

Evaluation of Antipyretic Activity of *Pedaliium murex* Against Brewer's Yeast-Induced Pyrexia in Rats

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The aqueous and ethanolic extracts of *Pedaliium murex* (Pedaliaceae) was investigated for antipyretic activity in rats using Brewer's yeast-induced pyrexia models. Brewer's yeast (15%) was used to induce pyrexia in rats. Both the extract (200 and 400 mg/kg body weight p.o) produced a significant ($p < 0.05$) dose dependent inhibition of temperature elevation compared with the standard drug Paracetamol (150mg/kg body weight). At doses of 200 mg/kg b.w, the aqueous extract significantly ($P < 0.001$) decreased yeast induced pyrexia in rats. These results indicate that leaf extracts of *Pedaliium murex* possesses potent antipyretic effects and thus pharmacologically justifying its folkloric use in the management of fever.

Abstract

Keywords: Acute toxicity, Antipyretic, Brewer's yeast, Prostaglandin, *Pedaliium murex*.

INTRODUCTION

Herbal medicines are assumed to be of great importance in the primary health care of individual and communities (Sheldon *et al.*, 1997). The World Health Organization has estimated that 80% of the population of developing countries still relies on traditional medicines, mostly plant drugs, for the primary health care needs. The high degree of efficacy and safety with herbal medicines make them more acceptable compared to other therapeutic invention (Chaturvedi *et al.*, 2007). Plant-based traditional knowledge has become a recognized tool in search for new sources of drugs and nutraceuticals (Ghosh, 2003; Sharma and Mujundar, 2003)

Pedalium murex Linn. (Pedaliaceae) is a diffuse, more or less succulent herb found near the coastal area of South India (Nadkarani, 1982). Mucilage obtained from leaves, stem as well as fruits is used to treat gonorrhoea (Mhaskar *et al.*, 2000). An infusion or extract prepared from leaves have diuretic and demulcent properties and also useful in treating disorders of the urinary system such as odour urine, dysuria, spermatorrhoea and incontinence of urine. As an emmenagogue, the juice is used in puerperal diseases and also to promote lochial discharge (Chopra *et al.*, 1996). The mucilage from leaves and young shoots is used as an aphrodisiac in seminal debility (Shukla and Khanuja, 2004). The aqueous extract of the whole plant has been found to possess analgesic and anti-inflammatory properties (Muralidharan and Balamurugan, 2008). *Pedalium murex* is rich in mucilage (Kirtikar and Basu, 1987), flavonoids (Harborne *et al.*, 1999) and saponin glycosides (Bhakuni *et al.*, 1992). Extensive phytochemical investigations on the plant have revealed the presence of Pedalitin and Pedalin (major flavonoids) along with Diosmetin, Dinatin, Dinatin-7-glucoronide, Quercetin, Quercimeritin and Quercetin-7- glucorhamnoside (Subramanian and Nair, 1972). Triterpenoids such as α amyryl acetate are also reported (Prasad and Thakur, 1983). Steroids such as β sitosterol (Shukla and Khanuja, 2004), sapogenins (Harvey, 1967) and diosgenin (Mangle and Jolley, 1998) have also been reported. Lipids (Bhakuni *et al.*, 1992), phenolic acids such as caffeic acid, ferulic acid, protocatechic acid and vanillic acid (Shukla and Khanuja, 2004) and amino acids such as aspartic acid, glutamic acid and histidine are other phytoconstituents present in *Pedalium murex* (Rastogi *et al.*, 1982).

Fever or pyrexia is the body's response to the presence of external or internal pyrogen (organisms causing fever). Pyrexia is caused as a secondary impact of infection, tissue damage, inflammation, graft rejection, malignancy or other diseased states. It is the body's natural defense to create an environment where infectious agent or damaged tissue cannot survive. Normally the infected or damaged tissue initiates the enhanced formation of pro-inflammatory mediator's (cytokines like interleukin 1β , α , β and TNF- α), which increase the synthesis of prostaglandin E₂ near preoptic hypothalamus area and thereby triggering the hypothalamus to elevate the body temperature. As the temperature regulatory system is governed by a nervous feedback mechanism, so when body temperature becomes very high, it dilate the blood vessels and increase sweating to reduce the temperature; but when the body temperature becomes very low hypothalamus protect the internal temperature by vasoconstriction (Chattopadhyay *et al.*, 2005).

The principle rationale behind the use of this plant for the study of antipyretic effects is that the tribal community of Kumaragiri hills of Salem district of Tamil Nadu has been using the leaf extract for fever (Alagesboobathy, 2009). However, there is not enough scientific report to support these supposed antipyretic activities. This has promoted us to study the antipyretic effect of leaves extract of *Pedalium murex* to ascertain the authenticity of these important claims of traditional potency.

MATERIALS AND METHODS

Plant Material

The plant specimen used for the study was collected from their natural habitat in Virudhunagar district, Tamil Nadu, India. The identity of the specimen was confirmed as *Pedalium murex*

using the local flora (Gamble, 1936). A voucher specimen (VHNSNCH A152) was deposited in the Research Department of Botany, V.H.N.Senthikumara Nadar College, Virudhunagar.

Chemical and drugs

All other chemicals and reagents were procured from authorized suppliers and of analytical grades.

Preparation of the extract

The fresh leaves of plant were taken and air dried in shade for ten days. Dried materials were blended into fine powder and extracted by continuous hot extraction process using Soxhlet apparatus not exceeding 60°C by ethanol. The marc was then extracted with distilled water to obtain aqueous extract. All the extracts were dried at 45°C in rotary evaporator to produce a semisolid mass. The dried extract was stored at 4°C until use. The aqueous and ethanol extract were dissolved in normal saline.

Phytochemical analysis

The plant extract was subjected to phytochemical screening through qualitative chemical analysis for confirmation of the phytoconstituents (Kokate *et al.*, 2004; Odebiyi and Sofowora, 1979).

Animals

In-bred Wistar albino rats weighing 150-200g were procured from the animal house of the Sangaralingam Bhuvanewari College of Pharmacy, Sivakasi, Tamil Nadu, India. The animals were grouped and housed in sanitized polypropylene cages (38 × 23 × 10) containing sterile paddy husk as bedding with not more than six animals per cage and maintained under standard laboratory conditions (temperature 25 ± 2°C; RH 60-70%) with dark and light cycle (12/12 h). The animals were fed with standard pellet diet supplied by VRK Nutritional Solution, Pune, India and fresh water ad libitum. All the animals were acclimatized to laboratory condition for a week before commencement of experiment to minimize if any of non-specific stress. All procedures described were reviewed and approved by the Institutional Animal Ethical Committee of the Sangaralingam Bhuvanewari College of Pharmacy, Sivakasi, Tamil Nadu, India. (Reg. No: 622/02/C/CPCSEA). All studies were performed in accordance with the guidelines for the care and use of laboratory animals, as adopted and promulgated by the Institutional Animal Care Committee, CPCSEA, New Delhi, India.

Acute toxicity study

Albino rats weighing 150-200 g selected by random sampling were used in this study. Acute oral toxicity was performed as per OECD-423 guidelines (Ecobichon, 1997). The animals were fasted overnight, provided only with water. Both the aqueous and ethanolic plant extract was administered orally at the dose level of 5mg/kg body weight by gastric intubations and the drug treated groups (4 animals each) were observed for 14 days. If mortality was observed in 2 or 3 animals, then the dose administered was identified as a toxic dose. If mortality was observed in one animal then the same dose was repeated again to confirm the toxic dose. If mortality was not observed, the procedure was repeated for further higher doses such as 50, 300 and 2000 mg/kg body weight. The animals were observed for toxic symptoms such as behavioral changes, locomotion, convulsions and mortality for 72 h.

Anti-pyretic activity

Anti-pyretic activity of *Pedaliium murex* was evaluated using Brewer's yeast-induced

pyrexia in rats (Loux *et al.*, 1972). Rats were weighed and randomized into six groups of four rats per group. The baseline body temperatures of the rats were taken by inserting a digital tele-thermometer into their anal cavities for about 2 min. The steady temperature readings obtained were recorded as the pre-temperatures. Pyrexia was induced in the rats by administering 1 ml/kg b.w of 15% aqueous suspension of Brewer's yeast in normal saline subcutaneously into the animal's dorsum region and 18 h later of yeast administration, the anal temperatures were measured again. Rats that did not show a minimum increase of 0.5°C were discarded from the study (Mukherjee *et al.*, 2002). Twenty four rats selected were grouped into six groups and treated as follows: Normal saline 10 ml/kg b.w were administered to group I, while group II were treated with Paracetamol 150mg/kg/b.w. Group III and IV were treated with aqueous extract of leaves of *Pedaliium murex* (200 mg and 400 mg/kg b.w respectively) and group V and VI were treated with ethanolic extract of leaves of *Pedaliium murex* (200 mg and 400 mg/kg b.w respectively). All the treatments were administered orally. Anal temperature was then measured after every sixty minutes interval of drug administration for each rat up to 4 h.

Statistical analysis

Results were expressed as Mean \pm Standard Error of Mean (SEM). The statistical significance of differences between groups was analyzed using student's t-test. Differences of $p < 0.05$ were considered statistically significant.

RESULTS

Phytochemical screening

The aqueous and ethanolic extract of *Pedaliium murex* were subjected to preliminary phytochemical screening revealed the presence of alkaloids, flavonoids, steroids, coumarins, phenols, saponins, tannins and sugars. (Table 1).

Acute oral toxicity study

Both the plant extracts produced no toxic symptoms or mortality up to a dose level of 2000 mg/kg body weight orally in rats, and hence the drug was considered safe for further pharmacological screening. So 1/10th and 1/5th (200mg and 400mg respectively) of that were selected for all *in vivo* experiments as sub maximal and maximal dose.

The percentage yield of the aqueous and ethanolic extract was 5.9% and 3.7% respectively.

Antipyretic study

The effect of aqueous and ethanolic extract of leaves of plant *Pedaliium murex* on Brewer's yeast induced pyrexia in rats are depicted (Table 2). *Pedaliium murex* leaf extract produced significant ($P < 0.05$) antipyretic effect in a dose dependent manner. Both the extract significantly reversed hyperthermia at either dose (200 & 400 mg/kg body weight). Time of peak effect was obtained from 2 to 4 h after oral administration of test drugs. The standard drug, Paracetamol suppressed hyperthermia induced by yeast significantly ($p < 0.01$) during all the observation times when compared with normal saline treated groups. 200 mg/kg of body weight aqueous extract showed extremely statistically significant ($p < 0.001$) from first hour and extended up to fourth hour after drug administration and ethanolic extract showed extremely significant ($p < 0.001$) reduction of elevated body temperature from second hour to consecutive fourth hour. Whereas the normal saline treated group remained hyperthermia throughout the experimental periods.

DISCUSSION

Search for herbal remedies with potent antipyretic activity received momentum recently as the available antipyretics, such as Paracetamol, Nimusulide etc. have toxic effect to the various

organs of the body (Guyton and Hall., 1998). The reduction in the Brewer's yeast induced fever by the extract in this study suggests some influence on the prostaglandin biosynthesis since it is believed to be a regulator of body temperature (Dascombe, 1985).

Flavonoids are known to inhibit prostaglandin synthetase (Ramaswamy *et al.*, 1985). The antipyretic activity observed can be attributed to the presence of flavonoids present in the plant extracts. Generally, plants showing the antipyretic activity also possess analgesic and anti-inflammatory activity (Dewan *et al.*, 2000). In our studies, the plant extract shows significant antipyretic activity, it may be attributed by its analgesic and anti-inflammatory activity.

CONCLUSION

Therefore, the plant extract of *Pedalium murex* possesses a significant antipyretic effect in Brewer's yeast induced elevation of body temperature in rats. These results support the traditional use of this plant in fever remedies. However, further studies are necessary to examine underlying mechanisms of antipyretic activities and to isolate the active compound (s) responsible for these pharmacological activities.

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Tables

Table1. Result of phytochemical constituents analysis of the aqueous and ethanol extract of *Pedaliium murex*.

Plant Extracts	Alkaloids	Flavonoids	Steroids	Coumarins	Phenols	Saponins	Tannins
Aqueous extract	+a	+	+	+	+	+	+
Ethanolic extract	+	+	+	+	+	- b	-

^a (+): Present

^b (-): Absent

Table 2. Anti-pyretic activity of leaf extract of *Pedaliium murex*

Group ^a	Dose (mg/kg)	Pretem- perature (°C)	Temp. after induced pyrexia (°C)	Temperature after drug administration (°C) (mean ± S. E. M)			
				1 hour	2 hours	3 hours	4 hours
I	Saline (10ml/kg)	36.38±0.253	37.20±0.204	37.20±0.204	37.68±0.165	37.78±0.165	37.68±0.131
II	Paracetamol (150mg/kg)	35.90±0.082b	36.95±0.065	36.95±0.065	36.23±0.075*** e	35.90±0.242***	35.75±0.240***
III	Aqueous (200mg/kg)	35.70±0.135	36.53±0.095	36.53±0.095	36.00±0.071***	35.85±0.133***	35.73±0.132***
IV	Aqueous (400mg/kg)	35.73±0.155	36.45±0.096	36.45±0.096	35.80±0.292**	35.93±0.125***	35.70±0.147***
V	Ethanol (200mg/kg)	35.85±0.150	36.85±0.065	36.85±0.065	36.45±0.087***	36.20±0.071***	36.00±0.204***
VI	Ethanol (400mg/kg)	36.08±0.229	36.88±0.278	36.88±0.278	36.45±0.185**	36.23±0.256**	36.20±0.252**

^a n=4 in each group,

^b Values are measured mean ± S. E. M and compared with control by Student't' test

^c*P<0.05,

^d ** P<0.01

^e *** P<0.001