

Somina (Herbal preparation): partial muscarinic agonist

Abstract

Purpose: To evaluate the agonistic property of somina (herbal drug) on muscarinic receptor.

Methods: For determination of effect of somina on receptor rabbit heart was in the Langendorff apparatus coupled with four channels Harvard Universal Oscillograph. The heart was perfused with different solutions like; Somina (20mg/ml), Ach 10^{-3} , Atr 10^{-3} + somina, Atr 10^{-3} + Ach 10^{-3} and Somina (20mg/ml) +Ach 10^{-3} and effect on heart rate was recorded. The records were used for the calculations of heart rate (beat per min).

Results: Somina and Ach 10^{-3} caused significant ($p < 0.05$) reduction in heart rate (28% and 52% respectively) however non significant reduction in heart rate was observed (3 and 11 %, $p > 0.05$) after atropine treatment. Receptor activity confirms that Somina act on Ach receptors. 33% reduction in heart rate was observed after perfusion with Somina (20mg/ml) +Ach 10^{-3} . Somina competing with Ach 10^{-3} (the full agonist) for the same muscarinic receptor and thereby reducing the ability of the full agonist to produce its maximum effect (Ach 10^{-3} 52%; Somina+Ach 10^{-3} 37% reduction) when both full agonist (Ach) administered simultaneously with somina.

Conclusion: Somina is a partial agonist at non-selective muscarinic receptors.

Keywords: somina, herbal preparation, heart rate, muscarinic receptor, partial agonist

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Introduction

Many herbal formulated preparations are used in folk medicine as remedies for the treatment of a variety of human ailments from time immemorial. One of the traditional medicine "Somina" is one of the traditional medicine, formulated by Hamdard laboratories (Waqf) Pakistan. It is claimed that Somina is a cephalic tonic having sedative, hypnotic and anxiolytic activities. It is also claimed that somina is effective in weakness of brain and memory. Previously researcher has suggested that somina affect brain serotonin levels and enhances the memory. Five Medicinal plants in different ratio are present in Somina. *Sesamum indicum* (14%), *Lagenaria vulgaris* (12%), *Prunus amygdalus* (12%), *Papaver somniferum* (10%) and *Lactuca scariola* (5%). These medicinal plants not only affect the brain activity but affect the cardiac activity like *Sesamum indicum* (14%) prevent the high blood pressure,¹ *Prunus amygdalus* (12%) decrease the coronary heart disease risk,² *Papaver somniferum* (10%) protect against heart attacks,³ *Lactuca scariola* (5%) is a vasorelaxant⁴ and *Lagenaria vulgaris* (12%) worked as cardio-protective.⁵ Previous studies suggest that somina stimulates the muscarinic receptor and reduced the heart rate and mean arterial Blood Pressure. In the light of previous reported data it was concluded the somina is a muscarinic receptor agonist. Now-a-days, common drugs have been classified according to their receptor activity like buspirone, aripiprazole and buprenorphine classified as partial agonists.⁶ However, still it is not confirmed that somina is a full agonist or partial agonist that's why the present study was planned to further confirm the agonistic property of somina on rabbit isolated heart preparation.

Materials and methods

Herbal preparations (Somina)

A patent formulation of Hamdard laboratories, Waqf. Pakistan (Somina) was obtained in the form of crumb/powder. 20mg/ml dose of somina were used in this experiment as this dose was said to be maximum effective dose. Somina (20mg/ml) were freshly prepared by dissolving somina in warm distilled water for experimental use.

Kreb's Henseleit buffer solution: Kreb's Henseleit Buffer solution was used for perfusion. The composition of solution was 118mM; NaCl, 4.70mM; KCl, 1.25mM; CaCl₂, 1.20mM; MgSO₄, 25mM; NaHCO₃ & 11mM Glucose. All chemicals were obtained from E-Merck, Germany.

Animals: Rabbits (*Oryctolagus cuniculus*) of either sex ranging from 1.0-2.0 Kg were used for experiments. The Standing Research Committee on Animal Research and Ethics from our institution approved the animal handling protocol.

Experimental procedure

These experimental animals were killed by decapitation and heart was isolated with intact aorta immediately and mounted in the Langendorff apparatus coupled with four channels Harvard Universal Oscillograph. The heart was perfused at a constant pressure retrogradely with filtered Krebs-Henseleit solution saturated with 95% O₂+5% CO₂ and regulated at 37°C. Ventricular activity of heart was recorded through isotonic transducer on Oscillograph. After

the stabilization of the heart, it was then perfused with different solutions like; Somina (20mg/ml), Ach 10^{-3} for comparison, Atr 10^{-3} + somina, Atr 10^{-3} + Ach 10^{-3} for receptor activity and Somina (20mg/ml) +Ach 10^{-3} for agonist activity on different animals. Care was taken to administer a single dose for at least 3 to 5 minutes before taking records of heart activity. After recording, the heart was washed with normal solution for 10-15 min, before the same/second dose was tested for next observation. For every observation, the activity recorded before administration of any dose was considered as control. A total of 15 rabbits were used in the present study. The records were used for the calculations of heart rate (beat per min).

Statistical analysis

All the data was normalized to percent of control. And the standard statistical tools, i.e., mean and Standard Errors were determined for its analysis.

Results

Somina (20mg/ml) produced a negative chronotropic effect on heart as compared to its control. The reduction in heart rate (negative chronotropic effect) was 28% as compare to their controls (Table 1). While, after Atr (10^{-3} M) pretreatment, 20mg/ml Somina was found to decrease the heart rate non significantly ($p>0.05$). This reduction was 3% than its control (Table 1). Ach 10^{-3} had demonstrated a decrease in heart rate that was 52% than its respective control. Further, in Atr (10^{-3}) pre-treated heart, the Ach (10^{-3}) did not show such decline in heart rate as shown earlier. The reduction in heart rate is decline with Atr (10^{-3}) pre-treatment was only 11% than its control. Single treatment of somina cause 28% and Ach 10^{-3} caused 52% reduction. For the determination of agonist activity both were administered at the same time cause a total 37% reduction in heart rate (Table 1).

Discussion

Literature reviews indicate that medicinal plant that is the constituent of somina possesses cardiac activity. Previous study on intact frog heart concluded that Somina (20mg/ml) is an active herbal medicine that affects cholinergic muscarinic receptors and decreases the heart rate. Another study revealed that somina also decreases the blood pressure (rats) by stimulating the muscarinic receptor. Present study confirmed that somina possess muscarinic receptor activity even when tested by using Langendorff heart assembly for rabbits. The partial agonist competing with the full agonist for receptor occupancy and producing a net decrease in the receptor activation observed with the full agonist alone.⁷ Further the present study revealed that somina is a partial agonists (28% reduction in heart rate), somina bind to and activate receptor (muscarinic receptor), but have only partial efficacy at the receptor relative to a full agonist (Ach 10^{-3} ; 52% reduction). Further present study is in agreement with previous research that in the presence of a full agonist (Ach 10^{-3}), a partial agonist Somina (20mg/ml) act as antagonist. In the present results the administration of combined therapy (Somina+Ach 10^{-3}), Somina competing with the full agonist (Ach 10^{-3}) for the same receptor and thereby reducing the ability of the full agonist to produce its maximum effect (Ach 10^{-3} 52%; Somina+Ach 10^{-3} 37% reduction shown in Figure 1.

Clinically this research is very important,

1. Partial agonists (somina) can be used to activate receptors (muscarinic) to give a desired sub-maximal response when small concentrations of the endogenous ligands (Ach) are present
2. They (Somina) can reduce the overstimulation of receptors when excess amounts of the endogenous ligand (Ach) are present.⁸

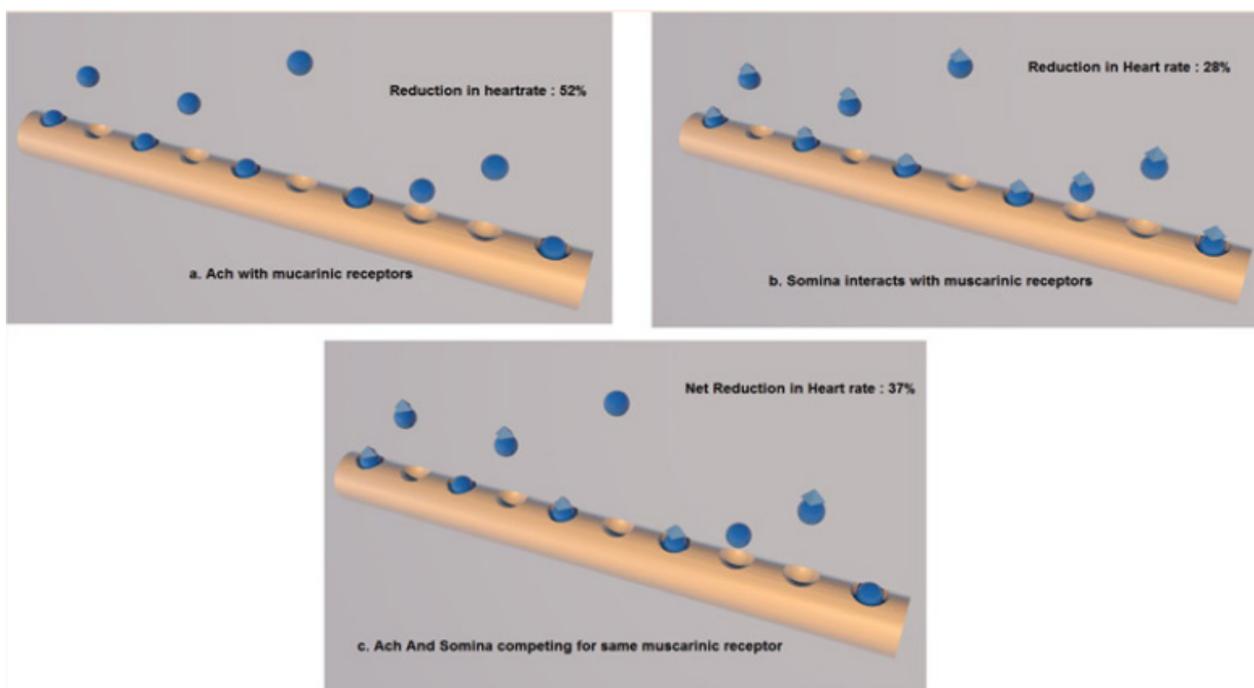


Figure 1 Proposed graphical illustration indicating the action of full (Ach) and partial (Somina) Agonist with muscarinic receptors.

Table I Effect of Somina (20mg/ml) and various treatments on Heart rate (beats/min).

S. No	Solution	Reduction in heart rate mean±S.E. (n)
1	Somina (20mg/ml)	28.03±0.08 (30)
2	Ach (10 ⁻³)	52.41±1.67 (30)
3	Atr 10 ⁻³ +Somina (20mg/ml)	03.43±1.02 (30)
4	Atr 10 ⁻³ +Ach (10 ⁻³)	11.06±2.35 (30)
5	Somina 20mg/ml + Ach (10 ⁻³)	36.95±0.14 (30)

The values has been presented as percent of control

Conclusion

It is concluded that Somina (Herbal preparation) worked as partial agonist.

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Conflict of interest

The author declares no conflict of interest.

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