 0.001$) weights.

Table-1: Effects of *L. hexandra* on heart and left ventricle weight

Parameters	Dw	Dw+Al	E100+Al	E200+Al	Nif+Al
Heart weight	0.626±0.016	0.724±0.013$^{\gamma}$	0.698±0.011^{a}	0.642±0.009^{b}	0.628±0.013^{b}
LVW	0.228±0.005	0.330±0.006$^{\gamma}$	0.280±0.008$^{\beta b}$	0.234±0.007^{c}	0.226±0.008^{c}
VHI	0.364±0.008	0.456±0.011$^{\beta}$	0.401±0.011	0.364±0.010^{b}	0.359±0.020^{b}

Each value presents means ± S.E.M. n = 6. $^{\alpha}p< 0.05$, $^{\beta}p< 0.01$: significantly different compared to normotensive rats. $^{a}p< 0.05$, $^{b}p< 0.01$: significantly different compared to hypertensive rats. Dw: distilled water 10mL/kg, Dw+Al: distilled water and alcohol l5g/kg, E100+Al: Extract 100mg/kg and alcohol, E200+Al: Extract 200mg/kg and alcohol, Nif+Al: Nifedipine 10mg/kg and alcohol; LVW: left ventricle weight; HVI: ventricular hypertrophy index.

Effects of *L. hexandra* on haemodynamic parameters

Table 2 summarizes the effect of *L. hexandra* aqueous extract on blood pressure and heart rate of the experimental animals. Administration of alcohol (5 g/kg) during 5 weeks resulted in a significant increase ($p < 0.001$) in blood pressure and a non-significant increase in heart rate. The increase in blood pressure was 60.95, 78.23 and 61.27% higher as compared to normotensive rats respectively for the systolic, diastolic and mean arterial blood pressure. In concomitant administration with alcohol, *L. hexandra* significantly ($p < 0.001$) prevented the increase in blood pressure. The systolic, diastolic and mean arterial blood pressures were decreased by 32.44, 38.25 and 32.35% with the dose 100 mg/kg and of 36.67, 44.48 and 37.34% with the dose 200 mg/kg respectively as compared to alcohol-induced hypertensive rats. Nifedipine in the same conditions significantly prevented the increase of

systolic blood pressures, diastolic blood pressures and mean arterial blood pressures by 32.64, 36.95 and 32.07% respectively as compared to alcohol-induced hypertensive rats.

Table-2: Effects of *L. hexandra* on haemodynamic parameters

	Dw	Dw+Al	E100+Al	E200+Al	Nif+Al
SBP (mm Hg)	108.75±2.07	175.04±2.64$^{\gamma}$	118.25±6.49^{c}	110.85±2.98^{c}	117.89±1.57^{c}
DBP (mm Hg)	90.13±4.83	160.54±2.67$^{\gamma}$	99.13±4.24^{c}	89.13±1.75^{c}	101.22±14.02^{c}
MBP (mm Hg)	102.54±2.91	165.37±2.64$^{\gamma}$	111.87±5.73^{c}	103.61±2.43^{c}	112.33±1.64^{c}
HR (beat/min)	370.59±1.17	379.84±5.12$^{\beta}$	380.72±8.98	375.04±3.60^{a}	364.28±2.05^{c}

Each value represents means ±S.E.M. n = 6. $^{\beta}p< 0.01$ and $^{\gamma}p< 0.001$: significantly different compared to normotensive rats (Dw). $^{a}p< 0.05$ and $^{c}p< 0.001$: significantly different compared to hypertensive rats (Dw+Al). Dw: distilled water 10 mL/kg, Dw+Al: distilled water and alcohol l5g/kg, E100+Al: Extract 100mg/kg and alcohol, E200+Al: Extract 200mg/kg and alcohol, Nif+Al: Nifedipine 10mg/kg and alcohol. SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, MBP: Mean Blood Pressure, HR: Heart Rate.

Effect of *Leersia hexandra* aqueous extract on the lipid profile

As shown in table 3, the administration of ethanol during 5 weeks resulted in a significantly ($p < 0.001$) increase of total cholesterol (TC), triglycerides (TG), LDL-cholesterol (LDL-c) and atherogenic index (AI).

The increase was 6.79, 35.87, 15.86 and 11.42% respectively as compare to normotensive group. At the same time, the rate of HDL-cholesterol (HDL-c) decrease by 20.74%. Administrated with ethanol, *L. hexandra* (100 and 200 mg/kg) significantly ($p < 0.001$) prevented HDL-c decrease by 31.29 and 22.96% respectively, and the increase of TC (5.11 and 9.33%), of TG (15.72 and 26.68%), LDL-c (15.30 and 17.03%) and of AI (11.53 and 10.25%) respectively as compared to alcohol-induced hypertensive rats. In the same conditions nifedipine prevented the decrease in HDL-c by 38.08% ($p < 0.001$) and the increase in TC, TG, LDL-c and IA respectively by 13.33 ($p < 0.001$), 15.16 ($p < 0.01$), 29.96 ($p < 0.001$) and 16.66% ($p < 0.001$) as compared to alcohol-induced hypertensive rats.

Table-3: Effect of *Leersia hexandra* aqueous extract on the lipid profile

	Dw	Dw+Al	E100+Al	E200+Al	Nif+Al
TG (mg/dL)	84.51±5.90	114.83±1.38$^{\gamma}$	96.77±2.10^{b}	84.19±2.35^{c}	97.42±2.52^{b}
TC (mg/dL)	190.67±0.77	203.62±2.83$^{\gamma}$	193.21±0.63^{b}	184.61±0.71^{c}	176.47±1.67$^{\gamma c}$
LDL-c (mg/dL)	117.27±1.28	135.87±3.29$^{\gamma}$	115.07±1.13^{c}	112.72±1.43^{c}	95.16±1.32$^{\gamma c}$
HDL-c (mg/dL)	56.49±0.26	44.77±0.93$^{\gamma}$	58.78±0.48^{c}	55.05±1.62^{c}	61.82±0.83$^{\beta c}$
AI	0.70±0.00	0.78±0.00$^{\gamma}$	0.69±0.00^{c}	0.70±0.00^{c}	0.65±0.00$^{\gamma c}$

Each value represents means ±S.E.M. n = 6. $^{\beta}p< 0.01$ and $^{\gamma}p< 0.001$: significantly different compared to normotensive rats (Dw). $^{b}p< 0.01$ and $^{c}p< 0.001$: significantly different compared to hypertensive rats (Dw+Al). Dw: distilled water 10 mL/kg, Dw+Al: distilled water and alcohol 5g/kg, E100+Al: Extract 100mg/kg and alcohol, E200+Al: Extract 200mg/kg and alcohol, Nif+Al: Nifedipine10mg/kg and alcohol. TC: total cholesterol, TG: triglyceride, AI: atherogenic index.

Effect of *Leersia hexandra* aqueous extract on liver and kidney function markers

As shown in Table 4, the levels of AST, ALT and creatinine levels in serum were significantly increased in alcohol-induced hypertensive rats as compared to normotensive rats. The increase of the level of these parameters was significantly and dose-dependently prevented in *L. hexandra*-treated animals as compared to alcohol-induced hypertensive rats. The values were decreased by 65.51, 23.49 and by 25.16% with the dose 100 mg/kg, and by 73.71, 33.34 and 46.38% with the dose of 200 mg/kg respectively for AST, ALT and creatinine levels as compared to alcohol-induced hypertensive rats. In the same conditions, nifedipine also prevented the increase in d'ALT, AST and creatinine respectively by 68.59, 25.81 and 45.07% as compared to alcohol-induced hypertensive rats.

Table-4: Effect of *Leersia hexandra* aqueous extract on liver and kidney function markers

	Dw	Dw+Al	E100+Al	E200+Al	Nif+Al
ALAT (U/L)	45.16±1.76	120.47±2.55$^{\gamma}$	41.55±1.82^{c}	31.66±3.02$^{\alpha c}$	37.83±4.82^{c}
ASAT (U/L)	202.15±3.62	250.26±13.32$^{\beta}$	191.47±2.04^{c}	166.80±2.13$^{\alpha c}$	185.65±8.31^{c}
Creatinine (mg/dL)	3.02±0.14	4.57±0.09$^{\gamma}$	3.42±0.09^{c}	2.45±0.11$^{\alpha c}$	2.51±0.10$^{\alpha c}$

Each value represents means ±S.E.M. n = 6.$^{\alpha}$p< 0.05; $^{\beta}$p < 0.01 and $^{\gamma}$p< 0.001: significantly different compared to normotensive rats (Dw). ^{b}p< 0.01 and ^{c}p< 0.001: significantly different compared to hypertensive rats (Dw+Al). Dw: distilled water 10 mL/kg, Dw+Al: distilled water and alcohol5g/kg, E100+Al: Extract100mg/kg and alcohol, E200+Al: Extract 200mg/kg and alcohol, Nif+Al: Nifedipine10mg/kg and alcohol.

Effect of *Leersia hexandra* aqueous extract on oxidative stress markers

Chronic feeding with alcohol resulted in a significant increased of MDA levels of 82.29% (p < 0.001) in liver, 94.80% (p < 0.01) in kidney, 50% (p < 0.05) in aorta and 51.42% (p < 0,01) in heart as compared to normotensive rats. When administered with ethanol, the plant extract (100 and 200 mg/kg) succeeded to prevent these increases. The values were 28.57 (p < 0.05), 35.33 (p < 0.05), 44.44 (p < 0.001) and 52.35% (p < 0.001) respectively in the liver, kidney, aorta and heart with the dose of 200 mg/kg, and 37.90 (p < 0.01) and 41.03% (p < 0.001) respectively in aorta and heart with the dose of 100 mg/kg lower as compared to alcohol-induced hypertensive rats. Nifedipine in the same conditions prevented the increase of MDA in all the investigated organs.

As shown in figure 2, ethanol 40° (5 g/kg) administration during 5 weeks led to a decrease in superoxyde dismutase (SOD) activity. The decrease was 50, 45.45, 61.90 and 70.83% respectively in liver kidney aorta and heart as compared to normotensive rats. Simultaneous administration of ethanol and plant extract significantly prevented that decrease with the two doses. Compared to alcohol-induced hypertensive rats, the values were increased by 183.33 % (p < 0.001) in the liver, 94.44 % (p < 0.01) in the kidney, 225% (p < 0.001) in the aorta and 342.85% (p < 0.001) in the heart with the dose of 100 mg/kg and of 241.66% (p < 0.001) in the liver, 88.88% (p < 0.05) in the kidney, 350% (p < 0.001) in the aorta and 385.71% (p < 0.001) in the heart with 200 mg/kg. Nifedipine (10 mg/kg) in the same conditions prevented the decrease in SOD activity by 258.33, 127.77, 425.00 and 457.14% respectively in the liver, kidney aorta and heart as compared to alcohol-induced hypertensive rats.

Chronic feeding with ethanol (5 g/kg) during 35 days resulted in a significant (p < 0.001) decrease in reduced glutathione level in all investigated organs as compare to normotensive rats. *L. hexandra* extract administration prevented that decrease. The rates of decrease were 64.89 and 65.02% in liver, 46.63 and 69.37% in kidney, 42.97 and 46.84% in aorta and 99.99 and 160.93% in heart respectively with the doses of 100 and 200 mg/kg as compared to alcohol-induced hypertensive rats. Concomitant administration of ethanol and nifedipine prevented significantly (p < 0.001) the decrease in reduced glutathione (GSH). The values were 86.68, 72.85, 49.49 and 140% higher as compared to alcohol-induced hypertensive rats.

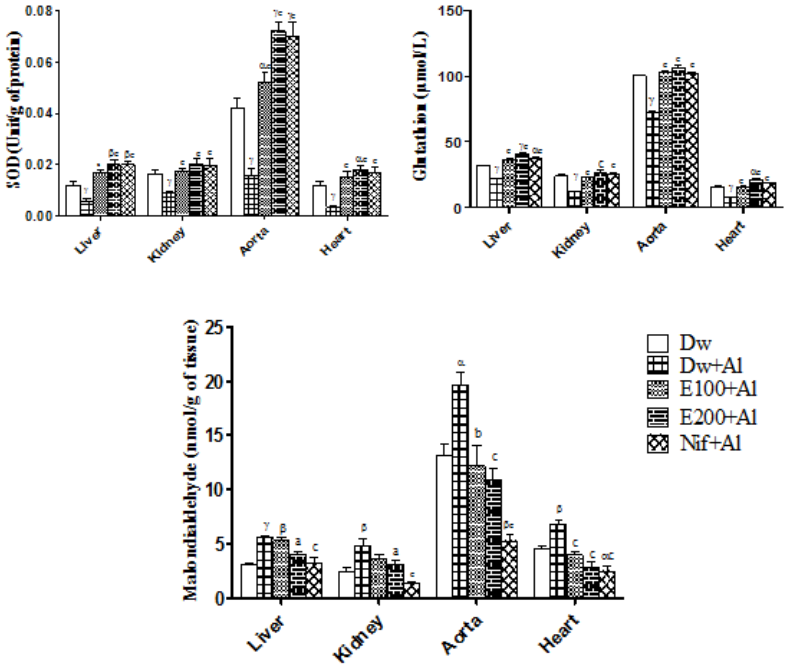

Fig-2: Effects of *L. Hexandra* aqueous extract on some markers of oxidative stress in ethanol induced hypertension

Each bar presents means ± S.E.M. n = 6. $^{\alpha}$p< 0.05, $^{\beta}$p< 0.01 and $^{\gamma}$p< 0.001: significantly different compared to normal rats. ^{a}p< 0.05, ^{b}p< 0.01 et ^{c}p< 0.001: significantly different compared to

hypertensive rats. Dw: distilled water 10mL/kg, Al: Alcohol 5g/kg, E100+Al: Extract 100mg/kg and alcohol, E200+Al: Extract 200mg/kg and alcohol, Nif+Al: Nifedipine 10mg/kg and alcohol.

Effects of *L. hexandra* on histological examination of the aorta

Table 5 summarizes the effect of *L. hexandra* aqueous extract on the section of aorta and stained with haematoxylin and eosin.The administration of ethanol during 5 weeks induced thickness in the arterial walls leading to the reduction in the blood vessel diameter. The thickness of the aorta of alcohol-induced hypertensive rats significantly ($p < 0.05$) increased by 30.82% when compared to normotensive rats. The aqueous extract of *L. hexandra* prevented the morphological modifications induced by ethanol in explored organ like aorta. As compared to alcohol-induced hypertensive rats, the thickness of aorta in rats treated with the extract at the doses of 100 and 200 mg/kg was reduced by 29.15 ($p < 0.05$) and 36.89% ($p < 0.01$) respectively.

Table-5: Effects of *L. hexandra* on the thickness of aorta

Parameter	Dw	Dw+Al	E100+Al	E200+Al	Nif+Al
Thickness of aorta (µm)	33.19±2.03	43.42±2.17$^{\alpha}$	30.76±2.68^{a}	27.40±2.29^{b}	28.19±1.10^{b}

Each bar presents means ± S.E.M. n = 18. $^{\alpha}p< 0.05$: significantly different compared to normotensive rats. $^{a}p< 0.05$, $^{b}p< 0.01$: significantly different compared to hypertensive rats. Dw: distilled water 10mL/kg, Dw+Al: distilled water and alcohol l5g/kg, E100+Al: Extract 100mg/kg and alcohol, E200+Al: Extract 200mg/kg and alcohol, Nif+Al: Nifedipine 10mg/kg and alcohol.

DISCUSSION

The present study aimed to evaluate the preventive effects of *L. hexandra* aqueous extract on alcohol induced hypertensive rat model. The chronic feeding with ethanol (5 g/kg/day) during 5 weeks resulted in a significantly increase of arterial blood pressure. This goes in line with the works of Hussain who reported as many others that chronic consumption of ethanol increases blood pressure [3]. Several possible mechanisms have been proposed such as increased vascular reactivity due to increase in intracellular calcium levels, stimulation of the endothelium to release vasoconstrictors and loss of relaxation due to inflammation and oxidative injury of the endothelium leading to inhibition of endothelium-dependent nitric oxide production [3]. According to some authors these mechanism mainly lead to an increase in vascular resistance [1, 3]. That in turn will increase the effort of the left ventricle, resulting in its development. Our results have confirmed that fact, suggesting that the hypertensive rats have their vascular resistance increase. Similarly it was observed an increase of the thickness of the media of the aorta wall in alcohol induced hypertensive rats. The prevention in the increase of the left ventricle weight as well as the aorta thickness both by our extract and nifedipine suggest that one way by which the extract prevented the hypertension may be by protecting the vessels against the damages that increase its resistance. Furthermore, younger animals as used in the present study seem to be more sensitive to the effect of ethanol-induced increase in blood pressure. The prevention in the increase of blood pressure by the aqueous extract of *L. hexandra* suggests that the extract possesses an antihypertensive activity. Weight lost can play an important role in the reduction of blood pressure. The consumption of alcoholic beverages contributes to weight gain because it provides extra calories and weight gain is one of the risk factors for hypertension [15]. In fact body weight reduction can improve vascular resistance and in turn blood pressure [16]. In our study, alcohol has reduced both body weight and food intake suggesting that the reduction in body weight is the result of the reduction in food intake. In fact body weight is closely link to the quality and the quantity of food intake. *L. hexandra* instead prevented the drop in body weight suggesting that the extract mechanism of antihypertensive activity does not pass through body weight lost.

It is well established that chronic consumption of ethanol can lead to dyslipidemia [17, 18] which can enhance vascular resistance and leads to the increase in blood pressure. In the present study, the chronic administration of ethanol to rats, as expected, resulted in a significant increase in serum total cholesterol, triglyceride levels and atherogenic index values. This confirms the fact that those with higher blood pressure values tend to have higher serum cholesterol [19]. Lipid profile parameters disturbance was significantly prevented with the aqueous extract of *L. hexandra*, implying that the improvement of lipid profile by the plant extract may be a way through which the plant prevented the increase in blood pressure [20-22]. This effect could be related to the presence in the extract of some flavonoids, terpenes and other phenolic compounds which lipid-lowering effects have been demonstrated [23]. Our results are consistent with those of Monsalve *et al.* who reported that lipid lowering canimprove vascular functions and some indices of oxidative stress [24].

Ethanol is believed to generate oxygen radicals, inhibit GSH synthesis and deplete GSH levels in tissues, increase MDA levels and generally impair the antioxidative defense system [25]. The significant increase in MDA level and decrease in glutathione level as well as SOD activity observed in alcohol-induced hypertensive rats confirmed that fact. Reactive oxygen

species (ROS) production is a naturally occurring process and a variety of enzymatic and non-enzymatic mechanisms are involved to protect cells against ROS [26]. Enzymes involved in the elimination of ROS include SOD, catalase and glutathione peroxidase. The role of ROS in the pathophysiology of hypertension is well established [27]. The causal relationship between ethanol, ROS and hypertension most likely occurs at the vascular level, where ethanol promotes oxidative stress, endothelial dysfunction, vascular inflammation, increased vascular reactivity and structural remodeling. Together, these responses lead to increased peripheral resistance and therefore increase blood pressure [1]. Our findings indicate that *L. hexandra* aqueous extract prevented the modification of GSH, SOD and MDA levels induced by ethanol, suggesting its antioxidant properties. These properties may be related to the presence in this extract of compounds like some flavonoids which are able to scavenge free radical and protect the cell membrane from destruction [28]. Our results have also indicated the presence of phenols, anthraquinones, tannins, alkaloids, saponins and flavonoids in the aqueous extract of *L. hexandra*. Indeed, dietary polyphenols are known to protect against oxidative stress and degenerative diseases [29]. Additionally, alkaloids are able to act as antihypertensive agents. Also, a number of flavonoids have been reported to increase nitric oxide (NO) production, thus dilate vascular smooth muscle and then reduce blood pressure in various animal models of hypertension [29]. Saponins are of great pharmaceutical importance because of their relationship to compounds such as the sex hormones, cortisones, diuretic steroids, vitamin D and cardiac glycosides [30]. Since this plant extract efficiently improved lipid profile and tissues oxidation, it might be more appropriate to prevent or alleviate dyslipidemia and tissue oxidation responsible of the development and progression of oxidation-associated diseases such as atherosclerosis and cardiovascular diseases. Ethanol administration can disturb the delicate balance between the pro- and anti-oxidant systems of the organism, leading to oxidative stress [31]. Increased generation of ROS/free radicals is able to cause auto-oxidation of the hepatic cells, kidney and other organs resulting in marked hepatic lesions [31]. ALT and AST are important enzymes produced by the liver and serum levels of these enzymes are widely used as biomarkers of liver Health [32].Our results revealed a significant increase in serum ALT and AST activities in untreated ethanol-induced hypertensive rats, indicating all impaired liver function. These enzymes have been reported to be sensitive indicators of liver injuries [33]. When the hepatocellular plasma membrane is damaged, the enzymes normally present in the cytosol are released into the blood stream. In this study, the aqueous extract of *L. hexandra* prevented the increase in levels of ALT and AST, suggesting that aqueous extract could have preserved the cells structural integrity as well as repaired the hepatic tissue damages caused by ethanol.

CONCLUSION

In conclusion, this study demonstrates the antihypertensive properties of aqueous extract of *Leersia hexandra* in ethanol-induced hypertension in rats. The plant extract may act on vascular resistance, lipid lowering activity and as antioxidant. Our data validate the use of this extract as traditional medicine against hypertension in Cameroon. This opens a way to the development of new traditional improved drug or isolation antihypertensive of bioactive compounds.

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Conflicts of Interest

The authors declare that there is no conflict of interest.

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