Anti-inflammatory activity of Shirishavaleha: An Ayurvedic compound formulation

Shyamlal Singh Yadav, Galib, B. Ravishankar¹, P. K. Prajapati, Ashok B. K.¹, Varun B.¹
Department of Rasashastra and Bhaishajya Kalpana Including Drug Research, Pharmacology Laboratory, Institute for Post Graduate Teaching and Research in Ayurveda, Gujarat Ayurved University, Jamnagar - 361 008, Gujarat, India.

ABSTRACT

The purpose of the present study was to evaluate the anti-inflammatory activity of Shirishavaleha prepared from two different parts of Shirisha (Albizia lebbeck Benth.), viz. the bark (Twak) and the heartwood (Sara). The activity was screened in the carrageenan-induced rat paw edema model in albino rats. The raw materials were collected and authenticated in the university and the trial formulations were prepared by following standard classical guidelines. Randomly selected animals were divided into four groups of six animals each. The test drugs were administered orally at a dose of 1.8 g/kg for 5 days. Phenylbutazone was used as the standard anti-inflammatory drug for comparison. Between the two different test samples studied, the formulation made from heartwood showed a weak anti-inflammatory activity in this model while that made from the bark produced a considerable suppression of edema after 6 h. It appears that the bark sample would be preferable for clinical use.

Key words: Albizia lebbeck, anti-inflammatory activity, Avaleha

INTRODUCTION

“Shirisharishta” is a well known Ayurvedic fermented formulation of Albizia lebbeck Benth, renowned for its utility in the treatment of different disorders. This formulation contains a combination of 12 ingredients, with Jaggery as a base and Shirisha (Albizia lebbeck Benth.) as the main ingredient (Table I lists all ingredients).¹¹

The bark of Shirisha is used traditionally in inflammatory conditions like toothache, diseases of the gums etc. The decoction of the bark is protective against bronchial asthma² and possesses an antihistaminic activity.³ The plant extract has also been proven to be efficacious in cases of allergic rhinitis.⁴ Other ingredients of the formulation, like Pippali (Piper longum Linn.),⁵ Haridra (Curcuma longa Linn.),⁶ Kustha (Saussurea lappa C. B. Clarke)⁷ Shunthi (Zingiber officinale Roscoe.)⁸ and Nagakesara (Mesua ferrea Linn.)⁹ etc. have been studied earlier individually for their anti-inflammatory activities.

However, “Shirisharishta” has a few disadvantages, such as complicated and time-consuming preparation procedure, poor palatability and acceptability at all age groups. Hence, we prepared the avaleha form of the same (“Shirishavaleha”) using the bark (SB) and heartwood (SH) because in fermentative preparations, Sara (heartwood) is the preferred part of Shirisha.¹⁰ A prior study carried out to evaluate the comparative efficacy of Shirisharishta prepared from Sara and Twak showed significant results¹¹ but, even then, the form (Arista) has certain disadvantages/inconveniences, and collection of Sara involves destruction of the plant. Therefore, it was planned to convert the formulation to an Avaleha with bark and heartwood. These were evaluated for their anti-inflammatory activities.

MATERIALS AND METHODS

Wistar strain albino rats of either sex weighing 200 ± 20 g were used for the study. The animals were obtained from the animal

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DOI: 10.4103/0974-7788.76781

Address for correspondence:
Dr. Galib, Department of Rasashastra and Bhaishajya Kalpana Including Drug Research, Institute for Post Graduate Teaching and Research in Ayurveda, Gujarat Ayurved University, Jamnagar - 361 008, Gujarat, India.
E-mail: galib14@yahoo.co.in
Submission Date: 04-04-10  Accepted Date: 29-01-11
house attached to the pharmacology laboratory of the Institute for Post Graduate Teaching and Research in Ayurveda. The animals were exposed to natural day and night cycles under ideal laboratory conditions in terms of ambient temperature (22 ± 2°C) and humidity (50–60%). They were fed with Amrut brand rat pellet feed supplied by Pranav Agro Industries and tap water given ad libitum. The experiment was carried out in accordance with the directions of the Institutional Animal Ethics Committee (IAEC) after obtaining its permission (Approval number; IAEC 09-10/05MD 07).

**Test formulations**

The raw materials [Table 1] for the test formulation were collected from the pharmacy attached to our institute and subjected to pharmacognostical studies in order to confirm their authenticity. From the raw materials, two samples of Shirishavaleha, viz. one from the bark (A) and the other from the heartwood (B) as main ingredient, were prepared by following the classical guidelines [12] in the Department of Rasashastra and Bhaishajya Kalpana of our institute.

**Animal grouping and dose selection**

The selected animals were divided into four groups of six animals each. Group I received tap water to serve as control while the test formulations A and B were administered to groups II and III. Dose of the test formulations (1.8 g/kg) (both A and B) was calculated by extrapolating the human dose to animals based on the body surface area ratio by referring to the standard table of Paget and Barnes (1969).[13] The test formulation was suspended in distilled water (180 mg/ml) and administered orally at a volume of 0.5 ml/100 g body weight with the help of a gastric catheter of suitable size sleeved on to a syringe nozzle. Group IV was administered phenylbutazone in the dose of 200 mg/kg.

**Experimental design**

The anti-inflammatory activity was carried out in the carrageenan-induced paw edema model.[14] The test drugs and vehicle were administered daily for 5 consecutive days. Standard drug, phenylbutazone, was administered 1 h before the carrageenan injection in a single dose. On the fifth day, initially, the left hind paw volumes up to the tibio-tarsal articulation were recorded by using a plethysmograph.[15] One hour after the drug administration on the fifth day, edema was induced by injecting 0.1 ml freshly prepared 1% carrageenan (Sigma type 1) in sterile saline solution to the sub-plantar aponeurosis of the left hind limb. The rats were administered tap water at a dose of 2 ml/100 g body weight to ensure uniform hydration and hence to minimize variations in edema formation. Paw volume was recorded 3 and 6 h after the carrageenan injection. Results were expressed as percentage increase in paw volume in comparison with the initial paw volumes and also in comparison with the control group.

### Table 1: Formulation composition of Shirishavaleha

| Ingredient | Botanical name                  | Part      | Quantity |
|------------|--------------------------------|-----------|----------|
| Shirisha   | Albizia lebbeck Benth.          | Bark/heartwood | 50 parts |
| Pippali    | Piper longum Linn.              | Fruit     | 1 part   |
| Priyangu   | Callicarpa macrophylla Vahl.    | Flower    | 1 part   |
| Kushtha    | Saussurea lappa C. B. Clarke    | Root      | 1 part   |
| Eta        | Elettaria cardemomum Maton.     | Seed      | 1 part   |
| Nilini     | Indigofera tinctoria Linn.      | Root      | 1 part   |
| Haridra    | Curcuma longa Linn.             | Rhizome   | 1 part   |
| Daruharidra| Berberis aristata DC.           | Stem      | 1 part   |
| Shunthi    | Zingiber officinale Roscoe.     | Rhizome   | 1 part   |
| Nagakesara | Mesua ferrea Linn.              | Stamen    | 1 part   |
| Guda       | Jaggery                        | -         | 200 parts|
| Jala (w/w) | Potable water                   | -         | 500 parts|

### Table 2: Effect of Shirishavaleha on carrageenan-induced paw edema

| Treatment    | Dose (g/kg) | 3 h Percentage increase | 6 h Percentage inhibition |
|--------------|-------------|-------------------------|---------------------------|
| Water        | Q.S.        | 61.25 ± 08.55           | 65.67 ± 07.52             |
| SB (bark)    | 1.8         | 40.53 ± 08.02           | 42.32 ± 06.85*            |
| SH (heartwood)| 1.8        | 41.90 ± 07.68           | 52.90 ± 05.61*            |
| Phenylbutazone | 0.2       | 16.35 ± 02.67***        | 26.17 ± 02.49***          |

Data: Mean ± SEM ↓ Decrease. The test formulations were administered by the oral route to groups of rats (n = 6) for 5 days. The percentage increase in paw volume was measured at 3 and 6 h. The data are expressed as mean ± SEM; significant differences in each group versus the control is *P < 0.05, **P < 0.01.
Statistical analysis
Student’s t test for unpaired data has been used for analyzing the data generated during the study. A P-value less than 0.05 was considered as statistically significant.

RESULTS
Data pertaining to the effect of the trial drugs on carrageenan-induced hind paw edema has been given in Table 2. After 3 h of carrageenan injection, the mean paw volumes in animals treated with the trial drugs were found to be decreased, although this was not statistically significant when compared with the control group. The anti-inflammatory effect of the trial drug SB was found to be significant at the end of 6 h (P < 0.05) when compared with the control group. The percent inhibition in paw edema after 6 h was recorded to be 60.14% in case of phenylbutazone and 35.55% with the trial drug SB.

DISCUSSION
It is well known that carrageenan-induced paw edema is characterized as a biphasic event with involvement of different inflammatory mediators. In the first phase (during the first 2 h after carrageenan injection), chemical mediators such as histamine and serotonin play a role, while in the second phase (4 h after carrageenan injection), kinins and prostaglandins are involved.[16]

In the present study, both the Shirishavaleha formulations have shown inhibition of carrageenan-induced edema in comparison with the control at both time intervals. However, the observed activity in the SB-treated group at the sixth hour was statistically significant, although less than that in the group treated with phenylbutazone. The observed effect may be due to inhibition of formation or activity of one or more than one of the phlogistic mediators, or it may be due to a general mechanism, like increasing the membrane stability in the cell. Further, Shirisha also possesses anti-allergic properties and a mast cell-stabilizing activity[17] and Haridra, another component of the compound, stimulates the adrenals resulting in the release of endogenous corticoids. Like other NSAIDs, it also inhibits the synthesis of prostaglandins.[18] In addition to all these, it also inhibits the activity of some proteolytic enzymes,[19] by which cell damage can be prevented at the local site to much extent. Curcumin was also reported to stabilize the lysosomal membrane and cause uncoupling of oxidative phosphorylation besides having a strong free radical scavenging activity,[20] which is probably responsible for the observed anti-inflammatory activity.

Our study suggests that the avaleha formulation (especially the one made from the bark), which would overcome the difficulties with the arishtha, is an effective formulation.

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Source of Support: Nil, Conflict of Interest: None declared.