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Studies on the Anti-Inflammatory and Antipyretic Properties of *Haldinia cordifolia*.

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ABSTRACT

Disadvantage in presently available synthetic drugs for inflammation is that they cause gastrointestinal irritation and reappearance of symptoms after discontinuation. Need for screening and development of novel, but better anti-inflammatory drugs and indigenous medicinal plants could be a logical source to find these. Herbal therapy is used to treat a large variety of ailment and symptoms, e.g., inflammation, fever and pain; however, there are no adequate experimental evidences about their effectiveness. The purpose of this investigation was study to the anti-inflammatory and anti-pyretic properties of stem bark extract of *Haldinia cordifolia* in rats. *Haldinia cordifolia* (rubiaceae) has been extensively used in folk medicine for the treatment of ulcers, burns, fevers, antiseptic, diarrhoea and dysentery. The ethanolic extract of dried stem bark of *Haldinia cordifolia* was investigated for anti-inflammatory (carragenan induced rat paw oedema) and anti-pyretic (brewer's yeast induced pyrexia) activities. Pre treatment with the extract (200 - 400 mg/kg, p.o.) significantly prevented increase in volume of paw oedema in dose dependent manner. Its effects on antipyretic activity were also significant and reduce fever at higher doses. In conclusion, this study has established the anti-inflammatory activity and antipyretic activity of *Haldinia cordifolia* and thus justifies the ethnic uses of the plant.

Key words: Inflammation, Pyretic, *Haldinia cordifolia*, Ethanol, Carrageenan, Paw oedema.

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INTRODUCTION

Medicinal plants are believed to be an important source of new chemical substances with potential therapeutic effects. Many plants synthesize substances that are useful to the maintenance of health in humans and other animals. These include aromatic substances, most of which are phenols or their oxygen-substituted derivatives such as tannins. Herbal therapy is used to treat a large variety of ailment and symptoms, e.g., inflammation, fever and pain; however, there are no adequate experimental evidences about their effectiveness. Inflammation is a body defense reaction to eliminate or limit the spread of an injurious agent and is characterized by five cardinal signs, redness, swelling, heat, pain and loss of function. The inflammatory process involves a cascade of events elicited by numerous stimuli that include infectious agents, ischemia, antigen-antibody interaction and thermal or physical injury^{1,2}. Disadvantage in presently available synthetic drugs is that they cause gastrointestinal irritation and reappearance of symptoms after discontinuation. Need for screening and development of novel, but better anti-inflammatory drugs and indigenous medicinal plants could be a logical source to find these.

Haldinia cordifolia (Roxb.) belongs to family Rubiaceae, is found throughout the India in deciduous and semievergreen forests in the lowland and lower hills. The plant fairly large and grows upto 30-40 meters tall. Used for its astringent, antipyretic and wound healing properties³ by tribal as traditional medicine. The group of flavanoids is famous for its anti-inflammatory, anti-allergic, antithromtic, vasoprotective and protection of gastric mucosa properties. These properties have been attributed to influence of flavanoids on production of prostaglandins and their antioxidant effects. Phytochemical evaluation of the bark extract showed the presence of alkaloids, tannins, flavanoids, and steroids etc., till now *Haldinia cordifolia* has not been the subject of any pharmacological research. Therefore, aim of this study was to carry out a pharmacological evaluation of ethanol extract of *Haldinia cordifolia* for its anti-inflammatory and antipyretic properties.

MATERIALS AND METHODS

Plant material:

The stem bark of *Haldinia cordifolia* was collected from Sri Venkateswara University, Chithoor Dist, Andhra Pradesh and identified by Prof. Sri Madhavachetty, voucher specimen (No.561) has been deposited at the Herbarium of the Department of Pharmacology, Bharathi College of Pharmacy, Karnataka. The plant material was air dried, powdered and extracted with ethanol in soxhlet apparatus. The extract was evaporated to dryness under reduced pressure.

Animals:

In breed Albino Wistar rats (150-200 g) were used for the experiments. All the animals were obtained from the laboratory animal centre, Bharathi College of Pharmacy, Karnataka. The animals were maintained under standard environmental conditions and fed with standard diet and water ad libitum. The experimental was approved by the Institutional Animal Ethics Committee (BCP/IAEC/PCL/03).

Phytochemical screening:

Preliminary phytochemical evaluation revealed the presence of alkaloids, flavonoids, tannins, sterols and saponins in the ethanolic extract of the *Haldinia cordifolia*.

Drugs and chemicals:

The drugs and fine chemicals were purchased from Sigma-Aldrich. All other chemicals and solvents were obtained from local firms (India) and were of highest purity and analytical grade.

Preparation of Extract:

The powdered drug was dried and packed well in Soxhlet apparatus and extracted with 1500 ml of ethanol for 72 hrs. The extract was concentrated and dried using Rotary vacuum evaporator. It was kept in desiccators until used.

Acute toxicity studies ⁴:

The result of acute toxicity study in rats indicated that the ethanolic extract did not produce any significant changes in the behavioral or neurological responses up-to 2000 g/kg b. wt.

Studies on inflammation**Acute inflammation study****Carrageenan-induced paw oedema in rats ⁵:**

The anti-inflammatory activity of the extract was determined using carrageenan induced rat paw oedema assay. The rats were divided into five groups of six rats each. The control group received distilled water p.o. at a dose of 2 ml/kg. The positive control group was treated orally with the standard drug, diclofenac (20 mg/kg). The test groups received the test drug in doses of 200 and 400 mg/kg p.o. All the doses were administered 30 min before the induction of oedema by administering 0.1 ml of 1% w/v carrageenan in saline in sub plantar region of hind paw of animal. The degree of paw oedema of all the groups was measured using a plethysmometer (Ugo Basile, Italy) at 30, 60, 120, 180 and 240 min after the administration of carrageenan to each group. The inhibitory activity was calculated according to the following formula⁶

$$\text{Inhibition (\%)} = 100 - \frac{(\text{Oedema volume in the treated})}{(\text{Oedema volume in the control})} \times 100$$

Antipyretic studies (Brewer's yeast induced hyperpyrexia method):

Animals of either sex were divided in to four groups of six each for this experiment. The normal body temperature of each rat was measured rectally at one hour interval on a thermometer and recorded. The antipyretic activity of extract was evaluated using Brewer's yeast induced pyrexia in Wister rats⁸. Before yeast injection the basal rectal temperature of rats was recorded and after recording animals were given subcutaneous injection of 10 ml/ kg of 15 % w/v yeast suspended in 0.5 % w/v methyl cellulose solution for elevation of body temperature of rats. Rats were then returned to their housing cages. At the 18hrs after yeast injection, the vehicle, standard drug and test drugs were administered in to different groups. Propylene glycol at dose of 5 ml/kg was administered orally to the control groups of animals and paracetamol at dose of 150mg/kg was administered orally to standard group of animals. The ethanolic extract of *Haldinia cordifolia* plant was administered orally at a dose of 100 mg/kg and 200 mg / kg of body weight to two groups of animals respectively. Rectal temperature was recorded by clinical thermometer at 0, 1, 2 3and 6hrs after drug administration and tabulated in Table 2⁷.

Statistical analysis:

The results are presented as Mean \pm SEM. Statistical analysis of data was performed using Student 't' test to study the differences amongst the means.

RESULTS & DISCUSSION:

Preliminary Phytochemical screening:

Phytochemical studies revealed that stem bark extract of *Haldinia cordifolia* contains phytosterols, alkaloids, flavanoids, glycosides, and saponins.

Carrageenan-induced paw oedema in rats:

The effect of ethanolic extract on Carrageenan induced hind paw edema test in rats was shown in Table. The results showed that the Ethanolic extract of *Haldinia cordifolia* (200 and 400 mg/kg) potently and significantly reduced the oedema in a dose-dependent manner as compared to the control animals. (Table1)

Anti pyretic activity test

The effect of ethanolic extract of *Haldinia cordifolia* plant on yeast induced pyrexia has been shown in table 1. Treatment with extract at dose of 200 mg/kg and 400 mg/kg body weight and Paracetamol at dose of 150mg/kg decreased body temperature of yeast induced rats. The results

obtained from both standards and extract treated groups were compared with the control group. A significant reduction in the yeast elevated rectal temp was observed in the test in a dose dependent manner. (Table2).

Table1. Effect of EEHC on paw oedema induced by carrageenan in rats

Treatment	Dose	Paw volume (in ml) at various times(%inhibition)				
Control	2 ml/kg	0.32±0.06	0.42±0.04	0.63±0.04	0.81±0.02	0.62±0.02
Diclofenac	20	0.21±0.07 (34)	0.26±0.05* (38)	0.41±0.07* (35)	0.52±0.02 * (36)	0.44±0.05 * (30)
EEHC	200	0.24±0.03 (25)	0.29±0.09* (31)	0.45±0.04* (29)	0.59±0.03 * (28)	0.48±0.06 * (23)
EEHC	400	0.22±0.03* (32)	0.24±0.02* (43)	0.42±0.09* (33)	0.54±0.06 * (33)	0.46±0.07 * (26)

Values are expressed as mean ± S.E.M. (n = 6); *p<0.05, ** p<0.01 Vs control.

Table2. Effect of EEHC on rectal temperature of rats

Treatment	Dose (mg/kg)	Rectal temperature (0C) after yeast injection						
		0hr	1hr	2hr	3hr	4hr	5hr	6hr
Control		37.39± 0.03	39.16 ±0.02	39.2±0 .15	39.2±0 .15	39.2±0 .15	39.05± 0.18	38.58± 0.21
Paracetamol	150	36.93± 0.41	38.6± 0.56	37.33± 0.21**	37.33± 0.31**	37.52± 0.17**	37.41± 0.2**	37.26± 0.16**
EEHC	200	37.26± 0.17	39.1± 0.18	38.5±0 .34	38.35± 0.335*	38.28± 0.17*	38.12± 0.21*	38.1±0 .106
EEHC	400	37.4±0. 17	38.78 ±0.45	37.86± 0.42*	37.63± 0.22**	37.45± 0.19**	37.45± 0.19**	37.4±0 .17**

Values are in mean ±SEM; (n=6) *p<0.05, ** p<0.01 Vs control

Carrageenan induced paw oedema is a commonly used primary test for the screening of new anti-inflammatory agents and is believed to be biphasic. The first phase (1-2 hr) is due to the release of histamine or serotonin and the second phase of oedema is due to the release of prostaglandin⁹. The results of this study indicate that the ethanolic extract of *Haldinia cordifolia* significantly reduced carrageenan induced paw oedema in rats. Therefore, the mechanism of action may be by inhibition of histamine, serotonin or prostaglandin synthesis. Usually most anti-inflammatory and analgesic drugs possess antipyretic activity. In general, non-steroidal anti-inflammatory drugs produce their antipyretic action through the inhibition of prostaglandin synthetase within the hypothalamus¹⁰. Therefore, the antipyretic activity of ethanolic extract of *Haldinia cordifolia* is probably by inhibition of prostaglandin synthesis in hypothalamus. The anti-inflammatory and antipyretic activities of methanolic extract may be due to the presence of alkaloids, sterols and flavonoids.

CONCLUSION:

The results of the present study indicate the anti-inflammatory and antipyretic activities of the stem bark of the *Haldinia cordifolia*. However, further investigation is being carried out to isolate the active constituents responsible for these activities and to elucidate the exact mechanisms of action.

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