

**ANTIHYPERTENSIVE AND LIPID LOWERING EFFECT OF
TERMINALIA ARJUNA (AQUEOUS EXTRACT) IN
SPONTANEOUSLY HYPERTENSIVE RATS (SHR): AN
EXPERIMENTAL STUDY**

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ABSTRACT

Hypertension is one of the leading causes of death in developed as well as in developing countries. Essential hypertension is accounting for 90 percent of all cases of hypertension. Alternative methods including supplementation with various herbs offer an effective way to decrease the rising number of people with high blood pressure. *Terminalia arjuna* (TA) is reported to be used in Indian medicinal system (*Ayurveda*) since thousands years. Exact mechanism responsible for reduction in blood pressure by *Terminalia arjuna* yet to be proved. In, present study we examined the effect of TA on various lipids in

hypertensive rats. The study was conducted on 30 spontaneously hypertensive rats (SHR) divided in to five groups. Group I treated as control and Group II a, b, c treated with aqueous extract of *Terminalia arjuna* (AETA) in various doses. Group III was treated with known hypotensive drug enalapril. After 4 weeks of experimental protocol, blood pressure, heart rate, total cholesterol, triglycerides, high density lipoprotein (HDL) cholesterol were measured. The present study shows that the *Terminalia arjuna* has potential to lower serum

cholesterol, serum triglyceride, very low density lipoprotein (VLDL) and low density lipoprotein (LDL) and significantly decreases the blood pressure and heart rate in SHR rats.

KEYWORD: Terminalia arjuna, SHR Rats, Hypertension, Lipid Profile.

INTRODUCTION

Essential hypertension, accounting for 90 percent of all cases of hypertension, is the leading member of the so called non communicable diseases and one of the leading causes of death in developed as well as developing countries including India.^[1,2] Alternative methods including supplementation with L-arginine, a nitric oxide precursor, Omega-3 Fatty Acids, vitamins C and E and various herbs^[3-5] offers an effective way to decrease the rising number of people with high blood pressure. Concomitant supplementation of the herbal extracts, diet intervention prevents cardiovascular complications and may be helpful in management of hypertension along with available anti-hypertensive drugs without any interference.

Terminalia arjuna (TA) is commonly known as Arjun is belongs to family Combretaceae is found to be distributed in India and Sri Lanka. In Indian medicinal system (*Ayurveda*), the bark of the tree TA is used since 1500 years for treatment of multiple cardiovascular ailments. The bark of Arjuna tree has been reported to contain's active constituents includes tannins, triterpenoid saponins, flavonoids, gallic acid several trace elements.^[6,7] Several studies have elucidated effects of TA on various cardiac disorders including congestive heart failure, liver diseases, and hyperglycemia, but there are terrified reports regarding effect of TA on various lipids in different doses. So in present study, we evaluated the effect of TA on lipids in spontaneously hypertensive rats. With, best of my knowledge this is the first report to reveal the effect of TA in SHR model.

MATERIALS AND METHODS

Animals: The present experimental study conducted in PG experimental laboratory of department of Physiology, King George's Medical University Lucknow India. The experimental protocols were conducted in accordance with CPCSEA guidelines. Thirty Spontaneous hypertensive rats weighing 120-180 gm procured from CDRI Lucknow. Spontaneous hypertensive rats (SHR), a genetic strain of hypertensive rat, are the animal of choice for screening antihypertensive agents in experimental hypertension as well as cardiovascular disease.^[8] The animals were fed with commercial pellet rat chow (From Bharat Science, Solution Company, Lucknow) and water *ad libitum*. They were placed

individually in wooden floored cages, in a room with temperature of about 27⁰C and 12 hour day night cycles. Animals were acclimatized in ambient conditions. Protocol of our experimental laboratory and procedures were performed in accordance with the CPCSEA guidelines. The study was approved by institutional ethics committee. (Approval No.31/IAH/Pharma/14 dated 17/05/14 No. 55/IAEC/2014).

Drug: Bark of *Terminalia arjuna* was procured by commercial supplier in refined powder form. The aqueous extract was prepared to store in cool and dry place. The aqueous extract of *Terminalia arjuna* was made in such a way that the aqua's dose does not exceed 0.2 ml/100 gm of body wt./day by oral gavages. The protocol of experiment was adopted for four weeks.

“Accurately” aqueous extract was administered orally to rats using feeding tube (oral gavages).

Experimental protocol: The animals were randomly, allocated to different experimental groups:

Group-I: (n=6 SHR rats) weighing 120-180 gm served as control, kept on rat chow and water *ad libitum*

Group-II a: (n=6 SHR rats) weighing 120-180 gm treated with aqueous extract of *Terminalia arjuna* (250mg/kg body wt) along with rat chow and water *ad libitum*.

Group-II b: (n=6 SHR rats) weighing 120-180 gm treated with aqueous extract of *Terminalia arjuna* (500 mg/kg body wt) along with rat chow and water *ad libitum*.

Group-II c: (n=6 SHR rats) weighing 120-180 gm treated with aqueous extract of *Terminalia arjuna* (750 mg/kg body wt) along with rat chow and water *ad libitum*.

Group-III: (n=6 SHR rats) weighing 120-180 gm Enalapril inj. (48 mg/kg, i.p.)^[9] Served as standard along with rat chow and water *ad libitum*.

Measurement of cardiac parameters

The cardiovascular parameters (systolic blood pressure (SBP) and heart rate (HR) were recorded in each animal at 9:30 a.m. every Monday of week for four weeks in all the groups. Heart rate and blood pressure were measured by using the non invasive blood pressure (NIBP) machine (manufactured by AD Instruments Australia). Non-invasive blood pressure methodology consists of utilizing a tail-cuff placed on the tail of rat to occlude the blood flow during inflation of cuff, non-invasive pulse transducer were placed distal to the occlusion

cuff; pulse was detected during deflation of tail cuff while the blood starts flowing, the pressure at the start of pulsation was assumed as systolic pressure.

Biochemical parameters: After 4 weeks of experimental protocol, blood was withdrawn from the dorsal pedal vein^[10] by help of insulin syringe. Serum was separated by centrifugation, lipid levels i.e. total cholesterol, triglycerides, and HDL-C, LDL and VLDL-cholesterol were estimated by using the reagent kit.

RESULTS

Effect of *Terminalia arjuna* on Blood Pressure and Heart Rate: Baseline systolic blood pressure and heart rate were recorded in animals of different groups. Our data showed that there was no significant difference ($p > 0.05$) in baseline systolic blood pressure and heart rate in various groups (Table-1).

After four weeks of treatment with TA, the SBP (mmHg) in group-I, group-II a, group-II b, group-II c, and group-III was 191.20 ± 7.47 , 190.00 ± 16.36 , 186.55 ± 15.67 , 181.40 ± 2.07 and 170.80 ± 1.92 mmHg respectively. Results imply that there was significant decrease in systolic blood pressure in group-II c and group-III after respective treatment. The baseline heart rate (beats per minute) in group-I, group-II a, group-II b, group-II c, and group-III was 373.80 ± 37.78 , 378.33 ± 10.98 , 347.33 ± 11.08 , 363.50 ± 13.23 and 369.17 ± 9.06 beats per minute respectively which was insignificant among various groups. Heart rate in group II c and group-III was 300.67 ± 14.58 and 294.33 ± 26.20 beats per minute after treatment with *Terminalia arjuna* and standard drug which was significantly lower than its basal values ($p < 0.005$) Table-2.

Effects of TA on lipids: After four weeks of administration serum lipids was estimated in each group, the results suggests that the total cholesterol and triglycerides were significantly reduced by administration of *Terminalia arjuna* in doses of 500mg and 750 mg / kg body weight while TA in dose of 250 mg/kg body weight did not show any kind of modulation on various lipids (Table -3) our data also revealed that VLDL cholesterol decreased and HDL/LDL ratio changed significantly. “Surprisingly” the *Terminalia arjuna* does not able to increase the HDL- cholesterol (a good cholesterol).

Table. 1: Effect of TA on Systolic blood pressure in different groups.

SBP in mmHg Mean \pm SD	Group -I n=6	Group-IIa n=6	Group-IIb n=6	Group-IIc n=6	Group-III n=6
baseline	194.60 \pm 13.35	195.10 \pm 11.17	191.40 \pm 10.95	189.20 \pm 2.59	197.20 \pm 3.96
Week-1	194.05 \pm 14.64	194.45 \pm 15.38	180.20 \pm 13.94	178.20 \pm 2.28	170.20 \pm 2.39
Week-2	196.40 \pm 13.93	192.20 \pm 2.41	175.00 \pm 4.24	177.20 \pm 4.15	164.80 \pm 3.83
Week-3	190.80 \pm 7.52	195.20 \pm 7.6	182.20 \pm 2.28	173.80 \pm 5.02	168.00 \pm 4.36
Week-4	191.20 \pm 7.47	190.00 \pm 16.36	186.55 \pm 15.67	181.40 \pm 2.07	170.80 \pm 1.92
p-value: basal vs Week-IV	p>0.05	p>0.05	p>0.5482	p=0.002	p=0.001

Table. 2: Effect of TA on heart rate in different groups.

Heart rate(BPM) Mean \pm SD	Group -I n=6	Group-IIa n=6	Group-IIb n=6	Group-IIc n=6	Group-III n=6
baseline	373.80 \pm 37.78	378.33 \pm 10.98	347.33 \pm 11.08	363.50 \pm 13.23	369.17 \pm 9.06
Week-1	373.62 \pm 17.90	370.05 \pm 10.54	344.83 \pm 12.70	357.33 \pm 15.44	350.67 \pm 17.24
Week-2	344.17 \pm 8.66	368.33 \pm 9.73	334.83 \pm 10.70	334.33 \pm 18.97	339.00 \pm 12.74
Week-3	384.83 \pm 12.44	368.67 \pm 9.37	329.50 \pm 9.91	321.83 \pm 13.48	315.50 \pm 4.09
Week-4	383.83 \pm 30.84	369.17 \pm 10.83	330.00 \pm 7.87	300.67 \pm 14.58	294.33 \pm 26.20
p-value: basal vs Week-IV	0.6253	0.1764	0.0108	0.0001	0.0001

Table. 3: Effect of TA on lipid profile.

Values in mg/dl	Group -I n=6	Group-IIa n=6	Group-IIb n=6	Group-IIc n=6	Group-III n=6	P value
Serum cholesterol	68.81 \pm 2.68	67.22 \pm 3.10	62.59 \pm 5.45	52.91 \pm 1.68**	67.92 \pm 2.07	P<0.03
Serum Triglyceride(TG)	62.83 \pm 1.26	62.10 \pm 2.32	58.97 \pm 1.92	53.74 \pm 2.68**	63.24 \pm 2.97	P<0.02
HDL-Cholesterol	29.32 \pm 3.37	30.84 \pm 4.69	31.84 \pm 5.95	34.86 \pm 6.30	30.24 \pm 5.44	P>0.05
LDL	34.62 \pm 3.37	32.36 \pm 3.73	20.48 \pm 1.64	19.84 \pm 2.90	33.26 \pm 4.84	P<0.01
VLDL-cholesterol	16.83 \pm 1.47	15.95 \pm 2.42	16.22 \pm 2.47	12.32 \pm 1.82**	16.07 \pm 1.96	P<0.01
HDL/LDL	0.84 \pm 0.18	0.95 \pm 0.32	1.55 \pm 0.22**	1.75 \pm 0.45**	0.90 \pm 0.16	P<0.01

*Group I vs Group II b, ** Group I vs Group II c, data given as mean \pm Standard deviation (SD)

DISCUSSION

Hypertension, the single largest disease amongst huge non communicable disease and is the leading causes of death. Essential hypertension, also known as primary hypertension, is accounting for 90 percent of all the cases of hypertension. Beside the dysfunctions of the rennin – angiotensin and aldosterone system, endothelial dysfunction and related imbalance between vasodilating and vasoconstricting factors must be considered for development of hypertension.^[11-13] It is well known fact that cardiovascular disease (CVD) is associated with hypertension and increased blood levels of low-density lipoprotein (LDL) and triglycerides (TG). In contrast, a low level of high density lipoprotein (HDL) is a risk factor for mortality from CVD. In this study, we assessed the effect of TA on the cardiovascular parameters and

serum lipid profile in SHR. Results showed that administration of aqueous extract of TA for four weeks has dose-dependent modulatory effect on systolic blood pressure and heart rate. The *Terminalia arjuna* in a dose of 250 mg did not show any significant effects while 500 mg/kg and 750 mg/kg treated group offered better cardio protection in hypertension and shows effect that are close to standard treated drug enalapril. *Terminalia arjuna* also decreases total cholesterol, LDL, VLDL and triglycerides. Earlier animal experiments have demonstrated that *arjuna* bark powder/extract reduces the total cholesterol (TC) and TG levels.^[14,15,16,17] Our data are in close agreement with these studies. Correction in serum lipid is associated with reduction in systolic blood pressure and decrease in mortality of cardiovascular diseases.^[18,19] The interaction of lipids and the endothelium has been widely studied by many authors and shows a strong relationship between endothelial function and cholesterol or oxidised cholesterol levels.^[20,21] In this way the administration of *Terminalia arjuna* in doses of 750 mg/kg body weight decreases lipids, hence correct the endothelial dysfunction, and decreases systolic and diastolic blood pressure. The ethanolic fraction of *Terminalia arjuna* possesses a potent antioxidant and hypolipidemic properties compared to other fractions, and this has been substantiated by other studies also.^[22,23] The hypolipidemic action is thought to be mediated through increased hepatic clearance of cholesterol, down-regulation of lipogenic enzymes, and inhibition of HMG-CoA reductase.^[24]

CONCLUSION

Our data indicate that the *Terminalia arjuna* has potential to lower various lipids including serum cholesterol, serum triglyceride, VLDL and LDL and significantly decreases the blood pressure in SHR rats. We still do not have sufficient data which would indicate the exact mechanism of lowering the blood pressure and correction of lipid profile in this study.

CONFLICT OF INTEREST

None declared.

Ethical approval: The study was approved by the Institutional Animal Ethics Committee no. - No. 55/IAEC/2014.

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