Antipyretic activity of *Cardiospermum halicacabum*

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*Cardiospermum halicacabum* extracts have been evaluated for their antipyretic activity against yeast-induced pyrexia in rats. The ethanol as well as n-hexane extracts (400 mg/kg) of the whole plant powder showed potent antipyretic activity. The water extract was devoid of significant activity. The antipyretic activity of the ethanol extract was concentration dependent.

In India, numerous invaluable plants are used in ethnomedical practices as well as in Ayurveda and Siddha. The pharmacological properties of many of these plants are not sufficiently evaluated in the light of modern science. One such plant is *Cardiospermum halicacabum* Linn. (Sapindaceae)`. In Ayurveda it is known as Karnasphota (synonymous: Kakathikta). The local vernacular name is uzhinja (Malayalam). *C. halicacabum* is a herbaceous twiny climber which is found throughout the plains of India`. This plant is used in Ayurveda and folk medicine for the treatment of rheumatism, lumbago, ear-ache, fever, etc.2 It has been investigated for various pharmacological actions in animal models3-5. The plant possesses significant analgesic, anti-inflammatory and vasodepressent activities3-5. The reported chemical constituents of the plant leaf include tannins, saponins and traces of alkaloids5.

Although this plant is used in traditional medicine to combat fever, its antipyretic effect has not been experimentally evaluated. Therefore, the present study was undertaken to determine the antipyretic effect of the plant's extracts against yeast-induced pyrogenesis in rats. The most commonly used antipyretic agent, paracetamol was used as a reference standard.

**Plant material—** *Cardiospermum halicacabum* was collected from the herbal garden of Regional Research Institute, Poojappura, Thiruvananthapuram and authenticated by the senior author. A voucher specimen was deposited in the herbarium of Tropical Botanic Garden and Research Institute. The whole plant was cut into small pieces, air-dried at room temperature and powdered.

**Preparation of extracts**—The plant powder (25g) was soxhlet-extracted with 350ml of absolute ethanol. The alcohol extract was evaporated to dryness at reduced temperature and pressure in a rotary evaporator to obtain the crude extract. (The yield of the alcohol extract was about 10%). The dried extract was suspended in 5% Tween 80 for the experiments. For the preparation of n-hexane extract also, the above procedure was followed. (The yield of n-hexane extract was 2.8%). For the water extract, 25 g of the powder was stirred continuously in 350 ml distilled water for 6 hr at room temperature, filtered and the filtrate was used for the experiments. (Tween 80 was added to the extract to make it in 5% Tween 80). This was done to facilitate comparison with alcohol and n-hexane extracts. The yield of the water extract was about 16%. This was determined in separate experiments by drying the extract to constant weight at 70°C.

**Paracetamol**—The standard antipyretic drug, paracetamol (Calpol, Burroughs Wellcome, India Ltd.) was suspended in 5% Tween-80 and used for comparison.

**Animals**—Adult male Wistar rats (150-200g.) obtained from the animal house of Tropical Botanic Garden and Research Institute, Palode, Thiruvananthapuram were used for the experiments. They were
maintained under standard laboratory conditions. Food (commercial pellet diet; Lipton, India) and water were given ad libitum.

*Yeast-induced pyrexia in rats*—Pyrexia was induced in rats by subcutaneously injecting a homogenised suspension of 12.5% yeast in normal saline at a dose of 1ml/100g body weight. The test was carried out in an air conditioned room (24°-26°C). The rectal temperature was recorded with a fine clinical thermometer, keeping the animal in a special restrained cage. The initial rectal temperature was taken and the pyrogen was injected. After the injection the temperature readings were recorded at 1, 2, 3, 4, 5 and 18 hr. The control group received normal saline in an identical manner. The percentage of pyrexia was calculated in each case.

**Determination of the antipyretic effects of C. halicacabum**—To determine the efficacy of various extracts (water, ethanol and n-hexane) of *C. halicacabum* in preventing yeast-induced pyrogenesis, yeast was administered to 4 groups of rats, after recording initial temperature. Immediately after yeast administration, each extract (in 5% Tween 80) was administered orally to a group of 6 rats at a dose of 400 mg/kg (1ml/rat). The control (pyrogen treated) rats received 1 ml 5% Tween 80 in an identical manner. The temperature was recorded at 1 hr intervals for 4 hr. To study the effect of various doses of the alcohol extract on the pyrogenesis, rats were divided into 5 groups of 6 animals each. After recording initial temperature, yeast was administered to all rats. Immediately after the pyrogen injection, Group I rats received 1 ml of 5% Tween 80 (po) and served as control. Groups II, III and IV were treated with 100, 200 and 400 mg/kg of the alcohol extract (in 5% Tween 80; 1 ml/rat) respectively. Group V received paracetamol (100 mg/kg; in 5% Tween 80, 1 ml/rat). The rectal temperature was recorded at 1 hr intervals for 3 hr.

To find out the efficacy of the alcohol extract, when administered 2 hr after pyrogen injection (after the development of fever), rats were divided into 4 groups, 6 animals in each group. Group I received the vehicle (5% Tween 80) and served as control (pyrogen treated). Groups II and III received 100 and 400 mg, respectively of the extract; group IV received 100 mg/kg paracetamol. The drugs (or vehicle) were administered 2 hr after pyrogen administration. The rectal temperature was recorded at 1 hr intervals for 4 hr after pyrogen injection.

**Acute toxicity and general behavior studies**—Doses of 100, 200, 400 and 800mg/kg of the alcohol extract of *C. halicacabum* were administered (po) to different groups of overnight fasted rats. They

![Fig. 1—Effect of yeast (pyrogen) administration on changes in rectal temperature with time in rats. Values are mean ± SD. n=6.](image)
were observed for mortality and gross behavioural changes continuously for 1 hr and intermittently for the next 6 hr and then again at 24 hr after dosing. The parameters observed were convulsion, hyperactivity, sedation, grooming, loss of righting reflex and increased respiration.

Statistical analysis—Values are expressed as mean ± S.D. Students 't' test was used to determine the significance of the difference of the mean of each group compared to control.

Yeast-induced pyrexia in rats reached a peak at 3 hr and then it slowly declined (Fig. 1). The increase in rectal temperature at 3 hr after pyrogen administration was about 3°F whereas that at 18 hr was 1.5°F (Fig. 1).

The effect of administration of C. halicacabum extracts immediately after the pyrogen injection on the pyrogenesis is given in Figs 2 and 3. All the ex-
Table 1—Effect of Cardiospermum halicacabum (ethanol extract) on yeast induced pyrexia in male albino rats

<table>
<thead>
<tr>
<th></th>
<th>Temperature in °F after pyrogen treatment (hr)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>0 (initial)</td>
</tr>
<tr>
<td>Control</td>
<td>99.9±.36</td>
</tr>
<tr>
<td></td>
<td>100 mg/kg</td>
</tr>
<tr>
<td>C. halicacabum</td>
<td>99.6±.45</td>
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<tr>
<td>100 mg/kg</td>
<td>[2.3]</td>
</tr>
<tr>
<td>400 mg/kg</td>
<td>99.8±.44</td>
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<tr>
<td></td>
<td>[2.2]</td>
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<tr>
<td>Paracetamol</td>
<td>99.7±.42</td>
</tr>
<tr>
<td>100 mg/kg</td>
<td>[2.2]</td>
</tr>
</tbody>
</table>

Drugs were administered 2 hr. after pyrogen administration. Time after drug administration is given in round parentheses. Values are mean ±SD of 6 animals in each group.

Values in [ ] represent % change in temperature.

** P < .01; * P < .05

extracts showed varying levels of antipyretic activity at 400 mg/kg. The alcohol extract was the most active which was closely followed by the n-hexane extract. The water extract was the least active (Fig. 2.). The alcohol extract remarkably controlled the pyrogenesis in a concentration dependent manner (Fig. 3). This effect of the plant drug (100 mg/kg) was almost comparable to that of paracetamol for the initial period of 2 hr. However, in the 3rd hr, the antipyretic effect of the extract declined as judged from the rise in temperature from the 2nd to 3rd hr (Fig. 3).

The extract, when administered 2 hr after pyrogen administration (after the development of fever), also showed a significant antipyretic activity (Table 1). The antipyretic activity observed at a higher dose (400 mg/kg) was significantly more than that at a lower dose (100 mg/kg). The efficacy of 100 mg/kg paracetamol was almost equal to that of 400 mg/kg of the extract at 2 hr after the drug treatment. (Table 1).

In the acute toxicity study, no mortality occurred within 24 hr in any of the doses of the plant extract studied. The LD₉₀ was, therefore, greater than 800 mg/kg, p.o. in rats. Besides, the treated animals did not show any changes in the general behavioural parameters observed during the 24 hr observation period.

Yeast-induced pyrexia is a classical method of testing antipyretic activity. Using this method several investigators recorded pyrexia 18 or 15 hr after yeast injection and then they administered the antipyretic drugs to be studied. In the present study the pyrexia observed at 18 hr after the pyrogen administration was almost 50% less than that at 3 hr. Pyrexia was also observed at 2 or 3 hr after the pyrogen injection in two recent studies⁷,⁸.

The present study reports for the first time the antipyretic activity of C. halicacabum extracts. This herbal drug is used in traditional medicine from time immemorial without any known adverse effects. Besides, our acute toxicity study did not show any toxic symptoms. C. halicacabum is readily available throughout India and can be developed into a phytopharmacology to combat common fevers.

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1. The wealth of India raw materials Vol II (Council of Scientific and Industrial Research New Delhi), 1950, 73.