Analgesic & Antipyretic activity profile on *Gymnostachyum febrifugum* Benth. A folk herb used in fever.

Abstract: **Introduction:** *Gymnostachyum febrifugum* Benth. commonly known as *Jwarahara soppu* in *Kannada* used by traditional healers in treating fever. It is a perennial herb commonly found in western ghats and coastal Karnataka. To prove traditional claim of herbal drug experimental activity planned. **Materials & Methods**: Brewer's yeast induced pyrexia and Eddy's hot plate models were used for antipyretic and analgesic activity respectively. Aerial part of the test drug collected and extract prepared. In both the models Wistar albino rats were divided into 4 groups with 6 rats in each group. Group 1- Normal Control, Group 2- Standard with administration of paracetamol (for antipyretic study) and diclofenac (for analgesic study), Group 3 (TED×1) and Group 4 (TED×2) with administration of single dose and double dose of test drug respectively. **Results**: Drug has shown significant antipyretic result in both single and double dose of test drug dose when compared to the standard drug. Analgesic activity of test drug has shown more significant result in single dose than double dose.

(Keywords: *Gymnosatchyum febrifugum* Benth.*, Jwara*hara, experimental, Brewer's yeast, Eddy's hot plate)

Introduction

India with 15 distinct agro-climatic zones offers a significant potential for the discovery of new herbal medicinal compounds[1]. The country's rich heritage in traditional medicine, especially practiced by folklore healers, showcases a treasure of natural remedies that have been effectively used since centuries. Scientific exploration of this biodiversity and traditional knowledge is essential to uncover novel therapeutic agents that can contribute in addressing healthcare challenges with more natural and sustainable solutions.

Gymnostachyum febrifugum Benth., known locally as *Nelamuchala*, *Biliagradaberu*, or *Jwarahara soppu*, is a perennial herb native to the Southern-Western Ghats of India[2]. Various parts of the plant have been used traditionally to treat ailments like fever, ulcers and cough[3]. It is a perennial herb native to the Southern-Western Ghats of India with highly reduced stems and ovate, dark green leaves. Its light pink flowers with a yellow lower lip are visually striking[4]. Roots of *G. febrifugum* Benth. have been scientifically evaluated for antimicrobial, antioxidant, antipyretic and hepatoprotective activities but stem & leaves remain unstudied[5]. This research aims to evaluate the antipyretic and analgesic potential on aerial part (stem and leaf) of this herb, providing a more comprehensive understanding of its medicinal property.

Material & method

Plant material

Aerial part (leaf and stem) of *Gymnostachyum febrifugum* Benth. was collected from its natural habitat near Udupi and was authenticated from the Department of Pharmaceutical Chemistry and Pharmacognosy, SDM Centre for Research and Allied sciences, Udupi, plant extract is prepared and used for study[6].

Methodology

Animals Selection[7]

The healthy Wistar albino rats of either sex weighing between 150-250 g were obtained from Animal house attached to the Pharmacology laboratory of SDM Centre for research in Ayurveda and Allied Sciences, Udupi. After IAEC approval (SDMCRA/IAEC/DG- 03) they were housed individually in polypropylene cages maintained under normal husbandry conditions at room temperature with relative humidity of 70– 80%. Animals were fed with standard laboratory pellet feed and water. They were acclimatized in the laboratory condition for two weeks prior to the experimentation.

Preparation and Administration of doses:

Dose of trial drug was calculated by extrapolating the human dose to animal dose based on the body surface area ratio using the table of Paget and Barnes (1964) and as per the previous work[8]. Recommended human dose of decoction converted into Rat dose by using formula. Rat dose =

Human dose x 0.018/100 grams per body weight. In all cases, the concentrations were prepared in 1 ml/100g of body weight. The test substances were administered in a single dose (TED×1) which is Human dose x 0.018/100 grams per body weight and double dose (TED×2) which is Human dose x 0.018/100 grams per body weight x 2. Dose formulation was prepared shortly prior to administration in distilled water and administered orally by oral feeding needle using an intubation needle fitted with a graduated syringe. This calculation was same for both antipyretic and analgesic activity.

Paracetamol IP tablets were used as standard drug for antipyretic activity whereas Diclofenac was taken as standard for analgesic study. In both activity both the standard drug of 0.1 mg tablet measured, powdered and mixed with 10 ml of distilled water separately and were administered orally by feeding needle.

Procedure:

Antipyretic activity- Brewer's yeast induced Pyrexia model [9]

Wister albino rats were randomly grouped into 4 groups with 6 animals each as normal group, standard group, Test Group 1 (TED×1) which receives plant extract dissolved in water(1gm/1ml) of aerial part (stem & leaf) *G febrifugum* Benth. in single dose, Test Group 2 (TED×2) which receives similar dosage form in double dose [Table 1]. Rats were kept under fasting for 18 hours before commencement of the experiment. Initial normal rectal temperature of all the animals were recorded by using a digital thermometer. Fever was induced by using 12.5% of brewer's yeast suspension in normal saline solution was injected subcutaneously in all albino rats in the dose of 1ml/100 g body weights. Then the rectal temperature of each rat was noted 18^{th} hour after the injection of the Brewer's yeast. This temperature was noted down to confirm the pyrexia. After 18^{th} hour of injection of yeast, corresponding standard and test drug was administered to respective groups. After administrating corresponding drugs to each group, hourly rectal temperature of each rat was noted for every 1 hour to get 4 readings and then after 24 hour to get 5^{th} reading. The data from the control group was compared with the data from the test drug administered and standard administered groups.

Table 1. Grouping of Experimental animal in Antipyretic activity

GROUPING	No. of Rats	Drug Received
Control group	6	Rat pellet & tap water
Standard group	6	Paracetamol
Test group 1 (TED×1)	6	Test drug (single dose)
Test group 2 (TED×2)	6	Test drug (double dose)

Analgesic activity- Eddy's hot plate model [10]

In this procedure Wister albino rats were randomly grouped into 4 groups with 6 animals each as normal group, standard group, Test Group 1 (TED×1) which receive test drug in single dose, Test Group 2 (TED×2) which receives test drug in double dos. Before starting the procedure, initial basal reaction time was recorded by observing hind paw licking or jump response (whichever appears first) in animals when placed on the hot plate maintained at constant temperature (55ºC). After recording the basal reaction time, test drug was administered (normal dose and double dose) by oral route to test group for 7 days. Diclofenac was administered to standard group. The reaction time was recorded on the hot plate in each group at the time period of 60 min, 120 min, 180 min, 240 minutes and 24 hours after drug administered. The mean time taken for the jump response or paw licking by the rat in control group, trial group and standard group was recorded and compared statistically.

Statistical Analysis [11]

The data were expressed as Mean ± SEM. Results were analyzed statistically by one-way analysis of variance (ANOVA) followed by Dunnet and Tukey's test. P value <0.05 was regarded as statistically significant.

Observation & Results

A. Antipyretic Activity

Effect of Brewer's yeast induced pyrexia in Wistar albino rats within the group:

Brewer's yeast injection led to an increase in rectal temperature across all groups ie., control, standard, and TED×1 and TED×2 groups. This increase was statistically significant compared to their basal rectal temperature, indicating a physiological response to the yeast injection. It was

observed that the control group showed a non- significant increase in rectal temperature at 1st, 2nd , 3rd , 4th , 5th and 24th hour when compared to initial temperature. In the standard group, a non- significant decrease in rectal temperature was observed at 1st, 2nd, 3rd, 4th, 5th, 24th hour. However, in the TED×1 and TED×2 groups, a significant decrease in rectal temperature was observed at the 24th hour compared to initial temperature of same group indicating that G febrifugum Benth. might have potential antipyretic effect. However, when compared to the standard group the decrease was not statistically significant, suggesting that more research may be needed to establish its effectiveness of therapy [Table 2].

Table 2: Effect of *Gymnostachyum febrifugum* Benth. on brewer's yeast induced pyrexia in Wistar albino rats within the groups

Group	Rectal temperature (℃)18hr after yeast induced pyrexia	Rectal temperature measured at the different time interval (18 hr after yeast induced pyrexia)					
		1st	2nd	3rd	4th	5th	24th
Control	38.6±0.081	39.96±0.53	39.0±0.31	39.05±0.37	39.38±0.39	39.3±0.42	38.71±0.23
Standard	39.3±0.17*	39.1±0.21	38.7±0.21	38.96±0.20	39.04±0.18	38.64±0.29	38.76±0.17
TEDx1	39.25±0.35**	39.23±0.26	39.3±0.32	39.3±0.31	39.7±0.36	39.33±0.28	37.98±0.28**
TEDx2	38.96±0.11**	39.18±0.14	38.95±0.022	39.4±0.15	38.96±0.11	30.01±0.10	38.46±0.23**

Therapeutic effective dose (Test single dose)- TEDx1,

Therapeutic effective Data: TEDx2

Data expressed in MEAN±SEM, *P<0.05, **P<0.

B. <u>Analgesic Activity:</u>

Analgesic activity of *Gymnostachyum febrifugum* Benth. using Eddy's Hot plate method, were documented in master charts and presented in the table 3 and statistical analysis was carried out to observe the efficacy and to compare the effect. Hot plate method was used to evaluate the analgesic effects of a drug that acts centrally or peripherally by observing behavior like paw licking and jump responses, which were indicative of neurogenic pain. In the present study hot plate method was employed to evaluate analgesic activity.

When compared to the control group, the standard drug showed a significant reduction in pain threshold at 60 min, 180 min, 240 min with non-significant elevation in pain threshold at 90, 120 min. TED×1(single dose*)* demonstrated a significant increase at 90 min and 240 min. When Standard drug administered group is compared with control, significant reduction in pain threshold was observed at 60 min, 180 min, 240 min and non-significant elevation in pain threshold was observed at 90, 120 min. TED×2 (double dose*)* showed non- significant reduction at 60min, 90 min, 180 min, a non- significant elevation at 120 min and significant elevation at 240 min indicating no analgesic action at double dose. Both the standard and the TED×1 increase the pain threshold, suggesting the presence of analgesic activity in the single dose of test drug group. The greater efficacy of the single dose compared to the double dose may be because of various factors are to be analyzed with further researches.

Table 3. Consolidated table on pain threshold at different time interval on administration of *Gymnostachyum febrifugum* Benth.

Groups	Pain threshold at different time interval in seconds				
	60 min	90 min	120 min	180 min	240 min
Control	10.83± 1.68	9.66± 2.08	11.5± 0.95	16.5± 7.95	10.0± 2.25
Standard	08.50± 0.99	12± 2.19	21.0± 5.15	12.5± 2.18	08.0± 1.18
TED×1	12.33± 2.33	17.8± 1.97*	20.1± 3.04	17.0±3.05	21.83±2.42**
TED×2	08.33± 1.22	8.33± 1.22	15.1± 3.70	12.3±1.58	16.66±1.05*

Therapeutic effective dose (Test single dose)- TEDx1,

Therapeutic effective dose (Test double dose): TEDx2

Data: Mean ± SEM, **P<0.01, *P< 0.05,

Discussion:

Gymnostachyum febrifugum Benth. an *Acanthaceae* perennial herb, endemic to the Western Ghats found in regions of Madras, Malabar and Travancore. Folk healers use this plant for treating various illness like fever, ulcers, pain, menorrhagia in coastal areas of Kerala and Karnataka, especially fever hence named as *Jwarahara soppu* in Kannada. Though root of this herb is scientifically evaluated for antimicrobial, antioxidant, antipyretic and hepatoprotective activities but stem & leaves remain unstudied[12].

Hence pharmacological study is planned to evaluate antipyretic and analgesic properties of aerial parts of test drug using Brewer'sYeast induced pyrexia model on Albino rats and Eddy's hot plate models for analgesic activity in Mice.

Aerial part of the test drug collected form its natural habitat shade dried and extract was prepared. In both the models Wistar albino rats were divided into 4 groups with 6 rats in each group. Group 1 served as normal Control, whereas group 2 as Standard with administration of paracetamol (for antipyretic study) and diclofenac (for analgesic study). Group 3 (TED×1) and Group 4 (TED×2) used for administration of single dose and double dose of test drug respectively.

The Yeast induced antipyretic model has shown significant result in both single and double dose of test drug dose within the group but not significant when compared to the standard drug 'paracetamol'. Analgesic activity of test drug has shown more significant result in single dose than double dose.

Thus, *Gymnosatchyum febrifugum* Benth.'s aerial part (stem & leaf) has shown both antipyretic and analgesic properties. Still further clinical studies are to be carried out to evaluate the efficacy of the drug in humans.

Conclusion:

The findings suggest that *Gymnostachyum febrifugum* Benth. aerial parts have shown significant analgesic action at a single dose. Additionally, the plant also showed antipyretic activity. Further research can be planned on other experimental models using different dosage forms, and also clinical studies cane be carried out.

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