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Short Report

Antipyretic activity of *azima tetracantha* in experimental animals

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ABSTRACT

In the present study, the ethanolic leaf extract of *Azima tetracantha* Lam (*A. tetracantha*) was investigated for antipyretic activity in rats using Brewer's yeast induced Pyrexia. The leaves of *A. tetracantha* were collected from Ponnamaravathi and cut into small pieces and shade dried. The dried powdered leaves (100 gm) were extracted in a Soxhlet apparatus by using 95% ethanol. Albino rats weighing (200-250g) were taken for the experiment divided into four groups of six animals each. Group 1 received 3% aqueous suspension of gum Acacia (1 ml/200g) as vehicle orally, group 2 and group 3 received ethanolic leaf extract of *A. tetracantha* 100 and 200 mg/kg with 3% aqueous suspension of gum Acacia orally and the group 4 served as standard received paracetamol 25 mg/kg with 3% aqueous suspension of gum Acacia orally. The subcutaneous injection of yeast suspension markedly elevated the rectal temperature after 18h of administration. Treatment with *A. tetracantha* extract at a dose of 100, 200 mg/kg decreased the rectal temperature of the rats in dose dependent manner. This effect was maximal at dose of 200 mg/kg and it caused significant lowering of body temperature ($P < 0.01$) up to 4 hour after its administration. The antipyretic effect started as early as 1h and the effect was maintained for 4h, after its administration. Both the standard drug paracetamol 25 mg/kg and tested drug *A. tetracantha* extract were significantly reduced the yeast elevated rectal temperature, at 2nd, 3rd and 4th hour compared to control group.

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1. Introduction

Pyrexia or fever is caused as a secondary impact of infection, malignancy or other diseased states. It is the body's natural defense to create an environment where infectious agent or damaged tissue cannot survive [1]. 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 (PGE₂) near peptic hypothalamus area and thereby triggering the hypothalamus to elevate the body temperature [2]. 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 increasing sweating to reduce the temperature; but when the body temperature become very low hypothalamus protect the internal temperature by vasoconstriction. High fever often increases faster disease progression by increasing tissue catabolism, dehydration and existing complaints, as found in HIV [3]. Drugs having anti-inflammatory activity generally possess antipyretic activity (e.g) non-steroidal anti-inflammatory drugs (NSAIDs). It has been suggested that prostaglandin (PGE) mediates pyrogen fever; the ability of NSAIDs, to inhibit prostaglandin synthesis could help to explain their antipyretic activity.

Search for safe herbal remedies with potent antipyretic activity received momentum recently as the available antipyretics, such as paracetamol, aspirin, nimusulide etc, which have toxic effect to the various organs of the body [4]. The subacute toxicity results

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revealed that *Azima tetracantha* (*A. tetracantha*) might be considered as a broad non-toxic one. The antipyretic activity exhibited that the ethanol extract of leaves possess a significant antipyretic effect in maintaining normal body temperature and reduced the elevated rectal temperature in rats and their effects are comparable to that of standard antipyretic drug paracetamol. Such reduction of rectal temperature of the tested animals appears to be due to the presence of a single bioactive substance or a mixture of compounds in them. Therefore, the present study aimed to evaluate the analgesic effect of ethanolic leaf extract of *A. tetracantha*.

2. Materials and Methods

2.1. Collection and Extraction

Fresh leaves of *A. tetracantha* were collected in Ponnmaravathi (Pudukkottai District) during the month of November-December. The drug was authenticated by botanist at the Rapinat Herbarium and Centre for Molecular Systemics, St. Joseph College Tiruchirappalli, Tamil Nadu, India. Plant material was dried under shade at room temperature, pulverized by a mechanical grinder, sieved through 40 meshes. The powdered material (100 g) was extracted with 95% ethanol by hot continuous Percolation method in a Soxhlet apparatus. The extract was then concentrated and dried under reduced pressure. The ethanol free semi solid mass obtained (13.65g) and suspended in 5% gum Acacia for pharmacological studies. This study was carried out in the animal house of Periyar College of Pharmaceutical Sciences for Girls, Tiruchirappalli (Regd. No. 265 / CPCSEA). Toxicity study was carried out as per the organisation for Economic Co-operation and Development (OECD) guidelines. The LD50 of the *A. tetracantha* ethanolic leaf extract as per OECD guidelines falls under class 4, values with no signs of acute toxicity <LD50> 2000 mg/kg). Hence the dosage was fixed in 100 and 200 mg/kg b.w.

2.2. Animals

Swiss albino mice of both sexes weighing between (18-25 g) were used for the experiment. The animals were kept in clean and dry plastic cages, with 12h: 12h light dark cycle at 25±2°C temperature and 45-55% relative humidity. The animals were fed with standard pellet diet and water was given ad libitum.

2.3. Antipyretic activity [5]

Brewer's yeast induced Pyrexia in Rats

Antipyretic activity on albino rats was studied with fever induced by 20% Brewer's yeast. Albino rats (200-250g) were fed uniformly till 24 hours, and food was withdrawn before giving drugs. After measuring rectal temperature of the rats by introducing 1.5 cm of digital thermometer in rectum, pyrexia was induced by injecting subcutaneously, 20% suspension of dried yeast in 2% gum Acacia in normal saline at a dose of 20 ml/kg of body weight. After 18 hour of yeast injection, rats which showed a rise in temperature of at least 1°C were taken for the study. Animals in the various groups were treated as follows:

Group 1: 3% aqueous suspension of gum Acacia (1 ml/200g) as vehicle, orally.

Group 2: Ethanolic leaf extracts of *A. tetracantha* 100 mg/kg (1 ml/200g) with 3% aqueous suspension of gum Acacia, orally.

Group 3: Ethanolic leaf extracts of *A. tetracantha* 200 mg/kg (1 ml/200g) with 3% aqueous suspension of gum Acacia, orally.

Group 4: Paracetamol 25 mg/kg (1 ml/200g) with 3% aqueous suspension of gum Acacia, orally

Rectal temperature was recorded every hour for four hours after administration of drugs.

3. Results

Effect of ethanolic leaf extract of *A. tetracantha* on rectal temperature in rats is presented in Table 1. The subcutaneous injection of yeast suspension markedly elevated the rectal temperature after 18h of administration. Treatment with *A. tetracantha* extract at a dose of 100, 200 mg/kg decreased the rectal temperature of the rats in dose dependent manner. It was found that the extract at a dose of 100 mg/kg caused significant lowering of body temperature at 4 hour following its administration (36.91 ± 1.15). This effect was maximal at dose of 200-mg/ kg and it caused significant lowering of body temperature ($P < 0.01$) up to 4 hour after its administration (36.16 ± 0.15). The antipyretic effect started as early as 1h and the effect was maintained for 4h, after its administration. Both the standard drug paracetamol 25 mg/kg and tested drug *A. tetracantha* extract were significantly reduced the yeast-elevated rectal temperature, at 2nd, 3rd and 4th hour compared to control group.

4. Discussion

A. tetracantha leaf extract possess alkaloids, flavonoids, tannins, β -sitosterol, terpenes, protein, coumarin, glycosides, protein and starch. The β -sitosterol is a plasminogen activator and promotes the formation of essential polyunsaturated fatty acids from linoleic acid, but linoleic acid is required for prostaglandin and leukotrienes synthesis [6] and thus beta sitosterol reduces prostaglandin and leukotrienes synthesis. β -sitosterol possesses potent anti-inflammatory and antipyretic activity [7] by reducing the secretion of proinflammatory cytokines and alpha-TNF [7, 8]. These phytosterols can enhance adaptive immunity through the stimulation of innate immune system termed as the "adaptogen" which promotes overall health without side effects [9].

In general, non-steroidal anti-inflammatory drugs produce their antipyretic action through inhibition of prostaglandin synthetase within the hypothalamus [10]. The ethanolic, butanolic and petroleum ether extracts of dried leaves of *Pergularia extensa* showed significant antipyretic activity in rats is due to the presence of the phytoconstituents flavanoids, steroids and saponins [11]. Presences of flavonoids were reported in *Dalbergia* species and flavonoids are known to inhibit prostaglandin synthetase [12]. Therefore it appears that antipyretic action of *Dalbergia* species may be related to the inhibition of prostaglandin synthesis in hypothalamus [13]. The antipyretic properties of *Acacia catechu* may be ascribed to the presence of flavonoids [14]. As some flavonoids are predominant inhibitors of cyclooxygenase or lipooxygenase [15, 16].

Chloroform extract of the *Solanum nigrum* leaves exhibited antipyretic activity when assessed against Brewers yeast induced pyrexia test is due to the presence of phyto constituents like

Table 1. Effect of ethanolic leaf extract of *A. tetracantha* on Brewer's yeast induced Pyrexia in Wistar albino rats

Treatment	Dose	Normal Temperature (°C)	Rectal Temperature (°C) 18 hrs after yeast induced pyrexia	Rectal temperature (°C) after treatment with extract			
				1h	2h	3h	4h
Control	-	35.23 ± 0.13	38.08 ± 0.18	38.09 ± 0.16	38.09 ± 0.16	38.09 ± 0.16	38.09 ± 0.16
<i>A. tetracantha</i> ethanolic leaf extract	100 mg/kg	35.49 ± 1.03	37.90 ± 2.10	37.7 ± 1.09	37.03 ± 0.95	36.94 ± 0.04	36.91 ± 1.15
<i>A. tetracantha</i> ethanolic leaf extract	200 mg/kg	35.29 ± 0.23	38.02 ± 0.19	38.04 ± 0.13	37.45 ± 0.10	36.53* ± 0.20	36.16* ± 0.15
Paracetamol	25 mg/kg	35.13 ± 0.25	38.01 ± 0.19	37.9 ± 0.08	37.26 ± 0.07	36.65* ± 0.15	35.88** ± 0.08

Values are expressed as Mean ± S.E, n = 6 by students "t" test

*P < 0.01 Vs control

** P < 0.001 Vs control

steroidal glycosides and steroidal oligoglycosides [17]. *Myrica salicifolia* root extract was found to have analgesic and antipyretic activity in mice. The phytoconstituents responsible for these activity is a variety of flavonoids among which myricitrin is generally considered [18].

The preliminary phytochemical screening of the petroleum ether and chloroform fraction of root of *Laportea crenulata* showed the presence of steroids, tannins and flavonoids [19]. The antipyretic activity of *Laportea crenulata* is due to the presence of steroids [20]. In many studies, flavonoids have been reported to exhibit antipyretic effect [21, 22]. Aqueous extract of *Untica macrorrhiza* a related species of *Laportea crenulata* suppressed yeast induced fever in rats [23]. The dry residue of fresh juice produced significant antipyretic effect in a dose dependent manner. The phytochemical analysis of the dry residue showed the presence of flavonoids, alkaloids, tannins and steroids. The antipyretic activity observed can be attributed to the presence of flavonoids [24].

Isoflavones have antipyretic effects [25]. Kerr and Collaborators 1981 [26], had isolated 12 different flavonoids from *Neurolaena lobata* and suggested that these could be some of the components responsible for *Neurolaena lobata* antipyretic effect. In a similar, but more detailed study was shown that *Pueraria lobata* isoflavones were responsible for the antipyretic activity [27].

5. Conclusion

The results of the present study suggest that the ethanolic leaf extract of *A. tetracantha* in doses of 100 and 200 mg/kg, significantly reduce the temperature of pyretic rats as revealed from the observation that the average percentage of antipyretic activity increased with the concentration of the extracts (200mg/Kg) compared with the control. It is also presumed that the presence of flavonoids may be contributing to antipyretic activities of ethanolic leaf extract of *A. tetracantha* in addition to the analgesic effect, as in the case of many of the established antipyretics.

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