ANTI-PYRETIC ACTIVITY OF ETHANOLIC EXTRACT OF MERREMA EMARGINATA (BURM. F) HALLIER F. IN RAT

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Abstract:
Pyrexia is the increase of body temperature than the normal due to metabolic disturbances. Antipyretic drugs are widely used in the treatment of fever and pain. But the greatest disadvantage in presently available synthetic drugs is that they cause gastrointestinal irritation and reappearance of symptoms after discontinuation. Merremia emarginata (Burm. f) Hallier f. (Convolvulaceae) is a perennial, much branched herb. In the indigenous system of medicine, Merremia emarginata has been claimed to be useful for cough, headache, neuralgia, rheumatism, diuretic, treatment of inflammation, epilepsy, troubles of nose etc. The ethanolic extract of the plant was prepared and screened for antipyretic activity. The acute toxicity studies also carried out. pyrexia was induced using cow’s milk 2ml/kg i.p.. The test drug M.emarginata at a dose of 200mg/kg i.p possessed significant antipyretic activity. The activity was very comparable to standard drug paracetamol 150 mg/kg i.p.

Keywords: pyrexia, ethanolic extract, paracetamol, rats and temperature.

Introduction
Pyrexia is the increase of body temperature than the normal due to metabolic disturbances [1]. Antipyretic drugs are widely used in the treatment of fever and pain. But the greatest disadvantage in presently available synthetic drugs is that they cause gastrointestinal irritation and reappearance of symptoms after discontinuation [2]. Merremia emarginata (Burm. f) Hallier f. (Convolvulaceae) is a perennial, much branched herb (creeper). Stems rooting at nodes, becoming tuberculate. Petiole 0.2-3.7 cm; leaf blade reniform to broadly ovate, 0.5-3.5 X 0.6-3.5 mm, glabrous or sparsely appressed pilose, base cordate, margin entire or coarsely crenate, apex obtuse to broadly rounded or slightly emarginated. Inflorescences sub sessile, 1(-3)-flowered; bracts unequal, ovate to linear, pubescent, apex acute. Seeds are grayish brown. Stems roots at the nodes, and is 10 to 80 cm in length. Leaves are small, kidney-shaped to somewhat heart-shaped, 6 to 15 mm long, often wider than long, and irregularly toothed. Flowers, one to three, occur in short stalks in the axils leaves. Sepals are rounded, about 4 mm long, with few too many white, weak hairs. Corolla is yellow, nearly twice as long as the calyx. Capsule is rounded and about 5 mm in diameter (www.efloras.org ).

It is found widely distributed all over the India, especially in damp places in upper gangetic plain, Gujarat, Bihar, West Bengal, Western- Ghats, ascending up to 900m in the hills, Goa, Karnataka in India, Ceylon and Tropical Africa [3-5]. Merremia emarginata is also known as ipomoea reniformis chois. In India it is known by various names in different regions viz., mooshakarni in Sanskrit, Underakani in Gujarat, Toinuatali in Telugu, Mushkani in Hindi, Goromusha in Persian, Paerattae-kirae in Tamil, Yellikkadukirai in Madras [6-10]. In the Philippines, decoction of leaves and tops used as diuretic. Leaves used as alterative; used in rheumatism and neuralgia. Also used for coughs and headache. In India, leaf juice given for migraine; also used as ear drops to relieve abscesses and ulcers. Root is used to treat diseases of the eyes and gums. In India, leaves eaten as greens. Young
leaves are fried with groundnut oil and other spices and used with bread, called “Roti” made from Sorghum flour. Leaves are also used in soups. [8,9,4,10,11,5]. Juice acts as purgative and the root is having diuretic, laxative, and applied in the disease of the eyes and gums. A little pharmacological investigation has been carried out on this plant. But a lot more can still be explored and utilized. The extract had spasmylytic action on guinea pig ileum but hypotensive effect not influenced by atropine sulphate in cats. The alcoholic extract appeared to be more musculotropic than neurotropic. (Aswal BS et al.,1984) [12], showed that the 50% ethanolic extract of Merremia emarginata (whole plant excluding roots) was screened for anti protozoal, anti viral, diuretic and effects on CVS, CNS and smooth muscles and was found inactive. EK Elumalai et al,[13], 2011 studied the aqueous and alcoholic extract of Merremia emarginata which showed antibacterial effect.

MATERIALS AND METHODS
Preparation of plant material:
The fresh samples of Merremia emarginata (Burm. f.) Hallier. Was collected from Villianur area of Puducherry during the month of February 2011 with help of Dr.A.Muthuvel, R.S. M.P., D.H.S., D.S.M. The voucher specimen of the plant is deposited in the Department of Pharmaceutical Analysis, College of Pharmacy, Mother Theresa Post Graduate and Research Institute of Health Sciences, Puducherry for the future references.

Preparation of plant extract:
The leaves were dried under shade and powdered by the help of mechanical process. The powder leaves have stored in airtight container for further studies. The powdered material (40g) was extracted in a Soxhlet apparatus using solvent 80% aqueous ethyl alcohol by continuous hot percolation technique for about 72 hrs. Temperature was maintained on an electric heating mantel with a thermostat control. The extract was then concentrated to 3/4th of its original volume by distillation. The concentrated extract was then transferred to a china dish and evaporated on a thermostat controlled water bath till it formed a thick paste. This thick mass was vacumm dried in desicator till it free from moisture. The concentrated aqueous ethanolic extract is 7g.

Animals:
The experiment was carried out on albino rats, weighing between 120-180gm. The animals were adapted to lab conditions for 7 days prior to the experiment free access to water. Number of rats in each group was five and divided into three groups.
1. Negative control (received normal saline 10ml/kg)
2. Positive control (Paracetamol 150mg as standard antipyretic agent).
3. Test control (Merremia emarginata 200mg/kg).

Acute Toxicity Studies
Acute toxicity study was conducted on mice to determine the minimum lethal dose of the drug. Swiss albino mice of either sex weighing between 20-25 g fasted overnight was used for the study. The test drug at the dose of 2 g/ Kg was given. The animals were observed for 24 hrs for symptoms like difficulty in breathing, sedation, decreased motor activity etc. The animals did not show any above said symptoms or any other toxic effects. No mortality was observed for 3 days, so it was found to be safe dose. A stock solution of 40mg/ml of alcoholic extract of the drug was prepared with distilled water.

Effect of Alcoholic Extract of M.Emarginata on Milk Induced Pyrexia in Rats
Before experiment rectal temperature of rat were recovered by inserting a bulb of digital thermometer in the rectum. Care was taken to insert it to the same depth each time. Milk was collected from local cow been boiled. When temperature of the boiled milk equilibrates to room temperature then rats were injected boiled milk at the dose of 2ml/kg (intraperitoneal route) body weight to induce pyrexia. Induction of fever was taken about in one to two hours. The aqueous ethanolic extract (200mg/kg, intraperitoneal route) was given on experimental
group; standard antipyretic agent paracetamol (150mg/kg, intraperitoneal route) was taken as positive control. Finally rectal temperatures were recorded for 3 hrs at consecutive time intervals.

**Results and Discussion:**
The tested drug *M. emarginata* (200 mg/Kg, i.p) did not show any toxic effect at the dose of 2g/kg. Hence the drug was found to be safe to use. It also possessed significant antipyretic activity which was very comparable to standard drug paracetamol(150mg/kg, i.p.). Pyrexia or fever is caused as a secondary impact of infection, malignancy or other diseased states. It is the body’s natural defence to create an environment where infectious agent or damaged tissue cannot survive [14]. Normally the infected or damaged tissue initiates the enhanced formation of pro-inflammatory mediator’s (cytokines like interleukin 1beta, alpha, beta and TNF- alpha), which increase the synthesis of prostaglandin E2 (PGE2) near peptic hypothalamus area and thereby triggering the hypothalamus to elevate the body temperature.[15] 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 increase 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 [16,]. Most of the antipyretic drugs inhibit COX-2 expression to reduce the elevated body temperature by inhibiting PGE-2 biosynthesis. Moreover, these synthetic agents irreversibly inhibit COX-2 with high selectivity but are toxic to the hepatic cells, golmeruli, cortex of brain and heart muscles, whereas natural COX-2 inhibitors have lower selectivity with fewer side effects [17]. A natural antipyretic agent with reduced or no toxicity is therefore, essential. As the plant had many pharmacological activity it was screened for antipyretic activity too. It also showed significant antipyretic activity. Hence it was an effective alternative medicine as antipyretic agents to synthetic drugs.

**REFERENCES**
1. www.bbc.co.uk/health/physical_health/conditions/fever1.shtml
10. Warden, H.J, Hooper, D, Bishen Singh, (1890), Pharmacographia Indica, 2, Delhi, 539.

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TABLE – 1: EFFECT OF ALCOHOLIC EXTRACT OF M.emarginata ON MILK INDUCED PYREXIA IN RATS

<table>
<thead>
<tr>
<th>SL. No</th>
<th>DRUG &amp; DOSE</th>
<th>RECTAL TEMPERATURE (°C) Before Treatment</th>
<th>After induction of Pyrexia</th>
<th>Temperature after Treatment (°C) 30 min 1 hr 2 hr 3 hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Normal Saline (0.1ml/10g, i.p.)</td>
<td>36.38± 0.07</td>
<td>40.62± 0.21</td>
<td>40.62± 0.30 40.34± 0.40 40.48± 0.34 40.44± 0.32</td>
</tr>
<tr>
<td>2</td>
<td>Paracetamol (150 mg/Kg, i.p.)</td>
<td>36.26± 0.18</td>
<td>40.08± 0.37</td>
<td>40.38± 0.19 37± 0.17* 36.84± 0.16** 36.09± 0.18**</td>
</tr>
<tr>
<td>3</td>
<td>M.emarginata (200 mg/Kg, i.p.)</td>
<td>36.44± 0.22</td>
<td>39.46± 0.26</td>
<td>38.8± 0.34 37.74± 0.75* 37.34± 0.20** 36.74± 0.10**</td>
</tr>
</tbody>
</table>

Values are given as mean ± S E M, n =5, *P > 0.01, ** P > 0.001 using student’t’ test