Research Article

ANTIHYPERTENSIVE ACTIVITY OF _JATEORHIZA MACRANTHA_ (MENISPERMACEAE) AQUEOUS EXTRACT ON ETHANOL-INDUCED HYPERTENSION IN WISTAR

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ABSTRACT

Ethnopharmacological information indicates that _Jateorhiza macrantha_ is used in traditional medicine to treat many diseases including hypertension. Taking into account this fact, this study was aimed to evaluate the antihypertensive effect of the leaves aqueous extract of _Jateorhiza macrantha_ (AEJM) on ethanol-induced hypertension in rats. Five groups of male albinos rats were respectively treated for 3 weeks with distilled water (10 mL/kg), ethanol 40° (6 g/kg), ethanol and captopril (20 mg/kg), ethanol and the AEJM (150 or 300 mg/kg). After 3 weeks, the hemodynamic parameters were recorded. The serum level of total cholesterol, triglycerides, HDL-cholesterol, LDL-cholesterol, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, gamma glutamyltransferase and creatinine were determined. Catalase, superoxide dismutase (SOD), reduced glutathione (GSH), malondialdehyde (MDA) and nitrites levels were measured in homogenised tissues. After 3 weeks, blood pressure and heart rate of ethanol treated rats were higher (P < 0.001) as compared with controls. Higher blood pressure was accompanied by the increase (P < 0.001) in all serum markers measured except that of HDL-cholesterol which decreased significantly. Ethanol treatment increased also the level of MDA in investigated tissues as compared to normal rats. However the nitrites, SOD, catalase and GSH levels decreased in tissues of ethanol hypertensive rats. AEJM prevented the increase of hemodynamic parameters induced by ethanol feeding and various modifications of biochemical and oxidative markers evaluated. This study shows that the AEJM prevents ethanol-induced hypertension in rats and attenuates hyperlipidemia, oxidative stress, liver and kidney's damages and endothelial dysfunction caused by ethanol consumption.

Keywords: Alcohol, Hypertensive rats, _Jateorhiza macrantha,_ Lipid profile, Oxidative markers.

INTRODUCTION

Several epidemiological studies have observed that alcohol has a biphasic cardiovascular effect which depends on the dose of alcohol ingested[1]. At low to moderate doses, alcohol has a favorable impact on cardiovascular outcome. However, chronic high dose alcohol intake has a direct relationship to elevate blood pressure, increase the likelihood of developing congestive heart failure, liver disease and other ethanol-related-diseases[1]. The risk of ethanol-associated cardiovascular disease is greater in men than women[2]. Chronic ethanol consumption is associated with vascular dysfunction and hypertension[3]. But the mechanisms involved in ethanol intake-related blood pressure increase are not yet completely understood. The following mechanisms have been proposed: activation of the renin-angiotensin-aldosterone axis, adrenergic nervous system discharge, cortisol secretion, reduction of insulin sensitivity, heart rate variability, direct effects of ethanol on peripheral muscle tone and endothelial dysfunction[1]. Hypertension can often lead to lethal complications if left untreated[4]. In fact, alcohol ingested is extensively metabolized in the liver, leading to the generation of acetaldehyde by the enzymatic activity in cytosol, microsomes, and peroxisomes. Acetaldehyde is further oxidized to acetate by acetaldehyde deshydrogenase in the mitochondria, which results in the generation of free radicals/reactive oxygen species (ROS)[5]. As a result, ROS have been implicated in a number of multifactor degenerative diseases and aging processes, such as diabetes, cancer, and cardiovascular diseases, as well as the initiation and maintenance of hypertension[6]. Antioxidants thus play an important role in protecting the human body against damage caused by reactive oxygen species[7]. It is known that superoxide rapidly inactivates endothelium-derived nitric oxide (NO), the most important endogenous vasodilator, thereby promoting vasoconstriction[8]. In addition, in arterial hypertension the endothelium-dependent nitric oxide dilation of coronary vessels is depressed, mainly because oxidative stress is enhanced by mechanical stress, thus impairing the adaptation of coronary circulation to changes in myocardial oxygen demand. Because oxidative stress also plays a major role in oxidation of LDL-cholesterol, consequences of arterial hypertension may be gathered in an integrative pathophysiological pattern. Many tribal people in the tropical regions use plants for their medicinal needs. _Jateorhiza_ _macrantha_ (Menispermaceae) which is the object of this study is used in Nigeria by the Edos of South east in association with other medicines to stop sail during pregnancy[9]. In Democratic Republic of Congo, the juice of the leaves is instilled in eyes, ears or nose against headache[9]. Information provided by practitioners of traditional medicine in Center Region of Cameroon indicates that the leaves of _Jateorhiza macrantha_ (_J. macrantha_) are used in the management of hypertension. This information is not cited in the national ethnobotanical survey of Cameroonian plants conducted by Adjanouhoun et al. (1996). The present study was designed to evaluate the antihypertensive effect of the aqueous extract of the leaves of _J. macrantha_ on ethanol-induced hypertension in rats.

MATERIAL AND METHODS

Preparation of plant extract and phytochemical screening

Fresh leaves of _J. macrantha_ were collected in the Center region of Cameroon (Nkolossan locality) in June 2009. The plant materials were identified by Dr Louis ZAPFACK of the Department of Vegetal Biology and Physiology of the University of Yaounde I. A specimen of this plant is conserved at the National Herbarium of Cameroon on the number 10050. Indeed, fresh leaves were dried at room temperature and reduced in powder. The powder (100 g) was macerated in 1L of distilled water for 24 h and filtered with Whatman N⊠ 3 filter paper. The solution obtained was evaporated at 45°C in drying-cupboard and gave 5.63 g of the aqueous extract (yield 5.63%). Phytochemical investigations of alkaloids, flavonoids, saponins, phenols, tannins, anthraquinones, cardiac glycosides, glycosides, triterpenes and saponosides were done according to the procedure described by Odebiyi and Sofowora[10].

Screening for alkaloid

0.5 g of the extract was stirred in 5 ml of 1% HCl on a steam bath and filtered while hot. Distilled water was added to the residue and 1 ml of the filtrate was treated with a few drops of Wagner's reagent. A reddish brown precipitate indicates the presence of alkaloids.

Screening for flavonoids

Two millilitres of dilute sodium hydroxide was added to 2 ml of the extract. The appearance of a yellow colour indicates the presence of flavonoids.

Screening for saponins

One millilitre of distilled water was added to 1 ml of the extract and shaken vigorously. A stable persistent froth indicated the presence of saponins.

Screening for phenols

Equal volumes (1 ml) of extract and Iron (III) chloride were mixed. A deep bluish green solution gave an indication of the presence of phenols.

Screening for tannins

A portion of the extract was dissolved in water, after which the solution was clarified by filtration. 10% ferric chloride solution was then added to the resulting filtrate. The appearance of a bluish black color indicates the presence of tannins.

Screening for anthraquinones

0.5 g of the extract was shaken with 10 ml of benzene and filtered. 10% of ammonia solution was added to filtrate and the mixture was shaken. The formation of a pink, red or violet colour on the ammoniacal phase indicates the presence of anthraquinones.

Screening for cardiac glycosides

0.5 g of the extract was dissolved in 2 ml glacial acetic acid containing 1 drop of ferric chloride solution. This was under layered with 2 ml of concentrated sulphuric acid. A brown ring formation at the inter phase indicates the presence of deoxy sugar characteristics of cardiac glycosides.

Screening for glycosides

1 g of the extract was dissolved in 5 mL of 5% HCl and neutralized by 5 mL of 5% NaOH. A few drop of Fehling's solution was added to the mixture. The formation of brick-red precipitate is an indication of the presence of glycosides.

Screening for terpenoids

0.5 ml of acetic anhydride was mixed with 1 ml of sample extract and a few drops of concentrated H_2SO_4. A bluish green precipitate indicates the presence of terpenes.

Animals

Twenty five male Wistar rats of 10 to 12 weeks old, weighing 150 - 180 g were housed in plastics cages and maintained in the animal house of the Department of Animal Biology and Physiology, Faculty of Science, University of Yaounde I, Cameroon. Animals were maintained under standard laboratory conditions with 12 h light/dark cycle, with free access to normal laboratory rat food and tap water. Prior authorization for the use of laboratory animals in this study was obtained from the Cameroon National Ethical Committee (Reg. N° FWA-IRD 0001954).

Experimental design

Rats were randomly divided into five groups of five rats each and treated daily for three consecutive weeks. Rats of Group 1 received tap water (10 mL/kg), rats of group 2 received ethanol 40° (6 g/kg), rats of groups 3, 4 and 5 received in addition to ethanol 40° (6 g/kg), captopril (20 mg/kg) or aqueous extract of *J. Macrantha* (150 or 300 mg/kg) respectively. At the end of this experimental period, arterial

blood pressure and heart rate of all rats were recorded as previously described[11]. The rats were sacrificed by decapitation and the free-running blood was collected.

Assay for lipid profile

Serum was separated by centrifugation (3600 rpm for 15 min) for the determination of serum total cholesterol (Chol), triglycerides (TG), HDL-Choleterol (HDL-Chol), alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatinine, alkaline phosphatase (ALP) and Gamma glutamyl transferase (GGT) levels using commercial diagnostic kits, Fortress, UK. The levels of LDL Cholesterol (LDL-Chol) was determined using the formula: LDL-Chol (mg/dL) = Chol - (TG/5) - HDL-Chol according to the commercial diagnostic kit, Fortress, UK indication.

Oxidative damage parameters in some organs

After blood collection, the abdominal cavity was opened; aorta, heart, liver and kidney were dissected out and homogenized in Mc Even solution for aorta and heart or Tris-HCl 50 mM buffer solution for liver and kidney to make a 20% homogenate. Tissues protein levels were assayed according to Gornall et al[12]. Catalase was determined according to Sinha[13], whereas reduced glutathione and superoxide dismutase were determined using the method described by Ellman and Misra and Fridovish, respectively[14, 15]. The end product of lipid peroxidation, malondylaldehyde (MDA) was determined using the procedure of Wilbur et al[16] and the nitrites levels in the tissues were determined using the Griess reagent method[17].

Statistical analysis

Data were expressed as mean ± standard error of mean. Statistical analysis was performed using one-way analysis of variance (ANOVA) followed by the Duncan post hoc test. A value of $P < 0.05$ was considered statistically significant.

RESULTS

Phytochemistry

The phytochemical screening of *J. macrantha* leaves aqueous extract revealed the presence of phenols, glycosides, anthraquinones, tannins, alkaloids, saponines, and flavonoids (Table 1). Cardiac glycosides, triterpenes and saponosides were absent (Table 1).

Table 1: Preliminary phytochemical screening of aqueous extract of *J. marantha*'s leaves

Screening number	Phytoconstituents	Aqueous extract of *J. marantha*
1	Alkaloids	+
2	Flavonoids	+
3	Saponins	+
4	Phenols	+
5	Tannins	+
6	Anthraquinones	+
7	Cardiac glycosides	-
8	Glycosides	+
9	Triterpenes	-
10	Saponosides	-

+ : presence; – : absence of phytochemical constituent.

Table 2: Effects of *J. macrantha* aqueous extract on hemodynamic parameters.

	Dw	Et	Et + Ex 1	Et + Ex 2	Et + Ca
SBP (mmHg)	116.26 ± 2.43	183.49 ± 3.71[α]	121.13 ± 3.96[a]	118.56 ± 2.10[a]	121.06 ± 2.92[a]
MBP (mmHg)	97.99 ± 0.97	173.17 ± 3.16[α]	112.30 ± 4.01[βa]	105.72 ± 1.68[a]	107.29 ± 2.31[γa]
DBP (mmHg)	88.86 ± 2.27	168.02 ± 2.93[α]	107.88 ± 4.23[βa]	99.30 ± 1.6[γa]	100.40 ± 2.70[γa]
HR (beat/min)	320.51 ± 3.10	365.08 ± 3.74[α]	360.15 ± 2.86[α]	351.44 ± 2.15[αb]	346.31 ± 1.25[αa]

Each value represents means ±S.E.M. of 5 rats; [γ]$P < 0.05$, [β]$P < 0.01$, [α]$P < 0.001$, significantly different compared to normal rats (Dw). [b]$P < 0.01$, [a]$P < 0.001$, significantly different compared to hypertensive rats (Et). Dw: distilled water 10 mL/kg, Et: Ethanol 6 g/kg, Ex 1: Extract 150 mg/kg, Ex 2: Extract 300 mg/kg, Ca: captopril 20mg/kg, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, MBP: Mean Blood Pressure, HR: Heart Rate.

Effects of *J. macrantha* aqueous extract on hemodynamic parameters

As shown in Table 2, systolic blood pressure (SBP), mean blood pressure (MBP) and diastolic arterial pressure (DBP) of ethanol 40° (6 g/kg) treated rats were significantly increased as compared to the control group. The *Jateorhiza macrantha* aqueous extract (150 or 300 mg/kg) or captopril (20 mg/kg) significantly prevented this increase of SBP, MBP and DBP as compared to ethanol hypertensive rats. At the doses of 150 and 300 mg/kg, the plant extract prevented, respectively by 35.15 % and 38.98 % the increase of MAP as compared to ethanol hypertensive rats. Ethanol consumption also leads to the enhancement of heart rate (HR) by 13.90 % (P< 0.001) compared to the control rats. This increase is reduced significantly

by the addition of the aqueous extract of *J. macrantha* (300 mg/kg) or captopril (20 mg/kg) by 3.73 % and 5.14 %, respectively.

Effects of aqueous extract of *J. macrantha* on lipid parameters

Table 3 shows that the administration of ethanol during 3 weeks increased significantly the level of total cholesterol, triglycerides and LDL-cholesterol by 45.47 %, 41.46 % and 160.38 %, respectively. The level of HDL cholesterol was decreased by 20.91 % (P < 0.001) in ethanol hypertensive rats compared to normal rats treated with distilled water. Aqueous extract of *J. macrantha* (150 and 300 mg/kg) and captopril (20 mg/kg) significantly (P < 0.001) prevented the decrease of HDL and the increase in total cholesterol, LDL-chol, and triglycerides levels compared to ethanol-hypertensive rats.

Table 3: Effects of *J. macrantha* aqueous extract on lipid profile.

	Dw	Et	Et + Ex 1	Et + Ex 2	Et + Ca
Chol (mg/dL)	48.88 ± 0.84	71.11 ± 1.19$^\alpha$	64.98 ± 0.34$^{\alpha a}$	50.14 ± 0.57^a	50.29 ± 0.38^a
TG (mg/dL)	28.53 ± 0.16	40.36 ± 1.32$^\alpha$	20.59 ± 0.78$^{\alpha a}$	18.44 ± 0.84$^{\alpha a}$	23.36 ± 0.57$^{\alpha a}$
LDL-Chol (mg/dL)	15.93± 0.89	41.48 ± 1.34$^\alpha$	31.61 ± 0.59$^{\alpha a}$	15.45 ± 0.71^a	14.52 ± 2.06^a
HDL-Chol (mg/dL)	27.25 ± 0.71	21.55 ± 0.82$^\alpha$	29.25 ± 0.65^a	31.00 ± 0.47$^{\gamma a}$	31.10 ± 1.71^a

Each value represents means ± S.E.M. of 5 rats; .$^\gamma$P < 0.05, $^\alpha$P < 0.001, significantly different compared to normal rats. ^{a}P < 0.001, significantly different compared to hypertensive rats. Dw: distilled water 10 mL/kg, Et: Ethanol 6 g/kg, Ex 1: Extract 150 mg/kg, Ex 2: Extract 300 mg/kg, Ca: captopril 20mg/kg.

Effects of aqueous extract of *J. macrantha* on some parameters of liver and kidney functions

The effect of aqueous extract of *J. macrantha* on liver and kidney functions was evaluated by the determination of AST, ALT, ALP, GGT and creatinine levels in serum. As shown in Table 4, the levels of these markers were significantly increased (P < 0.001) in ethanol

untreated hypertensive rats as compared to control rats. The levels of these parameters were significantly and dose-dependently reduced in *J. macrantha*-treated animals as compared to ethanol hypertensive rats. At the dose of 300 mg/kg, the aqueous extract of *J. macrantha* reduced the levels of these parameters by 72.03 % for AST, 49.81 % for ALT, 35.06 % for ALP, 50.42 % for GGT and 17.59 % for creatinine as compared to untreated hypertensive rats.

Table 4: Effects of *J. macrantha* aqueous extract on some parameters of liver and kidney functions.

	Dw	Et	Et + Ex 1	Et + Ex 2	Et + Ca
AST (U/L)	36.00 ± 0.89	131.60 ± 0.74$^\alpha$	42.6 0± 0.87$^{\alpha a}$	36.80 ± 0.24$^{\gamma a}$	37.24 ± 0.17^a
ALT (U/L)	11.30 ± 0.25	27.30 ± 0.68$^\alpha$	16.80 ± 0.71$^{\alpha a}$	13.70 ± 0.40$^{\beta a}$	11.70 ± 0.25^a
Creatinine (mg/dL)	0.92 ± 0.16	1.08 ± 0.03$^\alpha$	0.94 ± 0.02^b	0.89 ± 0.02$^{\gamma b}$	0.88 ± 0.07$^{\gamma b}$
ALP (U/L)	28.51 ± 0.78	45.88 ± 0.53$^\alpha$	31.99 ± 0.76$^{\gamma a}$	29.79 ± 0.98^a	30.89 ± 0.97^a
GGT (U/L)	3.57 ± 0.17	10.71 ± 0.67$^\alpha$	5.79 ± 0.59$^{\beta a}$	5.31 ± 0.40$^{\gamma a}$	4.68 ± 0.29^a

Each value represents means ± S.E.M. of 5 rats; .$^\gamma$P < 0.05, $^\beta$P < 0.01, $^\alpha$P < 0.001, significantly different compared to normal rats. ^{b}P < 0.01, ^{a}P < 0.001, significantly different compared to hypertensive rats. Dw: distilled water 10 mL/kg, Et: Ethanol 6 g/kg, Ex 1: Extract 150 mg/kg, Ex 2: Extract 300 mg/kg, Ca: captopril 20mg/kg.

Effects of aqueous extract of *J. macrantha* on some markers of oxidative stress

Figure 1 shows that ethanol treatment of rats for 3 weeks is associated to a significant decrease of catalase levels (Figure 1A) by 71.02 % in aorta, 54.15 % in heart, 79.89 % in liver and 28.96 % in kidney compared to control rats. Aqueous extract of *J. macrantha* (150 and 300 mg/kg) and captopril (20 mg/kg) prevented significantly (P<0.01) the decrease of catalase levels in various tissues investigated as compared to ethanol untreated hypertensive rats. As shown in Figure 1 B, the activity of SOD in ethanol hypertensive rats is reduced by 31.69 % (P < 0.05) in aorta compared to rats receiving distilled water during the experimental period. The content of SOD was significantly higher in heart and liver of *Jateorhiza macrantha*-treated groups as compared with the ethanol hypertensive rats. Ethanol treatment significantly (P < 0.001) decreased the levels of GSH by 74.42 % in heart, 61.99 % in liver and 76.35 % in kidney as compared to normal rats. The addition of *J. macrantha* aqueous extract to the treatment markedly suppressed the decrease of GSH in these tissues as compared to rats receiving ethanol (Figure 1C). Chronic feeding with ethanol also resulted of the significant increased of the level of the end product of lipid peroxidation (MDA) in aorta, heart, liver and kidney of rats untreated hypertensive animals as compared to rats receiving distilled water (Figure 1 D). The aqueous extract of *J. macrantha* dose dependently and significantly reduced the increase of MDA induced by ethanol in all tissues as compared with untreated hypertensive rats.

The effects of aqueous extract of *J. macrantha* on endothelial function of ethanol treated rats was determined by the measure of nitrites (NO_2^-) level in aorta, heart, liver and kidney of rats. The ingestion of ethanol 40° for 3 weeks leads to a decrease on NO_2^- levels in theses organs as compared to control rats (Figure 2). The level of nitrites was decreased by 24.60 % (P < 0.05) in aorta, 60.90 % (P < 0.001) in heart, 46.72 % (P < 0.001) in liver and 57.30 % (P < 0.001) in kidney of ethanol hypertensive rats as compared with normal rats. Aqueous extract of *J. macrantha* dose dependently and significantly prevented the decrease of nitrites levels as compared with the control hypertensive rats.

DISCUSSION

This study aimed to evaluate the antihypertensive effect of *J. macrantha* leaves aqueous extract on ethanol-induced hypertensive rats. Administration of ethanol 40° (6 g/kg) during 3 weeks leads to the increase of systolic, mean and diastolic arterial blood pressure. Our result is in accordance to previous studies[18, 19] and indicates the hypertensive effect of chronic consumption of higher amounts of ethanol. Additively, hypertension induced by ethanol consumption in this study is associated with significant increase of heart rate. Several mechanisms have been postulated for the ethanol induced hypertension. According to Leonardo et al[3], ethanol enhances secretion of hormones and neurotransmitters, stimulate the sympathetic nervous system and induce myogenic mechanism which involves alteration of contractile properties of vascular smooth muscle. The concomitant administration of ethanol and aqueous extracts of *J. macrantha* (150 and 300 mg/kg) in this study

dose-dependently prevent the raise in blood pressure and heart rate of ethanol treated rats. These results suggested that *J. macrantha* could act on some targets implicated in the genesis of hypertension such as vascular resistance, peripheral muscle tone, myocardiac contractility and volume overload to prevent hypertension. In this study, ethanol feeding significantly affected lipid profile by enhancing the level of total cholesterol, triglycerides, LDL-cholesterol and decreasing the level of HDL-cholesterol. Indeed, ethanol reduced the activity of the lipoprotein lipase and triglyceride lipase enzymes, thus resulting in the decreased uptake of triglyceride from serum causing its accumulation[20]. In addition, the elevation of cholesterol level observed may be due to the increased activity of the enzyme β-hydroxymethylglutaryl CoA (HMGCoA) which catalyses the rate limiting step in cholesterol biosynthesis leading to increased cholesterol synthesis in tissues and excess leaking out of cholesterol into the blood[20]. The decrease of HDL cholesterol in rats feed by ethanol 40° for three weeks in the present study may have important clinical implications in the pathogenesis of alcoholic hyperlipidemia and can be used as a marker for hepatic damage[21, 22]. *J. macrantha* aqueous extract administrations improved the lipid profile, suggesting that this extract may allow restraining fat storage and dyslipidemia. ALT

and AST are important enzymes produced by the liver and serum levels of these enzymes are widely used as biomarkers of liver health[23]. Ethanol treatment significantly increased the serum enzyme levels, namely ALT, AST, ALP and GGT indicating all impaired liver function. These enzymes have been reported to be sensitive indicators of liver injuries. When the hepatocellular plasma membrane is damaged, the enzymes normally present in the cytosol are released into the blood stream. In this view, the reduction in levels of ALT, AST, ALP and GGT by the aqueous extract of the leaves of *J. macrantha* could be an indicator of stabilization of plasma membrane. This stabilization could have then preserved the cells structural integrity as well as repaired the hepatic tissue damages caused by ethanol. This effect is in agreement with the commonly accepted view that serum levels of transaminases return to normal with the healing of hepatic parenchyma and regeneration of hepatocytes[24]. The regular alcohol consumption raises the blood pressure, which per se is a risk factor for renal damage[25]. This risk is verified in this study by the enhancement in serum creatinine levels. Our results show that *J. macrantha* aqueous extract prevented creatinine increases, suggesting that this extract might interfered with mechanisms of ethanol induced injuries in kidney.
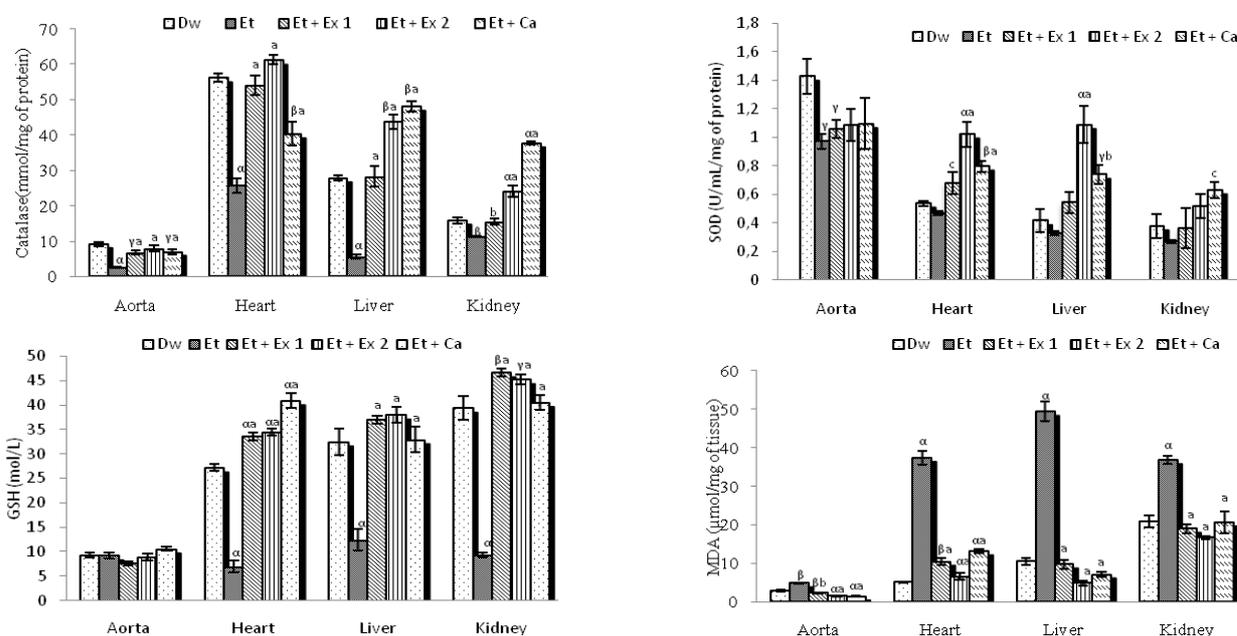

Fig. 1: Effects of *J. macrantha* aqueous extract on some markers of oxidative stress in ethanol induced hypertension.

Each bar represents means ± S.E.M. of 5 rats; .γP < 0.05, βP < 0.01, αP < 0.001, significantly different compared to normal rats. cP < 0.05, bP < 0.01, aP < 0.001, significantly different compared to hypertensive rats. Dw: distilled water 10 mL/kg, Et: Ethanol 6 g/kg, Ex 1: Extract 150 mg/kg, Ex 2: Extract 300 mg/kg, Ca: captopril 20 mg/kg.
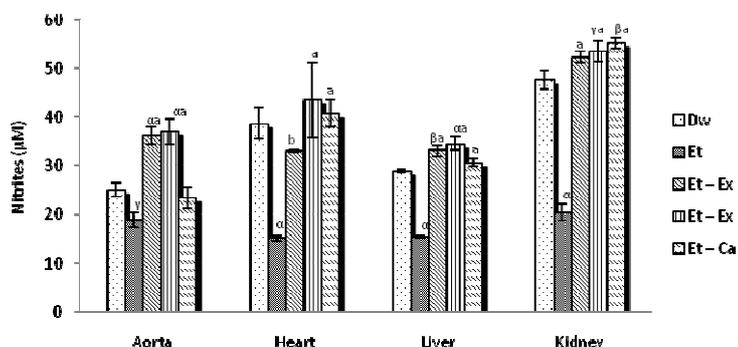

Fig. 2: Effects of *J. macrantha* aqueous extract on nitrites concentration in ethanol induced hypertension.

Each bar represents means ± S.E.M. of 5 rats; .γP < 0.05, βP < 0.01, αP < 0.001, significantly different compared to normal rats. bP < 0.01, aP < 0.001, significantly different compared to hypertensive rats. Dw: distilled water 10 mL/kg, Et: Ethanol 6 g/kg, Ex 1: Extract 150 mg/kg, Ex 2: Extract 300 mg/kg, Ca: captopril 20 mg/kg.

The metabolism of alcohol is inherently associated with the production of reactive oxygen (ROS) resulting in oxidative stress[26]. SOD and catalase are important enzymes, which protect against the free radical injury mediated by O_2^- and H_2O_2[27]. The levels of SOD, GSH, catalase and MDA in investigated tissues are significantly modified in ethanol treated rats when compared to normal rats. The significant decrease in the activity of antioxidant enzymes mainly SOD and catalase observed in aorta, heart, liver and kidney of hypertensive rats in the present work, may be due to cell membrane damage and alterations in dynamic permeability of membranes due to peroxidation, followed by the release of intracellular enzymes to the blood stream[28]. The decline of GSH, the endogenous antioxidant observed here is obviously connected with ethanol induced oxidative stress, which is characterized by the generation of toxic acetaldehyde and other reactive molecules in the cell[29]. Additionally, the level of MDA which increase in the various target organs of ethanol hypertensive rats could be linked to the generation of free radicals, resulting in the peroxidation of membrane lipids[29]. Our findings indicate that *J. macrantha* aqueous extract prevented the modification of GSH, catalase, 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 flavonoids which are able to scavenge free radical and protect the cell membrane from destruction[24]. Ours results have also indicated the presence of phenols, anthraquinones, tannins, alkaloids, saponins, and flavonoids in the aqueous extract of *J. macrantha.* Indeed, dietary polyphenols are known to protect against oxidative stress and degenerative diseases[30]. 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[30]. 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[31]. The presence of these compounds may justify the use of *J. macrantha* in traditional medicine as an antihypertensive agent.

In the present work the level of nitric oxide (NO) is also affected by ethanol consumption. Our results indicated the decreased of nitrites levels in investigated tissues of ethanol untreated rats. Indeed, one mean to investigate nitric oxide formation is to measure nitrite which is one of two primary, stable and non volatile breakdown products of NO[20]. These results correlated with many others and might indicate endothelium dysfunction after chronic ethanol feeding[32, 33]. Treatment of rats with aqueous extract of *J. macrantha* prevented the decrease on NO levels in various tissues explored in the present study, suggesting that this extract may have a benefic effect on endothelial function.

These results showed that the leaves aqueous extract of *Jaterohiza macrantha* might prevent the ethanol-induced hypertension in rats. Current findings also indicate that *J. macrantha* aqueous extract is able to normalize lipid profile, to fight against oxidative stress and cell damage in liver and kidney and to restore endothelial function in this type of animal model of hypertension. Thus, this study justifies the use of *Jateorhiza macrantha* in Cameroonian traditional medicine in the management of hypertension.

ACKNOWLEDGMENT

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