

Original Research Article

Pharmacological Evidence of Hypotensive Activity of Somina (Herbal drug) in Normotensive Rats

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Abstract

Purpose: To evaluate the effects of somina (herbal drug) on the arterial blood pressure.

Methods: Hypotensive activity was studied in pentothal sodium-anesthetized normotensive albino rats at various doses of somina (5, 10, 15, 20 and 35 mg/kg). The drugs were administered intravenously and changes in arterial blood pressure (systolic, diastolic and mean arterial blood pressure) were registered directly from the carotid artery. Acetylcholine (Ach, 10^{-4} M) was used as positive control for comparison while the receptor activity of Ach and somina was assessed using atropine (muscarinic receptor antagonist) on rat heart.

Results: Somina caused dose-dependent significant ($p < 0.05$) reduction in mean arterial pressure blood pressure (MABP). The 35 mg/kg dose caused 46.7 % fall in MABP, which was significant ($p < 0.05$) when compared with control. The results were comparable with those of acetylcholine (10^{-4} M) which showed 45.6 % fall in MABP. For receptor activity, atropine (10^{-4} M) was administered i.v., and then the Ach and somina (45 mg/kg) was administered one at a time. Non-significant fall in MABP was observed (1.2 and 20 %, $p > 0.05$) in rats that were pretreated with atropine.

Conclusion: Somina possesses potent hypotensive effect at different doses in normal rats by stimulating non-selective muscarinic receptors.

Keywords: Somina, Acetylcholine, Atropine, Herbal drug, Blood pressure, Hypotensive activity, Muscarinic receptor, Vascular relaxant activity

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INTRODUCTION

The herbal medicine (plant based medicine) has potential for improving health because plants have the ability to synthesize chemical compounds. These chemicals enable herbal medicines to be as effective as other synthetic medicines [1].

Hamdard Laboratories (Waqf) in Pakistan has been manufacturing and practicing herbal drugs for a long time. One of such drugs is somina. It is composed of five ingredients that belong to five

different medicinal plants - *Sesamum indicum*, *Prunus amygdalus*, *Papaver somniferum*, *Lactuca scariola*, and *Lagenaria vulgaris*.

Sesamum indicum belongs to family Pedaliaceae. It was reported previously that sesame seeds contain two chemicals, sesamin and sesamol known to have a cholesterol lowering effect in humans and it prevent high blood pressure [2]. *Prunus amygdalus* belongs to family Rosaceae, Scientists have suggested that almonds reduced LDL cholesterol and decrease the risk of coronary heart disease [3]. *Papaver*

somniferum belongs to family Papaveraceae, it is very important for protection against cardiovascular diseases and heart attacks [4]. *Lactuca scariola* (seed extracts) belongs to family Compositae/Asteraceae. The methanol extract of *Lactuca scariola* was found to possess vasorelaxant activities [5]. *Lagenaria vulgaris* belongs to family Cucurbitaceae, and possesses cardioprotective activity against isoproterenol-induced myocardial infarction [6].

On the basis of above activities reported in the literature regarding the individual constituents of somina, this study was conducted to investigate effect of somina on cardiac activity. In addition, its receptor activity was assessed.

EXPERIMENTAL

Drugs

Somina (herbal drug) used in the present study was obtained from Hamdard laboratories (Waqf) Pakistan in powdered form. The different doses of somina, viz, 5, 10, 15, 20 and 35 mg/ml, were prepared by dissolving it in warm distilled water. In addition, a cholinergic agent, i.e., acetylcholine chloride (Merck) (10^{-4} M) and anti-cholinergic agent, atropine (10^{-4} M) (Beohringer Ingelheim) were used for the purpose of comparison with the herbal drug. All dilutions were freshly prepared in warm distilled water before each experiment.

Animals

Adult Sprague dawley rats (200 - 225 g) of either sex were obtained from Dr. Hafiz Muhammad Ilyas of the Institute of Pharmacology and Herbal Sciences and were housed in groups of 6 per cage for seven days prior to experimentation with free access to food and tap water *ad libitum* and kept on a 12 h light/dark cycle. Each experimental group consisted of six animals. All animals were housed in an air-conditioned room at 23 ± 1 °C during the quarantine period. The experimental protocol was approved by the institutional ethics committee. The experimental procedures were performed according to Guidelines of National Institute of Health, USA. Public health service policy on humane care and use of laboratory animals [7]. All experimental procedure was approved by Review Board of Departmental Research Committee (Reg no. 2005/04/S/HMIIPHS).

Recording of blood pressure parameters

Normotensive Sprague-Dawley rats of either sex (200 - 250 g) were anaesthetized with pentothal

sodium (40 mg/kg, i.p.) [8]. Then the trachea was exposed and cannulated with polyethylene cannula to facilitate spontaneous respiration. Drugs were injected (0.20 - 0.25 ml) through a polyethylene cannula inserted into the external jugular vein followed by a saline flush (0.2 ml). The arterial blood pressure was recorded from the carotid artery via arterial cannula connected to a research grade blood pressure transducer (Harvard, 60-3003) coupled with four channels Harvard Universal Oscillograph (Curvilinear, 50-9307) (UK). The temperature of the animals was maintained at 37 °C by using the overhead lamp. Animals were allowed to equilibrate for at least 15 min before administration of any drug [9]. Mean arterial blood pressure was calculated as sum of the diastolic blood pressure plus one-third pulse width [10]. Changes in blood pressure were expressed as the percent of control values, obtained immediately before the administration of test substance [9]. Acetylcholine used as positive control as the dose of 10^{-4} m/kg. The hypotensive studies were carried out on different doses of somina.

Determination of receptor activity

Normotensive Sprague-Dawley rats of either sex (200 - 250 g) were anaesthetized and their blood pressure was recorded through carotid artery as described earlier. Atropine 10^{-4} m/kg were injected through a polyethylene cannula inserted into the external jugular vein followed by a saline flush (0.2 ml), to block the muscarinic receptors. The arterial blood pressure was continuously monitored from the carotid artery via arterial cannula connected to a research grade blood pressure transducer (Harvard, 60-3003) coupled with four channels Harvard Universal Oscillograph (Curvilinear, 50-9307) (UK). Animals were allowed to equilibrate for at least 5 min than Acetylcholine was administered to check the blockade of receptor than high doses of somina (35 mg/kg) was administered and change in blood pressure was monitored.

Statistical analysis

Changes in blood pressure were compared using Student's t-test Values of $p < 0.05$ were considered to be significant.

RESULTS

Effect of somina on blood pressure and receptor activity

The effect of intravenous administration of various doses of somina on various blood pressure parameters is presented in Table 1.

Intravenous administration of 0.2 ml of 0.9 % NaCl did not cause significant changes in the blood pressure parameters. However, intravenous administration of Ach 10^{-4} M produced a 45 % fall in SBP, DBP and MAP as shown in Table 1 which remained for 35 ± 2.43 s. Intravenous administration of somina at the different doses of 5, 10, 15, 20, and 35 mg/kg was found to reduce the systolic, diastolic and mean arterial blood pressure that was (16, 18, 21, 36 and 46 %) in comparison with their controls as shown in Table 1. This fall in blood pressure parameters was dose dependent. Decreases in various blood pressure parameters were statistically significant ($p < 0.05$). The maximum fall in MABP of 46 ± 1.7 % was recorded at the dose of 35 mg/kg (Table 1) which remained effective for 130 ± 1.22 s (Table 1).

Somina (35 mg/kg) has been found to decrease the MABP by 46 % than its control as shown in Table 2. While, on pretreatment with Atr (10^{-4} M), the 35 mg/kg dose of somina did not decrease MABP. In animal pretreated with Atr (10^{-4} M), the reduction in MABP was only 3 % than its control (Table 2).

Table 2: Receptor activity of somina and Ach compared with their antagonism with atropine

Parameter	% Fall*
Ach (10^{-4} M)	45.67** \pm 2.75
Somina (35mg/kg)	46.7** \pm 1.57
Atr (10^{-3}) + Ach (10^{-4} M)	1.20 \pm 0.70
Atr (10^{-3})+Somina (35mg/kg)	2.90 \pm 0.31

*Percent fall in receptor activity compared with atropine antagonism; **Indicate significant difference as compared to its control value $p < 0.05$

However, the use of Ach (10^{-4} M) has resulted in tremendous fall in MABP (Table 2) that was 46 % less than its respective control. Further, on pre-

treatment with Atr (10^{-4} M), the Ach (10^{-4} M) did not show decline in MABP as shown earlier without Atr (10^{-4} M) pre-treatment. This decline with Atr (10^{-3} M) pre-treatment was only 1 % than its control (Table 2).

DISCUSSION

The results of the present study demonstrate that intravenous injection of the somina produced a dose dependent significant fall in the systolic blood pressure, diastolic blood pressure and mean arterial pressure in normotensive rats.

Literature has shown that agents lower blood pressure by interfering either the inhibition of the sympathetic nervous system which decrease the arterial pressure [11] or parasympathetic stimulation results in hypotension due to the inhibitory effects of the cholinergic neurotransmitter, acetylcholine (Ach), on cardiac and vascular smooth muscle [12]. There is a possibility that the extract could be inducing its hypotensive effect via a sympatholytic or parasympathomimetic mechanism. The attenuation of the response to somina by atropine suggests that the extract may have an acetylcholine-like effect. Somina, used in the present study, reduces the blood pressure in anaesthetized normotensive rats. It is probably due to the presence of *Papaver somniferum*. *Papaver somniferum* has been reported to affect the vagus nerve and cause bradycardia [13]. Sesamin and sesamol, two unique phytoconstituents present in *Sesamum indicum*, is one of the important constituent of somina which also prevents high blood pressure in humans [14]. On the other hand, previously, methanolic extract of *Lactuca serriola* was found to possess vasorelaxant activities [5].

Table 1: Effect of different doses of somina on blood pressure parameters

Parameter	Systolic BP		Diastolic BP		MABP		%Fall	Duration
	Before	After	Before	After	Before	After		
Ach (10^{-4} M)	126.3 \pm 5.0	70.0* \pm 4.2	123.7 \pm 4.8	66.6* \pm 4.0	124.6 \pm 4.9	67.7 \pm 4.1	45.6* \pm 2.7	35.9 \pm 2.4
Somina (5 mg/kg)	104.3 \pm 8.3	80.0* \pm 6.8	101.6 \pm 8.4	77.3* \pm 6.7	102.0 \pm 8.4	78.2 \pm 6.8	16.5* \pm 6.7	30.0 \pm 0.05
Somina (10 mg/kg)	105.5 \pm 9.8	89.0* \pm 4.3	100.7 \pm 1.3	86.7* \pm 4.6	105.0 \pm 1.1	87.5 \pm 4.51	18.2* \pm 1.7	70.0 ^a \pm 4.4
Somina (15 mg/kg)	118.5 \pm 1.3	92.7* \pm 5.8	115.7 \pm 1.3	90.2* \pm 5.7	116.6 \pm 1.3	91.0 \pm 5.8	20.9* \pm 2.3	105.0 ^a \pm 9.8
Somina (20 mg/kg)	127.8 \pm 3.7	83.0* \pm 6.5	124.8 \pm 3.4	79.6* \pm 6.3	125.8 \pm 3.5	80.7 \pm 6.4	36.0* \pm 4.4	120.0 ^a \pm 4.1
Somina (35 mg/kg)	125.0 \pm 4.9	68.0* \pm 2.1	122.0 \pm 4.0	65* \pm 2.1	123.0 \pm 4.3	66.0 \pm 2.1	46.7* \pm 1.5	130.5 ^a \pm 1.2

*Indicate significant difference compared to control value ($p < 0.05$); ^aIndicate significant difference compared to positive control (Ach)

It was also suggested that methanolic extract of *L. serriola* have acetylcholine-like mechanism [5]. Our study is also in agreement with these suggestions that the presence of different constituents in somina showed the Ach like effect and causing a significant hypotensive activity in present study.

It is concluded that different doses of somina stimulates the muscarinic receptors (confirmed by receptor activity in atropine pretreated rats) located on the endothelial cells of the vasculature. This stimulation results in the release of endothelium-derived relaxing factors (EDRFs) or nitric oxide [15], that diffuse to smooth muscle cells and in this study, all exerted immediate and significant fall in systolic, diastolic and mean arterial blood pressure (MABP) in normotensive anaesthetized rats.

CONCLUSION

Somina is a pharmacologically-active drug with hypotensive activity when administered intravenously in rats. This lends some support for its use as a herbal remedy. The hypotensive effect is due to the stimulation of non-selective muscarinic receptors.

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