

Antipyretic effect of the ethanol extract obtained from leaves of *Mitragyna parvifolia* on a pyretic model induced by brewer's yeast

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ABSTRACT

The objective of the present study was to investigate the antipyretic activities of ethanol extract of *M. parvifolia* leaves. The antipyretic activity of *M. parvifolia* was studied in Brewer's yeast induced pyrexia in rats. The ethanol extract (25mg/kg, 50mg/kg and 100mg/kg) showed reduction in normal body temperature and yeast provoked elevated temperature in a dose dependant manner. The effect became significant at 60 min at the highest dose of 100 mg/kg. The results suggest that *M. parvifolia* contains biologically-active substances with potential values in the treatment of fever. These provide scientific evidence to support the isolation and development of biologically active components as antipyretic agents.

Key words: *Mitragyna parvifolia*, antipyretic, pyrexia, paracetamol.

INTRODUCTION

Mitragyna parvifolia (Roxb.) Korth (Family: Rubiaceae) is widespread throughout India, in deciduous tree and evergreen forests upto 1200m altitude¹. The bark and root reportedly used to treat fevers and colic among the santhalis, the bark, ground and made into a paste is applied to relieve muscular pain. In Ayurveda, the bark and fruit are used as substitute for those of *Anthocephalus chinensis* (Rubiaceae) to treat burning sensation, poisoning, wounds, gynaecological disorders, cough oedema, to alleviate kapha and pitta, and as an aphrodisiac. In siddha, the stem, bark, leaf, fruit and seed are used as a substitute for those of *Anthocephalus chinensis* to treat eye diseases, dropsy, diseases of vatam and urticaria². *M. parvifolia* has been reported, isolation and identification of some alkaloids N-oxides from the leaves³. Seven alkaloids from the leaves of *M. parvifolia*, from the sagar district of India, were

isolated and the pattern of alkaloid transformation over a period of 12 month is described⁴.

A review of the literature revealed that the antipyretic property of leaves of *M. parvifolia* has not been subjected to scientific evaluation. The present study was carried out in a experimental animal model to reports the antipyretic property on leaves of this plant.

MATERIAL AND METHODS

Plant material

The leaves of *M. parvifolia* were collected from the Putkaphar forest Korba, Chhattisgarh in the month of April. The collected material was authenticated by Dr. P. Jayaraman, Botanist, Plant Anatomy Research Centre (PARC), Chennai. The plant material was also compared with a herbarium specimen maintained at Minor Forest Produce (Trading and Development) Co-Op. Fed. Ltd.,

Shankar Nagar, Raipur, Chhattisgarh, by Expert Medicinal Plant, Mr. S.N.Khotele.

Preparation of extracts

The dried and powdered leaves (300 gm) were successively extracted on a Soxhlet apparatus, employing petroleum ether, chloroform, ethanol and distilled water respectively. The extracts were further concentrated under reduced pressure with a rotary evaporator. Leaves of *M. parvifolia* yielded 2.3%, 3.45%, 13.5% and 12.6% w/w powdered extract with petroleum ether, chloroform, ethanol and distilled water respectively.

Animals

For this study, male wistar albino rats (180-230 g) were employed throughout. They were obtained from the animal facility of Shree Venkateshwara Enterprises, Bangalore and quarantined for 10 days under standard conditions of temperature (27.3°C, 65±10% of relative humidity) and light (12-h light/dark cycle), and fed a standard diet and tap water *ad libitum*. All animals experiments had been approved by our institutional committee (reg. no. CPCSEA/265).

Acute oral toxicity study

Acute oral toxicity was performed by following OECD guideline – 420 fixed dose procedure for ethanolic extract and it was found that dose increasing upto 2000 mg/kg body wt. shown no toxicity or mortality in experimental rats. The LD₅₀ of the ethanolic bark extract as per OECD guidelines – 420 is greater than 2000 mg/kg (5).

Antipyretic studies

The procedure described by Al-Ghamdi (2001) was adopted for this study. The body temperature of each albino Wistar rat was recorded by measuring rectal temperature at predetermined intervals. Albino wistar rats were fasted overnight with water *ad libitum* before the experiments. Pyrexia was induced by subcutaneously injecting 20% (W/V) brewer's yeast suspension (10 ml/kg) into the animal's dorsum region. The rectal temperature of each rat was again recorded after 24 h of yeast administration. Rats that did not show a minimum increase of 0.5 °C in temperature 24 h after yeast injection were discarded. Thirty selected rats were grouped into five and immediately treated as follows: group I received normal saline, group II received 100 mg/kg Paracetamol, while groups III, IV and V received ethanol extracts 25, 50 and 100 mg/kg respectively i.p. Rectal temperature of all the rats was then recorded by inserting digital thermometer ((SK-1250 MC, Sato Keiryoki Mfg. Co., Ltd., Japan) into the rectum of each rat at thirty minutes in Table 1 (6-8).

Statistical analysis

The results are expressed as mean ± SEM of six independent experiments. Statistical significance between group was evaluated by one-way analysis of variance (ANOVA) followed by Turkey's multiple comparison test. A P < 0.05 value was considered as statistically significant.

RESULTS AND DISCUSSION

The extract caused a dose-dependent decrease in rectal temperature. The effect became

Table 1: Antipyretic activity of ethanol extract of *M. parvifolia* on Brewer's yeast induced pyrexia in rats

Treatment	Dose	Rectal Temperature (°C)				
		0.0h	0.5h	1.0h	1.5h	2.0h
Control	-	38.5±0.13	38.6±0.11	38.5±0.21	38.3±0.23	38.1±0.25
Paracetamol	100mg/kg	38.3±0.22	37.6±0.25*	37.3±0.24*	37.3±0.31*	37.2±0.32*
<i>M. parvifolia</i>	25mg/kg	38.31±0.31	38.4±0.22	37.7±0.41	37.7±0.25	37.82±0.23
	50mg/kg	38.2±0.35	38.5±0.41	38.12±0.31	38.02±0.34	37.7±0.323
	100mg/kg	38.1±0.21	38.0±0.43	37.5±0.32*	37.4±0.35*	37.4±0.34*

Results are expressed as Mean ± SEM from six observations, * Significantly different from the control at P<0.05

significant at 60 min at the highest dose of 100 mg/kg. However, Paracetamol caused a significant reduction in rectal temperature (Table 1).

Search for safe herbal remedies with potent antipyretic activity received momentum recently as the available antipyretic, such as paracetamol, aspirin, nimusulide etc. have toxic effect to the various organs of the body. The acute toxicity result reveals that this plant might be considered as a broad non-toxic one. The extract produced a significant reduction in yeast induced pyrexia in rats dose-dependently and its effect is comparable to that of the standard anti-pyretic drug (Paracetamol) used in this study. Pyrexia is a result

of secondary impact of infection, tissue damage, inflammation, graft rejection, malignancy or other diseased states. The infected or damaged tissue initiates the enhanced formation of pro-inflammatory mediators (cytokines like interleukin) which increase the synthesis of PGE₂ near pre-optic hypothalamus area thereby triggering the hypothalamus to elevate the body temperature (9). Most of the anti-pyretic drugs inhibit COX-2 expression thus inhibiting PGE₂ biosynthesis to reduce elevated body temperature. They are however toxic to the hepatic cells, glomerulus, cortex of the brain and heart muscle. A natural PGE₂ inhibitory antipyretic remedy like *M. parvifolia* with minimal toxicity is therefore essential.

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