Pharmacognosy Magazine
ISSN: 0973-1296

PHCOG MAG.
An official Publication of Phcog.Net

PHCOG MAG.: Research Article
Comparative Antipyretic activity of Patha: An Ayurvedic drug

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ABSTRACT – Different genera of Menispermaceae are being used by herbal manufacturers in formulations of the drug Patha. The important sources of Patha are roots of *Cissampelos pareira Var. hirsuta*, *Cyclea peltata* and *Stephania japonica*, and these genera are being used to treat ailments associated with pyrexia in Ayurvedic system of medicine. The objective of the present study was to evaluate the antipyretic effects of the methanol extracts of roots of above said plants using Yeast induced pyrexia in albino rats. Rectal temperatures were recorded before and after inducing pyrexia at interval of one hour for five hours. At the same time parallel experiments were run with a standard antipyretic (paracetamol) and the vehicle (1% Tween 80). Methanol extract of *Cissampelos pareira Var. hirsute* at dose of 200mg/kg body wt. showed significant antipyretic activity.

KEY WORDS – Antipyretic, *Cissampelos pareira*, *Cyclea peltata*, Patha, *Stephania japonica*.

INTRODUCTION

Cissampelos pareira Var. hirsuta Linn. (DC)., *Cyclea peltata* Lam and *Stephania japonica* Thunb. of the family Menispermaceae are commonly known as Patha in Ayurveda and have been used for the treatment of fever, urinary problems and skin infections (1). *C. pareira Var. hirsuta* is found very common in semidry forests of tropics, *C. peltata* in Western Ghats and Deccan region whereas *S. japonica* occurs in wet deciduous to semi evergreen forests of tropical temperate Asia (2). Various alkaloids and different pharmacological activities of these plants have been reported. Bisbenzylisoquinoline alkaloids, cissamperine with tumor inhibitor activity (3), tetrandrine (4), tropoloisoquinoline alkaloids such as pareirubrine A and B with antileukemic activity (5) have been isolated from roots of *C. pareira Var. hirsuta*. Root extracts were tested for antibacterial activity (6), antimalarial activity (7), diuretic activity (8), hypoglycemic activity (9) and anticonvulsant activity (10). Five bisbenzylisoquinoline alkaloids, cycleapeltine, cycleadrine, cycleacurine, cycleanorine , and cycleahornine chloride have been isolated from *C. peltata* (11). Antiplasmodial and cytotoxic activities of bisbenzylisoquinoline alkaloids (12) and antilithiatic activity (13) have been reported. Various alkaloids were isolated from roots of *S. japonica* such as tertiary phenolic biscoclaurine type alkaloid stepholine (14), hasubanonine (15), and water soluble quaternary base cyclanoline (16). The root extract was studied for its multidrug resistance modulator effect (17). A few ethnobotanical reports on treatment of fever (18), gastrointestinal tract disorders (19) were investigated.

MATERIALS AND METHODS

Plant material

Roots of *Cissampelos pareira* Var. hirsuta were collected from dry deciduous forests of Chamundi hills, Mysore. *Cyclea peltata* and *Stephania japonica* roots were collected from evergreen forests of Madikere. The taxonomical identification of the plants were done by Dr. G. Shivamurthy, Department of studies in Botany, University of Mysore, Mysore, and the voucher specimens were deposited at the herbarium, (specimen no. KKH-001/2006, KKH-002/2006 and KKH-003/2006 respectively). Roots were dried under shade, coarsely powdered and stored in airtight container for further use.

Preparation of extracts

The powdered plant materials were extracted using methanol as solvent in a Soxhlet apparatus. The solvent was completely removed by vacuum and semisolid mass was obtained (11.6%, 15.8% and 9.1% w/w with respect to the powdered material). The methanol extracts were stored in refrigerator and a weighed quantity was suspended in 1% Tween 80 for the experiment.

Phytochemical screening

Preliminary phytochemical investigation was carried out for all extracts. Presence of alkaloids was determined by *Mayer's*, *Dragendorf's*, *Wagner* and *Hager's* test, Flavonoids by *Shinoda*, Ferric chloride and lead acetate tests, Saponins by Foam and

haemolysis tests and Sterols by *Salkowaski* and *Libermann and Burchards* tests.

Animals used

Wistar albino rats of either sex weighing 250-300 g were used. The animals were maintained under suitable conditions (Temperature 25±2ºC) with dark and light cycle (14/10 hrs), and fed with standard dry pellets and water *ad libitum* throughout the experiment. The experiment was initiated after approval of Institutional Animal Ethical Committee [(IAEC) (NCP/IAEC/2/06-07)].

Toxicity study

Acute toxicity for the determination of LD_{50} value was performed with different doses of the extract according to the up and down method (20).

Yeast induced pyrexia

Rats were divided into eight groups of six rats each. The normal body temperature of each rat was measured rectally and recorded. Pyrexia was induced by injecting the Yeast suspension by subcutaneous rout of administration in hind limbs of the rats (21). The rats were acclimatized to remain quite in a restraint cage. A flexible thermister probe coated with the lubricant was inserted 3-4 cm deep into the rectum and fastened to the tail by adhesive tape. The temperature was measured on a thermometer (60 sec.). After measuring the basal rectal temperature, animals were given a subcutaneous injection of 10ml/kg body weight of 15% (w/v) yeast suspended in 0.5% (w/v) methyl cellulose solution. Rats were then returned to their housing cages. After 19 h of yeast injection, the animals were again restrained in individual cages for the recording of their rectal temperature as described previously.

Drug administration

After 19 h of yeast injection the extracts were administered orally at doses of 100 and 200 mg/kg body weight. to six groups of animals respectively. A similar volume of Tween 80 (1%) solutions was administered orally to the control group. The eighth group of animals received the standard drug paracetamol (200mg/kg body weight.) *p.o*. Rats were restrained for recording rectal temperature at the 19 h, immediately before extracts, Tween 80 or paracetamol administration, and again at one hour intervals up to the 24 h after yeast injection.

Statistical analysis

Values are expressed as Mean ± S.E.M. Statistical significance was analyzed using one way ANOVA.

Table 1: Effects of Methanolic extracts in yeast induced hyperthermia in rats.

Treatment with (mg/kg)	Mean ±S.E.M. rectal Temperature (°c)					
	Before yeast	After yeast	After treatment			
			1 hr	2 hr	3 hr	5 hr
Control	35.15±0.10	36.7±0.14	36.7±0.14	36.63±0.16	36.6±0.14	36.52±0.11
Paracetamol						
200	35.2±0.13	36.81±0.12	35.18±0.04***	35.1±0.09***	35.08±0.08***	35.11±0.11***
C. pareira						
100	35.2±0.09	36.53±0.08*	36.6±0.09	36.63±0.10	36.53±0.12	36.43±0.08
200	35.2±0.06	36.50±0.09*	36.08±0.15***	35.85±0.15***	35.53±0.12***	35.38±0.11***
C. peltata						
100	35.18±0.08	36.620.13	36.62±0.08	36.62±0.10	36.53±0.10	36.50±0.09
200	35.2±0.09	36.6±0.14	36.56±0.08	36.5±0.09	36.47±0.14	36.38±0.08*
S. japonica						
100	35.2±0.09	36.7±0.09	36.63±0.12	36.58±0.08	36.51±0.08	36.5±0.06
200	35.1±0.11	36.57±0.14	36.43±0.10**	36.42±0.08*	36.4±0.06**	36.37±0.08*

Values represent Mean ± S.E.M. (n = 6)

Control (1% Tween 80 solution)

****P<0.001, ** P<0.01, *P<0.05 significant as compared to corresponding data of the control.*

RESULTS

The LD_{50} study showed that all the three extracts are safe at a dose of 2 g/kg body weight. The methanolic extract of *C. pareira* at a dose of 200 mg/kg body weight has shown significant (P<0.001) antipyretic activity, it has shown significant fall in body temperature up to 4h following its administration. The antipyretic activity started as early as 1h and the effect was maintained for 4h. The response was comparable to that of antipyretic activity of paracetamol a standard antipyretic drug. But the same at a dose of 100 mg/kg body weight did not showed antipyretic activity. Methanolic extract of *C.peltata* failed to reduce yeast induced pyrexia at both the doses. The methanolic extract of *S. japonica* showed moderate antipyretic activity at a dose of 200 mg/kg body weight same at a dose of 100 mg/kg body weight did not showed significant activity.

DISCUSSION

Fever may be due to infection or one of the sequele of tissue damage, inflammation, graft rejection, or other disease states. Antipyretic are agents, which reduce the 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 elevates and a drug like paracetamol does not influence body temperature when it is elevated by the factors such as exercise or increase in ambient temperature (22). Yeast-induced fever is called pathogenic fever. Its etiology includes production of prostaglandins, which set the thermo-regulatory center at a lower temperature (23). The present results show that methanolic extract of *C. pareira* 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). At the same time the other two extracts *C. peltata* and *S. japonica* failed to show significant antipyretic activity. So inhibition of prostaglandin synthesis could be the possible mechanism of antipyretic action as that of paracetamol (24). Also, there are several mediators or multi-processes underlining the pathogenesis of fever. Inhibition of any of these mediators may bring about antipyresis (25). The results clearly indicate that the Ayurvedic drug Patha is roots of *Cissampelos pareira Var. hirsuta* in context of antipyretic activity. The detailed study is required in order to identify the actual active constituent from this drug.

ACKNOWLEDGMENTS

Authors are very much grateful to Dr. G. Shivamurthy, Professor, Department of studies in botany, university of Mysore for authentication of the plant materials. We are also thankful to principal National College of pharmacy, Shimoga for their timely help in these studies.

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