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# Antihypertensive Effect of a Standardized Aqueous Extract of *Hibiscus Sabdariffa (Zobo)*And *Hyphaene Thebaica (Goriba) In Cats*: In Vivo Approach to the Hypotensive Mechanism

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## ABSTRACT

Ethnopharmacologically, *Hibiscus sabdariffa* (HS) and *Hyphaene Thebaica* have been used as a folk remedy for the treatment of hypertension. The effects of *Hibiscus sabdariffa* (HS) in lowering blood pressure in human and animal hypertension have been documented. Moreover, several in vitro and in vivo ethnobotanical studies demonstrated evidence that extracts from the calyxes have been used in folk medicine to treat high blood pressure. More so, the evaluation of the physiological effects and health benefits of the extracts in clinical studies is most challenging. **Aim:** The aim of this study is to investigate the hypotensive and cardiac effects of the standardized aqueous extract of *Hibiscus sabdariffa* and *Hyphaene Thebaica* and to examine the evidence of its effectiveness on blood pressure based on ethnomedicinal, safety and toxicity. **Methods:** The study used a Randomized Clinical Trials, with three normotensive cats divided into three experimental groups: *Hibiscus sabdariffa, Hyphaene Thebaica,* and control. Each group had one cat. The cats were exposed to different treatments of single dose of standardized aqueous extracts which was inoculated intravenously through the femoral vein of the cats (0.2ml/1mg each of *Hibiscus sabdariffa & Hyphaene Thebaica,* 0.2ml/10mg*Hibiscus sabdariffa & Hyphaene Thebaica,* and 0.2ml/100mg *Hibiscus sabdariffa & Hyphaene Thebaica,* and placebo for the control) for three days. In each experimental group, various doses concentration were increased from 0.2ml/mg up to 0.8mls. The cats' blood pressure reaction or dose

response was measured using the recording microdynamometre. **Results:** Intravenous administration of the extracts resulted in a biphasic dose-related hypotensive effects across *Hibiscus sabdariffa* group at lower doses, while *Hyphaene Thebaica* extract resulted in a biphasic dose related increase of blood pressure at lower doses ,and hypotensive response was noted at higher concentration of 0.8ml/100 mg. Comparatively, blood pressure in *Hibiscus sabdariffa* treated cats showed exponential decrease in blood pressure as doses increase while *Hyphaene Thebaica* raised the blood pressure at lower doses and therefore demonstrated exponential decrease of blood pressure at higher doses. **Conclusion:** These results suggest that *Hyphaene Thebaica* exhibited its initial hypotensive effects at higher dose related while *Hibiscus sabdariffa* exhibited its hypotensive effects at lower doses. Moreover, no adverse effects were reported during the clinical trials. However, further in vivo, and in vitro studies are required to validate the clinical efficacy of *Hyphaene Thebaica* and *Hibiscus sabdariffa* in large-scale studies.

**Keywords:** Hibiscus sabdariffa; *Hyphaene Thebaica,* Clinical trials; Hypotension

## INTRODUCTION

*Hibiscus sabdariffa* L. (HS) (Malvaceae) and *H. Thebaica (Goriba)*tea is in widespread use across the world as a beverage and as a treatment of hypertension and hyperlipidemia (Herrera et al., 2004). Two systematic reviews have been published on the effectiveness of *Hibiscus sabdariffa* for the treatment of hypertension[1,2]. Hibiscus sabdariffa L. (Hs, roselle; Malvaceae) has been used traditionally as a food, in herbal drinks, in hot and cold beverages, as a flavouring agent in the food industry and as a herbal medicine [3]. In vitro and in vivo studies as well as some clinical trials provide some evidence mostly for phytochemically poorly characterised *Hibiscus sabdariffa and Hyphaene Thebaica* extracts. Extracts showed antibacterial, anti-oxidant, nephro- and hepato-protective, renal/diuretic effect, effects on lipid metabolism (anti-cholesterol), anti-diabetic and anti-hypertensive effects among others s [2,4]. This might be linked to strong antioxidant activities, inhibition of α-glucosidase and α-amylase, inhibition of

angiotensin-converting enzymes (ACE), and direct vaso-relaxant effect or calcium channel modulation [5]. Phenolic acids (esp. protocatechuic acid), organic acid (hydroxycitric acid and hibiscus acid) and anthocyanins (delphinidin-3-sambubioside and cyanidin-3-sambubioside) are likely to contribute to the reported effects s [6]. Most studies supported and provided the scientific basis for the statement that *Hibiscus sabdariffa* and their active constituents play an important role in the prevention of chronic and degenerative diseases that are associated with oxidative stress s [4]. Pytochemically, Hibiscus sabdariffa was found to be rich inanthocyanins which significantly decrease LDL oxidation, inhibit adipogenesis by regulating adipogenic signaling pathways and transcription factors, and modulate gene expression of certain micro RNAs. Hibiscus sabdariffa extracts was established to have a low degree of toxicity with a LD50 ranging from 2,000 to over 5,000mg/kg/day s [2]. Other studies further revealed that there is no evidence of hepatic or renal toxicity as the result of Hibiscus sabdariffa extract consumption, except at higher doses where evidence showed somehepatotoxic effects [2].There is evidence that *Hibiscus sabdariffa*acts as a diuretic without significantly influencing electrolyte levels [2]. Animal studies have consistently shown that consumption of *Hibiscus sabdariffa* extract dose-dependently reduces blood pressure [3]. In Ramdomized Control Trials, evidently showed that the daily consumption of a tea or extract produced from *Hibiscus sabdariffa* calyxes significantly lowered systolic blood pressure (SBP) and diastolic blood pressure (DBP) in adults with pre-hypertension, stage 1 hypertension and type 2 diabetes. Interestingly, in addition, *Hibiscus sabdariffa* tea was as effective in lowering blood pressure as the commonly used blood pressure medication Captropril, but less effective than Lisinopril [2,5]. Previous studies reported that over half of the Ramdomized Clinical Trials showed that daily consumption of *Hibiscus sabdariffa* tea or extracts had favorable influence on lipid profiles including reduced total cholesterol, LDL-C, triglycerides, as well as increased HDL-C [2]. Anthocyanins found in abundance in *Hibiscus sabdariffa* calyxes are generally considered the phytochemicals responsible for the antihypertensive and cholestrol

lowering effects, however evidence has also been provided for the role of polyphenols and hibiscus acid. A number of potential mechanisms have been proposed to explain the hypotensive and anticholesterol effects, but the most common explanation is the antioxidant effects of the anthocyanins inhibition of LDL-C oxidation, which impedes atherosclerosis, an important cardiovascular risk factors [3,2]. This comprehensive body of evidence suggests that extracts of *Hibiscus sabdariffa* are promising as a treatment of hypertension and hyperlipidemia. Anthocyanins of *H. sabdariffa* can inhibit low-density lipoprotein oxidation and therefore decrease the atherosclerotic process. Moreover, it has been showed that *H. sabdariffa* has a compound that causes nitric oxide release from vascular endothelium which follows by kidney filtration increase, a mechanism that clears its diuretic effect so on blood pressure [3,2].Studies have also shown that oral administration of *H. Thebaica (Goriba)* at 25mg/kg inhibit platelet function, reduce thrombus formation, and development of atherosclerosis in animal model s [7]. In the same reports, it was documented that *H. Thebaica (Goriba)* caused a significant decrease in systolic and diastolic blood pressure towards normal values[7].

## MATERIAL AND METHODS

**Design:** This study used an independent group randomized clinical trials to investigate the effects of *Hibiscus sabdariffa* and *H. Thebaica (Goriba)* on blood pressure response in cats. The subjects used for this study were divided into three groups: group one, administered with *Hibiscus sabdariffa* only, group two, administered with *H. Thebaica (Goriba)* only, group three, administered with placebo as control group. The independent variables were the different levels of intravenous administration of *Hibiscus sabdariffa* and *H. Thebaica (Goriba)* while the dependent variable was the blood pressure in (mmHg) response by the cats.

**Subjects:** The subjects for this study were three (3)African cats weighing between 350-450g. The cats were housed in separate metal cages and kept in a constant environmental condition of temperature (22±1°C) and humidity throughout the experiment. The cats were fed

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with mouse cubes on a constant diet and had access to fresh drinking water. The cats were acclimatized for a period of four days prior to the beginning of the study.

**Drug/Extracts:** The drugs/extracts used in the study were *Hibiscus sabdariffa and H. Thebaica* (0.2ml/1mg, 0.2ml/10mg and 0.2mls/100mg respectively .*Hibiscus sabdariffa* was administered intravenously through femoral vein at a dose of 0.2mls/1mg, 0.2mls/10mg and 0.2mls/100mg bodyweight, and *H. Thebaica* was administered at a dose of 0.2mls/1mg,0.2mls/10mg,0.2mls up to 0.8mls/100mg body weight.The arterial blood pressure,and heart rate were determined spectrofluorimetrically during the whole experimental period

**Instruments:** Materials and instruments used in the study included experimental cat cages, hand gloves, nose/face masks, distilled water/saline, recording sheets, disposable syringes, extracts/drugs, a laboratory coat, a stopwatch, an intravenous cannula, and microdynamometre .

**Extract Collection:** Hibiscus sabdariffa and *Hyphaene Thebaica*were collected from Kano, North-Western Nigeria. The authenticity of the plant were confirmed in the Plant Biology Department of Bayero University Kano, The voucher number of the specimensare Bayero University, Kano, Herbarium Accession Number BUKHAN0040 and BUKHAN0380 respectively. The flowers were harvested, and calyces were separated before they were subjected to air drying at room temperature and then powdered. Male and Female Wistar cats (350–450 g) were purchased from the Modern Veterinary Office for Laboratory Animals, Zaria, and housed in plastic cages at the animal house of the Faculty of Pharmacy, Ahmadu Bello University Zaria. Ethical approval was sought and protected under No. DRIP/IPTTO).

## Results

Figure.1 *Hyphaene Thebaica ( Goriba)*

It is clear from the figure below that there is almost 1mmHg exponential increase in blood pressure response to every corresponding

0.1ml increase in dose concentration from 0.2ml up to 0.8mls of the extract for 1ml/10mg concentration. A decline/reduction in blood pressure response was observed when the dose concentration was increasing from 0.9mls up to 1.5mls , there was corresponding decrease by 1mmHg geometrically. It is obvious that blood pressure increases at lower doses and decreased at lower doses.

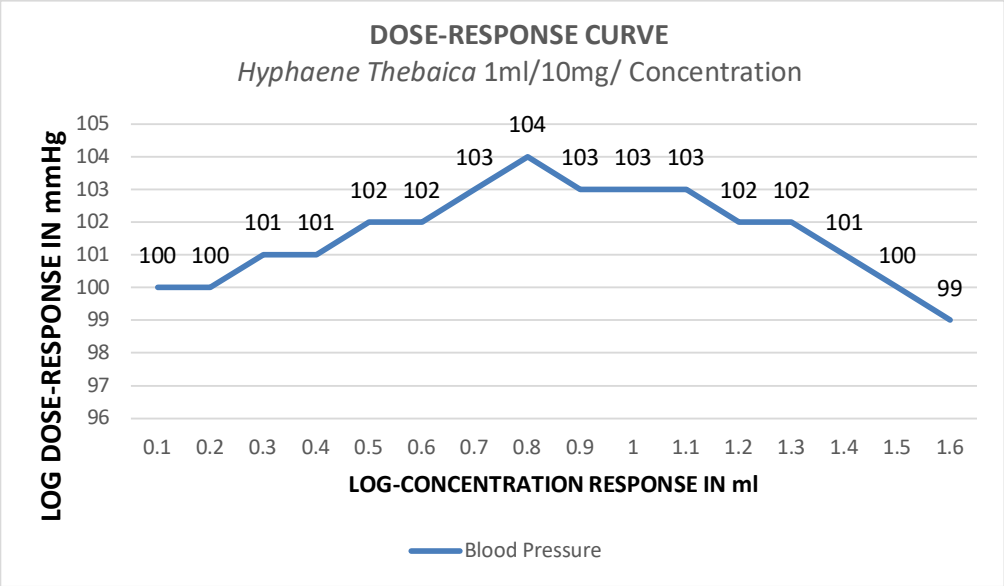


Figure 11. *Hyphaene Thebaica ( Goriba).*

It is obvious from the figure, below that for every 0.1mls administration there is corresponding exponential decrease in blood pressure response by 0.1mmHg. It is interesting that this pattern is observed at higher concentration of the extract preparation 100mg/1ml

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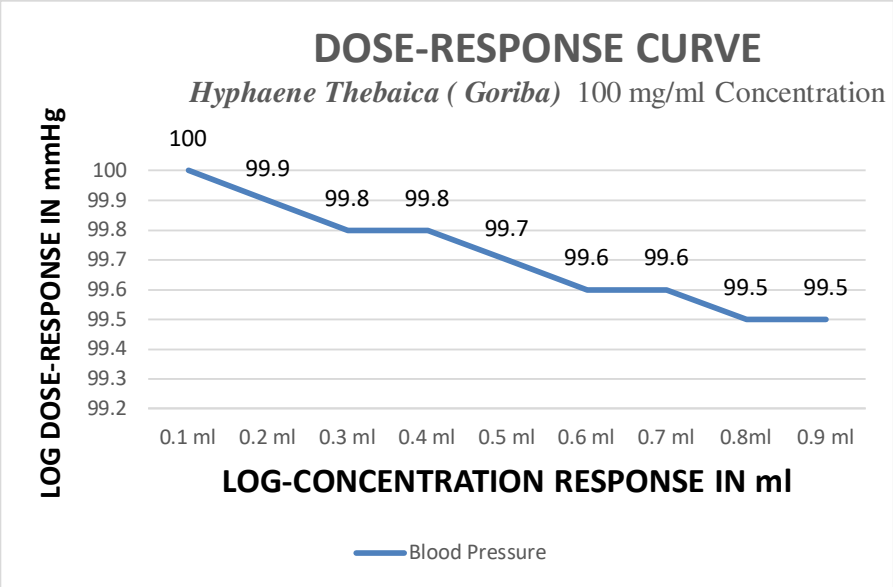


Figure. III *Hibiscus Sabdariffa (Zobo)*

It is clear from the figure, below that for every increase in dose concentration there is exponential decrease in blood pressure response by 0.1mmHg

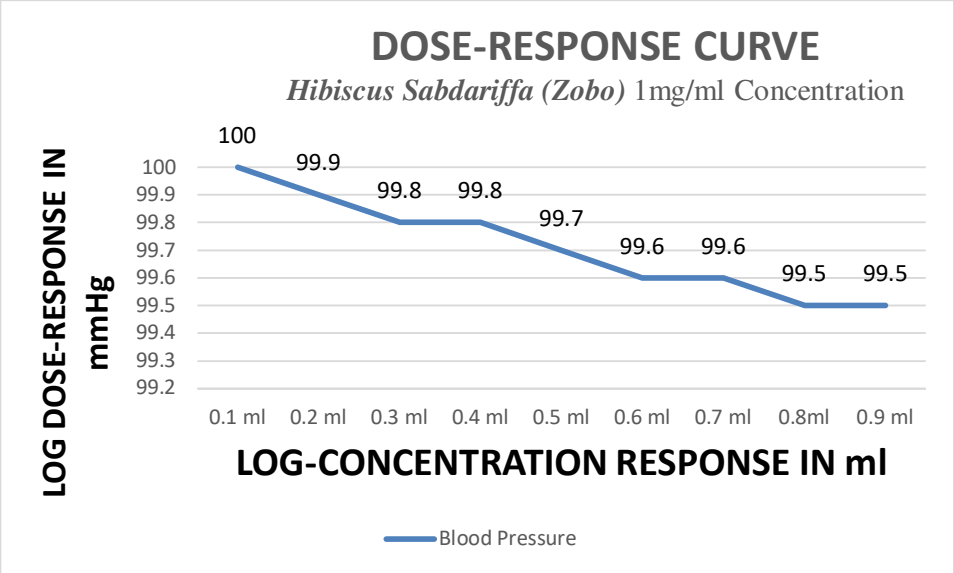


Figure.IV *Hibiscus Sabdariffa (Zobo)*

It is obvious from the figure , below that there is corresponding linear response in blood pressure for every increase in dose concentration of 10mg/ml preparation by 0.1mmHg

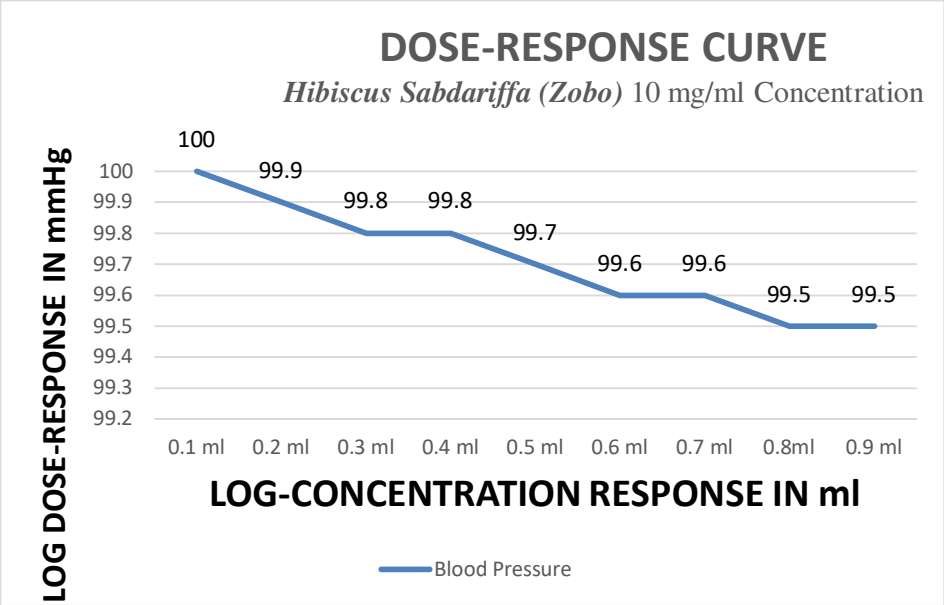


Figure .V *Hibiscus Sabdariffa (Zobo)*

It is clear from the figure below, that for every 0.1ml increase in dose concentration there is corresponding and exponential decrease by 0.1mmHg of blood pressure for 100mg/1ml preparation . It is however, noted that the responses is not linear to corresponding increase in dose concentration.

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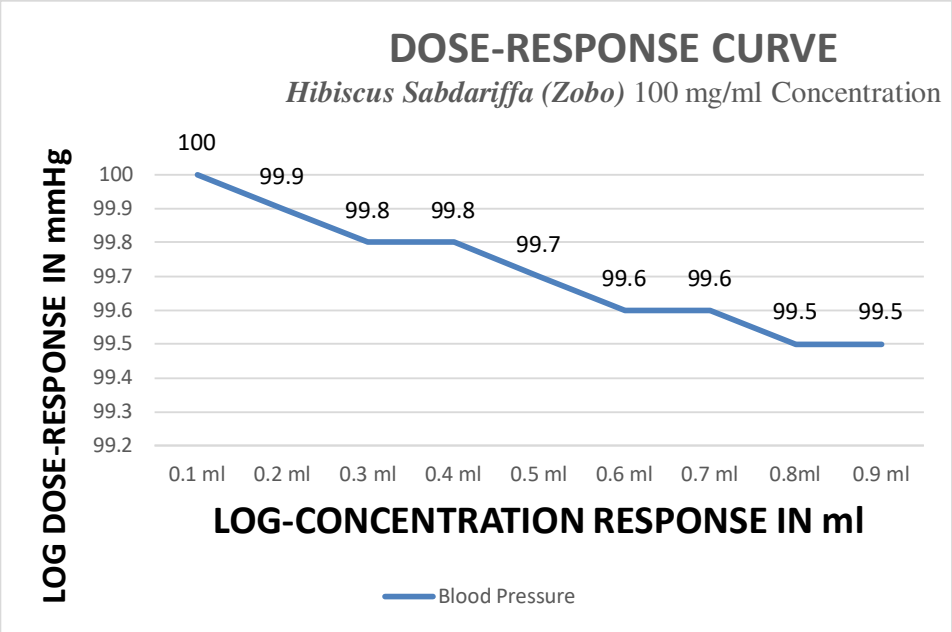


## DISCUSSION

In this study , it was found that *Hyphaene Thebaica* raises the blood pressure at lower doses peaking up to 20-25%, but with immediate reduction in blood pressure response at higher doses. This striking findings stands unique and contradicted with most previous studies. The probable explanation to this unique findings could be linked to lower concentration of anthocyanins at lower doses in *Hyphaene Thebaica* calyxes that are generally considered the phytochemicals responsible for the antihypertensive and lipid lowering effects as opposed to higher doses which is found in abundance. It was noted that at higher doses of *Hyphaene Thebaica* calyxes extract induces hypotensive effects, this findings is similar to what has been documented in the previous studies[8]. The probable explanation to this effect could be associated with the presence of high pytochemical concentration of anthocyanins, polyphenols and flavonoids. Comparatively, blood pressure in *Hibiscus sabdariffa* treated cats was found to have reduced by 10-15% in a dose related fashion. This findings is supported by some previous studies s [5,1,2]. The possible explanation to this hypotensive effects recorded in *Hibiscus sabdariffa* might be linked to strong antioxidant activities, inhibition of α-glucosidase and α-amylase, inhibition of angiotensin-converting

enzymes (ACE), and direct vaso-relaxant effect or calcium channel modulation. Phenolic acids (esp. protocatechuic acid), organic acid (hydroxycitric acid and hibiscus acid) and anthocyanins (delphinidin-3-sambubioside and cyanidin-3-sambubioside) are likely to contribute to the reported effects s [9,4,6]. This present findings on *Hibiscus sabdariffa* extracts provided a comprehensive body of scientific basis for its antihypertensive effects that mimic most ethnopharmacological relevance of some plants extracts [10]. However, evidences gathered provided that some extracts lowers blood pressure through a mechanism induced vasorelaxation by preventing carbonic anhydrase and stimulating KCa channels[11].In contrast, some growing evidences established that Organo-sulfur compounds have been correlated with reducing BP by sustaining the elasticity of the major arteries accompanied by lowering the blood viscosity, thereby preventing blood clotting. Aqueous extracts of *Hyphaene Thebaica and* onion (400 mg/kg/d) increased eNOS expression but decreased that of VCAM-1. The antioxidant effects of extracts seem to be the result of the inhibition of NADPH oxidase activity together with a simultaneous rise in antioxidant kinetics of glutathione peroxidase (GPX) enzymes and SOD [12].

Most herbal medicines control and reduce blood pressure by exerting antioxidant, anti-inflammatory, and anti-apoptosis properties, stimulating the eNOS-NO signaling pathway, suppressing endothelial permeability, and activating angiogenesis [4].

**Conclusion:** *Hyphaene Thebaica* raises blood pressure at lower doses while *Hibiscus sabdariffa* reduces blood pressure irrespective of the dosages.It is hypothesized that the biphasic doses induced hypotension by the extracts were thought to be acting on the cardiac pump efficiency and secondly through vasodilation. however more high quality animal and human studies informed by actual therapeutic practices are needed to provide recommendations for use that have the potential for widespread public health benefit. The extracts had a remarkable influence on the field of cardiology, and their role has one of the most prominent effects on the progress of cardiological science.

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## Conflict of interest statement:

All authors declare no conflict of interest.

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