

Protective Effects of *Tetrapleura tetraptera* Extract on High Salt-Induced Hypertension in Male Rats

¹Bella Ndzana Martin Thierry, ²Tsala David Emery, ³Ngo Lemba Tom Esther,
¹Aboubakar Oumarou Bibi Farouck, ¹Bilanda Danielle Claude and ¹Dimo Theophile

¹Laboratory of Animal Physiology, Department of Animal Biology and Physiology,
University of Yaounde I, P.O. Box 812 Yaounde, Cameroon

²Department of Life Sciences, Higher Teachers' Training College,
University of Maroua, P.O. Box 46 Maroua, Cameroon

³Laboratory of Animal Physiology, Department of Life and Earth Sciences,
Higher Teachers' Training College, University of Yaounde I, P.O. Box 47 Yaounde, Cameroon

Abstract: The stem bark of *Tetrapleura tetraptera* (Taub) [Mimosaceae] is used in cameroonian ethnomedicine for the treatment of hypertension and diabetes. This experiment was conducted to evaluate the possible effects of *Tetrapleura tetraptera* Aqueous Extract (TAQE) against hypertension and investigate its antioxidant effect in salt-induced hypertensive rats. High-salt hypertensive rats (9%) received vehicle (distilled water, 10 mL/kg/day), TAQE (100 or 200 mg/kg/day) or captopril 20 mg/kg/day. After a period of 4 weeks, Systolic Blood Pressure (SBP) was measured by invasive method. The lipid profile, oxidative status and liver function were evaluated by colorimetric method. There were significant rise in SBP and heart rate in salt treated rats. The malondialdehyde and antioxidative enzymes (catalase and superoxyde dismutase) levels were significantly elevated and decreased respectively in high salt as compared to control. The oral co-administration of TAQE with high salt reduced the SBP and improved the antioxidant status, lipid profile and liver function. Captopril associated with high salt prevented the some alterations induced by salt consumption in rats. This study supports the traditional used of *Tetrapleura tetraptera* against hypertension. *Tetrapleura tetraptera* could prevent the rise in blood pressure and improved the oxidative status in salt model of hypertension.

Key words: *Tetrapleura tetraptera*, salt, hypertension, rat, captopril

INTRODUCTION

Tetrapleura tetraptera stem bark is widely used in Cameroon for treatment of hypertension and diabetes. The fruit consists of a fleshy pulp with some small, brownish black seeds. In Nigeria, the fruits are used traditionally in flavouring, pomades and soaps preparation. An infusion of the whole fruit is usually taken in bath against fever or orally as a recuperative tonic (Ojewole and Adesina, 1983a,b). The insect repellent property of the fruits has been reported (Ojewole and Adewunmi, 2004). Cardiovascular and neuromuscular actions of scopoletin from these fruits were described (Ojewole and Adesina, 1983a,b). The stem bark aqueous decoction of *Tetrapleura tetraptera* is usually imbibed for the relief of stomach ulcerative pain in Ghana (Irvine, 1961). *Tetrapleura tetraptera* is a potential molluscicide (Maillard *et al.*, 1989; Adewunmi *et al.*, 1991). The soft parts of the fruit and the stem bark are known to contain

sugars, tannins, traces of saponin and amino acids (Adesina *et al.*, 1980). This plant has also many other traditional medicinal uses dealing with the management of convulsion, leprosy, inflammation and rheumatic pains (Aladesanmi, 2007). The stem bark is used in Cameroon, against diabetes and hypertension.

Hypertension or chronic High Blood Pressure (HBP) is a major contributor to ischemic heart disease, cerebrovascular disease, heart and renal failure and is estimated to cause >7 million premature deaths per year worldwide (Whitworth *et al.*, 2003). Appropriate treatment and even prevention of hypertension depends upon better understanding of the underlying causes and mechanisms of the elevated blood pressure. Despite extensive research during the past few decades some critical questions about the pathogenesis of elevated blood pressure remain unanswered. The results of many studies in humans and laboratory animals showed a clear relation between high salt intake and the development of

hypertension (Stamler *et al.*, 1991; Kassab *et al.*, 1998; Huang and Johns, 2000). Many mechanisms by which high salt intake can initiate the development and maintenance of hypertension have been reported. There are changes in vascular reactivity (Mulvany *et al.*, 1978; Adegunloye and Sofola, 1997; Nishida *et al.*, 1998; Lenda *et al.*, 2000) in sympathetic reflexes (Miyajima and Bunag, 1985; Ferrari and Mark, 1987) on calcium mobilization, in Na⁺, K⁺-ATPase activity (Obiefuna *et al.*, 1991a,b; Li *et al.*, 1994), on endogenous sodium pump ligands levels (Fedorova *et al.*, 2001) and in the balance between blood volume and cardiac output (Simchon *et al.*, 1991).

However, these factors explain only part of attributable cardiovascular diseases. For instance, excessive production of Reactive Oxygen Species (ROS) has been suggested to contribute to the genesis of vascular diseases including hypertension (Griendling and Alexander, 1997; Landmesser and Harrison, 2001). Free radicals have been implicated in the causation of several diseases such as liver cirrhosis, atherosclerosis, cancer, hypertension, etc. and compounds that can scavenge free radicals have great potential in ameliorating these disease processes (Wilson, 1998). Free radical scavenger enzymes namely superoxide dismutase, catalase and peroxidase glutathione represent the enzymatic part. Therefore, prevention of oxidative stress-induced hypertension is an area growing interest. Earlier study showed a protective effect of *T. tetraptera* against dyslipidemia, stress and hypertension induced by salt-sucrosed enriched diet (Thierry *et al.*, 2012). The present study was then designed to investigate antihypertensive and antioxidant activities of *Tetrapleura tetraptera* in salt-induced hypertension rats.

MATERIALS AND METHODS

Preparation of the aqueous extract of *Tetrapleura tetraptera*: The stem bark of *Tetrapleura tetraptera* were collected in the center region of Cameroon and authenticated at the National Herbarium of Cameroon (voucher specimen No. 31310/HNC). The 0.3 kg dried stem bark of *Tetrapleura tetraptera* was extracted in 3 L distilled water and macerated during 24 h following the traditional method. The filtered aqueous extract was concentrated in drying-cupboard (45°C) and gave 18.75 g of a brown powder. A solution (20 mg mL⁻¹) was prepared from this powder each in distilled water.

Experimental design: The study was performed on male Wistar rats from the Laboratory of Animal Physiology of the University of Yaounde I, Cameroon. All animals (180-220 g of body weight) were maintained at room temperature 25±1°C with a 12 h light/dark cycle. Prior

authorization for the use of laboratory animals in this study was obtained from the Cameroon National Ethical Committee (Reg. No. FWAIRD 0001954). Rats were randomly divided into five groups of five animals each: normal control, fed with standard chow diet and tap water; a high-salt control group (Se) receiving salt (9%, 1.8 g/kg/day) by gavage and normal diet, 3) three groups received high salt with *Tetrapleura tetraptera* aqueous extract (100 or 200 mg/kg/day) or captopril 20 mg/kg/day.

Blood pressure and heart rate measurements: After 4 weeks, arterial blood pressure and heart rate of all rats were measured (Bopda *et al.*, 2007). Briefly, Systolic Blood Pressure (SBP) measured from right carotid artery via an arterial cannula connected to a pressure transducer coupled with a hemodynamic recorder Biopac Student Lab. (MP35) and computer. Changes in final Mean Arterial Blood Pressure (MABP) were calculated by the equation:

$$\text{MABP} = \text{SBP} + \frac{1}{3} (\text{SBP} - \text{DBP})$$

where, DBP is the diastolic blood pressure.

Serum and tissue sampling: At the end of the experimental period, animals were sacrificed by cervical decapitation. Blood samples were collected in dried tubes and the serum was obtained by centrifugation at 1000 g during 15 min at 4°C for serum enzymes activities, lipids and glucose determination. Heart, aorta, liver and kidney were rapidly dissected out, weighted and homogenized (20%) in McEwen solution (mM NaCl, 147; CaCl₂, 2.6; CO₂HNa, 11.6; D-glucose, 11; KCl, 5.6; NaH₂PO₄, 0.66; MgCl₂, 0.24) for aorta and heart or in Tris-HCl 50 mM buffer solution for liver and kidney. Homogenates were centrifuged at 10,000 g during 30 min at 4°C for the determination of various oxidative stress parameters.

Biochemical analysis: Aspartate aminotransferase (AST), Alanine Aminotransferase (ALT), Alkaline Phosphatase (ALP) and Gamma Glutamyltransferase (GGT) activities as well as Total Cholesterol (TC), High Density Lipoprotein (HDL-C), Triglycerides (TG) and glucose contents in the serum were spectrophotometrically measured by commercial kits Fortress Diagnostics. Atherogenic Index (AI) was calculated according to Wakayashi and Kobaba (2002) method using the following equation:

$$\text{AI} = \frac{(\text{TC} - \text{HDL-C})}{\text{TC}}$$

LDL-Cholesterol (LDL-C) was estimated according to Fortress kits using the following equation:

$$\text{LDL-C} = \text{TC} - \left(\frac{\text{TG}}{5} \right) - \text{HDL-C}$$

Superoxide Dismutase (SOD) was measured by the method of Misra and Fridovich (1972). Reduced Glutathione (GSH) was determined as described by Ellman (1959). Catalase Cctivity (CAT) was assayed colorimetrically at 570 nm and expressed as imoles of H₂O₂ consumed/min/mg protein as described by Sinha (1972). Lipid Peroxidation was estimated by measuring the Thiobarbituric Acid Reactive Substances (TBARS) and was expressed in terms of Malondialdehyde (MDA) content (Wilbur *et al.*, 1949). Nitrite contents of the tissue were determined as described by Ikeda *et al.* (2003).

Statistical analysis: All data were expressed as mean±SEM. The statistical significance was evaluated by using Statistical Package for the Social Sciences (SPSS) 16.0. The difference between the groups was compared using one-way Analysis of Variance (ANOVA) followed by the Duncan post hoc test. The p<0.05 was considered statistically significant.

RESULTS AND DISCUSSION

Effects of *T. tetraptera* on systolic blood pressure and heart rate: After 4 weeks of treatment, SBP increased significantly (p<0.001) by 20.77% in Se compared to control group. This enhancement was reduced by 15.69, 21.12 and 24.18% in SeEx 100, SeEx 200 and SeCap 20 groups, respectively compared to Se (Table 1). Chronic treatment with TAQE (100 mg kg/day, PO) or captopril (20 mg kg/day, PO) significantly decreased the blood pressure by 6.00 and 4.30%, respectively, compared to control rats.

The heart rate in normotensive rats was 361.51±4.34 beats per minute. In hypertensive rats, the corresponding

value was 406.03±3.89 beats per minute (p<0.001). Chronic treatment with plant extract significantly decreased the heart rate in SeEx 100 by 8.12%, SeEx 200 by 13.05% and SeCap 20 by 14.76% compared to Se. Captopril (10 mg kg⁻¹) also inhibited the elevation of heart rate as compared to normal control. No significant change in heart rate was observed in SeEx 200 group as compared to control.

Effects of treatments on body weight: As shown in Table 2, the Body Weight (BW) gained was 33.42, 17.74, 30.83 and 29.47% in Control, SeEx 100, SeEx 200 and SeCap 20, respectively 4 weeks after the beginning of the experiment. Table 2 also shows a weight loss of 25.37% in Se group during the same period.

Lipid profile of rats treated with *T. Tetraptera*: Table 3 shows the changes in serum TC, TG, LDL-C, glucose and HDL-C concentrations in the four groups at the end of treatment. At the end of the experimental period (week 4), high salt feeding significantly increased (p<0.001) plasma levels of triglycerides, LDL-C and total cholesterol by 93.58, 79.41 and 77.26%, respectively as compared to control rats. Salt also reduced HDL-cholesterol by 84.46% as compared to control rats. Treatment with *Tetrapleura tetraptera* stem bark aqueous extract or captopril, succeeded to prevent rise in TC, LDL-C and TG serum levels in SeEx 100, SeEx 200 and SeCap 20. The reduction in LDL-C levels was 84.25 and 89.75% for the aqueous extract at 100 and 200 mg kg⁻¹, respectively and 80.04% for captopril. The reduction in TG levels was 93.31, 95.09% for the extract at doses of 100 and 200 mg kg⁻¹, respectively and 95.27% in captopril treated group. TC decreased by 82.55, 87.38% for the extract at doses of 100 or 200 mg kg⁻¹, respectively and 78.19% for captopril treated group. Chronic treatment with aqueous extract (100 or 200 mg/kg/day, PO) and captopril (20 mg/kg/day,

Table 1: Effect of *T. tetraptera* on arterial blood pressures and heart rate

Parameters	Haemodynamic				
	Control	Se	SeEx 100	SeEx 200	SeCap 20
SBP (mmHg)	133.63±2.23	168.66±0.98 ^c	142.16±1.38 ^{ab}	133.04±2.27 ^b	127.88±1.91 ^{ab}
MABP (mmHg)	118.53±1.81	151.98±1.27 ^c	125.92±2.28 ^{ab}	117.99±1.83 ^b	112.32±2.18 ^{ab}
DBP (mmHg)	110.98±2.14	143.64±1.79 ^c	117.80±2.88 ^{ab}	110.48±1.77 ^b	104.55±2.45 ^{ab}
Heart rate (BPM)	361.51±4.34	406.03±3.89 ^c	373.05±3.39 ^{ab}	353.05±4.52 ^b	346.11±2.91 ^{ab}

Se: High salt alone (9%), SeEx 100 and SeEx 200: High salt associated with *Tetrapleura tetraptera* stem bark aqueous extract 100 and 200 mg/kg/day, respectively, SeCap 20: High salt associated with captopril 20 mg/kg/day. ^ap<0.05, significantly different compared to control rats, ^bp<0.001, significantly different compared to control rats, ^cp<0.001, significantly different compared to salt hypertensive rats. Data were expressed Mean±SEM (n = 5)

Table 2: Effect of *T. tetraptera* on body weight

Parameters	Control	Se	SeEx 100	SeEx 200	SeCap 20
Initial body weight (g)	198.40±5.06	215.20±0.63	183.60±2.85	185.80±0.32	202.00±0.32
Final body weight (g)	298.00±3.48	160.60±1.26	223.20±3.79	268.60±0.63	286.40±0.95
BW variation (%)	+33.42	-25.37	+17.74	+30.83	+29.47

Se: High salt alone (9%), SeEx 100 and SeEx 200: High salt associated with *Tetrapleura tetraptera* stem bark aqueous extract 100 and 200 mg/kg/day, respectively, SeCap 20: High salt associated with captopril 20 mg/kg/day. Data were expressed Mean±SEM (n = 5)

Table 3: Effect of *Tetrapleura tetraptera* on lipid profile, liver and kidney functions parameters of salt-loaded hypertensive rats

Parameters	Control	Se	SeEx 100	SeEx 200	SeCap 20
TC (mg dL ⁻¹)	44.75±2.42	196.78±3.88 ^e	34.33±2.42 ^d	24.83±0.97 ^{ad}	42.91±4.36 ^d
TG (mg dL ⁻¹)	1.41±0.14	21.98±3.59 ^e	1.47±0.34 ^d	1.08±0.14 ^d	1.04±0.24 ^d
HDL-C (mg dL ⁻¹)	5.02±0.39	0.78±0.05 ^e	3.87±0.63 ^{bd}	4.97±0.01 ^d	4.46±0.21 ^d
LDL-C (mg dL ⁻¹)	39.44±2.85	191.60±4.55 ^e	30.16±2.99 ^d	19.64±0.99 ^{ad}	38.24±4.52 ^d
Atherogenic index	0.89±0.01	0.99±0.00 ^e	0.87±0.04 ^d	0.80±0.01 ^{bd}	0.89±0.01 ^d
Bilirubine (mg dL ⁻¹)	0.58±0.07	2.20±0.16 ^e	0.61±0.18 ^d	0.51±0.04 ^d	0.57±0.04 ^d
Creatinine (mg dL ⁻¹)	0.27±0.09	0.87±0.15	0.79±0.79	0.38±0.05	0.38±0.05
AST (U L ⁻¹)	4.04±0.25	27.92±0.88 ^b	12.44±1.20 ^b	6.68±0.76 ^a	3.08±0.38 ^d
ALT (U L ⁻¹)	7.60±0.16	17.30±2.53 ^e	12.80±1.58 ^e	9.70±0.47 ^{bd}	8.48±1.58 ^d
ALP (U L ⁻¹)	6.21±1.73	63.25±5.20 ^e	22.48±6.07 ^{bd}	18.28±4.02 ^{ad}	19.92±4.05 ^{bd}
GGT (U L ⁻¹)	4.60±5.39	10.07±0.75 ^e	6.82±0.88 ^{ad}	3.97±0.00 ^{ad}	2.62±1.13 ^{ad}

Se: High salt alone (9%), SeEx 100 and SeEx 200: High salt associated with *Tetrapleura tetraptera* stem bark aqueous extract 100 and 200 mg/kg/day, respectively, SeCap 20: High salt associated with captopril 20 mg/kg/day. ^ap<0.05, significantly different compared to control rats, ^bp<0.01 significantly different compared to control rats, ^cp<0.001, significantly different compared to control rats, ^dp<0.01 significantly different compared to salt hypertensive rats, ^ep<0.001, significantly different compared to salt hypertensive rats. Data were expressed Mean±SEM (n = 5)

PO) significantly (p<0.001) increased HDL-C by 79.84%, 84.30 and 82.51%, respectively as compared to Se. At the dose of 100 mg kg⁻¹, extract prevented the decrease of HDL-C as compared to normal control.

Effects of *T. tetraptera* on some parameters of liver and kidney functions: The effects of *Tetrapleura tetraptera* on liver and kidney functions shows also that high salt intake resulted in a significant increased of bilirubine by 73.64%, AST by 85.53%, ALT by 56.07%, ALP by 90.18% and GGT by 54.32% in high salt, respectively as compared to normal rats. After *Tetrapleura tetraptera* treatment, bilirubine values were near to the normal range by 72.27, 76.82 and 74.09%, respectively compared to high salt. Levels of ALP and GGT significantly (p<0.001) decreased in *Tetrapleura tetraptera* (100 and 200 mg kg⁻¹) or captopril (20 mg kg⁻¹) treated compared to untreated hypertensive rats. ALT significantly (p<0.001) decreased in *Tetrapleura tetraptera* (100 and 200 mg kg⁻¹) or captopril (20 mg kg⁻¹) treated and AST significantly (p<0.01) decreased in captopril (20 mg kg⁻¹) compared to untreated hypertensive rats.

Effects of *Tetrapleura tetraptera* on oxidative stress markers: As shown in Fig. 1 a decreased (p<0.001) in antioxidant enzymes activity (SOD and catalase) were observed in aorta, heart, liver and kidney in Se group when compared with normal control. TAQE significantly improved catalase and SOD activity at all the doses studied. High-salt fed resulted in significant decrease in tissues of GSH and NO (Fig. 2a and b) level as compared to control group. Administration of TAQE (100 and 200 mg/kg/day) for 4 weeks resulted in a significant (p<0.001) increase in tissues GSH and in NO level as compared with Se control group. High-salt control rats showed significant increase in MDA (Fig. 3) level by 99.56, 80.99, 65.01 and 73.13% in aorta, heart, liver and

kidney, respectively. TAQE administration significantly decreased MDA tissues level as compared with Se rats in dose dependent manner.

The aim of the present study was to evaluate the possible effects of *Tetrapleura tetraptera* Aqueous Extract (TAQE) against hypertension and to investigate whether this extract could protect against salt-induced oxidative stress in rats. Excess sodium intake induces hypertension by increasing fluid volume and preload thereby increasing cardiac output. Sodium may also increase blood pressure through other mechanisms that affect vascular reactivity and renal function (Sanjay and Tiwari, 2001). In the study, high salt feeding increased blood pressure. Serum parameters such as TG, TC and LDL-C levels were higher in salt treated rats as compared to control. These results also indicate a decreased in body weight in Se and increased body weight in SeEx 100, SeEx 200 and SeCap 20 as compared to control rats. It is well known that low salt intake stimulates the sympathetic nervous system which increases brown adipose tissue activity (Coelho *et al.*, 2006). Coelho *et al.* (2006) showed that body weight was higher on a low-salt diet and the opposite was observed on a high salt intake. These metabolic effects are possibly due to an increase and a decrease brown adipose tissue activity, respectively induced by low and high salt intake. The increased body weight in rats treated with the plant extract suggested a possible role of its compounds on salt absorption. The data showed a significant increased of systolic blood pressure in Se as compared to control rats. Administration of TAQE significantly prevented this rising. These results suggest that the extract could decrease blood pressure and could contain compounds which are responsible for its antihypertensive activity.

The causes of hypertension in humans are not fully understood but are correlated with salt intake, obesity, insulin resistance and of course, genetic factors. The rat

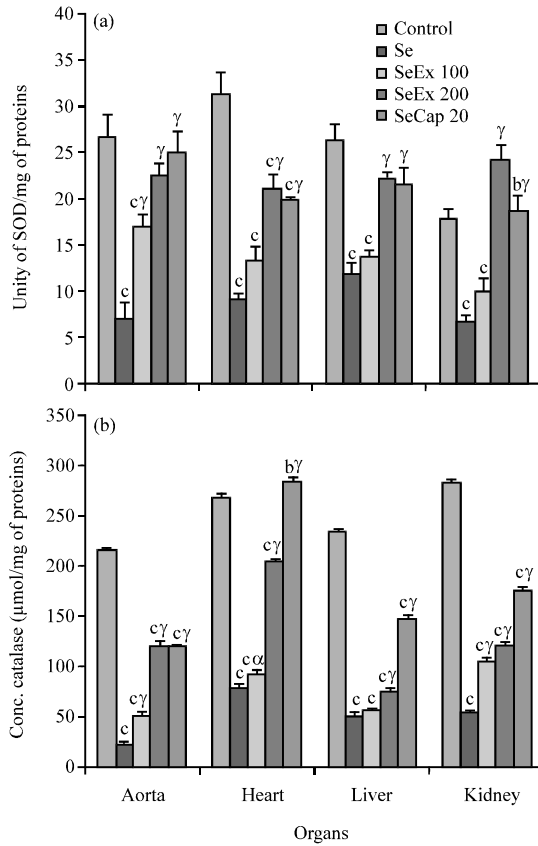


Fig. 1: Effects of *Tetrapleura tetraptera* on tissues SOD and Catalase levels of salt-induced hypertensive rats. Se: High salt alone (9%), SeEx 100 and SeEx 200: High salt associated with *Tetrapleura tetraptera* stem bark aqueous extract 100 and 200 mg/kg/day, respectively, SeCap 20: High salt associated with captopril 20 mg/kg/day. Data were expressed Mean±SEM from five separate experiments. ^ap<0.01 significantly different compared to control rats, ^bp<0.001 significantly different compared to control rats, ^cp<0.05 significantly different compared to salt hypertensive rats, ^dp<0.001 significantly different compared to salt hypertensive rats. a) Unity of SOD/mg of proteins; b) Conc. catalase (µmol/mg of proteins)

is the historically preferred small animal model for diet-induced hypertension, perhaps because of its size, the amount of physiological data available and strong blood pressure response that some strains present (Gajda *et al.*, 2007). According to Gu *et al.* (2008), high salt consumption induced hypertension and renal injury in normotensive rodent animals. Similar results were obtained in this study.

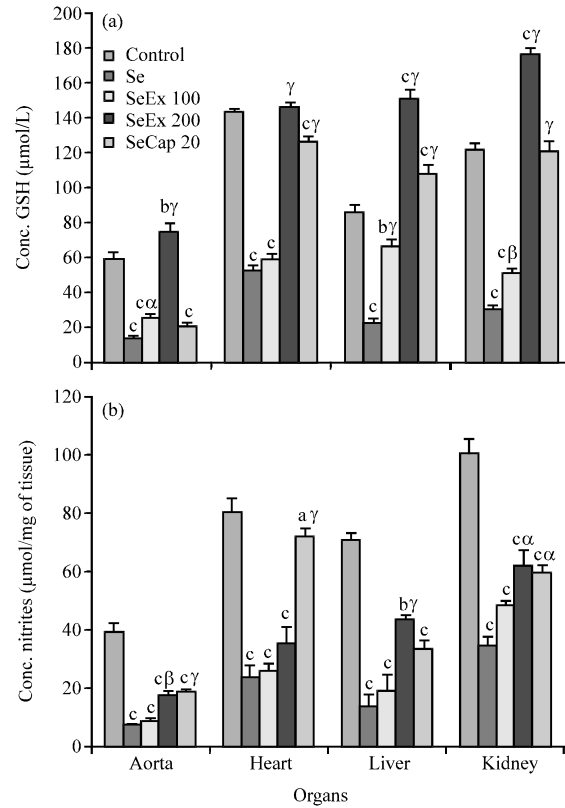


Fig. 2: Effects of *Tetrapleura tetraptera* on GSH and nitrites levels of salt-induced hypertensive rats. Se: High salt alone (9%), SeEx 100 and SeEx 200: High salt associated with *Tetrapleura tetraptera* stem bark aqueous extract 100 and 200 mg/kg/day, respectively, SeCap 20: High salt associated with captopril 20 mg/kg/day. Data were expressed Mean±SEM from five separate experiments. ^ap<0.05, significantly different compared to control rats, ^bp<0.01 significantly different compared to control rats, ^cp<0.001 significantly different compared to control rats, ^dp<0.05 significantly different compared to salt hypertensive rats, ^ep<0.01 significantly different compared to salt hypertensive rats, ^fp<0.001 significantly different compared to salt hypertensive rats. a) Conc. GSH (µmol/L) and b) Conc. nitrites (µmol/mg of tissue)

In fact, the hypertension observed in high salt treated rats in the present research could be explained by an enhanced reactivity to the activation of α -adrenoceptors (Adegunloye and Sofola, 1997; Obiefuna *et al.*, 1991a, b) and changes on calcium mobilization in Na^+ , K^+ -ATPase activity (Obiefuna *et al.*, 1991b; Li *et al.*, 1994) on endogenous sodium pump ligands levels (Fedorova *et al.*,

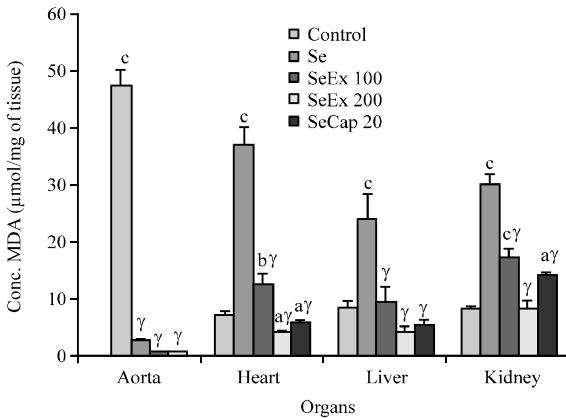


Fig. 3: Effects of *Tetrapleura tetraptera* on tissues MDA levels of salt-induced hypertensive rats. Se: High salt alone (9%), SeEx 100 and SeEx 200: High salt associated with *Tetrapleura tetraptera* stem bark aqueous extract 100 and 200 mg/kg/day respectively, SeCap 20: High salt associated with captopril 20 mg/kg/day. Data were expressed Mean±SEM from five separate experiments. ^ap<0.05, significantly different compared to control rats, ^bp<0.01 significantly different compared to control rats, ^cp<0.001 significantly different compared to control rats, ^γp<0.001 significantly different compared to salt hypertensive rats

2001) and in the balance between blood volume and cardiac output (Simchon *et al.*, 1991). The plant extract in the study, significantly prevented the increase in blood pressure in the high salt model with an increase on the heart rate. This significant difference on the heart rate of experimental animals corroborate with the findings of Bunag *et al.* (1983) who obtained hypertension associated with tachycardia in hypertensive animals.

The results suggested a probable role of oxidative stress in the pathogenesis of hypertension during high salt feeding. Earlier studies (Kitiyakara *et al.*, 2003) showed that graded increases in oxidative stress occur in the normal rat renal cortex, evidenced by an increase in nicotinamide phosphate dehydrogenase and nicotinamide dehydrogenase stimulated superoxide anion generation in response to increased dietary salt. Moreover, they also showed a decrease in expression of the antioxidant superoxide dismutase with increasing salt intake. In the present study, the responses of SOD, CAT enzyme activities, GSH, nitrites (NO₂⁻) and MDA content suggest that oxidative stress is an important component of high salt feeding. The results revealed a significant increase in MDA as well as a decrease of SOD, CAT, GSH and NO₂⁻. *Tetrapleura tetraptera* aqueous extract given simultaneously with high salt, reduced MDA, the end

product of lipid peroxidation. The increased observed in antioxidant concentrations, SOD and CAT and in GSH content in all extract treated groups and captopril group may be due to a reduction of oxidative stress. To maintain sodium and water homeostasis, the NOS system play a role in the regulation of renal interstitial hydrostatic pressure (Majid *et al.*, 2001) and renal medullar blood flow (Cowley *et al.*, 2003) and it maintains normal blood pressure by enhancing NO production in the kidney in response to exposure to a high-sodium diet. In particular, NO in the renal medulla is important to the regulation of sodium and water reabsorption (Cowley *et al.*, 1995; Fujiwara *et al.*, 1999). The results suggested that one of the mechanisms by which blood pressure is maintained normal during exposure to high levels of salt can be attributed to the protective effects of eNOS expression and consequent NO synthesis in the renal medulla by the plant extract. Oxidative stress induces tissue damage leading to impairment of kidney and liver functions (Bilanda *et al.*, 2010).

In the study, researchers evaluated the toxicity of high salt on these function by assessing the level of blood creatinine, bilirubine, transaminases (AST and ALT), ALP and GGT. High salt intake may be directly nephrotoxic by increasing oxidative stress and indirectly harmful by increasing blood pressure (Weir and Fink, 2005). Oxidative stress induces tissue damage leading to impairment of kidney and liver functions accompanied by an increase kidney and liver serum parameters (Bilanda *et al.*, 2010). The data are consistent with previous information. The hepatic injury induced by high salt, probably resulted in an increase in serum ALT, AST, ALP and GGT levels due to the leakage of cellular enzymes in the circulation. Serum creatinine level also increased in high salt feeding, indicating deterioration of residual renal function. *Tetrapleura tetraptera* and captopril reduced significantly the elevation in serum levels of AST, ALT, ALP and GGT, creatinine and bilirubine at values above the normal control one's that is similar with the effect on oxidative stress markers. This may indicate that oxidative stress contributed in mechanism (s) of hepatotoxicity due to chronic consumption of high salt. The low level of serum enzymes following the concomitant treatment with *Tetrapleura tetraptera* or captopril suggested a liver and kidney protective effects of the stem bark TAQE. This effect is probably due to the reduction in cell membrane disturbance.

CONCLUSION

In this study, the results are consistent with the fact that salt is a factor progression of renal and hepatic

damage. High salt intake was related to hypertension and oxidative stress. The data showed the efficacy of the aqueous extract of the stem bark of *Tetrapleura tetraptera* against salt-induced hypertension which may be related at least partly to its antioxidative *in vivo* activity. Hence, *Tetrapleura tetraptera* characterization of active constituents responsible for this activity and further *in vivo* and *in vitro* studies are required to understand the mechanism of action of this plant as an antioxidant and/or antihypertensive.

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REFERENCES

- Adegunloye, B.J., O.A. Sofola, 1997. Effect of dietary salt loading and high-calcium diet on vascular smooth muscle responses and endothelium function in rats. *Clin. Exp. Pharmacol. Physiol.*, 24: 814-818.
- Adesina, S.K., C.O. Adewunmi and V.O. Marquis, 1980. Phytochemical Investigation of the molluscicidal Properties of *Tetrapleura tetraptera* (Taub). *J. Afr. Med. Plants*, 3: 7-15.
- Adewunmi, C.O., H.C. Andersson and L. Busk, 1991. A potential molluscicide, aridan (*Tetrapleura tetraptera*), neither induces chromosomal alterations in Chinese Hamster ovary cells, nor mutations in *Salmonella typhimurium*. *Toxicol. Environ. Chem.*, 30: 69-74.
- Aladesanmi, A.J., 2007. *Tetrapleura tetraptera*: Molluscicidal activity and chemical constituents. *Afr. J. Trad. Complementary Alternative Med.*, 4: 23-36.
- Bilanda, D.C., T. Dimo, P.D.D. Djomeni, N.M.T. Bella and O.B.F. Aboubakar *et al.*, 2010. Antihypertensive and antioxidant effects of *Allanblackia floribunda* Oliv. (Clusiaceae) aqueous extract in alcohol- and sucrose-induced hypertensive rats. *J. Ethnopharmacol.*, 128: 634-640.
- Bopda, M.O.S., T. Dimo, T.B. Nguiefack, D.D. Dzeufiet, S.V. Rakotonirina and P. Kamtchouing, 2007. Effects of *Brillantaisia nitens* Lindau (Acanthaceae) methylene chloride/methanol leaf extract on rat arterial blood pressure and heart rate. *Pharmacologyonline*, 1: 495-510.
- Bunag, R.D., J. Butterfield and S. Sazaki, 1983. Hypothalamic pressor responses and salt-induced hypertension in Dahl rats. *Hypertension*, 5: 460-467.
- Coelho, M.S., M.D. Passadore, A.L. Gasparetti, T. Bibancos and P.O. Prada *et al.*, 2006. High- or low-salt diet from weaning to adulthood: Effect on body weight, food intake and energy balance in rats. *Nutr. Metab. Cardiovasc. Dis.*, 16: 148-155.
- Cowley, A.W. Jr., D.L. Mattson, S. Lu and R.J. Roman, 1995. The renal medulla and hypertension. *Hypertension*, 125: 663-673.
- Cowley, A.W. Jr., T. Mori, D. Mattson and A.P. Zou, 2003. Role of NO production in the regulation of medullary blood flow. *Am. J. Physiol. Regul. Integr. Comp. Physiol.*, 284: R1355-R1369.
- Ellman, G.L., 1959. Tissue sulfhydryl groups. *Arch. Biochem. Biophys.*, 82: 70-77.
- Fedorova, O.V., D.E. Anderson, E.G. Lakatta and A.Y. Bagrov, 2001. Interaction of NaCl and behavioral stress on endogenous sodium pump ligands in rats. *Am. J. Physiol. Regul. Integr. Comp. Physiol.*, 281: R352-R358.
- Ferrari, A.U. and A.L. Mark, 1987. Sensitization of aortic baroreceptors by high salt diet in Dahl salt-resistant rats. *Hypertension*, 10: 55-60.
- Fujiwara, K., K. Hayashi, H. Matsuda, E. Kubota, M. Honda, Y. Ozawa and T. Saruta, 1999. Altered pressure-natriuresis in obese Zucker rats. *Hypertension*, 33: 1470-1475.
- Gajda, M.A., A.M. Pellizzon, R.M. Ricci and A.E. Ulman, 2007. Diet-induced metabolic syndrome in rodent models. A discussion of how diets made from purified ingredients influence the phenotypes of the MS in commonly used rodent models.
- Griendling, K.K. and R.W. Alexander, 1997. Oxidative stress and cardiovascular disease. *Circulation*, 96: 3264-3265.
- Gu, J.W., P.A. Bailey, W. Tan, M. Shparago and E. Young, 2008. Long-term high salt diet causes hypertension and decreases renal expression of vascular endothelial growth factor in sprague-dawley rats. *J. Am. Soc. Hypertens.*, 2: 275-285.
- Huang, C.H. and E.J. Johns, 2000. Impact of angiotensin II in the brain on renal sympathetic nerve activity in anaesthetized rats raised on a high salt diet. *J. Physiol.*, 523: 213-214.
- Ikeda, U., M. Takahashi and K. Shimada, 2003. C-reactive protein directly inhibits nitric oxide production by cytokine-stimulated vascular smooth muscle cells. *J. Cardiovasc. Pharmacol.*, 42: 607-611.
- Irvine, F.R., 1961. *Woody Plants of Ghana*. 1st Edn., Oxford University Press, London.
- Kassab, S., M.T. Miller, J. Novak, J. Reckelhoff, B. Clower and J.P. Granger, 1998. Endothelin-A receptor antagonism attenuates the hypertension and renal injury in Dahl salt-sensitive rats. *Hypertension*, 31: 397-402.

- Kitiyakara, C., T. Chabrashvili, Y. Chen, J. Blau and A. Karber *et al.*, 2003. Salt intake, oxidative stress and renal expression of NADPH oxidase and superoxide dismutase. *J. Am. Soc. Nephrol.*, 14: 2775-2782.
- Landmesser, U. and D.G. Harrison, 2001. Oxidant stress as a marker for cardiovascular events: Ox marks the spot. *Circulation*, 104: 2638-2640.
- Lenda, D.M., B.A. Sauls and M.A. Boegehold, 2000. Reactive oxygen species may contribute to reduced endothelium dependent dilation in rats fed high salt. *Am. J. Physiol.*, 279: H7-H14.
- Li, P.W.C., C.S. Ho and R. Swaminathan, 1994. The effect of high salt intake on Na⁺, K⁺-ATPase activity of tissues in the rat. *Clin. Exp. Hypertens*, 16: 327-340.
- Maillard, M., C.O. Adewunmi and K. Hostettman, 1989. New triterpenoid N-acetylglycoside with molluscicidal activity from *Tetrapleura tetraptera* Taub Helvetica. *Chim. Acta*, 72: 668-672.
- Majid, D.S., K.E. Said, S.A. Omoro and L.G. Navar, 2001. Nitric oxide dependency of arterial pressure-induced changes in renal interstitial hydrostatic pressure in dogs. *Circ. Res.*, 88: 347-351.
- Misra, H.P. and I. Fridovich, 1972. The role of superoxide anion in the autoxidation of epinephrine and a simple assay for superoxide dismutase. *J. Biol. Chem.*, 247: 3170-3175.
- Miyajima, E. and R.D. Bunag, 1985. Dietary salt loading produces baroreflex impairment and mild hypertension in rats. *Am. J. Physiol.*, 249: H278-H284.
- Mulvany, M.J., D.K. Hansen and C. Aalkjaer, 1978. Direct evidence that the greater contractility of resistance vessels in SH rats is associated with narrowed lumen and thickened media and an increased number of smooth muscle cell layer. *Circ. Res.*, 43: 854-864.
- Nishida, Y., J. Ding, M.S. Zhou, Q.H. Chen, H. Murakami, X.Z. Wu and H. Kosaka, 1998. Role of nitric oxide in vascular hyper-responsiveness to norepinephrine in hypertensive Dahl rats. *J. Hypertens.*, 16: 1611-1618.
- Obiefuna, P.C.M., O.A. Sofola and A.B. Ebeigbe, 1991a. Dietary salt-loading attenuates endothelium dependent relaxation in response to histamine but not to acetylcholine in rat aortic rings. *Exptl. Physiol.*, 76: 135-138.
- Obiefuna, P.C., A.B. Ebeigbe, O.A. Sofola and C.P. Aloamaka, 1991b. Altered responses of aortic smooth muscle from Sprague-Dawley rats with salt-induced hypertension. *Clin. Exp. Pharmacol. Physiol.*, 18: 813-818.
- Ojewole, J.A. and C.O. Adewunmi, 2004. Anti-inflammatory and hypoglycaemic effects of *Tetrapleura tetraptera* (Taub.) (Fabaceae) fruit aqueous extract in rats. *J. Ethnopharmacol.*, 95: 177-182.
- Ojewole, J.A. and S.K. Adesina, 1983a. Mechanism of the hypotensive effect of Scopoletin isolated from the fruit of *rapleura tetraptera*. *Planta Med.*, 49: 46-50.
- Ojewole, J.A. and S.K. Adesina, 1983b. Cardiovascular and Neuromuscular actions of scopoletin from fruit of *Tetrapleura tetraptera*. *Planta Medica*, 49: 99-102.
- Sanjay, V. and S.C. Tiwari, 2001. Essential hypertension-pathogenesis and pathophysiology. *J. Indian Acad. Clin. Med.*, 2: 141-161.
- Simchon, S., W.M. Manger and T.W. Brown, 1991. Dual hemodynamic mechanisms for salt-induced hypertension in Dahl salt-sensitive rats. *Hypertension*, 17: 1063-1071.
- Sinha, A.K., 1972. Colorimetric assay of catalase. *Anal. Biochem.*, 47: 389-394.
- Stamler, J., G. Rose, P. Elliot, A. Dyer, M. Marmount, H. Kestelot and R. Stamler, 1991. Findings of the international cooperative intersalt study. *Hypertension*, 17: 9-15.
- Thierry, B.N.M., N.L.T. Esther, A.O.B. Farouk, T.D. Emery and D. Theophile, 2012. Aqueous extract of *Tetrapleura tetraptera* (Mimosaceae) prevents hypertension, dyslipidemia and oxidative stress in high salt-sucrose induced hypertensive rats. *Pharmacologia*, 3: 397-405.
- Wakayashi, I. and W.R. Kobaba, 2002. Effet de l'age sur le rapport entre le boire et les rapports artherosclerotiques. *Gerontology*, 48: 151-156.
- Weir, R.M. and C.J. Fink, 2005. Salt intake and progression of chronic kidney disease: An overlooked modifiable exposure? A commentary. *Am. J. Kidney Dis.*, 45: 176-188.
- Whitworth, J.A., WHO and ISHWG, 2003. 2003 World Health Organization (WHO)/International Society of Hypertension (ISH) statement on management of hypertension. *J. Hypertens*, 21: 1983-1992.
- Wilbur, K.M., F. Bernheim and O.W. Shapiro, 1949. Determination of lipid peroxidation. *Arch. Biochem. Biophys.*, 24: 305-310.
- Wilson, R.L., 1998. Free Radicals and Tissue Damage, Mechanistic Evidence from Radiation Studies. Academic Press, New York, pp: 123.