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ANTIPYRETIC ACTIVITY OF *CRATEVA MAGNA* BARK ON TAB-VACCINE INDUCED PYREXIA

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ABSTRACT

Objective: *Crataeva magna* is a potent medicinal plant in the Indian systems of medicine. Traditionally used for inflammation, fever, arthritis, bronchitis, urinary calculi and cough. The objective of the present work was to study the antipyretic activity of plant *Crataeva magna* (Lour.) DC belonging to family Capparaceae.

Materials & Methods: In the present study the alcoholic extracts of the bark of *Crataeva magna* were studied for their antipyretic activity by TAB (Typhoid) vaccine-induced pyrexia in rabbits.

Result: In TAB vaccine-induced fever, the fever was significantly reduced and the body temperature was normalized by administration of 200 and 400 mg/kg dose orally and the property was comparable to the reference drug.

Conclusion: This study has established the antipyretic activity of *Crataeva magna* and thus, justifies the anecdotal, folkloric and ethnomedical uses of this plant for fever.

Keywords:

Crataeva magna,
Typhoid vaccine,
Hyperpyrexia,
Rabbits,
Antipyretic activity

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INTRODUCTION: *Crataeva magna* (Lour.) DC. (Capparaceae) is a high-value medium sized deciduous medicinal tree of tropical climate found in tropical regions of the world and also grows almost all over India, especially in the semi-arid regions. Medicinal usage has been reported in traditional systems of medicine, such as Ayurveda and Unani, wherein the plant is frequently preferred in the treatment of urinary disorders that reoccur owing to development of antibiotic resistance by the infecting organism^{1, 2}. It has lithotriptic, diuretic, demulcent and tonic properties³⁻⁵.

It is one of the medicinal plants in India, which possess anti-inflammatory and anti-arthritic activity. Various parts of this plant, including the root, stem, flower and leaves are recommended for the treatment of fever in combination and separately. The root juice is given for the relief of fever in whole part of India. It is also useful in disorders of urinary organs, urinary tract infections, pain, intermittent fever, asthma, bronchitis, renal and vesicle calculi. Bark yields triterpenoids (α and β - amyrin, ceryl alcohol, lupeol, friedelin, betulonic acid, 4-taraxasterol, lupenone), flavonoids (rutin, catechin, quercetin) and alkaloids (cadabicine)^{6,7}.

However, it has been best known for its action on urinary calculi and it has an official status in the Indian herbal pharmacopoeia-2002, as an anti-lithiatic drug. There are no scientific studies in support of this traditional claim for its antipyretic activity. In the present communication the alcohol extract derived from the aerial part of *C. magna* was evaluated for its antipyretic activity in experimental animals.

MATERIALS AND METHODS:

Plant Materials: Bark of *Crataeva magna* which was reported to be used against fevers by folk doctors in TamilNadu and bark, were collected in the month of June 2008. The twigs of the plant

along with flowers were submitted and Chief botanist at Department of Botany, St Joseph's college, Trichirappalli, authenticated it. A voucher specimen (PPRL/No.-1596/09A) has been deposited in the herbarium of the Pharmacology Department, Periyar College of Pharmaceutical Sciences, Thiruchirappalli, India.

Preparation of Plant Extract: The barks of *C. magna* were shade dried and powdered, passed in sieve 22. The powdered material was extracted using 95% ethanol in Soxhlet apparatus. The alcoholic extract obtained was filtered and the process was repeated for four days. The resulting filtrates were pooled for further processing. This pooled ethanolic extract was concentrated on rotavapour (Buchi R-114) and subjected to freeze drying in a Lypholizer (Heto Fd 3 drywinner). The dried extract was weighed to calculate the yield. This extract (yield 6.67%) and the dried plant extracts were freshly dissolved or suspended in normal saline prior to before administration.

Animals: White rabbits (1.50-2.0 g) of either sex, maintained in the Animal Experimental Laboratory of Periyar College of Pharmaceutical Sciences, at room temperature of $25 \pm 2^\circ\text{C}$, relative humidity of $75 \pm 5\%$ and 12 h dark-light cycle. Food and water were given *ad libitum*. The project was approved by Institute Animal Ethical Committee. Each experimental group consisted of six animals housed in separate cages. The animals had access to standard laboratory feed (M/s. Hindustan Lever Ltd.)

TAB vaccine-induced pyrexia: This was studied in rabbits. The animals were maintained in the laboratory for 24 h prior to the experiment⁸. The antipyretic activity was assessed by the method of TAB (Typhoid) vaccine-induced pyrexia with some modification⁹. In this method the rabbits were divided into groups, each group consisted of six animals. The control group was treated with 2

ml/kg of saline. The normal rectal temperature of a group of rabbits was recorded by a telethermometer at hourly intervals for a period of 4 h. TAB vaccine was administered intravenously into the marginal ear vein of rabbits at a dose of 0.5 ml/rabbit. *C. magna* was administered orally in doses of 100 and 200 mg/kg, 60 min after TAB vaccine when there was significant pyrexia. Subsequently, the rectal temperature was recorded every 30 min up to 3 h. Paracetamol 100 mg/kg (po) was used for comparison.

Statistical analysis: The significance of difference among the various treated groups and control group were analyzed by means of one-way ANNOVA followed by Dunnett's multiple comparison tests using Graphat Instat Software

(SanDiego, CA, USA) $p < 0.05$ accepted as significant. The experimental results are represented as mean \pm SEM (standard error mean). Student's *t*-test was used

RESULTS AND DISCUSSION: In the preliminary phytochemical screening *C.magna* revealed the presence of alkaloids, terpenoids, phytosterols, flavonoids and flavonones. Several traditional claims, the usefulness in pain, inflammation and fever have been emphasized more in literature¹⁰. Hence, *C.magna* was considered that investigations for these medicinal properties may give scientific authentication to the traditional claims. **Table 1** shows the antipyretic activity of *C.magna* on TAB Vaccine induced hyperpyrexia in experimental white rabbits.

TABLE 1: ANTIPIRETIC EFFECT OF ALCOHOLIC EXTRACT OF C. MAGNA BARK ON TAB VACCINE INDUCED HYPERPYREXIA IN RABBITS

Treatment & Dose	Basal °C	°C 2 hrs after TAB Vaccine	° C after treatment with drugs/hr			
			1 st hr	2 nd hr	3 rd hr	4 th hr
Control (saline) 1ml/100 gm	35.2 \pm 0.13	38.28 \pm 0.30	37.71 \pm 0.10	37.33 \pm 0.15	37.26 \pm 0.31	37.11 \pm 0.07
<i>C. magna</i> 150 mg/kg, p.o.	35.6 \pm 0.21	38.06 \pm 0.34	38.01 \pm 0.28	37.75 \pm 0.18	37.26 \pm 0.48	36.16 \pm 0.11*
<i>C. magna</i> 300 mg/kg, p.o.	35.92 \pm 0.18	38.25 \pm 0.38	38.12 \pm 0.36	37.88 \pm 0.79	36.91 \pm 0.24*	35.96 \pm 0.39**
Paracetamol 100 mg/kg, p.o.	35.3 \pm 0.14	38.01 \pm 0.29	37.96 \pm 0.45	37.15 \pm 0.13	36.36 \pm 0.13*	35.45 \pm 0.23**

Values are expressed as mean \pm SEM of six animal per group (n=6). * $p < 0.05$, ** $p < 0.001$ significant when compared with reference drug paracetamol

When the extract was administered to rats with established TAB vaccine-induced fever, the fever was significantly reduced and the body temperature was normalized by administration of 150 and 300mg/kg dose intraperitoneally. However, 100mg/kg dose of extract had no effect on the rectal temperature of rabbits (Not shown). The response in higher doses was almost comparable to that of paracetamol.

TAB vaccine is a sterile suspension, 1ml containing 1×10^9 *S. typhi* and 7.5×10^8 each of *S. paratyphi* A and B organisms in 5 and 10ml vials. It is probable that the TAB induced hyperpyrexia indirectly by causing release of endogenous pyrogen. It was of interest to note that the extracts

of *C. magna* aerial parts produced a rather modest decrease in the body temperature in hyperthermic rats. Regulation of body temperature requires a delicate balance between the production and loss of heat, and the hypothalamus regulates the set point at which body temperature is maintained. The cause of this decrease may be central and/or peripheral in origin. Clinically available antipyretic drugs, such as paracetamol and the non-steroidal anti-inflammatory drugs are able to lower the body temperature only in feverish patients. In general, non-steroidal anti-inflammatory drugs produce their antipyretic action through inhibition of prostaglandin synthetase within the hypothalamus^{11, 12}. Therefore, it appears that the antipyretic action of the extract may also be related to the

inhibition of prostaglandin synthesis. It is one of the medicinal plants in India which possess anti-inflammatory and anti-arthritic activity.

The antipyretic effect of *C. magna* indicated a likelihood of intervention with prostaglandin synthesis, as prostaglandins have been established as a common mediator in all these responses. However, this possibility remains to be investigated in detail. Moreover, the active compounds responsible for these pharmacological actions also remain to be identified. This result seems to support the view that the plant has some influence on prostaglandin biosynthesis, since prostaglandin is believed to be a regulator of body temperature¹³.

The preliminary phytochemical analysis reveals that the major chemical Constituents of the alcoholic extract of *C. magna* are terpenoids and flavonoids. The major chemical components of *C. magna* are known to be betulinic acid, lupeol, 4-taraxasterol, rutin and quercetin. Thus phytochemicals found in alcoholic extract, which might be responsible for the antipyretic activity. Thus, the results of the present study provide support to the traditional usage of *C. magna* in fever, even if further studies are needed to better evaluate these activities and the potential of the plant.

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