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Pharmacological Study

Evaluation of polyherbal formulation (SJT-HT-03) for antihypertensive activity in albino rats

Hardik S. Ghelani, Bipin M. Patel[1], Rina H. Gokani[1], Manish A. Rachchh[1]

The National Institute of Complementary Medicine (NICM), University of Western Sydney, Campbelltown, NSW, Australia, [1]Department of Pharmacology, S. J. Thakkar Pharmacy College, Rajkot, Gujarat, India

ABSTRACT

Background: Hypertension is an incurable pathological condition and lifelong therapy is required. Long term use of conventional synthetic anti-hypertensive drugs is associated with a spectrum of toxic effects. However, therapeutic interventions using herbal drugs for hypertension have gained considerable attention worldwide. **Aim:** To evaluate the anti-hypertensive activity of polyherbal formulation (SJT-HT-03). **Materials and Methods:** The polyherbal formulation (SJT-HT-03) comprises of leaves of *Aegle marmelos* L., fruits of *Benincasa hispida* Thunb., *Garcinia indica* Thouars, and flowers of *Musa paradiasica* L., *Rosa indica* L., *Hibiscus rosa sinensis* L. Selected plants as mentioned above were collected, dried and extracted with different solvents. Formulation SJT-HT-03 (250 mg/kg, p.o.), was evaluated using two kidney one clip (2K1C) model and deoxycorticosterone acetate (DOCA)-salt-induced hypertension model using the enalapril (10 mg/kg, p.o.) and hydrochlorothiazide (5 mg/kg, p.o.) as a reference standard drug in respective models. **Results:** SJT-HT-03 significantly reduced ($P < 0.001$, one-way analysis of variance followed by Turkey's multiple comparison tests) systolic as well as diastolic blood pressure (BP) in 2K1C and DOCA-salt model. Further, SJT-HT-03 has shown a significant reduction ($P < 0.01$) in angiotensin converting enzyme (ACE) activity in serum, clipped kidney as well as in lungs in 2K1C model, whereas significant reduction ($P < 0.05$) in serum Na^+ and increase in serum K^+ level in DOCA model. **Conclusion:** Polyherbal formulation SJT-HT-03 possess significant anti-hypertensive activity by producing direct depressant effect on heart, inhibition of ACE, aldosterone antagonistic as well as diuretic effect and thereby act on multiple targets to achieve optimal effect.

Key words: *Aegle marmelos*, anti-hypertensive, polyherbal, two kidney one clip model

Introduction

Hypertension is the most common cardiovascular disease. It is reported to be the fourth contributor to premature death in developed countries and the seventh in developing countries. The prevalence of hypertension and pre-hypertension were higher in males when compared to females and increasing trend was observed in both males and females with increasing age.[1] Treatment of hypertension involves the use of vasodilators, β adrenergic blockers, central sympatholytic, α adrenergic blockers, β + α adrenergic blockers, angiotensin converting enzyme (ACE) inhibitors, angiotensin (AT_1) antagonists, calcium channel blockers, diuretics etc., Although these drugs have brought about remarkable changes in hypertension therapy, the efficacy of these drugs are still debatable. Reports on clinical evaluation of these drugs show that there are incidences of relapses, adverse effects and danger of drug interaction during hypertension therapy.[2] Hence alternative therapy is need based innovation in current cardiovascular science.

In search of alternative treatment of hypertension, today world is moving toward the herbal options. Most herbal medicines are well-tolerated by the patient, with fewer unintended consequences than pharmaceutical drugs. Another advantage is that herbs cost much less than prescription medications.[3] There are many plants which are traditionally used and reported to possess anti-hypertensive effects, but as hypertension possess different etiological and pathological origin, no single drug can able to effectively control the condition. Hence in the proposed study, we have selected different plants, which are already reported to possess hypotensive or anti-hypertensive effect individually and act through a different mechanism.[4-10] The summary of

Address for correspondence: Mr. Hardik S. Ghelani,
The National Institute of Complementary Medicine (NICM),
University of Western Sydney, Campbelltown, NSW,
Australia - 2751.
E-mail: h.ghelani@uws.edu.au

Table 1: Summary of selected plants of SJT-HT-03

Biological name of plant	Family	Sanskrit name	Part selected	Solvent used for extraction	% yield obtained (% w/w)	Activity reported
Aegle marmelos Linn.	*Rutaceae*	*Bilwa*	Leaves	Distilled water	26.87	Direct depression of the myocardium
Benincasa hispida Thunb.	*Cucurbitaceae*	*Kushmanda*	Fruits	Methanol	18.03	Angiotensin converting enzyme inhibition activity
Garcinia indica Thouars	*Clusiaceae*	*Vrikshamala*	Fruits	Distilled water	21.02	Anti-oxidant activity, cardiotonic activity
Musa paradiasica Linn.	*Musaceae*	*Kadali*	Flower	Chloroform	9.90	Diuretic activity, direct vasodilation activity
Rosa indica Linn.	*Rosaceae*	*Gulab*	Flower	Distilled water	21.8	Hypocholesterolaemic activity
Hibiscus rosa sinensis Linn.	*Malvaceae*	*Japa*	Flower	Ethanol: water (7:3)	12.85	Decreasing heart rate

extraction including parts used, solvent used and percentage yield obtained has given in Table 1. More particularly present invention reveals the use of different herbal ingredients comprises leaves of *Aegle marmelos* L. (*Bilva*), fruits of *Benincasa hispida* Thunb. (*Kushmanda*), *Garcinia indica* Thouars (*Vrikshamala*), and flowers of *Musa paradiasica* L. (*Kadali*), *Rosa indica* L. (*Shatpatrika*), *Hibiscus rosa sinensis* L. (*Japa*) to prepare novel composition. The main objective of the present study is to prepare novel polyherbal formulation which can give synergistic effect in the experimentally induced hypertension in rats. Another object is to provide unique formulation, which can able to control hypertension by a different mechanism, so that better effectiveness can be achieved.

Materials and Methods

Animals

A total of 60 Wistar albino rats, weighing 200-250 g, were procured from Zydus Research Center, Ahmedabad. Animals were fed with standard chew diet. All animals were kept under a controlled light/dark cycle each of 12 h, temperature (22 ± 2°C) and humidity (73-75%) with free access to food and water *ad libitum* animals were fasted for the prescribed time in the individual models before anti-hypertensive activity. Coprography was prevented by fasting the animals in cages with grating on the floor. Throughout the experiment, the animal house was maintained in the same identical conditions as per the standard guidelines of Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) of India and protocol (SJT/027-2011) of the present study was approved by Institutional Animal Ethics Committee (CPCSEA Reg. No: 920/ac/CPCSEA/05).

Plant extraction and preparation of polyherbal formulation

In all plants were procured from a commercial source and identified by Department of Botany, Christ College; Rajkot. All mentioned plants were dried and powdered. The summary of extraction including parts used, solvent used and percentage yield obtained has given in Table 1. All extracts were labeled and stored in the cold condition at 4°C throughout the study period. Proposed herbal formulation namely, SJT-HT-03 was prepared according to previously reported [Table 1] effective doses (ED_{50}) of individual plant extract. The % contents of polyherbal formulation were also calculated from individual ED_{50} of the plants extracts as, aqueous extract of leaf of *A. marmelos* (10%), methanolic extract of fruit of *B. hispida* (15%), aqueous extract of fruit of *G. indica* (20%), chloroform extract of flowers of *M. paradiasica* (20%), aqueous extract of flowers of *R. indica* (20%) and hydroalchoholic extract of flowers of *H. rosa sinensis* (15%). They were well-mixed in a mortar and pestle along with the addition of 0.5% w/v sodium carboxymethylcellulose (CMC) (suspending agent) until the stable and homogeneous suspension formed.

The acute oral toxicity

The acute oral toxicity study was carried out as per the guideline set by the Organization for Economic Co-operation and Development (OECD guidelines 423) received from the CPCSEA.

Pharmacological models used to screen anti-hypertensive activity

Two kidney one clip model for hypertension

Animals were fasted 24 h before surgery. Ketamine (25 mg/kg, i.m) was given to produce anesthesia. A retroperitoneal flank incision was made and the left renal artery was exposed and cleared. Then a U-shaped silver clip (2 mm wide, 10 mm long) with a gauge of 0.25 mm was placed around the renal artery and secured in place and the incision was sutured and the animals were returned to their cages. In 2K1C model, the renal artery is constricted on only one side while the other artery (or kidney) left untouched. After 4 weeks, renin-angiotensin dependent BP increased.

All operated animals were divided into total four groups (Groups II to V) comprising six animals in each group while Group I served as a normal control (0.25% w/v sodium CMC; 10 ml/kg, p.o.) with no operated animals. Group II served as a Sham control (0.25% w/v sodium CMC; 10 ml/kg, p.o.). Group III served as a hypertensive control (0.25% w/v sodium CMC; 10 ml/kg, p.o.). Group IV received polyherbal formulation SJT-HT-03 (250 mg/kg, p.o.) while Group V received standard drug enalapril (10 mg/kg, p.o.). All above drug treatments were given for 28 days on a daily basis, starting from the day of clipping of kidney.[11]

Following parameter has been evaluated in this model:

- Serum ACE activity (in blood) was measured on a weekly

basis (on 7th, 14th and 21st day)
- ACE activity in kidney and lung were measured on 28th day of the completion of the protocol
- BP was measured after 28 days of the protocol using invasive technique.

Measurement of ACE activity in serum

Serum ACE activity was measured using Hippuryl-His-Leu (HHL) as a synthetic substrate. After 7, 14 and 21 days of treatment, blood was collected and serum was separated. Then 100 µl of rat serum was added to 150 µl of HHL (5 mM) in phosphate buffered saline (NaCl 300 mM) at pH 8.3. Test and control tubes were incubated for 30 min at 37°C with shaking. The enzymatic reactions were terminated by the addition of 0.25 ml of 1N HCl; HCl was added before the serum in 0-time control assays. The hippuric acid formed by action of the ACE on HHL is extracted from acidified solution into 1.5 ml of ethyl acetate by vortex mixing. After a brief centrifugation, 1 ml aliquots of each ethyl acetate layer was transferred to a clean tube and heated at 120°C for 30 min. The hippuric acid was then re-dissolved in 1 ml distilled water and the amount formed was determined from its absorbance at 228 nm using ultraviolet (UV) spectrophotometer[12] (Shimazdu 1800).

Measurement of ACE activity in kidney and lungs

At the end of 28 days of protocol, kidney and lung were rapidly removed, cleaned of fatty and connective tissues, blotted dry and then weighted. Tissues were homogenized at 4°C in cold Tris-HCl buffer (pH 7.8) containing 30 mM KCl, 5 mM magnesium acetate, 0.25M sucrose and 1% of Triton X-100. The homogenate was centrifuged at 5000 × *g* for 15 min at 4°C and the supernatant was used for the assay.[13]

Spectrophotometric assay of ACE

Incubations for the spectrophotometric assay of HHL hydrolysis by angiotensin-converting enzyme was carried out at 37°C in disposable 13 mm × 100 mm tubes. Each 0.25 ml assay mixture contains the following components at the indicated final concentrations: Potassium phosphate buffer 100 mM; sodium chloride 300 mM, HHL 5 mM. The enzymatic reactions were terminated by the addition of 0.25 ml of 1 N HCI; the HCI was added before the enzyme in 0-time control assays. The hippuric acid formed by action of the angiotensin-converting enzyme on HHL was extracted from the acidified solution into l. 5 ml of ethyl acetate by vortex mixing for 15 s. After a brief centrifugation, l ml aliquot of each ethyl acetate layer was transferred to a clean tube by means of an Eppendorf pipette. The ethyl acetate aliquots were evaporated by heating at 120°C for 30 min. The hippuric acid was dissolved in 1 ml water and the amount formed was determined from its absorbance at 228 nm using UV spectrophotometer[14] (Shimazdu 1800)..

Measurement of BP in 2K1C model

On the 28th day of experiment, rats were anesthetized with ketamine (25 mg/kg, i.m.). Left carotid artery (for recording BP) was cannulated under aseptic conditions with polyethylene cannula filled with 1% heparin in normal saline. A pressure tube filled with 200 U/ml heparin in saline was tied to the implanted catheter and connected to a pressure transducer and then to the pre-amplifier and recorded on the physiograph. Height obtained in mm was converted into mmHg after calibration of physiograph using sphygmomanometer.[15]

Deoxycorticosterone acetate -salt induced hypertension model

Wistar albino rats having average body weight of 150 g were selected and put on 2% w/v sodium chloride solution instead of plain water until they achieved the body weight of 200 gm. Wistar albino rats treated as above were divided into total five groups comprising six animals in each group.

Group I: Normal control; 0.25% w/v sodium CMC (10 ml/kg, p.o.).

Group II: Sham control; 0.25% w/v sodium CMC (10 ml/kg, p.o.) + sesame seed oil (1 ml/kg, s.c. twice in a week).

Group III: Hypertensive group; 0.25% w/v sodium CMC (10 ml/kg, p.o.) + DOCA salt (10 mg/kg, s.c., twice in a week).

Group IV: Test group; SJT-HT-03 (250 mg/kg, p.o.) + DOCA salt (10 mg/kg, s.c. twice in a week).

Group V: Standard group; hydrochlorothiazide (5 mg/kg, p.o.) + DOCA salt (10 mg/kg, s.c. twice in a week).

All above drug treatments were given for 43 days on a daily basis. DOCA salt dissolved in sesame seed oil was given twice weekly up to 43 days. In sham control group, instead of DOCA only sesame seed oil was given twice in a week.[11]

Following parameter has been evaluated in this model:
- Serum sodium and potassium level were measured after 43 days of treatment protocol
- BP was measured after 43 days of the protocol using invasive technique.

Measurement of serum sodium and potassium level

Blood samples were collected after 43 days of treatment by retro orbital method. Animals were anesthetized by ether. After blood collection, centrifuge it at 6000 RPM for 15 min at 25°C. Supernant were used for assay of sodium and potassium. Serum Na^+ and K^+ levels were estimated by using semi auto analyzer (RA-50, Bayer Diagnostics), using specific kits (Auto span, India) at 500 and 550 nm respectively.[16] Both Na^+ and K^+ levels were determined in mmol/L.

Measurement of BP

On 43rd day of experiment, rat were anesthetize with ketamine (25 mg/kg, i.m.). Left carotid artery (for recording BP) was cannulated under aseptic conditions with polyethylene cannula filled with 1% heparin in normal saline.[15] Rest procedure, which was mentioned under the 2K1C-model was followed and BP was observed in terms of mm of Hg.

Statistical analysis

All values were representing in terms of mean ± standard error of the mean. After completion of the study, one-way analysis of variance followed by Tukey's multiple range tests was applied to check the level of significance using commercially obtained computer software. $P < 0.05$ was considered as statistically significant activity when compared to the control group and hypertensive group.

Results

Acute oral toxicity test

In the acute toxicity study, the administration of the polyherbal formulation (SJT-HT-03) at various doses did not elicit any mortality up to 5000 mg/kg dose in the rat. Even at this high dose there were no gross behavioral changes or any clinical symptoms observed.

2K1C animal model

In this model, SJT-HT-03 has shown significant reduction ($P < 0.001$) in serum ACE activity after 7 days, 14 days and after 21 days treatment when compared to hypertensive group. The reduction in ACE activity in case of SJT-HT-03 group was comparable with that of enalapril treated group [Table 2]. Further, polyherbal formulation SJT-HT-03 also significantly reduced ($P < 0.001$) ACE activity in lungs as well as clipped kidney after 28 days of treatment when compared to hypertensive groups. The reduction in ACE activity in lung and clipped kidney case of SJT-HT-03 group was comparable with that of enalapril treated group [Table 3]. Further, SJT-HT-03 has shown significant reduction ($P < 0.001$) in systolic and diastolic BP after 28 days of treatment as compared to hypertensive groups. The reduction in systolic as well as diastolic BP in case of SJT-HT-03 group was comparable with that of enalapril treated group [Table 4].

DOCA-induced hypertension animal model

SJT-HT-03 has shown significant reduction ($P < 0.05$) in serum sodium level and significant increase ($P < 0.05$) in serum potassium level after 43 days of treatment as compared to hypertensive groups. These results were comparable with that of standard hydrochlorothiazide treated group [Table 5]. Further, polyherbal formulation SJT-HT-03 also significantly reduced ($P < 0.01$) systolic and diastolic BP after 43 days of treatment as compared to hypertensive group. The reduction in systolic as well as diastolic BP in case of SJT-HT-03 group was comparable with that of hydrochlorothiazide treated groups [Table 6].

Discussion

2 kidney 1 clip (2K1C) is a renovascular type animal model for hypertension. This is a very commonly used model of hypertension. In 2K1C model, the renal artery is constricted on only one side while the other artery (or kidney) left untouched. This result in a sustained increase in BP due to increased plasma rennin activity, which in turn increases circulating angiotensin-II, a potent vasoconstrictor. However, there is no salt and water retention because other kidney being intact. Thus, the resultant hypertension at this stage is renin-angiotensin dependent only. Moreover, it has been shown that other vasoactive agents may also be involved in producing hypertension in 2K1C, such as: Thromboxane A_2 and prostaglandin $F_2\alpha$. In renovascular hypertension, there is an alteration in sympathetic function with increased sympathetic drive and impaired catecholamine's extraction.[17] The sympathetic nervous activity may be augmented by the angiotensinergic mechanism in 2K1C hypertension. Many mechanisms appear to be responsible

Table 2: Effect of SJT-HT-03 on serum ACE activity after 7th, 14th and 21st day's treatment in 2K1C-induced hypertension model, 2K1C: Two kidney one clip

Groups	ACE activity (µmol/g.min)		
	After 7 days	After 14 days	After 21 days
Normal control	13.19±0.54	12.98±0.80	13.20±0.55
Sham control	13.32±0.47	12.49±0.58	13.72±0.77
Hypertensive	22.08±0.90$	24.23±0.99$	50.00±3.00$
SJT-HT-03	04.46±0.38*	04.42±0.65*	03.16±0.72*
Enalapril	05.79±0.36*	05.55±0.41*	05.33±0.53*

All values are in mean±SEM, n=6. $$P<0.001 when compared with normal control group, *P<0.001 when compared with hypertensive group. SEM: Standard error of the mean, ACE: Angiotensin converting enzyme

Table 3: Effect of SJT-HT-03 on ACE activity in lungs and clipped kidney after 28 days treatment in 2K1C-induced hypertension model

Groups	ACE activity (µmol/g.min)	
	Lungs	Clipped kidney
Normal control	2.19±0.13	1.47±0.07
Sham control	2.02±0.09	1.30±0.07
Hypertensive	5.24±0.15$	2.43±0.10$
SJT-HT-03	0.85±0.04*	0.41±0.02*
Enalapril	0.74±0.04*	0.35±0.04*

All values are in mean±SEM, n=6. $$P<0.001 when compared with normal control group, *P<0.001 when compared with hypertensive group. SEM: Standard error of the mean, ACE: Angiotensin converting enzyme, 2K1C: Two kidney one clip

Table 4: Effect of SJT-HT-03 on systolic and diastolic blood pressure after 28 days treatment in 2K1C-induced hypertension model

Groups	Blood pressure in mmHg	
	Systolic	Diastolic
Normal control	108.55±2.71	88.22±2.42
Sham control	115.09±2.76	100.18±4.05
Hypertensive	168.36±6.16$	150.72±6.79$
SJT-HT-03	106.37±2.80*	88.26±3.10*
Enalapril	106.66±2.89*	85.94±3.20*

All values are in mean±SEM, n=6. $$P<0.001 when compared with normal control group, *P<0.001 when compared with hypertensive group. SEM: Standard error of the mean, 2K1C: Two kidney one clip

Table 5: Effect of SJT-HT-03 on serum sodium and potassium level after 43 days treatment in DOCA-induced hypertension model

Groups	Serum level (mmol/L)	
	Sodium	Potassium
Normal control	221.65±3.79	5.65±0.26
Sham control	218.37±3.22	5.14±0.32
Hypertensive	252.19±9.46$	4.11±0.26$
SJT-HT-03	227.45±2.97*	5.53±0.47*
Hydrochlorthiazide	238.84±4.98*	5.72±0.38*

All values are in mean±SEM, n=6. $$P<0.01 when compared with normal control group, *P<0.05 when compared with hypertensive group. SEM: Standard error of the mean, DOCA: Deoxycorticosterone acetate

Table 6: Effect of SJT-HT-03 on systolic and diastolic blood pressure after 43 days of treatment in DOCA-induced hypertension model

Groups	Blood pressure in mmHg	
	Systolic	Diastolic
Normal control	115.65±2.72	84.26±2.42
Sham control	105.43±3.23	81.55±3.23
Hypertensive	174.73±1.55$	145.43±2.83$
SJT-HT-03	106.05±2.63*	74.73±3.83*
Hydrochlorthiazide	102.70±2.74*	70.88±2.82*

All values are in mean±SEM, n=6. $P<0.001 when compared with normal control group, *P<0.001 when compared with hypertensive group. SEM: Standard error of the mean, DOCA: Deoxycorticosterone acetate

for the hypertension-related sympathoexcitation, including an "adrenergic reinforcement" due to the excitatory effects exerted on sympathetic neural function, both at the central and peripheral level, by various humoral agents (such as nitric oxide, endothelins, etc.)[18]

In the present study, SJT-HT-03 has shown significant reduction in systolic and diastolic BP in 2K1C model as compared to hypertensive rats. These findings suggest that SJT-HT-03 may act via ACE inhibitor activity and thereby remove the action of angiotensin II. This probable mechanism of SJT-HT-03 was confirmed after estimation of ACE activity in serum, lungs and clipped kidney, where it has shown significant reduction when compared to hypertensive groups. Another mechanism for anti-hypertensive activity of SJT-HT-03 includes, increased in level of bradykinin due to ACE inhibition. Blockage of angiotensin II formation by SJT-HT-03 through inhibition of ACE has been demonstrated to lower BP in renovascular hypertensive subjects by acute vasodilation[19] and chronically to cause a reversal of cardiac[20] and vascular hypertrophy.[21] One of the drugs of our formulation SJT-HT-03 was methanolic extract of *B. hispida*, which already reported to possess anti-oxidant and ACE inhibition activity. Total phenolic contents of *B. hispida* might be responsible for this action.[5]

Mineralocorticoids cause retention of sodium and water in the body until escape dieresis occurs due to increased pressure on the kidneys. No further retention of sodium and water occurs, but the general level of body sodium and water is slightly raised. Selye *et al.*[22] was the first to demonstrate that DOCA produces hypertension in rats. DOCA induced hypertension is salt dependent since neither administration of DOCA nor partial removal of renal mass is effective in increasing BP when applied without salt administration.[23] Previous studies have shown that the administration of mineralocorticoid together with salt results in sodium retention, potassium depletion, hypertension, extensive tissue damage and even death, whereas activating natriuretic systems and suppressing sodium- and water-retaining systems to increase sodium excretion.[24,25]

SJT-HT-03 has shown significant reduction in systolic and diastolic pressure as compared to hypertensive rat. The probable mechanism would be the increase in sodium excretion through kidney and retention of potassium in its exchange. This leads to reduction in volume overload. This mechanism fit well in our study, as after 43 days of DOCA salt treatment in SJT-HT-03 treated group animals, there was a significant decrease in serum sodium level and side by side significant increase in serum potassium level. These results were also comparable with standard drug hydrochlorothiazide. One of the content of our formulation SJT-HT-03 was *M. paradiasica*, whose chloroform extract was reported to possess diuretic activity.[26] Thus our formulation SJT-HT-03 possesses anti-hypertensive effect in DOCA-salt-induced model due to its diuretic property and thereby reduce volume overload.

Conclusion

SJT-HT-03 produce anti-hypertensive effect by acting on multiple targets, which includes reduce the level of angiotensin-II by inhibiting ACE activity as well as decreased volume overload by antagonizing effect of DOCA and by producing diuretic effect. Further investigation is projected be focused to undertake its preclinical toxicity and followed by clinical studies.

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हिन्दी सारांश

बहुऔषधी योग - 'SJT-HT-03' का उच्च रक्तचाप पर प्रभाव – एक प्रायोगिक अध्ययन

हार्दिक एस. घेलाणी, बिपिन एम. पटेल, रिना एन. गोकाणी, मनिष ए. रच्छ

उच्च रक्तचाप यह असाध्य व्याधी अवस्था है, जिसकी जीवनभर चिकित्सा जरूरी है। प्रस्तुत अध्ययन बिल्व, कूष्माण्ड, वृक्षाम्ल, कदली, तरुणी एवं जपा इन वनस्पतियों से निर्मीत बहुऔषधी योग `SJT-HT-03' का उच्च रक्तचाप पर होनेवाले प्रभाव का परिक्षण करने हेतु किया गया है। उल्लेखित वनस्पतियों को संग्रह कर, सूखाकर, उनके विविध द्रव्यों के साथ अर्क निकाले गये। योग (SJT-HT-03) का परिक्षण २ किडनी १ क्लिप मॉडेल (2 K1C) एवं डिओंक्सिकोर्टिकोस्टिरॉन ॲसिटेट (DOCA) सॉल्ट इन्डयुस्ड हायपरटेन्शन मॉडेल के सहायता से किया गया। इनमें क्रमशः एनाल्प्रिल (10 mg/kg p.o.) एवं हायड्रोक्लोरोथायाझाइड (5mg/kg p.o.) का निर्देश अंक मानक के तौर पर प्रयोग किया गया। योग (SJT-HT-03) वन वे ॲनालिसिस ऑफ व्हेरियन्सफ के बाद 2K1C एवं DOCA सॉल्ट मॉडेल तुर्कीज कम्पॅरिजन टेस्ट सिस्टोलिक एवं डायास्टोलिक ब्लड प्रेशर में महत्त्वपूर्ण घटाव में कारणीभूत रहा एवं योग के कारण सिरम में ॲन्जियोटेन्सिन कनव्हर्टिंग एन्झाइम ॲक्टिविटी, 2K1C मॉडेल में क्लिप्ट किडनी, लन्गस में महत्वपूर्ण घटाव, DOCA मॉडेल में सिरम सोडियम में महत्त्वपूर्ण घटाव एवं सिरम पोटॅशिअम में वृद्धि हुई। योग में महत्त्वपूर्ण उच्च रक्तचाप विरोधी क्षमता है जिसका कारण हृदय पर प्रत्यक्ष अवसादक कर्म, ACE का अवरोध, अल्डोस्टेरॉन प्रतिरोधक एवं मूत्रल कर्म यह है। योग के द्वारा विविध लक्ष्यों पर कर्म करके महत्त्वपूर्ण प्रभाव प्राप्त हुआ।