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Annals of Biological Research, 2012, 3 (11):5114-5118
(http://scholarsresearchlibrary.com/archive.html)

Annals of Biological Research
Scholars Research Library
ISSN 0976-1233
CODEN (USA): ABRNBW

Effect of activity directed administration of ethanolic extracts of *Nauclea Latifolia* on the body and organ weights of hypertensive induced albino wistar rats

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ABSTRACT

Hypertension is a relatively common disorder that is probably the most important public health problem in developed countries. It is common, asymptomatic, readily detectable, usually easily managed and usually leads to lethal complications if left unmanaged. This study evaluates the body and organ weights changes of hypertensive rats gavaged with ethanolic root and stem bark extracts of Nauclealatifolia. The stem extract produced a significant decrease ($p<0.05$) in the relative liver weight in the group treated with 300mg/Kg body weight of stem extract, compared to the normal control. There was a significant decrease ($P < 0.05$) in the relative heart weight of rats treated with 150mg/kg body weight of stem extract and that of the standard (Captopril) treated, compared to the normal control. There was a significant increase ($P < 0.05$) in the body weight of rats treated with 150mg/kg of stem extract, compared to the hypertensive control. Also, there was a significant decrease ($P< 0.05$) between the relative heart weight of rats treated with 150mg/kg of root extract and that of standard (Captopril) treated, compared to the normal control. The body weight of rats treated with 150mg/Kg and 300mg/Kg body weight of root extract were also significantly increased ($P < 0.05$) compared to the hypertensive control.These changes showed that N. latifoliahave antihypertensive potentials

Keywords: *Nauclealatifolia, antihypertensive treatment, body and organs weight changes.*

INTRODUCTION

Hypertension is a complex condition whose root cause is largely unknown andis rarely accompanied by any symptoms, therefore making it difficult to manage. As of 2000, nearly one billion people or approximately 26% of the adult population of the world had hypertension [1, 2].7.1 million Deaths per year may be attributable to hypertension [3]. It is common in both developed and developing countries[1]. However, rates vary markedly in different regions with rates as low as 3.4% (men) and 6.8% (women) in rural India and as high as 68.9% (men) and 72.5% (women) in Poland [2]. Hypertension is an intermittent or sustained elevation in systolic blood pressure (above 110 mm Hg) or diastolic blood pressure (above 70 mm Hg) or a systolic and diastolic pressure 20 mm Hg above the individual's baseline pressure. [20, 4].High blood pressure is said to be present if it is persistently at or above 140/90 mmHg. This requires the heart to work harder than normal to circulate blood through the blood vessels. Hypertension can be described into two types; Primary and secondary. Primary hypertension is a type of

high blood pressure with no obvious underlying medical cause while secondary hypertension are caused by other conditions affecting the kidneys, arteries, heart or endocrine system. Although mild to moderate hypertension is usually asymptomatic, accelerated hypertension is associated with headache, somnolence, confusion visual disturbances and nausea and vomiting [5]. Despite the fact that our understanding of the pathophysiology of an elevated arterial pressure has increased in 90% to 95% of cases, the etiology (and thus potentially the prevention or cure) is still largely unknown. Consequently, in most cases, the hypertension is treated non- specifically resulting in a large number of minor side effectsand a relatively high non- compliance rate [6, 7, 8]. Although the etiology of hypertension is directly unknown, there are many risk factors such as sedentary lifestyle,[6]obesity[9], (more than 85% of cases occur in those with a body mass index greater than 25),salt (sodium) sensitivity[10], alcohol intake [9], and vitamin D deficiency[11, 12]. It is also related to aging and some inherited genetic mutations[11]. Family history increases the risk of developing hypertension [13]. Renin elevation is another risk factor. Renin is an enzyme secreted by the juxtaglomerular apparatus of the kidney and linked with aldosterone in a negative feedback loop [14]. Also sympathetic over-activity is implicated[15]. Insulin resistance which is a component of metabolic syndrome is also thought to cause hypertension [9]. According to [16], low birth weight has recently been questioned as a risk factor for adult essential hypertension. Hypertension is a major risk factor for stroke, myocardial infarction (heart attacks), heart failure, aneurysms of the arteries (e.g. aortic aneurysm), peripheral arterial disease and is a cause of chronic kidney disease. Even moderate elevation of arterial blood pressure is associated with a shortened life expectancy. [17]. Severalclasses of medications, collectively referred to as antihypertensive drugs, are currently available for treating hypertension. The majority of people require more than one drug to control their hypertension. Joint National Committee on High Blood Pressure,advocates starting treatment with two drugs when blood pressure is >20 mmHg above systolic or >10 mmHg above diastolic targets[18]. Preferred combinations are renin–angiotensin system inhibitors and calcium channel blockers, or renin–angiotensin system inhibitors and diuretics [19]. Acceptable combinations include calcium channel blockers and diuretics, beta-blockers and diuretics, dihydropyridine calcium channel blockers and beta-blockers, or dihydropyridine calcium channel blockers with either verapamil or diltiazem.

In Africa and in most Asian countries where the use of folk medicine is in prevalence, the search for herbal cures is but a common practice. [20, 4].*Nauclealatifolia*(family: Rubiaceae) commonly known as pin cushion tree is a straggling shrub or small tree native to tropical Africa and Asia. Parts of the plant are commonly prescribed traditionally as a remedy for diabetes mellitus. The plant is also used in the treatment of ailments like malaria [21, 22, 4,23], gastrointestinal tract disorders [24, 4], sleeping sickness, prolong menstrual flow [25], hypertension [22, 4] and as a chewing stick [26].

MATERIALS AND METHODS

Collection and preliminary processing of plant materials

The root and stem of pin cushion tree (Nauclealatifolia) were collected from the Teaching Hospital premises of the University of Calabar, Calabar in Cross River State, Nigeria. The plant was authenticated by the Department of Botany, Faculty of Sciences, University of Calabar. The plant parts were washed thoroughly with tap water and then rinsed with distilled water. The bark of both the stem and root were carefully peeled using a kitchen knife. The peeled bark was chopped into small pieces and dried under shade.

Preparation of extracts

The dried bark was blended into power using an electric blender. The powder was weighed using an electric weighing balance and soak in 80% ethanol at the ratio of 1:4 of powder to ethanol respectively. The mixture was agitated using an electric blender and kept under a regulated temperature of 0-8^{0}C for 48 hours (2 days). The extracts were doubly filtered, using a Cheese cloth and then a filter paper. The filtrate was concentrated using a rotary evaporator at a regulated temperature of 37-45^{0}C. The extracts were finally evaporated to dryness using a Freeze Drier. The percentage yield of the root and stem extracts were 19.9% and 18.3% respectively.

Animals

Sixty rats (males and females) of Wistar albino strain weighing 180-220g were used for this study. The rats were obtained from the Department of Biochemistry, Faculty of Basic Medical Sciences, University of Calabar.

The rats were used for sub-chronic toxicity study and antihypertensive screening. The animals were allowed one week acclimatization, after which they were reweighed and housed in plastic cages with plastic bottom and wire-

mesh top (North Kent Co. Ltd), under controlled environmental conditions of Temperature (28±2^{0}C), Relative Humidity (50±5%) and a 12 hour light/dark cycle. The animal facility was adequately ventilated and the animals maintained regularly on the commercial rat chow. Tap water and food were provided ad libitum throughout the experimental period.

Experimental Design

The experimental design employed consisted of 50 white wistar rats divided into two equal batches; A and B. Each batch of 25 animals consisted of 5 groups of 5 rats per groups. Batch A animals received the stem extract, while batch B received the root extract. The animals in group 1 were the normal rats that served as the control group. Group two animals were induced hypertensive rats that received no treatment and also served as controls. Groups 3-5 were all hypertensive rats that were treated with 150mg/Kg extract (group 3), 300mg/Kg extract (group 4). The last group (group 5) were treated with a standard antihypertensive drug (captopril 20mg/Kg). The groups 1, 2 and 5 were common to the two batches of the experimental design. The duration of the experiment was two weeks, and all animals (treated and untreated) were allowed food and water ad libitum.

RESULTS AND DISCUSSION

Table 1: Body and organ weights of rats treated with crude ethanolic stem bark extracts of *nauclealatifolia* for 14 days

EXTRACT	PARAMETER	NC (GP7)	HC (GP6)	T1 (GP1)	T2 (GP2)	T5 (GP5)
STEM EXTRACT	Body weight	188.68 ±17.87	159.22 ±2.64	200.68 ±6.82[a]	191.30 ±7.95	179.74 ±27.10
	Liver weight	7.35 ±0.72	5.66 ±0.19	7.06 ±0.46	6.44 ±0.29	6.78 ±1.10
	Relative Liver weight	3.51 ±0.19	3.55 ±0.10	3.51 ±0.19	3.37 ±0.10*	3.77 ±0.17
	Kidney weight	1.23 ±0.09	1.06 ±0.04	1.28 ±0.07	1.24 ±0.05	1.24 ±0.14
	Relative Kidney weight	0.65 ±0.03	0.66 ±0.02	0.64 ±0.02	0.65 ±0.01	0.71 ±0.05
	Heart weight	0.70 ±0.01	0.52 ±0.04*	0.58 ±0.02	0.62 ±0.04	0.56 ±0.07
	Relative Heart weight	0.38 ±0.03	0.32 ±0.02	0.29 ±0.01*	0.33 ±0.02	0.31 ±0.02*

Values expressed as mean±SEM, n = 5.
** =P<0.05 compared to the normal control, GP7.*
a=P<0.05 compared to the hypertensive control, GP6.
b=P<0.05 compared to the standard treated, GP5.
c=P<0.05 compared to GP2 treated with 300mg/Kg of stem extract.

Table 1 presents the result of the body and organ weights of activity directed administration of ethanolic stem extract of *Nauclealatifolia*. There is a significant decrease at (P < 0.05) between therelative liver weight of rat treated with 300mg/kg of stem extract (3.37±0.10) and that of the normal control (3.51±0.19). This might be due to the effect of the extract on the liver of the treated animal. The increased requirement of the liver to handle the xenobiotic load is probably responsible for this decrease in relative size, as most of its metabolites are channeled towards the detoxification of these xenobiotics [3]. There is a significant decrease at (P< 0.05) of the relative heart weight of rats treated with 150mg/kg of stem extract (0.29 ±0.01) and that of the standard (Captopril) treated (0.31 ±0.02) in relation to that of the normal control (0.38 ±0.03). The decreased heart weights might be due to the heart's increase activities in hypertensive conditions, with possible tissue degeneration/atrophy[4]. There is a significant increase at (P < 0.05) between the body weight of rat treated with 150mg/kg of stem extract (200.68 ±6.82) and that of hypertensive control (159.22 ±2.64). The increased body weight may be due to the recovery effect elicited by the extracts [3]. Generally, hypertension affects the body's homeostatic and metabolic conditions. This could result to a negative energy balance with a consequent significant lose in body weight. However, the elicited a recovery effects, typified by the increased in body weight [7]. This might be a strong pointer to the fact the extract had and elicited antihypertensive properties.

Tabe2: Body and organ weights of rats treated with crude ethanolic root bark extracts of *nauclealatifolia* for 14 days.

EXTRACT	PARAMETERS	NC (GP7)	HC (GP6)	T3 (GP3)	T4 (GP4)	ST (GP5)
ROOT EXTRACT	Body weight	188.68 ±17.87	159.22 ±2.64	218.96 ±10.36[a, b]	197.46 ±10.68[a]	179.74 ±27.10
	Liver weight	7.35 ±0.72	5.66 ±0.19	7.74 ±0.62[a]	7.10 ±0.24	6.78 ±1.10
	Relative Liver weight	3.51 ±0.19	3.55 ±0.10	3.53 ±0.20	3.64 ±0.22	3.77 ±0.17
	Kidney weight	1.23 ±0.09	1.06 ±0.04	1.38 ±0.07[a]	1.42 ±0.10[a]	1.24 ±0.14
	Relative Kidney weight	0.65 ±0.03	0.66 ±0.02	0.63 ±0.01	0.72 ±0.03	0.71 ±0.05
	Heart weight	0.70 ±0.01	0.52 ±0.04*	0.64 ±0.04	0.62 ±0.05	0.56 ±0.07
	Relative Heart weight	0.38 ±0.03	0.32 ±0.02	0.29 ±0.02*	0.32 ±0.02	0.31 ±0.02*

Values expressed as mean±SEM, n = 5.
** =P<0.05 compared to the normal control, GP7.*
a=P<0.05 compared to the hypertensive control, GP6.
b=P<0.05 compared to the standard treated, GP5.

Table 2 presents the result of the body and organ weights of activity directed administration of ethanolic root extract of *Nauclealatifolia*. There is a significant decrease at (P< 0.05) between the relative heart weight (0.29 ±0.02) of rats treated with 150mg/kg of root extract and that of standard (Captopril) treated (0.31 ±0.02) in relation to the normal control (0.38 ±0.03).this might be due to the reasons given for table 1 above. There is a significant increase at (P <0.05) between the body weight (218.96 ±10.36) of rats treated with 150mg/kg of root extract and that treated with 300mg/kg of root extract (197.46 ±10.68) in relation to the hypertensive control (159.22 ±2.64). There is a significant increase at (P< 0.05) between the body weight (218.96 ±10.36) of rats treated with 150mg/kg of root extract and that treated with the standard (Captopril) antihypertensive drug (179.74 ±27.10).

The results of the effects of administration of the extracts showed that the extracts possessed antihypertensive potential.

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