

Investigation of Antihypertensive Effectiveness and Tolerability of *Hibiscus Sabdariffa* in Mild to Moderate Hypertensive Subjects in Enugu, South-east, Nigeria

Nwachukwu DC*¹, Aneke E², Obika LFO³ and Nwachukwu NZ⁴

¹Department of Physiology, College of Medicine, University of Nigeria, Enugu Campus, Enugu State, Nigeria.

²Department of Medicine, Enugu State University of Science and Technology, Enugu, Enugu State, Nigeria.

³Department of Physiology, School of Basic Medical Sciences, University of Benin, Benin City, Edo State, Nigeria.

⁴Department of Ophthalmology, University of Nigeria Teaching Hospital, Enugu, Enugu State, Nigeria

ABSTRACT

Objective: *Hibiscus sabdariffa* (HS) is widely consumed in Nigeria as a refreshing drink called 'Zobo'. Most Nigerians drink 'Zobo' because of the belief that it has antihypertensive action. Several animal studies have demonstrated the antihypertensive effects of HS but there is paucity of information on clinical studies on antihypertensive activity of HS in black subjects. This study investigated the antihypertensive effectiveness and tolerability of HS in mild to moderate hypertensive subjects in Enugu, South East, Nigeria.

Method: Ninety-Five newly diagnosed but untreated mild to moderate hypertensive subjects attending Medical out-Patients (MOP) unit of Enugu State University Teaching Hospital, Enugu were recruited for the study. They were randomly divided into two groups: A and B. Those in group A were given HS (150mg/kg) once daily while those in group B received twice daily. All infusions were administered orally daily for 4 weeks. Clinical evaluation and treatment adherence were monitored weekly. Sitting blood pressure was measured at baseline and weekly during treatment.

Result: At the end of 4 weeks, HS once daily decreased systolic blood pressure (SBP) by 17.08 ± 4.25 mmHg (-11.38%) and diastolic blood pressure (DBP) by 11.13 ± 3.92 mmHg (-12.13%) whereas HS twice daily caused 10.56 ± 3.39 mmHg (-6.9%) and 7.36 ± 2.54 mmHg (-7.4%) decrease in SBP and DBP respectively. No side effect was

Address for Correspondence

Department of Physiology, College of Medicine, University of Nigeria, Enugu Campus, Enugu State, Nigeria

E-mail: danychukwu@yahoo.com

reported during treatment in both groups.

Conclusion: The result of the present study suggests that low dose of HS was more effective in reducing blood pressure than high dose and that both doses were tolerated in mild to moderate hypertensive Nigerian subjects.

Keywords: *Hibiscus sabdariffa*, Essential hypertension, Clinical trial and alternative medicine.

INTRODUCTION

Hibiscus sabdariffa (HS) Linn belongs to the family of *Malvaceae* which has about 85 genera with *Hibiscus* having about 300 species. The calyx of the plant is used to produce a popular beverage called 'Zobo' in most parts of Nigeria¹. HS has been used in traditional medicine to treat high blood pressure, liver diseases, anemia, cancer and fever²⁻⁴. There is a growing public belief in Nigeria that HS has antihypertensive action and this has led to increased consumption of its aqueous infusion (Zobo) both in private homes and social gatherings⁵. Among its ethnomedicinal uses, its antihypertensive effect has been well researched; studies have shown that HS has a relaxing effect on rat vascular smooth muscle via inhibition of calcium influx^{6,7}. Intravenous injection of extract of HS calyx to anaesthetized cats⁸ and anaesthetized rats⁹ lowered blood pressure in a dose-dependent manner. In a study, methanolic extract of the calyces of HS produced a vasodilator effect in isolated aortic rings of male spontaneously hypertensive rats via endothelium-dependent and -independent pathways with the endothelium dependent vasodilator effect resulting from 'activation of endothelium-derived nitric oxide/cGMP- relaxant pathway' and that of endothelium-independent effect possibly due to 'inhibition of calcium (Ca^{2+}) influx'¹⁰. The antihypertensive action of HS was also demonstrated in rats with experimental renovascular hypertension where chronic

administration of its aqueous extract was shown to attenuate both systolic blood pressure (SBP) and diastolic blood pressure (DBP)¹¹.

In a clinical trial involving 54 patients with moderate essential hypertension, daily consumption of aqueous extract of HS resulted in 11% decrease in both SBD and DBP 12 days after commencement of treatment¹². It was postulated that the antihypertensive action may be mediated through diuretic, vasodilatory and/or inhibition of ACE. In a similar study involving mild to moderate hypertensive Mexicans, HS caused 14.15 ± 11.7 mmHg and 11.18 ± 6.91 mmHg reductions in SBP and DBP respectively¹³. Most of the reported antihypertensive studies on HS in Nigeria were animal based studies. In order to justify the ethnomedicinal claims and usage and also confirm previous reports from animal studies, the present study investigated the antihypertensive effectiveness and tolerability of aqueous extract of HS calyx in mild to moderate hypertensive Nigerians.

MATERIALS AND METHODS

Plant collection

Dried calyces of *Hibiscus sabdariffa* were purchased from Ogbete main market, Enugu. They were authenticated by Mr A. Ozioko of the herbarium section of Botany Department, University of Nigeria, Nsukka and a specimen voucher number UNH/314b was assigned to it.

Human subjects

95 mild to moderate hypertensive subjects attending medical out-patient (MOP) clinic of Enugu State University Teaching Hospital, Parklane, Enugu, were recruited for study but only 90 (55 males

and 35 females) completed it. The study was carried out in line with the Guidelines of the Helsinki Declaration for human studies¹⁴ and approved by the institutional ethical committee.

Inclusion criteria

WHO/ISH (2003) Classification of Hypertension		
Category	Systolic BP (mmHg)	Diastolic BP (mmHg)
Optimal	<120	<80
Normal	<130	<85
High normal	130-139	85-89
Mild (Grade 1) hypertension	140-159	90-99
Moderate (Grade 2) hypertension	160-179	100-109
Severe (Grade 3) hypertension	≥ 180	≥ 110

- (i) Newly diagnosed but untreated mild to moderate hypertension.
- (ii) Adequate briefing was done and consent obtained from the subjects.

Exclusion criteria

- (i) Patients with diabetes, nephropathy, cardiopathy, hepatic disease and cancer were excluded from this study.
- (ii) Pregnant women, individuals with evidence of secondary hypertension, chronic smokers and alcoholics were also excluded.

All participants were prohibited from participating in other clinical studies for the duration of this study.

Preparation of HS infusion

The method of Herrera-Arellano et al.¹³ was used to prepare HS infusion with 2 modifications. 20g of dry calyces were weighed and ground in electric mill to obtain particles <2mm. It was used to make an infusion by adding 1L of boiling clean bottle water (Aquafina, Pepsi Nig. Ltd) and allowed to stand for 30 minutes.

The solution was filtered using Whatman's no.1 filter paper. The filtrates

were stored in clean plastic containers at room temperature.

The following two modifications were made:

- (i) Infusions were prepared and given to patients.
- (ii) Time allowed for extraction was extended from 10 to 30 minutes.

HS dosage calculation

$$\text{Daily dose} = 150 \text{ mg / kg}$$

$$1 \text{ kg} = 150 \text{ mg}$$

$$\text{Weight of Patient} = W \text{ kg}$$

$$W \text{ kg} = 150 \times W \text{ mg} = 0.15 \times W \text{ g}$$

From extraction,

$$20 \text{ g} = 1 \text{ L}$$

Thus,

$$0.15 \times W \text{ g} = (0.15 \times W / 20 \times 1) \text{ L} = (0.0075 \times W) \text{ L}$$

150mg/kg was chosen because it produced

approximately the same colour as the locally brewed 'Zobo' drink.

Blood pressure measurement

Participants who met the inclusion criteria were randomly divided into 2 groups: A and B.

Group A - Subjects were given 150mg/kg of HS infusion orally once daily before breakfast for 4 weeks.

Group B- Subjects took 150mg/kg of HS infusion orally twice daily (before breakfast and dinner) for 4 weeks.

All the subjects were given weekly appointments and a week worth of infusion. BP was measured before (baseline) and at weekly intervals during treatment. Clinical evaluation and treatment adherence were also evaluated weekly.

Sitting BP was measured by a physician who was not aware of the treatment group assigned to subjects. BP was measured using Accoson® mercury sphygmomanometer. SBP was taken as first appearance of Korotkov sounds and the DBP the point of disappearance of the sounds (Phase V). Two consecutive readings were taken from each subject at 5 minutes interval and the average of these was taken as the mean blood pressure reading. Measurement was taken between 8.00am to 10.00am. Any constrictive clothing on the arm was removed before measurement was taken.

STATISTICAL ANALYSIS

Results were presented as Mean± SEM. Data were classified by groups and weeks of treatment and analyzed using SPSS version 20. One way analysis of variance (ANOVA) was used to compare differences between groups. P values ≤ 0.05 was considered significant.

RESULTS AND DISCUSSION

Baseline characteristics of subjects who participated in the present study are presented in table 1. At the end of 4 weeks, both SBP and DBP decreased in both groups (Table 2). In group A (HS once daily), SBP decreased by 17.08 ± 4.25 mmHg at the end of week 4 whereas in group B (HS twice daily), it reduced by 10.56 ± 3.39 mmHg. This represents a decrease of 11.38% and 6.9% respectively in the two groups (Table 3). Similarly, DBP decreased by 11.13 ± 3.92 mmHg and 7.36 ± 2.54 mmHg in groups A and B respectively; which represents a percentage decrease of 12.13% and 7.4% in the two groups respectively (Table 3). MAP followed a similar pattern; at the end of week 4, a reduction of 13.58 ± 3.15 mmHg was observed in group A while 8.45 ± 2.78 mmHg reduction was recorded in group B (Table 2). At the end of treatment, blood pressure was reduced to normal in group A (133.80 ± 1.77 mmHg for SBP and 88.08 ± 1.12 mmHg for DBP) whereas this was not achieved in group B (143.44 ± 2.39 mmHg for SBP and 92.32 ± 1.54 mmHg for DBP). No side effects were reported by subjects in both groups during the period of study.

The result of the present study showed that at a low dose (150mg/kg once daily), HS calyx infusion was effective in reducing both SBP and DBP in mild to moderate hypertensive subjects. This finding is consistent with earlier reports of antihypertensive activity of HS in laboratory animals^{5,8, 9} and in human subjects^{12,13}. A decrease of 11% in both SBD and DBP was reported in a study¹² while 11% decrease in SBP and 12% reduction in DBP was reported in another study¹³ while a decrease of 11.38% (SBP) and 12.13% (DBP) was observed in group A (low dose) of the present study. Since similar method of preparing HS infusion was used in these studies, racial differences obviously did not

affect the antihypertensive activity of HS. However, at a higher dose (150mg/kg twice daily), the antihypertensive effectiveness of HS was reduced; this may not be unconnected with earlier reports of its toxicity on heart and kidney when administered at high doses^{15,16}.

The duration of treatment does not seem to have much effect on blood pressure outcome. The present study and that done in Mexico¹³ lasted 4 weeks while that done in Iran¹² lasted 2 weeks and similar results were obtained in all the studies.

No side effect was reported in this study as well as previous human studies showing that HS was tolerated in the different races studied. This also suggests that HS consumption is safe as earlier reported¹⁷.

CONCLUSION

The present study has shown that HS at low dose can effectively reduce blood pressure in mild to moderate hypertensive Nigerians and thus validates the numerous animal antihypertensive studies on HS. This study also provides evidence that daily consumption of HS at a low dose has no side effect. These findings in addition to its cheapness and availability amplify its desirability as an alternative antihypertensive agent in mild to moderate hypertensive subjects. However, caution has to be applied in ensuring that it is not consumed in high or undesirable dosage.

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Table 1. Baseline clinical characteristics of the subjects

Parameter	Group A (n= 48)	Group B (n= 42)
Age (years)	47.80±9.07	48.00±2.02
Weight(Kg)	78.48±10.15	76.54±8.32
BMI(Kg/m ²)	28.10±3.59	28.21±0.58
SBP(mmHg)	150.88±1.33	154.20±6.30
DBP(mmHg)	99.21±0.96	99.68±1.48
MAP (mmHg)	116.96±5.38	117.77±3.70

Results presented as Mean± SEM

Table 2. SBP, DBP and MAP (mmHg) in both groups at baseline and during treatment

Weeks	SBP (mmHg)		DBP (mmHg)		MAP (mmHg)	
	GroupA	Group B	GroupA	Group B	Group A	Group B
Baseline	150.88±1.33	154±2.3	99.21±0.96	99.68±1.48	116.96±5.38	117.77±3.70
Week 1	146.32±1.51	150.52±2.3	97.44±1.01	97.60±1.45	113.74±3.13	115.27±3.68
Week 2	142±1.65	147.68±2.26	94.80±1.01	95.72±1.45	110.66±4.15	113.04±5.17
Week 3	138.44±1.62	145.32±2.28	91.88±1.01	94±1.48	107.47±3.16	111.10±3.58
Week 4	133.80±1.77	143.44±2.39	88.08±1.12	92.32±1.54	103.28±2.29	109.32±3.12

Results presented as Mean± SEM

Table 3. Percentage (%) change in blood pressure at weeks 2 and 4

Weeks	SBP		DBP		MAP	
	GroupA	Group B	GroupA	Group B	Group A	Group B
Week 2	-5.92±0.48	-4.12±0.14	-5.40±0.26	-3.98±0.17	-5.40±2.25	-1.48±2.19
Week 4	-11.38±0.53	-6.90±0.36	-12.13±0.48	-7.42±0.40	-7.84±1.57	-4.03±2.15

Results presented as Mean± SEM