

Original Research Article

An experimental study on wistar rats to see the effect of *Gymnema sylvestre* on blood pressure

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ABSTRACT

Background: Hypertension is a leading cause of morbidity and mortality globally. It is a well-known risk factor for an array of adverse cardiovascular outcomes. Obesity is considered as one of the major contributing factors to essential hypertension in humans. Obesity in itself is a risk factor for conditions like insulin resistance, hypertension, stroke, ischemic heart diseases, CHF etc. Undoubtedly in recent times we have achieved great advances in terms of management of hypertension but still we have miles to cover to have dominance over it. *Gymnema sylvestre* is a valuable indigenous herb. A number of animal and human studies have shown the potential role of *Gymnema sylvestre* (GS) as an anti-diabetic and anti-obesity agent.

Methods: Adult Female Wistar rats, weighing between 150-200 gm, were included in the study. They were randomly divided into five groups with six rats in each group. High Fat Diet (HFD) was given for 4 weeks to induce hypertension in all the groups except group I which was fed with normal chow. Drugs along with respective diets were given to the rats for next 4 weeks by oral feeding cannula. Systolic blood pressure was measured by NIBP controller machine.

Results: On feeding rats with HFD for 4 weeks the mean systolic blood pressure increased significantly. After giving drugs GS (100mg/kg), GS (200mg/kg) and Amlodipine (10mg/kg) to groups III, IV, V respectively for next 4 weeks, mean systolic blood pressure fell significantly ($p < 0.05$) as compared to group II (HFD control group). At final evaluation at week 8 (as compared to Group 2) SBP got maximally reduced in Group 5 (35.1%) followed by Group 4 (26.4%), Group 3 (20.1%). On comparing Amlodipine standard (group 5) with other groups, a significant difference was found. This showed that *Gymnema sylvestre* reduced the elevated systolic blood pressure significantly but this anti-hypertensive effect was inferior to Amlodipine.

Conclusions: The present study concludes that *Gymnema sylvestre* has a potent dose-dependent antihypertensive action but the effect is inferior to Amlodipine. Hence it can be used as an add-on to standard drugs for hypertension.

Keywords: Hypertension, High fat diet, *Gymnema sylvestre*, Obesity

INTRODUCTION

Hypertension is one of the leading causes of morbidity and mortality globally. It is a well-known risk factor for an array of adverse cardiovascular outcomes.¹ The increase in the blood pressure above the normal levels gets in positive correlation to the rise in incidence of coronary disease, stroke as well as associated

cardiovascular co-morbidities.^{2,3} A number of risk factors attribute to the development of primary (essential) hypertension. Some of them are advancing age, race, obesity, family history, physical inactivity etc.^{4,5} Obesity stands tall as one of the major contributing factors to essential hypertension in humans.⁶ Obesity in itself is a risk factor for conditions like insulin resistance, hypertension, stroke, ischemic heart diseases, CHF etc.

Going as per to Framingham Heart Study, obesity has been attributable for around 78% and 65% of essential hypertension in men and women respectively.⁷

Hypertension, diabetes, hypercholesterolemia, obesity, and smoking are the five leading modifiable risk factors that together toll to more than half of cardiovascular mortality.⁸ Undoubtedly in recent times we have witnessed better treatment protocols and improved control over hypertension but still we have miles to cover to have dominance over it. Time and again recent researches have shown the prowess of natural products to counteract hypertension and other chronic non-communicable diseases. A number of natural products and their various combinations may act in a synergistic way to increase their bioavailability and have some noteworthy advantages over chemical treatments.

Gymnema sylvestre is a well-known indigenous herb, belonging to the family "Asclepiadaceae". Traditionally, extract of the plant has been used in constipation, dyspepsia, renal calculi, jaundice, haemorrhoids, bronchitis, asthma, menorrhoea, leucoderma etc.⁹ A number of animal and human studies have shown the potential role of *Gymnema sylvestre* as an anti-diabetic and anti-obesity agent.¹⁰

METHODS

The present study was approved (Approval No. -Research project No. 69/IAEC/2015) by the Institutional Animal Ethics Committee (IAEC), King George's Medical University, Lucknow, Uttar Pradesh, India.

Experimental procedure

Healthy adult female wistar rats weighing 150- 200 g were procured from Indian Institute of Toxicology Research (IITR), Lucknow. They were housed in the Institutional animal house of King George's Medical University, Lucknow, Uttar Pradesh, India under standard conditions of temperature ($25\pm 2^\circ\text{C}$), humidity ($55\pm 10\%$) and light-dark cycle controlled environment. Animals were provided with pellet diet and free access to drinking water.

After an acclimatization period of 7 days, rats were randomly divided into five groups with six rats in each group. Group1 (Normal Control) was fed on normal chow diet while group 2 to 5 were fed with High Fat Diet (HFD) for 4 weeks. HFD was purchased from Bharat Science Solution Company, Lok Nagar, Unnao, Uttar Pradesh. HFD contained crude fat 25%, crude protein 18%, carbohydrate 44%, fiber 13%, moisture 8 %, vitamins, minerals and other ingredients in appropriate quantity.

From 5th week to 8th week, group 1 was continued with normal chow, group 2 was given HFD while other groups were fed with HFD along with respective drugs. Test

drug used was powdered leaves extract of *Gymnema sylvestre*. It was obtained from Ekgaon Company, New Delhi. Group 3 was given *Gymnema sylvestre* (100mg/kg), group 4 was on *Gymnema sylvestre* (200 mg/kg) and group 5 was given Amlodipine 10 mg/kg. All the drugs were given by oral route as a suspension using distilled water.

The present study was done to evaluate the anti-hypertensive action of *Gymnema sylvestre* and to compare it with Amlodipine in high fat diet induced hypertension in Wistar rats.

Measurement of systolic blood pressure

Systolic blood pressure (SBP) was measured with the help of NIBP controller machine (ML 125), AD Instruments (Australia) by using TAIL CUFF METHOD. Blood pressure was recorded at day 0, week 4 and week 8.

Statistical analysis

Statistical analysis was done using SPSS Statistics 20 (Armonk, NY: IBM Corp.) Results were expressed as mean \pm standard error of mean (S.E.M.). To make an intergroup comparison, one way analysis of variance (ANOVA) followed by Dunnett's t-test was used while to compare similar group at different time intervals, paired t-test was applied. p-value <0.05 was considered statistically significant.

RESULTS

At Day 0 application of ANOVA showed that all the groups were comparable as there was no significant difference found among the groups ($F = 0.901$, p value 0.479) in terms of SBP as shown in Figure 1.

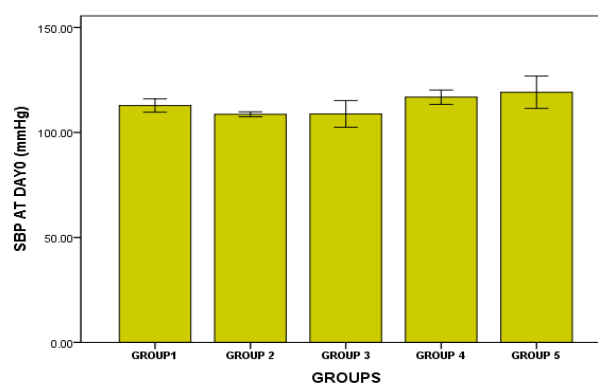
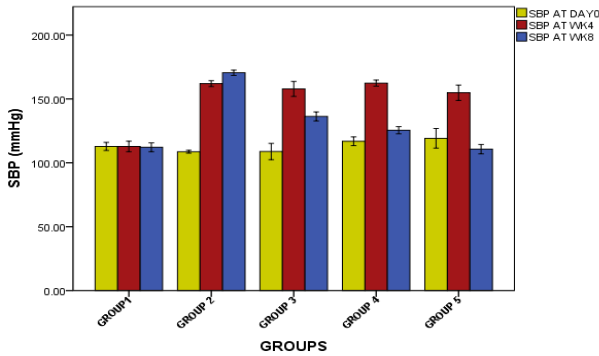


Figure 1: SBP (mmHg) of different groups at day 0 (Mean \pm SEM, N=6).

On feeding groups 2 to 5 with high fat diet for 4 weeks, SBP increased significantly in groups 2 to 5 (from their baseline values) as shown in Table 1 and Figure 2. When they were compared to group 1 (Normal control)

significant difference in SBP (F=3.990, p-value <0.001) was observed. After giving drugs to group 3 to 5 for next 4 weeks, significant changes were found (Figure 2).



*Significant as compared to Baseline (Day 0); #Significant as compared to week 4; \$Significant as compared to Baseline (Day 0)

Figure 2: Pre and Post treatment SBP (mmHg) of different Groups (Mean ± SEM, n=6).

SBP in individual groups at different time intervals (day 0 to week 4, week 4 to week 8 and day 0 to week 8) were compared by paired t-test. SBP at week 4 increased significantly (p-value <0.05) in all the Groups on HFD (2 to 5) as compared to their baseline values. SBP at week 8 decreased significantly in all drug Groups as compared to the values at week 4.

Values at week 8 were found significantly different from that of Day 0 only in group 2 and 3. This showed that the test drugs reduced the SBP significantly and in drug group 4 and 5, values were found comparable to the baseline.

At final evaluation at week 8 (as compared to Group 2) SBP got maximally reduced in Group 5 (35.1%) followed by Group 4 (26.4%), Group 3 (20.1%). ANOVA revealed a significant difference (F= 59.34, p-value<0.001) among the Groups at week 8. Dunnett’s post hoc test (comparison with Group1, 2 & 5) showed a significant decrease in all the Groups as compared to Group 2 (Disease Control Group).

Table 1: Pre and post treatment SBP (mmHg) of wistar rats of different groups (Mean ± SEM, n=6).

Groups	Day 0	Week 4	Week 8	% change at week 8 as compared to Group 2
Group 1	112.8±3.2	112.8±4.2	112.2±3.5	34.2
Group 2	108.7±1.2	162.0±2.3*	170.5±2.0\$	-
Group 3	116.8±3.4	162.3±2.3*	136.3±3.5#\$	20.1
Group 4	108.3±9.2	151.3±7.8*	125.5±7.6#	26.4
Group 5	119.2±7.7	154.8±6.0*	110.7±3.7#	35.1

*Significant as compared to Baseline (Day 0); #Significant as compared to week 4; \$\$Significant as compared to Baseline (Day 0)

On comparing with group 1, SBP in group 5 was found comparable to the normal control group. On comparing Amlodipine standard (group 5) with other groups, a significant difference was found. This showed that *Gymnema sylvestre* reduced the elevated systolic blood pressure significantly but this anti-hypertensive effect was inferior to Amlodipine.

DISCUSSION

Hypertension, or high blood pressure, is considered as the leading cause of cardiovascular mortality. It is a major risk factor for various cardiovascular complications including coronary artery disease, stroke, heart failure, chronic kidney disease, vision loss and peripheral vascular disease.¹¹ Obesity, hypertension, dyslipidaemia, diabetes, and smoking are the major risk factors that are responsible for more than half of the cardiovascular mortality. Obesity is a multi-factorial disease characterized by increased fat stores and eventually body weight. Overweight or obesity leads to various hazardous

complications like insulin resistance, diabetes, dyslipidaemia, hypertension, gout, some cancers etc. The basic underlying cause behind obesity is the disparity between energy uptake and energy expenditure. HFD fed rats resembles humans in many regards so it can act as a ‘humanized’ model for obesity and its related co-morbidities.^{12,13} In present study, hypertension was introduced in Wistar rats by feeding them HFD for 4 weeks. Systolic blood pressure increased significantly in rats fed on HFD as compared to the normal control group.

From 4th week onwards group 2 to 5 were given HFD along with *Gymnema sylvestre* (100mg/kg) to Group 3, *Gymnema sylvestre* (200mg/kg) to Group 4 and Amlodipine (10 mg/kg) to Group 5. Assessment of SBP at the end of the 8th week showed a significant decrease in SBP in Groups 3, 4 and 5 as compared to Group 2 (Disease control) but on comparing with group 5, the effect was found inferior to the standard drug Amlodipine (10mg/kg). The main chemical which could be

responsible for the anti-hypertensive action is gymnemic acids. The leaf extract of *Gymnema sylvestre* is known to possess weight reducing property.¹⁴ Studies have shown that the extract of the plant can suppress the levels of insulin, leptin, lipids besides reducing the oxidative stress in HFD fed obese model of rats. This may directly or indirectly reduce the systolic blood pressure. These mechanisms could possibly be responsible for the anti-hypertensive action of *Gymnema sylvestre*. Hence, it can be concluded that *Gymnema sylvestre* has a significant anti-hypertensive action and can be used as an add-on therapy for hypertension. But the effects need to be confirmed beforehand through trials on higher animals and humans.

CONCLUSION

The present study concludes that *Gymnema sylvestre* has a potent dose- dependent antihypertensive action but the effect is inferior to Amlodipine. Hence it can be used as an add-on to standard drugs for hypertension.

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