Comparative Analgesic and Antipyretic activity of ethanolic extract of *Tragia involucrata*

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Abstract

The present study investigates the analgesic and antipyretic activity of ethanolic extract of *Tragia involucrata*, is a valuable medicinal plant. Phytochemical analysis of *Tragia involucrata* plant extracts revealed the presence of various bio-chemical compounds such as flavonoids, glycosides, alkaloids, saponins and terpenoids. Since flavonoids have remarkable analgesic activity, the present work aims at evaluating the in-vivo analgesic activity of *Tragia involucrata* by acetic-acid induced writhing response method and Eddy's hot plate method. Brewer's yeast induced hyperpyrexia method was used for antipyretic activity study. The data of the present studies suggests that *T. involucrata* extract showed significant anti-pyretic and analgesic activity. Therefore the present studies support the isolation and use of active constituents of *Tragia involucrata* in treating pain. Key Words: *Tragia involucrata*, flavanoids, analgesic activity, antipyretic activity

Introduction

Plant-based medicinal agents are used worldwide to treat a myriad of ailments in both humans and animals (Cordell and Colvard, 2007). Natural products are undeniably the best source for the diversity in the chemotype for the discovery of novel therapeutics (Manly et al., 2002). There is a growing interest in correlating phytochemical constituents of a plant with its pharmacological activity (Gupta, 1994; Vaidya and Antarkar, 1994). Scientists have even started correlating the botanical properties of plants with their pharmacological activity (Rawat et al., 1997). *Tragia involucrata* L. commonly known as (Tamil name: Kanchori) and Indian stinging nettle (English) is a widely used indigenous medicinal plant.

Experimentally, it shows wound healing, anti-inflammatory, anti-microbial, psychopharmacological, anti-cancer, anti-diabetic, hypolipidaemic, diuretic and antioxidant activities (Warrier *et al*., 1994). However, there is no systematic scientific report published indicating utility of this plant material in the treatment of pain and fever. Thus the presence of therapeutically active flavonoids as major constituents was the basis of selection and evaluation ethanol extract of *Tragia involucrata* leaves for their Analgesic and Antipyretic activity.

Materials and Methods

Preparation of Drug

Fresh leaves of the plant *Tragia involucrata* were collected from Tirunelveli district, tamil Nadu, India. It was confirmed with voucher specimen deposited at the Survey of Medicinal Plants Unit, Govt. Siddha Medical College, Palayamkottai. The taxonomic features of the plant confirmed with the Flora of Presidency of Madras (Gamble, 1915 – 1921) and The Flora Tamil Nadu Carnatic (Mathew 1983 – 1988). The leaves were dried under shade and then powdered with a mechanical grinder and stored in airtight container. Ethanol extract of the coarsely powdered material was prepared by employing Soxhlet method. The extract was concentrated and stored in brown bottles for future use.

Animals

Wister adult Albino rats (100-150 g), were procured from lab animal house, Dept. of Pharmacology, Govt. Siddha Medical College, Palayamkottai. The animals were housed in microlan boxes in a controlled environment (temperature 25^{o}C and 12 hrs dark and light cycle) with standard diet and water *ad libitum*. They were divided into three groups as follows:

- Group I: Vehicle control (VC) (given 150 mg/kg plus yeast injection)
- Group II Paracetamol (reference standard) (150 mg/kg plus yeast injection)
- Group III: *Tragia involucrata* ethanol extract (500 mg/kg plus yeast injection)

Antipyretic activity (Brewer's yeast induced hyperpyrexia method

(Turner, 1965)

Animals of either sex (100-150 g) were divided into three groups each consisting of six animals. The normal body temperature of each rat was measured rectally at one hour interval on a thermometer and recorded. Before yeast injection, the basal rectal temperatures of rats were recorded. After recording animals were given subcutaneous injection of 10 ml/kg body weight of 15% w/v yeast

suspended in 0.5% w/v methyl cellulose solution for elevation of body temperature of rats. At the end of 18 hr after yeast injection, the vehicle, the standard drug and the test drug were administered into different groups. Normal saline at a dose of 5 ml/ kg bw was administered orally to the control groups of animals. Paracetamol at a dose of 150 mg/kg bw was administered orally at a dose to standard group of animals. To the test group alcoholic extract at a dose of 500 mg/kg bw (body weight) was administered orally. Rectal temperature was recorded by clinical thermometer at regular interval of 0, 1, 2, and 3 hrs after drug administration and results are tabulated (Vogel, 2002).

Analgesic studies

Analgesic activity of alcoholic extract evaluated by acetic-acid induced writhing response (Seigmund *et al*., 1957) Adult wistar albino rats (100-150 gms) were divided

into three groups of six rats each. The first group was given 10 ml/kg bw of normal saline I/P (Intra Peritoneal) and served as control, group II was given Piroxicam 10 mg / kgbw I/P and served as standard. Group III was received 100 mg/kgbw of the extract given orally. Thirty minutes later, rats in all groups were treated with acetic acid (0.06% of 1 ml/100 gm I/P). Five minutes after Acetic acid injection rats were placed in individual cage and the number of abdominal contractions was counted for each rat for a period of 10 min. Percentage of inhibition of writhing was calculated using the following expression:

$$\text{Inhibition (\%)} = \frac{\text{Mean number of writhing (control)} - \text{Mean number of writhing (test)}}{\text{Mean number of writhing (control)}} \times 100$$

Analgesic activity of alcoholic extract was evaluated by using Eddy's hot plate method

(Eddy and Leimbach, 1953)

Adult Wister albino rats (100-150 g) were divided into three groups of six rats each. The first group was given 10 ml / kgbw of normal saline IP and served as control, group II received 10 mg of Piroxicam / kgbw IP and served as standard, group III received 100 mg/kgbw of extracts orally respectively and served as treated group. The

Eddy's hot plate was maintained between 55°C. The animals were placed on the hot plate and the time taken for licking or jumping was recorded using stopwatch. The reaction was observed at 0, 15, 30, 60, &120 mins.

Results

AntiPyretic acitivity

Pain is an ill-defined, unpleasant, sensation usually evoked by an external or internal noxious stimulus. It is a warning signal and primarily protective in nature, but causes discomfort. Analgesics are the drugs that selectively relieve pain by acting on the CNS (central nervous system) or on peripheral pain mechanisms, without significantly altering consciousness.

The effect of ethanolic extract of *T. involucrata* on Yeast induced pyrexia has been shown in Table - 1. Yeast injection in experimental animals caused significant rise in body temperature at the various time intervals as recorded rectally with the help of a tele-thermometer. Treatment with extract at a dose of 500 mg /kg bw and Paracetamol at a dose of 150 mg / kgbw decreased body temperature of yeast induced rats. The vehicle itself had a moderate antipyretic effect in the initial stages; at the later stages, however, the observed antipyretic activity was only marginal. The effect of ethanolic extract of *Tragia* has little higher rectal temperature in C° after 18 hrs of yeast injection. The results obtained from both standards and extract treated groups were compared with the control group. A significant reduction in the yeast elevated rectal temperature was observed in the test groups. It might be due to the presence of alkaloid compound in *Tragia involucrata.*

Analgesic activity

Analgesic activity of ethanolic extracts of *Tragia involucrata* in acetic acid induced writhing method has been tabulated (Table:2). Number of abdominal writhings *in Tragia plukenetii* was high, but the percentage of inhibition was very much reduced than *Tragia involucrata. Tragia involucrata* has more analgesic activity than control (Piroxicam 10 mg).It may be due to the presence of crude chemical constituents. The results indicated that extracts considered for analysis have little more analgesic activity than those from control group. *Tragia involucrata* has a higher effect (68.20%). This indicates that plant extracts are little more potent active as analgesic agent.

Significant reduction of licking response in Eddys hot plate method has also been tabulated (Table: 3).

Discussion

Yeast induced fever is called pathogenic fever. Its aetiology includes production of prostaglandins, which set the thermoregulatory centre at a lower temperature (Howard, 1993). The present results show that *Tragia* possesses a significant antipyretic effect in yeast-provoked elevation of body temperature in rats, and its effect is comparable to that of paracetamol (standard drug). So inhibition of prostaglandin synthesis could be the possible mechanism of antipyretic action as that of paracetamol (Chandrashekaran et al., 2009). The antipyretic activity observed can be attributed to the presence of flavonoids, saponins, glycosides, tannins [Mutalik et al., 2003].

The analgesic activity was assessed by writhing test which has been reported to be useful for investigation of peripheral antinociceptive activity and performed as a chemical pain model (Abdollahi et al., 2003). The hot plate test was performed as a thermal pain model which is known useful for study of the central mechanism of analgesic activity.

Phytochemical screening of *Tragia involucrata* revealed the presence of considerable quantities of flavonoids, saponins, terpens, alkaloids, tannins and phenols. Several reports have shown the analgesic and anti-inflammatory properties of flavonoids, tritrepenoids, tannins and other polyphenolic compounds in different experimental animal models (Krasteva *et al.*, 2007). Moreover, tritrepenoids, flavonoids and tannins are known to inhibit prostaglandin synthesis and the effect of *Tragia* in chronic phase of inflammation could be attributed to inhibition of prostaglandin release due to the presence of these components.

Kanthal *et al.*, (2011) revealed the presence of antioxidative constituents such as terpenoids and flavonoids in plant has been shown to have diuretic, laxative, anti hypertensive, anti inflammatory and analgesic activity. Anita Singh *et al*., (2012) reported that the plant *Cassia fistula* L. belonging to family Leguminosae, The methanolic extract of plant pod showed the presence of glycoside, steroids, amino acids, flavanoids have been focused to evaluate antipyretic activity, which was significantly ($P<0.05$) higher than control rats.

It can be concluded that alcoholic extract of the *T. involucrata* possesses anti-nociceptive and anti-pyretic properties which are probably mediated via inhibition

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of prostaglandin synthesis as well as central inhibitory mechanisms which may be of potential benefit for the management of pain and inflammatory disorders.

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Table 1: Antipyretic Studies of Ethanolic extract of *Tragia involucrata*

Group	**Treatment**	**Dose**	**Initial rectal temperature in C° before yeast injection**	**Rectal temperature in C° after 18 hrs of yeast injection (Mean± SEM)**			
				0 hr	**1 hr**	**2 hr**	**3 hr**
I	Saline	5 ml/kg	37.65±0.1	40.92±o.l	40.48±0.17	39.21±0.14	39.13±0.16
II	Paracetamol	150 mg/kg	37.25±0.2	40.43±0.19	38.65±0.17	3846±0.09*	37.88±0.18*
III	*Tragia involucrata*	500 mg/kg	37.71±0.4	40.61±0.14	39.63±0.19	38.21±0.24*	**37.63±0.18***

n= 6 in each group * indicates p<0.01 compared to control

Table 2: Analgesic activity of ethanolic extract of *Tragia involucrata* in acetic acid induced writhing method

Group	Treatment (mg/kg)	No. of abdominal writhings	% Inhibition
I	Saline	21 ± 3.8	00.00
II	Piroxicam 10	10.2 ± 2.1	45.00
III	*Tragia involucrata* 100	5.6 ± 2.3	68.20

The results were considered statistically significant if the p- value were 0.05 or less.

Table 3: Analgesic activity of ethanolic extract of *Tragia involucrata* in Eddy's hot plate method.

Group	Treatment (mg/kg)	Reaction time in minutes				
		0	**15**	**30**	**60**	**120**
I	Saline	5.1±0.21	5.7±0.20	5.6±0.24	5.5±0.40	5.4±0.23
II	Piroxicam 10	5.6±0.21	6.2±0.20	6.8±0.30*	6.2±0.36**	5.8±0.37**
III	*Tragia involucrata* 100	5.6±0.25	8.1±0.20	**9.0±0.54***	8.0±0.41*	7.1±0.30*

All values are mean ± SEM, n =6,

***p<0.05 indicates significant and**

****p<0.001 is more significant when compared to control.**