



Antipyretic and Analgesic effects of *Aristolochia tagala*

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Abstract

The indiscriminate use of non-steroidal anti-inflammatory drugs as antipyretic and analgesic agents causes potential side effects in patients. Therefore, the quest for the identification of analgesic drugs without side effects is continuing. In this process, the efficacy of plant-based drugs used in the traditional medicine system is gaining momentum nowadays due to their cost effectiveness, greater availability and lesser side effects. In the present study, the methanolic leaf extract of *Aristolochia tagala* was tested for the antipyretic and analgesic effect in Swiss albino mice. The antipyretic activity was investigated by the brewer's yeast induced pyrexia method. The rectal temperature was measured after 18 h of yeast injection. The temperature decrease was recorded for four hours after the administration of plant extract. For the determination of analgesic effect, tail immersion test was followed. The animals were treated with the plant extract at the doses of 200 mg/ kg and 400 mg/ kg. The reaction time was recorded after the drug treatment. The results were subjected to statistical analysis using one-way ANOVA for their significance. The results indicate that *Aristolochia tagala* methanolic extract possesses antipyretic and analgesic effect, which are dose dependent.

Keywords: antipyretic, analgesic, *Aristolochia tagala*, albino mice, yeast induced pyrexia, tail immersion test

Introduction

Plants play an essential role in the traditional medicine system since time immemorial. Around 2500 plant species belonging to 1000 genera are routinely being used in the Indian Medical system such as Ayurveda, Unani, Siddha and Homeopathy for the treatment of various illnesses. The phytochemicals and related drugs are used to treat nearly 87% of human diseases (Newman *et al.*, 2007). The usage of synthetic drugs for prolonged period results in deleterious side effects and after effects to the human

body. The cost of the medicines is also relatively high. Hence the people living in third world countries still rely on plant-based medicines for their cost-effectiveness and easy availability. It is also a known fact that herbal medicines cause lesser side effects. The extracts obtained from different parts of the plants exhibit an array of pharmacological activities which include anti-inflammatory, hypoglycemic, hepatoprotective, analgesic, antipyretic, wound healing, etc. Fever or pyrexia is a form of patient's discomfort. It is caused by the secondary response of microbial infection, inflammation, tissue damage or other diseased states. Pyrexia is considered as a natural defense mechanism to inhibit the growth of infectious agents to protect the body from tissue damage. Various species of *Aristolochia* have been used in herbal medicines used for the treatment of snake-bite, wound healing and tumours (Rates, 2001; Dey and Nath, 2012). *Aristolochia tagala* is a rare medicinal plant which has been less explored for its pharmacological effects. The antipyretic effect of this plant is yet to be determined despite the increased use of this herb. Therefore, the present study seeks to evaluate the antipyretic and analgesic effects of methanolic extract of leaves of *Aristolochia tagala* in Swiss albino mice.

Materials and Methods

Collection of plant materials

The leaves of *Aristolochia tagala* were collected from Shenbagathoppu region of Southern Western Ghats, Virudhunagar district, Tamil Nadu, India during the month of August 2015. It is an evergreen climbing plant growing up to 20m tall. They grow usually in mountains at the altitude ranges between 800 and 1350m. The leaves are simple, oval to oblong, 6 – 25 cm long by 4 – 10 cm wide. They were identified and authenticated by Dr. R. Ramasubbu (a taxonomist) of the Department of Biology, Gandhigram Rural Institute, Dindigul, India. The voucher specimens were deposited in the Department of Botany Herbarium, VHNSN College, Virudhunagar, India for future references.

The leaves were washed in clean water and air dried under shade. The dried leaves were pulverized in a mixer grinder to fine powder. The dried powdered material was extracted with methanol in a Soxhlet apparatus by continuous heat extraction for about 48 h. The extract was concentrated at 40°C in vacuum.

Animals

Male Swiss albino mice weighing 110-150g were employed for the study. The animals were maintained in polypropylene cages with paddy husk bedding under natural 12 h light/ dark cycle. They were allowed to acclimatize the laboratory conditions for two weeks before the commencement of experiment. The animals were fed with standard diet obtained from Poultry Research Station,

Chennai and provided with water *ad libitum*. The experimental protocol was approved by the animal ethics committee constituted for the purpose as per CPCSEA guidelines.

Experimental design

Antipyretic activity

Pyrexia was induced in all the animals by subcutaneous injection of 15% (w/ v) concentration of Brewer's yeast (10ml/kg) in distilled water. The animals were divided into four groups each comprising 4 animals and were administered with standard drug and extract (oral administration) as follows:

Group I : received saline (10ml/kg) and served as control

Group II : were treated with yeast (10ml/kg) and Paracetamol (33mg/kg)

Group III : administered with yeast (10ml/kg) and *Aristolochia tagala* extract (200mg/kg)

Group IV : administered with yeast (10ml/kg) and *Aristolochia tagala* extract (400mg/kg)

The basal rectal temperature was measured using a telethermometer at a depth of 2 cm before the injection of yeast. After 18 h of injection, the temperature was recorded at 1st, 2nd, 3rd and 4th hour.

Analgesic activity

Swiss albino mice of either sex were divided into 4 different groups each containing 4 animals. The control group animals were administered with saline solution. The standard drug Diclofenac sodium (100mg/ kg) was administered to the animals of Group II. The methanolic leaf extract of *Aristolochia tagala* were given orally to Group III and IV at the concentration of 200mg/ kg and 400mg/ kg respectively. The lower 5 cm position of the tail was marked individually. This part of the tail was immersed in a water bath maintained at 55 °C. The withdrawal time (in seconds) of the tail from the water bath was recorded as reaction time or tail-flick latency (Stasi *et al.*, 2012). The cut-off time for immersion was 15 s in order to avoid injury to the tail. Initial reading was measured immediately before the administration of test and standard drugs. After 60 minutes of injection, the responses were recorded at the time interval of 1, 2, 3 and 4 h.

Statistical analysis

The results of antipyretic and analgesic activity were statistically analyzed using one way ANOVA. The results were compared with the control group. *P*-values <0.05 and <0.01 were considered statistically significant.

Results

The efficacy of methanolic extract of leaves of *Aristolochia tagala* against yeast induced pyrexia is presented in Table 1. The control group showed increased level of rectal temperature up to 4h after the drug administration while the treatment group responded well to the yeast induced pyrexia (Fig.

1). The temperature decreased to a significant level in all the treatment groups after 1h of drug administration. The standard drug paracetamol exhibited peak effect after 4h which was followed by the animals administered with 400mg/ kg of *Aristolochia tagala* extract. The animals responded to *Aristolochia tagala* extract at 200mg/ kg significantly lower than at 400mg/ kg. At 4h after the drug administration, about 86% reduction in temperature was observed in the animals treated with 400mg/ kg of methanolic extract. This is very close to the effect exerted by the standard drug Paracetamol which showed 88% reduction in rectal temperature. A maximum of 47% reduction in temperature was recorded in the animals that received the plant extract at 200mg/ kg. In contrast to the treatment groups, the control group exhibited an elevated level of rectal temperature up to 3h after the beginning of experiment.

The results of analgesic activity of *Aristolochia tagala* methanol extract is shown in Table 2. It is evident that the plant extract exhibited significant response at the dose of 400 mg/ kg. Maximum effect was observed with the standard drug Diclofenac Sodium after 3h of drug administration. Similar response was also recorded in the animals treated with extract at 400 mg/ kg. The animals administered with 200 mg/ kg of *Aristolochia tagala* leaf extract showed moderate response as evidenced by the reaction time. In control group, there was no significant change in the analgesic effect.

Discussion

The experimental results showed that the methanolic leaf extract of *Aristolochia tagala* possesses significant antipyretic effect against the yeast-induced pyrexia in Swiss albino mice. The extract has reduced the rectal temperature as the standard drug paracetamol. Generally, non-steroidal anti-inflammatory drugs inhibit the synthesis of prostaglandins in hypothalamus thereby exert antipyretic effect. These antipyretic drugs perform their action by inhibiting the action of an enzyme, cyclooxygenase (Rajani *et al.*, 2011). The methanolic leaf extract of *Aristolochia tagala* showed more pronounced effect in lowering the rectal temperature at the dose of 400 mg/kg. The activity was less at 200 mg/ kg dosage level but it was significant when compared to the control animals. These results clearly indicate that the methanolic extract has suppressed the fever likely by inhibiting the prostaglandin synthesis. The antipyretic effect of plant extract at 400 mg/ kg level was almost equivalent to the standard drug paracetamol. Similar results were obtained with the leaf extract of *Vitex negundo* Linn. (Murthy *et al.*, 2010)

As evident from Table 2, the leaf extract of *Aristolochia tagala* showed potential analgesic effect as determined by tail immersion method. A perusal at the results revealed that the effect was dose dependent. At 200 mg/ kg dose of extract, the reaction time was lesser than those at 400 mg/ kg. The

response was comparable with the standard drug Diclofenac Sodium. Peak effect was observed after 3 h of pyrexia induction in all the groups. The saline could not exert any effect on the animals. There was no significant difference in reaction time between the positive control and extract treated group (400 mg/ kg). Inhibition of pain induced by thermal stimuli may be due to the extract which can probably work by suppressing the release of prostaglandin, bradykinin and histamine (Mehemet, 2002). The phytochemicals present in the extract may be responsible for the analgesic activity. Further investigation in the line of isolation and identification of these bioactive principles is required to establish that *Aristolochia tagala* can be used as an antipyretic and analgesic substitute.

Conclusion

Hence, it can be concluded that methanolic extract of *Aristolochia tagala* leaf possesses antipyretic effect against yeast-induced pyrexia in Swiss albino mice as evidenced by the decrease in rectal temperature. This study also provides the evidence for the analgesic effect of the extract. These pharmacological effects may be due to the presence of bioactive principles such as phenolics, flavonoids and other phytochemical constituents present in the extract.

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Table 1. Effect of methanolic leaf extract of *Aristolochia tagala* (AT) against yeast induced pyrexia in Swiss albino mice

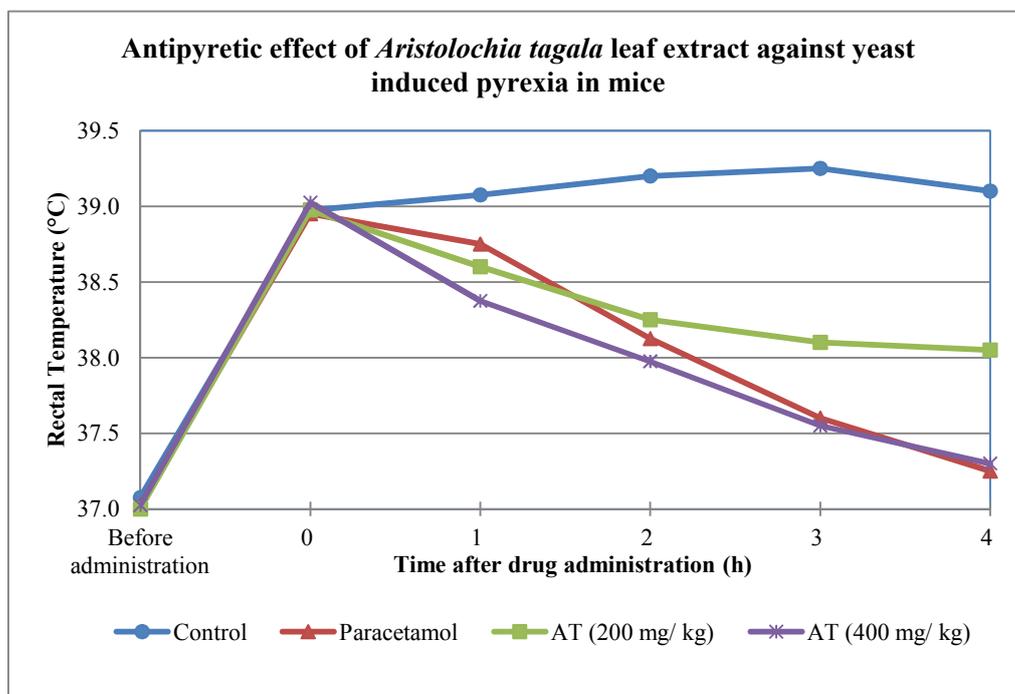
Drug & Dose	Before yeast injection (°C)	Rectal Temperature at different time intervals after 18h of yeast injection (°C)				
		0 h	1 h	2 h	3 h	4 h
Control (Saline 10ml/ kg)	37.075±0.048	38.975±0.063	39.075±0.103 (-5.26%)	39.200±0.082 (-11.84%)	39.250±0.065 (-14.47%)	39.100±0.041 (-6.58%)
Paracetamol (33 mg/ kg)	37.025±0.048	38.950±0.065	38.750±0.253* (10.39%)	38.125±0.202# (42.86%)	37.600±0.178# (70.13%)	37.250±0.104# (88.31%)
AT Extract (200 mg/ kg)	37.000±0.041	38.975±0.085	38.600±0.041* (18.99%)	38.250±0.065* (36.71%)	38.100±0.041# (44.30%)	38.050±0.029# (46.84%)
AT Extract (400 mg/ kg)	37.025±0.048	39.025±0.111	38.375±0.085# (32.50%)	37.975±0.085# (52.50%)	37.550±0.087# (73.75%)	37.300±0.041# (86.25%)

The values are expressed as Mean ± SEM (n = 4 animals/ group). The symbols # and * represent significant levels at p<0.01 and p<0.05 respectively when compared with control. The values in parentheses represent percentage reduction in rectal temperature after drug administration.

Table 2. Evaluation of analgesic activity of methanolic leaf extract of *Aristolochia tagala* (AT) by tail immersion method

Groups	Dose	Before drug administration (in seconds)	Reaction time (in seconds) after administration of drugs at different time intervals			
			1 h	2 h	3 h	4 h
Control (Tween 80)	1 ml/ kg	1.75 ± 0.41	2.00 ± 0.35	1.75 ± 0.41	2.50 ± 0.56	2.00 ± 0.61
Diclofenac Sodium	100 mg/ kg	2.00 ± 0.35	8.75 ± 0.41 [#]	10.25 ± 0.41 [#]	10.75 ± 0.41 [#]	10.25 ± 0.41 [#]
AT Extract	200 mg/ kg	1.50 ± 0.25	5.75 ± 0.41*	5.75 ± 0.41*	6.50 ± 0.56*	5.75 ± 0.41*
AT Extract	400 mg/ kg	2.75 ± 0.41	7.00 ± 0.35 [#]	10.50 ± 0.56 [#]	10.75 ± 0.22 [#]	10.00 ± 0.35 [#]

The values are expressed as Mean ± SEM (n = 4 animals/ group). The symbols [#] and * represent significant levels at p<0.01 and p<0.05 respectively when compared with control

Figure 1. Effect of *Aristolochia tagala* extract on the change in rectal temperature

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