Antipyretic and Phycopharmacological activity of leaf extract of *Gonostegia hirta* (Blume ex Hasskarl) Miquel: An important wild food plant of Arunachal Pradesh, India

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ABSTRACT

The main objective of this work was to study the antipyretic and analgesic activity of ***Gonostegia hirta (Blume ex Hasskarl) Miquel*** *of leaf extract in an experimental albino rat model. Antipyretic was evaluated on normal body temperature and Brewer's yeast-induced pyrexia in albino rat's model. While phycopharmacological activity of MEGHL was investigate by general behavior and phenobarbitone sodium-induced sleeping time methods.Yeast suspension (10ml/kg b.w) was recorded rectal temperature after 19h of subcutaneous injection. The MEGHL at oral doses of 100, 200 and 300 mg kg-^{1}b.w showed significant reduction in normal body temperature and yeast provoked elevated temperature (37.9±0.2 and 37.6±0.5) in a dose-dependent manner and the anti-pyretic effect was comparable to that of the standard anti-pyretic drug paracetamol(150 mg/kg b.w). MEGHL extract at 100-300 mg kg^{-1} caused not much reduction in spontaneous activity (general behavior profile) as well as in phenobarbitone sodium-induced sleeping time. This study revealed that the methanol extract of G.hirta possess significant antipyretic activity in the tested models but does not have much activity of phycopharmacological, and may validated its popular use as a antipyretic agents as well as food plant in Adi community of Arunachal Pradesh.*

KEY WORDS: *Antipyretic, Phycopharmacological activity, Gonostegia hirta, Adi community*

Introduction

Gonostegia hirta (Blume ex Hasskarl) Miquel (synonym: *Pouzolzia hirta* Blume ex Hasskarl) of family Urticaceae is reported to be distributed in Pakistan (N.W.F. Province, Kashmir), India (Punjab, Kumaon, Uttar Pradesh, Sikkim, Khasia, Behar, Assam, Arunachal Pradesh), China, Malaysia, Australia. The plant is found to be growing at an altitude ranging from (200-2500) m from the mean sea level. *Gonostegia hirta* is a famous wild edible food plant used by the *Adi* tribe of Arunachal Pradesh which is ideally found in weedy places, thickets by ditches and rice field and moist as well as semi-dry secondary forest patches. The roots, the leaves or the whole plant are used to treat boils and abscesses, abdominal cramps in females and leucorrhoea, bone dislocations and fractures (Chen *et al*, 2003). In the North Eastern States of India and Eastern Himalayan range, the plant is reported to be used as vegetable, and also used for treatment of constipation, gastric ulcer, stomach flatulence and laxative agent (Tag *et al*, 2008, Ranjay *et al*, 2010).

Materials and Methods

Plant material

The leaves of G. hirta **(Blume ex Hasskarl) Miquel were** collected from the Kebang forest of Siang district, Arunachal Pradesh, India. The plant material was taxonomically identified and authenticated by SFRI, Itanagar. A voucher specimen was deposited in the herbaum of the department of Botany, Rajiv Gandhi University for future reference. The leaves were dried under shade, powered (1kg) and passed through 40 mesh sieve, and stored for further use.

Preparation of extract

The powdered plants material (1kg) was extracted by using Soxhlet extraction apparatus in cold with 90% methanol as solvent for 72 h at room temperature. The whole extract of leaves containing solvent was separately collected and filtered with Whatman No. 1 filter paper. The solvent was then evaporated to dryness under reduced pressure in rotary evaporator at 45–70 ◦C. The concentrated methanol extracts of *G. hirta* leaf (MEGHL) (yield of ±110 g (11.1%, w/w)) was stored in a desiccator for further use. A weighed amount of the dried extract (prepared in 2%, w/v Tween-80) was used in the present pharmacological studies.

Animals used

Healthy albino rats (Wistar strain) of either sex weighing 100-200g were housed at 23±4 ◦C, relative humidity 60–70% used with access to healthy food at regular intervals and water *ad libitum*, and all the animal experiments were carried out according to the institutional regulations and national criteria for animal experimentation.The experimental data were statistically evaluated using one-way analysis of variance (ANOVA) (ORIGIN version 8.0). Paired statistical analyses were performed using the Student's *t*-test and the *p*-value were considered statistically significant at $p < 0.05$ and $p < 0.001$.

Study on normal body temperature of rats:

Healthy albino rats of either sex were divided into five groups which comprises five in each group. Only healthy rats with constant normal body temperature were selected for this experiment. The body temperature of each rat was rectally measured at time intervals before and 4h after the administration of either propylene glycol (vehicle control) or MEGHL at doses of 100, 200, 300 mg kg^{-1} body weight orally.

Yeast induced hyperthermia in rats:

Rats of either sex were divided into five groups, comprising five rats in each group. The normal body temperature of each rat was measured with digital thermometer rectally and recorded. The rats were trained to remain quiet in a reserve cage. Fever was induced by a subcutaneous injection of 10ml/Kg 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 third, fourth and fifth group of animals received MEGHL orally at doses of 100, 200 and 300 mg/kg, respectively. The first group received 5 ml/kg body weight of 2% (v/v) aqueous Tween-80 solution orally (vehicle control group). The second group received standard drug paracetamol (150mg/Kg). Rectal temperature of all the rats was recorded at 19 h, immediately before the extract or vehicle or paracetamol administration, and again at 1h intervals upto 4 h, after yeast injection.

Phycopharmacological test

Gross behavioral studies:

Evaluation of general behavioral profile was performed by the method of Dixit and Varma (1976). Rats of either sex were divided into five groups, comprising five rats in each group. The first three groups of animals were administered with MEGHL at the doses of 100, 200, and 300 mg kg^{-1} subcutaneously. While the last two groups receive either chlorpromazine (5mg/Kg) as a drug control or propylene glycol (5ml kg^{-1}) as vehicle control. The animals were under observation for their behavioral changes if any, at 30 min intervals in the first hour and at hourly intervals for the next 4h for the following parameters (Mukherjee et al., 1996; Murugesan et al., 1999).

Awareness, alertness and spontaneous activity

The awareness and alertness were recorded by visual measure of the animal's response when placed in different positions and its ability to orient itself without bumps or falls (Turner, 1965). The normal behavior at resting position was recorded as 0, little activity (+), moderate flexibility (++), strong response (+++) and abnormal restlessness as (++++). The spontaneous activity of the rats was recorded by placing the animal in a bell jar. It usually shows a moderate degree of inquisitive behavior. Less or moderate activity was scored as ++, strong activity as +++. If there is slight or little motion, the score was +, while if the animals sleeps, the score was −. Excessive or very strong inquisitive activity like constant walking or running was scored ++++. A similar test was performed with the same scoring, when the animals are removed from the jar and placed on a table (Turner, 1965; Mukherjee et al., 1996).

Phenobarbitone sodium-induced sleeping time

Rats were divided into five groups of five rats each. Animals received (40mg kg^{-1}) (s.i) phenobarbitone sodium 30 min after the injection of MEGHL at a dose of 100, 200 and 300 mg kg^{-1}, chlorpromazine (5mg kg^{-1}) standard and vehicle control propylene glycol (5ml kg^{-1}).The sleeping time was recorded, measured as the time interval between the loss and regaining of the righting reflex (Dandiya and Collumbine, 1959; Mandel et al., 2001).

Results

Effects of MEGHL on normal and yeast- induced hypertherma

It was found that the leaf extract at 100 mg kg^{-1} caused significant lowering of the body temperature up to 4h ($p < 0.01$) following extract administration. This effect was maximal at 4 h and MEGHL at doses of 200 and 300 mg kg^{-1} in dose-dependent manner causing significant lowering of body temperature of rats from 36.3 ± 0.8 to 34.8 ± 0.6 upto 5 h after extract administration (Table 1). The antipyretic effect of *G.hirta* leaf extract on yeast induced is shown in Table 2. It was found that the subcutaneous injection of 15% w/v of yeast suspension markly elevated the rectal temperature after 19h of administration (38.8°C) and treatment with *G.hirta* leaf extract (100, 200 and 300 mg kg^{-1} doses) decreased the rectal temperature. The result obtained from both, the standard drug paracetamol (150mg kg^{-1}) and *Gonostegia hirta* leaf extract (100, 200 and 300 mg kg^{-1}) treated groups, were compared with the control (5 ml kg-1 propylene glycol) group. It is also evident that the antipyretic effect was started within 2 h and the effect was maintained for 4 h following its administration. The antipyretic effects of MEGHL on normal body temperature and hyperthermic rats were dose-dependent [Table 1 and 2].

Effect on general behavioral profiles

The results obtained from the different experiments are presented in Table 3. The MEGHL produced slight depression in spontaneous activity, alertness and sound response at doses of 300 mg kg^{-1}. However, the standard drug chlorpromazine hydrochloride caused a significant depression of all these responses compared with the methanolic extract.

Effect on phenobarbitone sodium-induced sleeping time

The MEGHL not significantly potentiated the phenobarbitone sodium-induced sleeping time when compared with the control drug (Table 4).

Table 1:
Antipyretic activity of MEGHL on normal rat body temperature

Treatment (mg/kg)	***Rectal temperature(° C) before and after treatment***					
	0 h	***1 h***	***2 h***	***3 h***	***4 h***	***5 h***
Control (mL/kg)	36.4±0.2	36.6 ± 0.3	36.5±0.3	36.8±0.12	36.6 ± 0.4	36.5± 0.3
Paracetamol, 150	36.1±0.13	36.4 ± 0.6	36.1± 0.5	35.3 ± 0.2	35.7 ± 0.2*	36.1 ± 0.4*
MEGHL, 100	36.5 ± 0.4	35.7± 0.4*	35.4± 0.5	35.3 ± 0.4*	35.1±0.13**	35.0±0.6**

MEGHL, 200	36.3 ± 0.8	35.02±0.7**	35.04±0.6**	36.12±0.7**	35.5±0.3*	35.6±0.2*
MEGHL, 300	36.5±0.5	34.92±0.6**	35.3±0.4*	35.5±0.22**	35.02±0.4*	34.8±0.6**

Data represents mean ± SE (standard error) *(n=5)*; *$p < 0.001$ and** $p < 0.01$, significant from the control; control 2 % (v/v) aqueous Tween-80 solution; MEGHL, methanol extract of *G. hirta* leaf

Table 2:
Antipyretic activity of MEGHL on yeast-induced hyperthermia test in rats

Treatment (mg/kg)	***Rectal temperature(° C)***					
	Before yeast	***19 h after yeast***	***Time after MEGHL treatment (min)***			
			60	***120***	***180***	***240***
Control (mL/kg)	36.62±0.3	37.9±0.6	37.8±0.5	37.7±0.62	36.6±0.4	37.8±0.3*
Paracetamol, 150	36.9±0.4	38.6±0.42	37.3±0.3	37.02±0.3	36.9±0.4	36.7±0.3
MEGHL, 100	37.0±0.8	38.1±0.4*	37.9±0.2*	37.6±0.23*	37.6±0.2*	37.4±0.3*
MEGHL, 200	37.8 ±0.5	38.7±0.4*	37.7±0.5**	37.6±0.4*	37.5±0.4*	37.4±0.7**
MEGHL, 300	36.7±0.9	38.8±0.5**	37.6±0.5**	37.7±0.4*	37.5±0.3*	36.7±0.7**

Data represents mean ± SE (standard error) *(n=5)*; *$p < 0.001$ and** $p < 0.01$, significant from the control; control 2 % (v/v) aqueous Tween-80 solution; MEGHL, methanol extract of *G. hirta* leaf

Table 3
Effect of the MEGHL on general behavioral profiles in rats

Behavior type	**MEGHL (mg Kg^{-1})**			**Chlorpromazine (5mg Kg^{-1})**	**Propylene glycol (5mg kg^{-1})**
	100	**200**	**300**		
Spontaneous activity	-	+	+	++++	-
Alertness	-	-	+	++++	-
Sound response	-	+	+	++++	-

MEGHL, methanol extract of *G. hirta* leaf: '-'no effect; '+' slight depression; '++' moderate depression; '+++' strong depression' '++++' severe depression; *n*=5

Table 4
Effect of the MEGHL on Phenobarbitone sodium-induced sleeping time

Experiment	**Dose**	**Sleeping time (min)**
Propylene glycol	(5ml kg^{-1})	54.8 ± 4.8*
Chlorpromazine	(5mg kg^{-1})	93.8 ± 13.02*
MEGHL	(100 mg kg^{-1})	17 ± 1
	(200 mg kg^{-1})	19.14 ± 1.3
	(300 mg kg^{-1})	19.8 ± 2.5

MEGHL, methanol extract of *G. hirta* leaf. Values are mean ± S.E., *n*=5; *$p < 0.001$

Discussion

Fever may be a result of infection or tissue damage, inflammation or other disease states. In fever, this set point is elevated and drug like paracetamol do not influence body temperature when it is elevated by factors like exercise or increase in ambinent temperature (Goodmann and Gilman, 1996). Antipyretic are drug, which reduce elevated body temperature. The present study showed that the methanol extract of *Gonostegia hirta* leaf at 100, 200 and 300 mg kg^{-1} doses possess a significant antipyretic property in an experimental brewer's yeast-induced hyperthermia in rats. The yeast provoked elevation of body temperature (38.8°C) in rats as the temperature reduced to 37.4°C, 37.4°C and 36.7°C respectively, and this effect is comparable to that of the standard antipyretic drug paracetamol which at 150 mg kg^{-1} reduced the temperature to 36.7°C. This study reveals that the MEGHL causes a significant antipyretic effect in yeast-provoked elevation of body temperature in rats [Table 1]. The MEGHL caused a significant lowering of body temperature whose antipyretic effect is comparable to that of paracetamol in both the experimental conditions. The body temperature requires a delicate balance between the production and loss of heat and is regulated by hypothalamus (Goodmann and Gilman, 1996). However, the *Gonostegia hirta* leaf extract also significantly reduced the normal body temperature of the animals tested, this effect needs further study to know the exact mechanism of action.

MEGHL showed slight influences in general behavior profiles as evidence in the spontaneous activity and sound response. The results of MEGHL was compared with the vehicle control and standard drug which shows that the control and standard drug exhibit significantly potentiated the phenobarbitone sodium-induced sleeping time while the MEGHL showed no activity. From the present investigation it is confirms that the plant may not have antipsychotic activity, due to this reason the plant can be used to consumed as vegetables for providing the nutrition requirement as well as therapeutic potentials.

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