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Role of Antioxidant-Rich Nutraceutical on Body Weights and Mean Arterial Blood Pressure of Salt-Induced Hypertensive Rats

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Research Article

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Abstract

Hypertension or high blood pressure is a medical condition in which blood pressure in the vessels is persistently elevated. The study aim to formulate an antioxidant rich nutraceutical from locally available food stuff (onion, garlic, ginger, tomato, lemon, palm oil, water melon seeds) and investigate their effects on blood pressure and body weight in salt-induced rats. The rats were placed on 8% salt diet for 6 weeks and then supplementation and treatment with nutraceutical and nifedipine in the presence of salt diet for additional 4 weeks. Feeding rats with salt diet for 6 weeks increased blood pressure and body weight of the salt-loaded rats relative to control. Both supplementation and treatment (nifedipine) lowered the blood pressure but only supplementation lowered the body weight. Antioxidant-rich nutraceutical might be beneficial in the managements of patients with hypertension and obesity.

Keywords: Supplementation; High Blood Pressure; Vessels; Obesity; Nifedipine

Abbreviations: BP: Blood Pressure; STG: Standard Treatment Guidelines; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; MABP: Mean Arterial Blood Pressure; PR: Pulse Rate; RAAS: Renin Angiotensin Aldesterol System; MR: Mineralocorticoid Receptors; ROS: Reactive Oxygen Species; ACE: Angiotensin Converting Enzyme

Introduction

Hypertension is the major public health problem worldwide and it is among the common cardiovascular disease in black Africans and a major cause of morbidity and mortality among Nigerians [1]. According to hypertension is a condition in which the systolic blood pressure (BP) equal is greater than 140mmHg or diastolic blood pressure equal or greater than 90mmHg [2].

Excess of sugar and salt or deficiencies of antioxidant vitamins in diet play a vital role in the etiology of hypertension which directly poses damage to the vital organs such as brain, kidney and vascular tissues [3].

Hypertension represents one of the major factors for the development and progress of cardiovascular diseases and it is an important threat to the health of individuals in sub – Saharan Africa [4].

The prevalence of hypertension varies within different countries. The overall global prevalence among adults was estimated to be 26.6% in men and 26.1% in women [5].

In Nigeria, hypertension is the commonest non-communicable disease with over 4.3 million Nigerians above the age of 15 years classified as being hypertensive (systolic BP ≥ 160 mmHg and diastolic BP ≥ 90 mmHg). This gives a prevalence rate of about 25% which is even higher when the current standard treatment guidelines (STG) of ≥ 140 and ≥ 90 mmHg systolic and diastolic BPs respectively, are used as a landmark [6]. Prevalence rates of this magnitude place a significant burden on the limited health facilities of developing countries.

Furthermore, epidemiological studies and clinical trials suggested that, diets known to contain significant amount of naturally occurring antioxidants appear to ameliorate most of the traits of metabolic syndrome and may reduce cardiovascular risk [7]. Some locally available foodstuff contains significant amount of antioxidants and may be use for formulation of an antioxidant rich nutraceutical.

The research was conducted to determine the effect of salt diet on body weight and blood pressure in albino rats at 6 weeks of salt loading and to evaluate the effects of antioxidants rich nutraceutical on body weight and blood pressure of salt induced hypertensive rats.

Materials and Methods

Experimental Animals

Wistar albino rats of both sexes weighing between 150-220g were used for the study. The animals were purchased from the Department of Biological Science, Usmanu Danfodiyo University, Sokoto, Nigeria and were allowed to acclimatize for two weeks before the commencement of the experiment. The animals were grouped into 6 groups of eight rats each and were fed with pelletized growers' feed (Vital feed, Jos, Nigeria) and allowed access to water *ad libitum* before and during the experimental period.

Experimental Design

The animals were randomly divided into 6 groups of eight rats each.

Group I Salt-loaded, treated with 250mg/kg of nutraceutical

Group II Salt-loaded, treated with 500mg/kg of nutraceutical

Group III Salt-loaded, treated with 10mg/kg of nifedipine

Group IV Salt-loaded, treated with 500mg/kg of nutraceutical + 10mg/kg of nifedipine

Group V Salt-loaded, untreated

Group VI Normal, control

Induction of Hypertension in Rats

The rats were placed on 8% w/w salt diet except the control group, for 6 weeks and treatment with nutraceutical for additional 4 weeks [8].

Measurement of Blood Pressure

The baseline blood pressure was measured by tail-cuff method using non-invasive Ugo Basile, series 58500 blood pressure recorder. The average of three readings was taken for each rat and the blood pressure of the rats were monitored throughout the experimental period. Mean arterial blood pressure was calculated according to the following equation: DP +1/3 (SP- DP) where SP and DP are systolic and diastolic pressure respectively. Subsequent measurements were done every week.

Preparation of Antioxidant Micronutrients Supplements

The nutraceutical was prepared from onions, garlic, tomatoes, ginger, water melon seeds, lemon and palm oil in ratio of 4:4:4:4:2:1:1. This was done by mixing 20g of onions; 20g of garlic, 20g of tomatoes and 20g of ginger in 100ml distilled water and blended using electric blender. 10g of ground water melon seeds were then added and blended once again. To this, 5g of lemon juice and 5g of palm oil were added, mixed. The nutraceutical solution was packaged into clean dry containers and stored frozen at -20^{o}C until required.

The appropriate dosages of the nutraceutical and drug were administered to the animals orally once daily by intubation using intravenous cannula tube for 4 weeks, weight changes of the rats were monitored throughout the experimental period.

Estimation of % Protection against Atherogenesis

This was calculated using the following equation:

$$\% \text{ protection} = \frac{AI\ of\ HC - AI\ of\ treated\ group}{AI\ of\ HC} \times 100$$

Statistical Analysis

Values are expressed as mean ± standard deviation of 6 rats per group.

Results

The effect of nutraceutical on systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MABP) and pulse rate (PR) are presented in Figures 1, 2, 3 and 4 respectively. The result indicated that salt-loading to rats for 6 weeks increased the SBP, MABP and PR but no variation on DBP between salt-loading groups and control group. Supplementation with nutraceutical lowered the SBP, MABP and PR. The salt loading untreated group showed a progressive increase of SBP, MABP and PR throughout the experimental period while controls group no increase was observed.

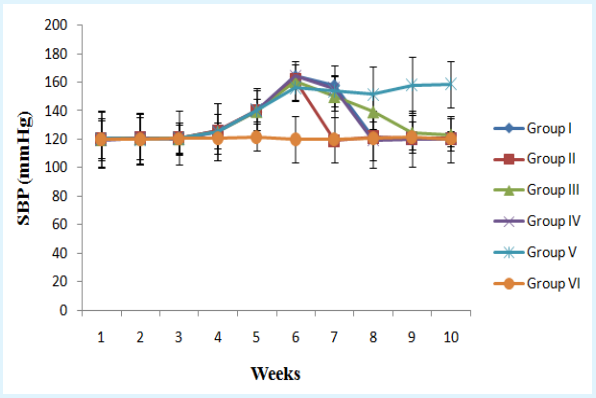

Figure 1: Effect of salt diet and nutraceutical supplementation on systolic blood pressure of salt-loaded rats

Week 1-6: salt diet only, week 6-10: salt diet plus supplements, Group I: salt loaded treated with 250mg/kg of nutraceutical, Group II: salt loaded treated with 500mg/kg of nutraceutical, Group III: salt loaded treated with 10mg/kg of nifedipine, Group IV: salt loaded treated with 500mg/kg of nutraceutical + 10mg/kg of nifedipine, Group V: salt-loaded untreated, Group VI: control.

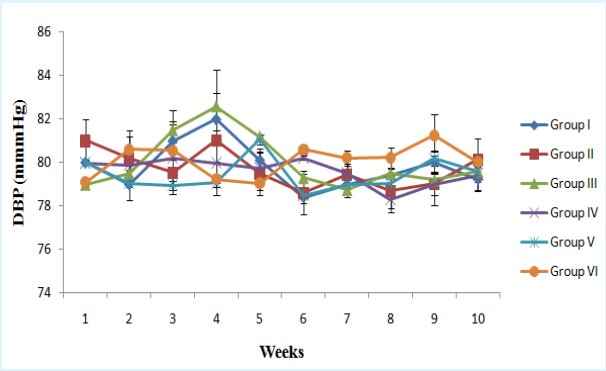

Figure 2: Effect of salt diet and nutraceutical supplementation on diastolic blood pressure of salt-loaded rats

Week 1-6: salt diet only, week 6-10: salt diet plus supplements, Group I: salt loaded treated with 250mg/kg of nutraceutical, Group II: salt loaded treated with 500mg/kg of nutraceutical, Group III: salt loaded treated with 10mg/kg of nifedipine, Group IV: salt loaded treated with 500mg/kg of nutraceutical + 10mg/kg of nifedipine, Group V: salt-loaded untreated, Group VI; control.

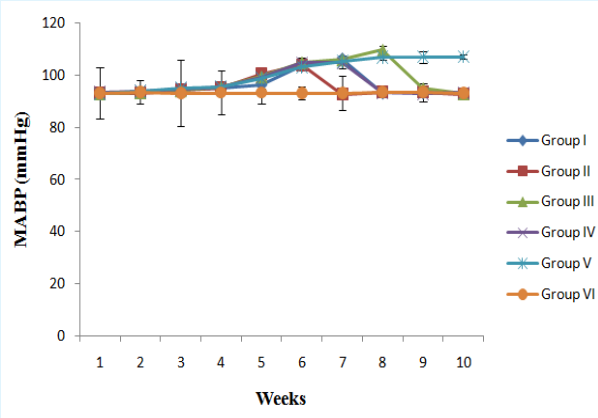

Figure 3: Effect of salt diet and nutraceutical supplementation on mean arterial blood pressure of salt-loaded rats.

Week 1-6: salt diet only, week 6-10: salt diet plus supplements, Group I: salt loaded treated with 250mg/kg of nutraceutical, Group II: salt loaded treated with 500mg/kg of nutraceutical, Group III: salt loaded treated with 10mg/kg of nifedipine, Group IV: salt loaded treated with 500mg/kg of nutraceutical + 10mg/kg of nifedipine, Group V: salt-loaded untreated, Group VI: control.

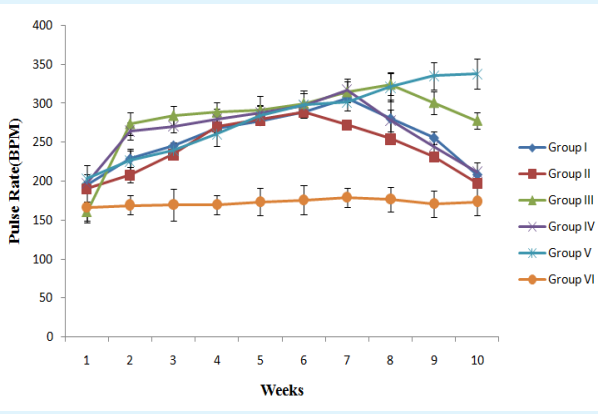

Figure 4: Effect of salt diet and nutraceutical supplementation on pulse rate of salt-loaded rats.

Week 1-6: salt diet only, week 6-10: salt diet plus supplements, Group I: salt loaded treated with 250mg/kg of nutraceutical, Group II: salt loaded treated

with 500mg/kg of nutraceutical, Group III: salt loaded treated with 10mg/kg of nifedipine, Group IV: salt loaded treated with 500mg/kg of nutraceutical + 10mg/kg of nifedipine, Group V; salt-loaded untreated, Group VI: control.

The result of the mean percentage weight gain of the rats in all the groups and mean percentage reduction in SBP, MABP and PR are presented in Figures 5 and 6 respectively. The result indicated that the salt-loaded untreated and salt-loaded treated with 10mg/kg of nifedipine are gained more weight (42.4±1.76%) and (37.02±0.88%) respectively than all other groups. The group that gained the least weight (18.3±0.65%) was the group supplemented with 500mg/kg of nutraceutical.

The result also showed that supplementation decreases the SBP, MABP and PR, rats supplemented with 500mg/kg of nutraceutical have the highest % reduction (27.42±2.52%) and (12.85±1.22%) in SBP and MABP respectively while groups supplemented with 10mg/kg of nifedipine have the lowest % reduction (23.22±0.97%) and (10.23±0.76%) in SBP and MABP respectively.

It was observed that rats supplemented with 500mg/kg of nutraceutical + 10mg/kg have the highest % reduction (47.78±0.05%) in PR while group supplemented with 10mg/kg of nifedipine have the lowest % reduction (39.46±0.24%) in PR.

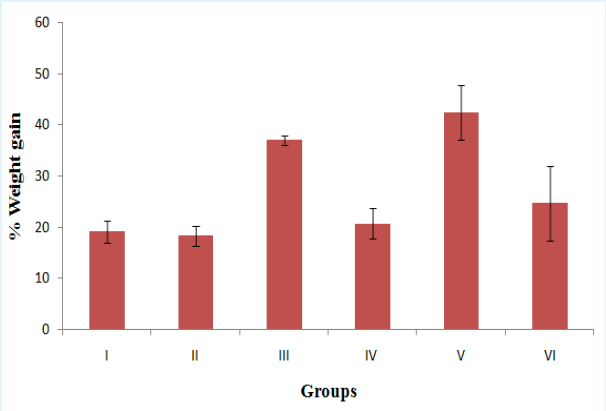

Figure 5: The mean percentage weight gain of salt-loaded rats treated with nutraceutical

Group I: salt loaded treated with 250mg/kg of nutraceutical, Group II: salt loaded treated with 500mg/kg of nutraceutical, Group III: salt loaded treated with 10mg/kg of nifedipine, Group IV: salt loaded treated with 500mg/kg of nutraceutical + 10mg/kg of nifedipine, Group V: salt-loaded untreated, Group VI: control.

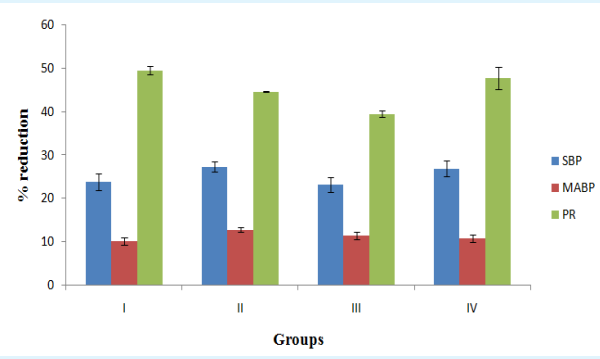

Figure 6: The mean percentage reduction in SBP, MABP and PR of salt loaded rats' supplemented with nutraceutical.

SBP-systolic blood pressure, MABP-mean arterial blood pressure, PR-pulse rate, Group I: salt loaded treated with 250mg/kg of nutraceutical, Group II: salt loaded treated with 500mg/kg of nutraceutical, Group III: salt loaded treated with 10mg/kg of nifedipine, Group IV: salt loaded treated with 500mg/kg of nutraceutical + 10mg/kg of nifedipine, Group V: salt-loaded untreated, Group VI: control.

The result of mean percentage protection against atherogenesis is presented in Figure 7. The result indicated (76.5±2.13%) mean average percentage protection in all the groups supplemented with nutraceutical while non-supplemented group gave the lowest (13.02±1.77%) protection against atherosclerosis.

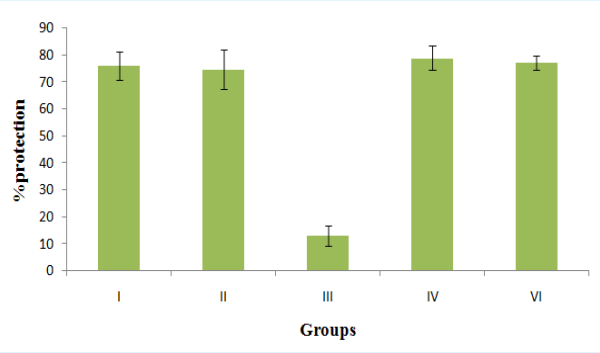

Figure 7: Mean percentage protection of nutraceutical against atherosclerosis.

Group I: salt loaded treated with 250mg/kg of nutraceutical, Group II: salt loaded treated with 500mg/kg of nutraceutical, Group III: salt loaded treated with 10mg/kg of nifedipine, Group IV: salt loaded treated with 500mg/kg of nutraceutical + 10mg/kg of nifedipine, Group V: salt-loaded untreated, Group VI: control.

Discussion

The onset of hypertension is caused by complex interaction between genetic predisposition and environmental risk factors [9]. Hypertension is associated with the incidence of arthrosclerosis [10]. Thus, development of therapeutic/management strategies that may delay the onset and prevent complications associated with hypertension is critical to improve the life of patients with hypertension. This study was designed to formulate an antioxidant rich nutraceutical from locally available foodstuff and to evaluate whether supplementation with antioxidant rich nutraceutical could play vital role in delaying the onset and progress of hypertension. In our model, a diet containing 8% salt was used to induce hypertension in Wistar albino rats for a period of 6 weeks. Our model fit the scenario of high salt diet caused hypertension in experimental rats and humans [11,12].

The results of this study indicated that salt-loading to rats for 6 weeks increased blood pressure and body weight. The mechanism of high salt diet-induced hypertension could be attributed to increase concentration of sodium in circulation which turned activates sympathetic nervous system and renin-angiotensin-aldesterol-system (RAAS) as well as increased signaling through the mineralocorticoid receptors (MR) [13,14]. These may lead to increase production of reactive oxygen species (ROS) and oxidative stress, and finally contribute to aetiopathology of insulin resistance, high blood pressure, impaired glucose homeostasis and dyslipidaemia [15].

The finding confirms the reports that salt loading to various strains of rats such as Sprague-Dawley rats, Wistar rats and Dahl salt-sensitive rats result in increased mean arterial blood pressure [11,12,16].

Elevation of systolic blood pressure (SBP) indicates the risk of cardiovascular disease which is more important than increase in diastolic blood pressure (DBP) and is more difficult to control than DBP [9]. The lack of effect on DBP observed in this study could be attributed to salt diet does not have much effect on resting state of the heart during cardiac relaxation.

The blood pressure lowering effect of nutraceutical could be attributed to combine effects of the nutraceutical with calcium channel blocking activity and diuretic effect [17]. It may also be attributed to high level of flavonoids, in the nutraceutical as flavonoids inhibit the activity of angiotensin-converting enzyme (ACE) which raises blood pressure [18]. Other possible mechanism could be due to the presence of antioxidant vitamins and minerals in the nutraceutical thereby exhibiting antioxidant activity either by serving as nucleophilic species or scavenge superoxide anions as reported by [19].

The highest percentage weight gain observed in non-supplemented rats with hypertension. The possible mechanism by which salt diet increases body weight could be attributed to sodium levels can activate RAAS via increase in sympathetic outflow thereby stimulating adipokines that contribute to increase in abdominal weight [20]. The lowest percentage weight gain was observed in rats supplemented with 500mg/kg of nutraceutical. The weight lost could be attributed to anti-obesity effects of the nutraceutical through modification of lipid and carbohydrate metabolism, increased insulin sensitivity, and regulation of both appetite and adipocytokines [21]. Other possible mechanism could be attributed to inhibitory effects of the nutraceutical in proliferation, differentiation, angiogenesis in pre-adipocytes and induction of apoptosis in mature adipocytes [22,23]. Other possibility could be associated with the regulation of brown adipose tissue metabolism and increase thermogenesis, decrease adiponectin and leptin gene expression in adipocytes [24,25].

Conclusion

Antioxidant rich nutraceutical lowered the blood pressure and body weight and may have promising effect in the management of cardiovascular complications of hypertension and obesity.

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