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ANALGESIC AND ANTIPYRETIC ACTIVITIES OF *HELIOTROPIUM INDICUM*

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ABSTRACT

Heliotropium indicum, a herbaceous medicinal plant belonging to the family Boranginaceae, used in Siddha system of medicine to cure inflammation, ulcers, wounds, all types of fevers, particularly used in scorpion sting to reduce the inflammation and pain. The present study deals with its analgesic and antipyretic activity in rat models. Aqueous and chloroform extracts of the herb *Heliotropium indicum* were prepared and analyzed for its pharmacological activity. Albino rats of either sex are used for analgesic and antipyretic property of the extract by using hot plate method and brewer's yeast induced pyrexia method. Analgesic activity showed significant effect even at a minimal dose over the standard drug. The antipyretic activity revealed that the extracts showed an effective result at 75mg/kg dosage. The findings in the study suggest that the aqueous and chloroform extract of the herb *Heliotropium indicum* possesses analgesic and anti-inflammatory activities. These results may prove the fact that the herb may be used as analgesic and anti-inflammatory along with its adaptogenic properties.

Key words: *Heliotropium indicum*, Antipyretic, Analgesic, Brewer's yeast, Hot plate method.

INTRODUCTION

Herbal drugs have gained importance in recent years because of their efficacy and cost of effectiveness. Numerous plants synthesize substances that are useful in the maintenance of Health in human and animals (Sawarkar *et al*., 2011). The therapeutic benefits of traditional medicines are often attributed to a combination of active constituents (Chindo *et al*., 2003). *Heliotropium indicum* belongs to the family Boranginaceae. It is a small herb distributed throughout India, Ceylon, Tropical Africa and America. The plant is bitter, astringent, cures all fevers. The juice of the leaves is rubbed where the scorpion has sting, it acts as an antidote (Kirtikar and Basu, 1975). The leaves of the plants used as an external application to ulcers, wounds and local inflammations. Srinivas *et al*., (2000) reviewed that *Heliotropium indicum* produced significant anti inflammatory activity in both acute and sub acute models of inflammation. Three pyrrolizidine alkaloide, acetyllasiocarpine, europine and heliosupine have been isolated from the whole plant *Heliotropium indicum* (Singh *et al*., 2005). The present study was designed to screen the analgesic and antipyretic activity of the plant *Heliotropium indicum* in rats so as to scientifically describe the potential values of the plant, which is already used in Traditional Siddha System of Medicine.

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Pyrexia or fever is caused as a secondary impact of infection, malignancy or other diseased states. It is the body's natural defense to create an environment where infectious agent or damaged tissue cannot survive (2). Normally the infected or damaged tissue initiates the enhanced formation of pro-inflammatory mediators (cytokines like interleukin and TNF-a), which increase the synthesis of prostaglandin E2 (PGE2) near peptic hypothalamus area and there by triggering the hypothalamus to elevate the body temperature (3). As the temperature regulatory system is governed by a nervous feedback mechanism, so when body temperature becomes very high, it dilated the blood vessels and increase sweating to reduce the temperature; but when the body temperature become very low hypothalamus protect the internal temperature by vasoconstriction.

MATERIALS AND METHODS

Collection of plants: The plants *Heliotropium indicum* was collected from Vallam, Thanjavur dist, Tamil Nadu, India and the collected plants were carefully examined and identified with the help of Regional Floras; Gamble, 1967; Mathew, 1983. A voucher specimen was deposited at the Dept. Herbarium, Dept. of Siddha Medicine, Tamil University, Thanjavur.

Table 1. Analgesic effect of aqueous extract of *Heliotropium indicum*

S.No	GROUP	Reaction Time in Seconds				
		0	+30	+60	+120	+180
1.	I	3.3±0.93	3.6±0.05	3.9±0.03	3.1±0.04	3.4±0.07
2.	II	3.3±0.46	5.7± 0.05	7.7± 0.05	9.5±.0.07	11.0±0.05
3.	III	3.4±0.31	6.2± 0.07	8.5± 0.06	10.1±0.04	11.7±0.02
4.	IV	3.4±0.04	6.7± 0.08	9.2± 0.01	10.1±0.09	10.7±0.02
5.	V	3.4±0.04	5.8±0.05	7.8±0.03	10.1±0.07	9.8±0.05

Table 2. Analgesic effect of chloroform extract of *Heliotropium indicum*

S.No	GROUP	Reaction Time in Seconds				
		0	+30	+60	+120	+180
1.	I	3.3±0.88	3.6±0.01	3.9±0.04	3.1±0.02	3.4±0.06
2.	II	3.3±0.48	5.9± 0.04	8.1± 0.03	10.1±0.01	11.8±0.04
3.	III	3.4±0.35	6.4± 0.03	8.9± 0.04	10.6±0.05	12.5±0.03
4.	IV	3.4±0.08	6.9± 0.07	9.6± 0.04	10.7±0.8	11.5±0.02
5.	V	3.4±0.04	5.8±0.05	7.8±0.03	10.0±0.07	9.8±0.05

I-Control-5ml saline II-25mg/kg test drug III-50 mg/kg test drug IV-75 mg/kg test drug V-Standard drug (100mg/kg Acetylsalicylic acid)

Table 3. Antipyretic activity of aqueous extract of *Heliotropium indicum*

S.No	GROUP	Mean Total Temperature ± S.E.M. (°C)				
		Before yeast	After yeast	After treatment (minutes)		
		0h	20h	+90	+180	+270
1.	I	37.00±0.02	38.68±0.08	38.66±0.22	38.66±0.03	38.62±0.17
2.	II	37.00±0.00	38.74±0.10	38.54±0.07	38.47±0.05	38.41±0.19
3.	III	37.00±0.01	38.72±0.06	38.48±0.05	38.33±0.07	37.98±0.08
4.	IV	37.00±0.00	38.78±0.15	38.62±0.10	37.95±0.02	37.27±0.17
5.	V	37.00±0.00	38.70±0.12	38.76±0.21	37.58±0.06	37.33±0.07

Table 4. Antipyretic activity of chloroform extract of *Heliotropium indicum*

S.No	GROUP	Mean Total Temperature ± S.E.M. (°C)				
		Before yeast	After yeast	After treatment (minutes)		
		0h	20h	+90	+180	+270
1.	I	37.01±0.02	38.62±0.08	38.67±0.04	38.66±0.03	38.69±0.11
2.	II	37.01±0.00	38.71±0.05	38.55±0.02	38.47±0.05	38.49±0.12
3.	III	37.01±0.01	38.70±0.07	38.58±0.05	38.33±0.07	38.46±0.06
4.	IV	37.01±0.00	38.76±0.16	37.49±0.05	37.95±0.02	37.42±0.15
5.	V	37.01±0.00	38.74±0.12	37.58±0.06	37.58±0.06	37.33±0.07

I-Control-5ml saline II-25mg/kg test drug III-50 mg/kg test drug IV-75 mg/kg test drug V-Standard drug (100mg/kg Paracetamol)

Extraction of plant material: Aqueous and chloroform extracts of study plant was prepared according to the methodology of Indian Pharmacopeia (Anonymous, 1966). The shade dried plants were subjected to pulverization to get coarse powder.

The coarse powder was subjected to soxhlet extraction separately with chloroform and distilled water. These extracts were concentrated to dryness in flush evaporator under reduced pressure and controlled temperature (40-50c) and stored in a refrigerator. The extracts were involved in phytochemical screening and pharmacological studies.

Pharmacological studies

Animals: Adult albino rats of either sex kept in polypropylene cages under standard environment conditions. Animals were provided with commercial food pellet and water *ad libitum*. Drugs were administered orally through the sterile syringe.

Experimental Protocol

Group I: Animal induced with specific substances for this study without any treatment (control group).

Group II, Group III and Group IV of animals were induced with specific substances for inducing particular specifications and treated with plant extracts 25 mg/kg body weight, 50mg/kg body, 75mg/kg body respectively.

Group IV: This group of animal was induced with specific substance for inducing particular specification and treated with standard drug.

Analgesic activity

Hot plate method: The modified method of Hunskaar *et al*., (1986) as previously adopted (Adzu *et al*., 2001) was used in this activity. Rat that showed noeciptive responses within 20 hours when placed a hot plate maintained at 55± 0.5°c were selected and group into five. Group I was treated with normal saline and treated as control group. The treated group II, III and IV received 25mg, 50mg and 75mg/animal of the extracts respectively and group V received the standard drug acetyl salicylic acid 100mg/animal and kept as standard control. Each rat was placed singly on the hot plate and the latency to exhibit thermal stimulus were determined before and at 0, 30, 60, 120 and 180 minutes after treatment. Licking of paws and jumping were the parameters evaluated as the thermal stimulus. Sixty seconds were taken as the cut - off time to avoid rat tissue

damage. Analgesic activity was expressed as mean percent maximal effect (% MPE calculated as % MPE = Post drug latency-Pre-drug latency / cut-offtime-pre drug latency).

Anti pyretic studies: Yeast induced pyrexia was used to screen the effect of the plant extracts (Turner, 1965). The initial rectus temperature was recorded. Pyrexia was produced by injecting 2ml of 15% suspension of dried brewer's yeast, subcutaneously below the nape of the neck. Extracts were administered orally to those animals that showed a rise in body temp. of 1.2 ºc or more i.e., after 20h of the yeast infection. The rectal temperate was then recorded at 1-4 hr after the drug administration and compared with the initial temperature. Control group was administered with equivalent volume of the vehicle used. Paracetamol was used as the standard drug (100mg/kg).

RESULTS AND DISCUSSION

Analgesic activity of aqueous and chloroform extracts of the study plant, *Heliotropium indicum* was evaluated by hot plate method. The results were recorded in table 1 & 2. Aqueous and chloroform extracts of the plant showed a highly significant activity over the standard control acetyl salicylic acid. After 180 minutes of drug administration, the plant extracts, showed significant effect even at 25mg/kg dosage. The most significant effect was observed at the do dosage of 50 mg/kg.
The subcutaneous injection of yeast elevated the rectal temperature. The antipyretic activity of the both extracts of the plant analyzed and the results were recorded in table 3 & 4. Treatment with the plant extract (aqueous & chloroform) at the dosage of 50 and 75 mg/kg, decreased the rectal temperature compared to the standard drug paracetamol (100mg/kg). The result obtained from both the treated and standard group were compared with the control group and significant reduction in fever that induced by brewer's yeast suspension. Chloroform extract (treated group) showed better effect than the aqueous extract.

In analgesic activity, the two extracts of the plant *Heliotropium indicum* was significantly ($P<0.05$) increased the reaction time compared to control. Analgesic activity of both extracts was more effective than the standard drug acetyl salicylic acid. The hot plate reaction test is used specifically to screen the central nervous system acting analgesic activity of a drug. The upload agents exert their analgesic effects via supra spinal and spinal receptors (Nemirovsky *et al.,* 2001). The aqueous and chloroform extract of the plant showed a good analgesic action in 30 min after drug administration in group II, III and IV. But After 180 minutes, the effect of the action in both extracts were reduced in group IV. The reduction of the rectal temp of the extracts appear to be due to the presence of bio active compounds such as tannin and flavonoid in them (Vimala *et al.,* 1992). Phytochemical screening of *Heliotropium indicum* revealed that the presence of flavonoids, tannin, alkaloids and saponin (Singh *et al*., 2005).

Anti pyretic activity is a characteristic of drugs which have a inhibitory effect an prostaglandin-biosynthesis (Vane, 1987). The extracts produced a significant reduction in brewer's yeast induced pyrexia and its effect is comparable to that of the standard drug paracetamol. So inhibition of prostaglandin synthesis could be the possible mechanism of antiphyretic action as that of paracetamol (Chandrasekaran *et al*., 2009). These findings lend pharmacological support to the reported uses in Siddha Medicine and previous research work on pharmacology of the plant in the treatment of pain, inflammation, scorpion sting, wound, painful ulcers and fevers.

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