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SHORT COMMUNICATION

Evaluation of Anti-Pyretic Potential of *Ichnocarpus frutescens* Roots

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ABSTRACT

The methanolic extract of *Ichnocarpus frutescens R.Br.* root (MEIF) was evaluated for its anti-pyretic potential on normal body temperature and yeast-induced pyrexia in albino rats. Yeast suspension (10 ml/kg body wt.) increased rectal temperature 19 h after subcutaneous injection. The MEIF, at doses of 100, 200, and 300 mg/kg body wt., p.o., produced significant reduction in normal body temperature and yeast-provoked elevated temperature in a dose dependent manner. The effect extended up to 5 h after the drug administration. The anti-pyretic effect of MEIF was comparable to that of paracetamol (150 mg/kg body wt., p.o.), a standard anti-pyretic agent.

Keywords: *Ichnocarpus frutescens, methanol extract, Anti-pyretic effect*

Ichnocarpus frutescens R. Br (Apocynaceae), commonly known as siamlata, is an evergreen, laticiferous, woody creeper with rusty red appearance, found almost throughout India. A decoction of the shoots is used in fevers. Leaves are boiled in oil and applied in headaches and fevers; they are also applied to wounds between fingers. [1, 2].The whole plant is used as a tribal medicine in atrophy, bleeding gums, cough, simple fevers, liver disorder and dysentery**.** Stalk and leaves in decoction is used in the treatment of skin eruptions and also useful in simple fever. A decoction of the roots of Colocynth, Anantamul, Sariva (Sanskrit) and *Hedyotis biflora* prepared in the usual way is administered with the addition of powdered long pepper bdellium in chronic skin diseases, syphilis, loss of sensation and hemiplegia [3]. Studies on chemical constituents of the plant revealed the presence of phenylpropanoids, phenolic acids, coumarines, flavonoids, sterols and pentacyclic triterpenoids. [4, 5] Pharmacological investigations have demonstrated that *I. frutescens* possess anti-inflammatory and antioxidant activity [6]. There are no scientific papers reporting on the other pharmacological properties of this Plant. The aim of this study was to evaluate the anti-pyretic activities of the methanolic extract of *Ichnocarpus frutescens* (MEIF).

MATERIALS AND METHODS

Plant material

Roots of *Ichnocarpus frutescens* R. Br were collected during the month of June 2005 from Chennai, Tamilnadu, India. The plant material was taxonomically identified and authenticated by Prof. *p*. Jayaraman, Taxonomist, Plant Anatomy Research Centre, Chennai, India. A voucher specimen (PARC/24/06) has been deposited in the Herbarium of the Department of Pharmaceutical Technology, Meerut Institute of Engineering and Technology, India, for future reference. The roots of the plants were dried under controlled temperature, powdered and passed through a 40 mesh sieve and stored in an air tight container.

Extraction procedure

The powdered plant material was extracted using 95% methanol as a solvent in a soxhlet hot extraction apparatus. The solvent was completely removed by vacuum distillation to yield a reddish-brown residue (yield 5.4% w/w). The methanolic extract (MEIF) was examined chemically and was found to contain flavonoids, terpenoids, and sterols. Further the chemical natures of constituents were confirmed using thin-layer chromatography (TLC).The extract was stored in refrigerator until use. Requisite amount of MEIF was suspended in 2% aqueous Tween 80 solution and used for the present study.

Table1. Effect of MEIF on normal body temperature

Treatment	Rectal temperature (°C)					
	0 h	1 h	2 h	3 h	4 h	5 h
Control	37.40 ±0.05	37.35 ±0.05	37.12 ±0.03	37.30 ±0.03	37.22 ±0.04	37.13 ±0.02
MEIF (100 mg/kg)	37.13 ±0.05	36.22 ±0.08	36.42 ±0.11[a]	36.50 ±0.10[a]	36.63 ±0.07[a]	36.73 ±0.10[b]
MEIF (200mg/kg)	37.30 ±0.05	36.80 ±0.11	36.95 ±0.05[a]	37.08 ±0.03[b]	37.15 ±0.04[b]	37.20 ±0.05[b]
MEIF (300 mg/kg)	37.30 ±0.10	36.67 ±0.13	36.75 ±0.16[b]	36.95 ±0.13[b]	37.08 ±0.10[b]	37.25 ±0.12[b]

Data are shown as mean ± S.E.M., n = 6. [a] < 0.01, [b]< 0.05 *c*ompared with the control values at corresponding hour.

Animals used

Albino (Wister) rats weighing between 180-200 g of either sex were obtained from the animal house, Department of Pharmaceutical Technology, Meerut Institute of Engineering and Technology, Meerut. The animals were housed in the standard polypropylene cages and provided with food and water *ad libitum.* The animals were acclimatized to laboratory environment for period of 14 days prior to performing the experiments. The experimental protocols were approved by Institutional Animal Ethics Committee (Regn No: 711/02/A/CPESEA).

Acute toxicity study

Acute toxicity study was performed as per OECD-423 guidelines [7]. Swiss Albino mice of either sex (20-25 g) were used. The animals were fasted for 4 h, but allowed free access to water throughout the course of experimentation. The fasted mice were divided into different groups of six animals each. MEIF was administered orally at a dose of 5 mg/kg. The control animals received a similar volume of 2% (v/v) aqueous Tween 80 solution. Mortality in each group was observed for 7 days. The mortality was not observed, the procedure was repeated at doses 50, 300, 1000 and up to 3000 mg/kg.

Study on normal body temperature

Rats of either sex were divided into five groups (n=6) of six each. The body core temperature of each rat was measured rectally at predetermined intervals before and for 5 h after administration of either aqueous Tween 80 solution (control) or MEIF at oral doses of 100, 200 and 300 mg/kg body wt.

Development of yeast induced pyrexia

Rats of either sex were divided into five groups (n=6) of six each. The normal body temperature of each rat was measured rectally at predetermined intervals and recorded. Fever was induced according to the method described by Murugesan et al., [8]. The rats were trained to remain quiet in a restraint cage. A thermister probe was inserted 3-4 cm deep into the rectum and fastened to the tail by adhesive tape. Temperature was measured on a digital thermometer. After measuring the basal rectal temperature, animals were injected subcutaneously with 10 ml/kg body wt. of 15% w/v yeast, suspended in 0.5% w/v methyl cellulose solution and the animals were returned to their housing cages. After 19 h of injection, the animals were again restrained in individual cages for rectal temperature determination.

Drug administration

After 19 h of yeast- injection, the MEIF was administered orally at doses of 100, 200 and 300 mg/kg body wt. to three groups of animals, respectively. A similar volume (5 ml/kg body wt.) of 2% aqueous Tween 80 solution was administered orally to the control group. The animals of fifth group received the standard drug, Paracetamol (150 mg/kg body wt.) orally [8]. Rats were restrained for rectal temperature recording at the 19th hour, immediately before MEIF or vehicle or Paracetamol administration, and again at 1 h intervals up to the 23rd hour after yeast injection.

Statistical analysis

The results are presented as mean ± SEM. One way analysis of variance (ANOVA) followed by Dunnett's *t*-test for multiple comparisons were used for statistical evaluation. p values less than 0.05 were considered as stastically significant.

RESULTS

Acute toxicity study

There was no mortality at doses up to 3 g/kg (p.o) in mice. During observation the animals exhibited decreased mobility but no signed of convulsions or loss of writhing reflex. This result indicates MEIF extract has low toxicity profile.

Effects on normal body temperature and yeast induced pyrexia

The hypothermic effect of MEIF on normal body temperature in rats is presented in Table.1. It was found that MEIF at doses of 100 mg/kg body wt. caused significant lowering (p<0.01) of body temperature up to 4 h following its administration. This effect was maximal at 4 h and doses of 200 and 300 mg/kg body wt. in a dose dependent manner and caused significant (p<0.05) lowering of body temperature up to 5 h after administration. The subcutaneous injection of yeast suspension elevated the rectal temperature markedly after 19 h of challenge. Treatment with MEIF at doses of 100, 200 and 300 mg/kg body wt. decreased the rectal temperature of the rats in a dose dependent manner. The antipyretic effect started as early 1 h and the effect was maintained for 4 h, after its administration. The standard drug Paracetamol at 150 mg/kg body wt. reduced the yeast-provoked elevation of

Table 2. Effect of MEIF on yeast induced pyrexia in rats

Treatment	Rectal temperature (°C)					
	Initial 0 h	19 h after yeast injection	20 h	21 h	22 h	23 h
Control	37.3 ± 0.14	39.4 ±0.09	39.4 ±0.11	39.4 ±0.11	39.4 ±0.08	39.4 ± 0.12
Paracetamol (150 mg/kg)	37.3 ± 0.10	39.3 ±0.11	38.4 ± 0.15[a]	38.2 ± 0.09[a]	37.6 ± 0.05[b]	37.2 ± 0.06[b]
MEIF (100mg/kg)	37.3 ± 0.14	39.4 ±0.13	38.8 ± 0.13[a]	38.1 ± 0.10[a]	37.7 ± 0.12[b]	37.3 ± 0.09[b]
MEIF (200 mg/kg)	37.1 ± 0.11	39.5 ±0.12	38.6 ± 0.09[a]	38.0 ± 0.12[a]	38.0 ± 0.10[a]	37.4 ± 0.10[b]
EIF 00mg/kg)	37.3 ±0.10	38.7 ±0.16	38.4 ±0.12[a]	38.4 ±0.10[a]	37.8 ±0.11[b]	37.6 ± 0.10[b]

Data are shown as mean ± S.E.M., n = 6. [a]$p < 0.01$ [b]< 0.05, compared with the control values for the corresponding hour

body temperature significantly. The results obtained for standard, drug treated and MEIF treated rats were compared with the control (2% aqueous Tween 80 solution) group and we observed a significant reduction in the yeast-elevated rectal temperature. (Table.2)

The present results show that the methanolic extract of *Ichnocarpus frutescens* (MEIF) 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). Further more the MEIF also reduced normal body temperature significantly, and this effect will be studied further to ascertain the exact mechanism of action.

DISCUSSION

This study examined the hypothermic and antipyretic activity of a methanolic extract of the root of *Ichnocarpus frutescens* (MEIF) in an experimental animal model using rats. We observed that MEIF lower the body temperature in a dose-dependant manner up to 5 h after its administration. Pyrexia or fever is caused as a secondary impact of infection, tissue damage, inflammation, graft rejection 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 mediators (Cytokines like interleukin α, β, 1β and TNF-α), which increase the synthesis of prostaglandin E_2 (PGE_2) near preoptic hypothalamus area and thereby triggering the hypothalamus to elevate body temperature. Antipyretics are the drugs, which reduce elevated body temperature. Regulation of body temperature requires a delicate balance between production and loss of heat, and the hypothalamus regulates the set point at which body temperature is maintained. In fever this set point is elevated and a drug like Paracetamol do not influence body temperature when it is elevated by factors such as exercise or increases in ambient temperature [9].The present result show that the MEIF possesses a significant antipyretic effect in yeast-provoked elevation of body temperature (Table 2) as well as normal body temperature (Table 1) in rats. In both cases, the extract caused a significant lowering of body temperature, with the effect being comparable to that of Paracetamol. (150 mg/kg,).The results suggest that the plant has some influence on prostaglandin biosynthesis because prostaglandin is believed to be a regulator of body temperature [10]. Earlier study revealed that *Ichnocarpus frutescens* contain β-sitosterol as one of the major compound [5] and β-sitosterol is reported to have significant antipyretic activity [11]. Hence the antipyretic activity of *Ichnocarpus frutescens* root extract studied by us may be due to the presence of β-sitosterol. Thus the present pharmacological evidence provides support for the folklore claim as an antipyretic agent.

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