DOSE-RESPONSE CURVE OF SOMINA
(HERBAL PREPARATION): A STUDY ON FROG HEART

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ABSTRACT
Dose response relation is important with respect to pharmacological efficacy of drug substances and must be known for herbal preparation. Herbal preparations Somina (Hamdard Patent), having five ingredients is not yet screened for its dose response relation. In the present study Somina is used for the determination of dose response on exposed Frog’s heart preparation. U’s shape dose response curve was obtained which shows maximum response at 20mg/ml while it was found to reduce at low and higher doses. The dose response curve is discussed on the basis of properties of ingredients available in this herbal preparation.

INTRODUCTION
Many herbal formulated preparations are traditionally used in folk medicine as remedies for the treatment of a variety of human ailments from time immemorial. However, pharmacological data is not available for all of them. In addition, Dose response relationship is also not known for such medicines. This relation is very important in therapeutic decisions and in experimental pharmacology. Rossum (1963) stresses the importance of studying dose-response curves for the analysis of the mechanism of action. Further, Dose-response theory is also important with respect to toxicology. Vom Saal (1997) has discovered a series of Non-Monotonic Dose-Response Curves. He suggested that in a Non-Monotonic Dose-Response Curve (NMDRC), the shape of the dose response curve reverses as the level of contamination goes up. Some NMDRC are shaped like U’s, with high responses at low and at high levels of contamination. Others are shaped like inverted U’s with the greatest response in intermediate ranges. He suggested that observable fact is that low doses may actually cause greater impact than high doses for a specific response. The same effect has been found by Gupta (2000). In view of the above information in the literature, the study for the determination of Dose response relation is carried out on one of the traditional medicine “Somina” formulated by Hamdard laboratories (Waqf) Pakistan. Somina is composed of five ingredients that belong to five different medicinal plants. Sesamum indicum (14%), Prunus amygdalus (12%), Papaver somniferum (10%), Lactuca scariola (5%) and Lagenaria vulgaris (12%). It is claimed that Somina is a cephalic tonic having sedative, hypnotic, anxiolytic activities. It is also effective in weakness of brain and memory.

i) Sesamum indicum belongs to family Pedaliaceae. Aftab (1995) reported that Sesamum indicum, reduces the blood pressure and heart rate in anaesthetized normotensive rats.

ii) Prunus amygdalus belongs to family Rosaceae, has been found to exhibit hypotensive and antisclerotic actions (Vulpe, 2002).

iii) Papaver somniferum belongs to family

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Papaveraceae, in minute doses it stimulates brain, heart and respiration (Khan, 1997). Clarke (2000) reported that *Papaver somniferum* causes Palpitation.

iv) *Lactuca scariola* (seed extracts) belongs to family Compositae/Asteraceae. It is useful against nervousness, palpitation (Khan, 1997).

v) *Lagenaria vulgaris* belongs to family Cucurbitaceae, its pulp is diuretic (Khan, 1997).

**MATERIALS AND METHODS**

**Herbal Preparations (Somina)**

It is (a patent of Hamdard laboratories, Waqf. Pakistan) obtained in powdered form. Its different doses (5mg/ml to 35mg/ml) were freshly prepared by dissolving its powder in warm distilled water for experimental use.

**Normal Ringer Solution**

All chemicals that are used in preparation of normal ringer solution were obtained from E-Merck, Germany. Composition of solution was similar as quoted by Ahmed et al (1999). The composition is as follows:

NaCl, 115mM; KCl, 2.5mM; CaCl₂, 1.8mM; Na₂HPO₄, 2.15mM; NaH₂PO₄, 0.85mM

**Animals**

Both male and female adult Frogs (*Rana cyanophlictis*) were used. The Standing Committee on Animal Research from our institution approved the animal handling protocol.

**EXPERIMENTAL PROCEDURE**

This study was carried out on exposed and intact Frog’s heart by using the method described previously by Ahmed *et al* (1999). During experiment, normal Ringer solution was continuously poured on heart after removing pericardium to maintain vitality and prevent drying. The heart activity was recorded through an ink stylus on Harvard Kymograph Universal Model (Cat. No.50-7392). After getting the normal record, the heart was continuously poured with individual doses of Somina (5mg/ml to 35mg/ml) one by one on different animals. Care was taken to pour a single dose for at least 3 to 5 minutes before taking traces of systole and diastolic phase on kymograph paper. After recording, the heart was washed with normal Ringer solution for 3 to 5 min, before the same dose was tested again for next observation. One animal was used for 3-5 observation taken with a single dose. For every observation, the activity recorded before pouring of somina was considered as control. A total of 57 Frogs were used in the present study.

**Measurements**

The records obtained were used for the measurements and calculations of heart rate (per min).

**Statistical Analysis**

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

**RESULTS**

**Effect of Somina on Heart rate:**

Different doses of Somina (5mg/ml to 35mg/ml) had demonstrated negative chronotropic effect on heart when compared with control. However, at low doses from 5mg/ml to 10mg/ml the negative chronotropic effect was only 11% in comparison with their controls. At 15mg/ml dose of Somina this effect was 15% (Fig. 1). An increase in its dose to 20mg/ml has resulted in a maximum effect that was 20%. Further, increase in its dose to 25mg/ml has reduced this effect being 17% of control. Later, at 30mg/ml, it was only 12%. At highest dose (35mg/ml) used in this study has shown 6% negative chronotropism being least among various doses (Fig. 1).

**DISCUSSION**

Somina has tested as active preparation that decreases the heart activity and it has been
earlier reported that *Sesamum indicum* (ingredient of Somina) reduces the blood pressure and heart rate (Aftab, 1995). Present study demonstrates that the negative chronotropic effect caused by Somina is dose dependent (Fig. 1). At low doses from 5 to 15 mg/ml gradual increase in negative chronotropism was followed by $E_{\text{max}}$ at 20 mg/ml dose. It is clearly indicating increased interaction (Katzung, 1996) of somina with its receptors for negative chronotropism. The ingredients responsible for this negative chronotropism is the *Sesamum indicum* present in Somina. Maximum response ($E_{\text{max}}$), at 20 mg/ml suggest that this dose is maximum effective dose with maximum receptor activity for negative chronotropism. It is therefore confirmed that the intensity of the effect of somina is dependent on its concentration (Gilberto & Vinicio, 2000). Later, reduced negative chronotropism beyond the dose of 20 mg/ml indicate the effect of its next ingredient *Papaver somniferum* which is reported to increase heartbeat (Khan, 1997) and cause palpitation (Clarke, 2000). In our opinion, since, Somina is a poly herbal preparation. Therefore, at low doses effect of *Sesamum indicum* dominates over Papaver somniferum, while at high doses the *Papaver somniferum*, dominates with the suppression of *Sesamum indicum*. Therefore, the U shape of dose response curve indicate first dominancy and then suppression of *Sesamum indicum* which is one of the active ingredient in Somina

**CONCLUSION**

It is concluded that Somina (Herbal preparation) possesses dose dependent activity and the dose response reverses at 25 mg/ml. This reversal indicates cumulative effects of its ingredients. It is proposed that somina increases negative chronotropism at low doses and decrease it at high doses.

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