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ANTI-PYRETIC EFFECT OF *FLACOURTIA JANGOMAS* EXTRACT IN BREWER'S YEAST-INDUCED PYREXIA IN RATS

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Abstract

Objective: To evaluate the effect of methanolic extract of *Flacourtia jangomas* (MEFJ) leaf and stem in brewer's yeast-induced pyrexia in rats

Methods: Pyrexia was induced by subcutaneously injecting 20% w/v brewer's yeast suspension (10ml/kg) into the animal's dorsum region (below the nape of the neck). 18h after the injection, the rectal temperature of each rat was measured using a digital thermometer (HICKS, digital thermometer with beeper). Only rats that showed an increase in temperature of at least 0.7℃ were used for experiments. MEFJ (100mg/kg, 200mg/kg and 400mg/kg b.w.) or paracetamol (150mg/kg b.w.) or vehicle was administered orally and the temperature was measured at 1, 2, 3, and 4h after treatment.

Results: The methanolic extract (200, 400mg/kg) of *Flacourtia jangomas* significantly reversed yeast induced fever at 1, 2, 3 and 4 hr, while at 100mg/kg dose shown both significant and non-significant action. The reference drug paracetamol (150mg/kg) also suppressed fever induced by yeast in rats. Methanolic extract did not show any toxicity and mortality up to maximum dose of 2000 mg/kg of body weight. Phytochemical screening revealed the presence of flavonoids, saponins and carbohydrate, Tannins and Phenolic Compounds in methanolic extract.

Conclusion: The result of the present study concludes that the MEFJ shown significant antipyretic activity. Further investigations are required to isolate the active constituents responsible for this activity and to elucidate the exact mechanisms of action.

Key words: Brewer's yeast, Pyrexia, *Flacourtia jangomas*,antipyretic

Introduction:

Pyrexia or fever is caused as a secondary Impact of infection, tissue damage, inflammation, graft rejection, malignancy or other diseased states. (Spacer CB & Breder CD, 1994).

Pyrogens act on the hypothalamus, which releases prostaglandins that reset the hypothalamic thermostat to a higher temperature. (Anne Waugh *et al*, 2001).

Fever occurs due to bacteremia. It is thought to be mediated through release of factors like prostaglandin, interleukin-1, tumer necrosis factor in response to infection. (Harsh Mohan, 2005).

Most of the antipyretic drugs inhibit COX-2 expression to reduce the elevated body temperature by inhibiting PGE-2 biosynthesis. 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. (Cheng, L.et al 2005)

A natural antipyretic agent with reduced or no toxicity is therefore, essential.

Flacourtia jangomas(family Flacourtiaceae), is large shrubs or small trees, 5–10 m tall, deciduous; trunk and older branches usually unarmed, young branches with simple or divaricate spines; bark yellow-brown, reddish brown, or light brown, flaky; young branches smooth, glabrous or sparsely pubescent, lenticellate. (Qiner Y, Zmarzty S 2007). The fruit, stem bark and bark yielded a coumarin, ostruthin. (Khare CP 2007) Infusion of bark is used as a gargle. (Prajapati narayan das and Kumar U. 2003)Bark, leaves, fruits are used as refrigerant. (Joy PP 2008) The fruit is sweetish at first and then sour; stomachic, alexipharmic; helps digestion and allays thirst; useful in biliousness; dispels "tridosha" and other fevers; removes "vata" (Ayurveda). (KR Kirthikar and BD Basu 1993)

Materials and methods

Animals

Normally healthy adult Wistar strain rats of either sex weighing of 150-200gm were used in the experiment. Animals maintained under standard environmental conditions, were fed with a standard diet and water ad libitum. The animals were fasted for 18h prior to the experimentation, but allowed free access to water only.

The experimental protocol has been approved by the Institutional Animals Ethics committee (Reg. No. 003/2009/IAEC/jnu.)

Drugs and Chemicals

Brewer's yeastused as a pyrogen for producing pyrexia;Paracetamol, a standard anti-pyretic agent and Sodium chloride (Quqligens Fine Chemicals A division of GlaxoSmithKline pharmaceutical Ltd. Mumbai) were used in this study.Other chemicals used for extraction purpose and phytochemical tests were of laboratory grade.

Collection and authentication of plant

Leaves and stem of plant were collected from local region of Kushinagar, District of Gorakhpur, India in the month of March 2009. The botanical identity was confirmed by a taxonomist Prof Kamal, Department of Botany; Gorakhpur University, Gorakhpur where voucher specimen (No. GU0309186) has been deposited for further reference.

Preparation of methanolic extract

The leaves and stem of *Flacourtia jangomas* were washed, shade dried and powdered. The powdered material was defatted with petroleum ether (60-80 ºC) and then extracted with methanol in Soxhlet apparatus (40 cycles). The extract was concentrated for further studies at reduced pressure and temperature in a rotary evaporator. Methanolic extract of *Flacourtia jangomas* (MEFJ) was tested for presence of secondary metabolites by different phytochemical tests.

Preliminary phytochemical screening

Standard screening test of the extract was carried out for various plant constituents. The crude extract was screened for the presence or absence of secondary metabolites such as alkaloids, carbohydrate, phenolic compounds, flavonoids, saponins and tannins by using standard procedures. (Khandelwal KR 2005; Kokate C K 1997)

Acute toxicity test

Acute oral toxicity study for the test extract of the plant was carried out using OECD/OCED guideline.

*Limit Test at 2000 mg/kg:*Dose 2000mg/kg body weight was administered orally to one animal. This first test animal survived. Since, four other animals were dosed (orally) sequentially, so that a total of five animals were tested. Animals are observed individually at least once during the first 30 minutes after dosing, periodically during the first 24 hours (with special attention given during the first 4 hours), and daily thereafter, for a total of 14 days. No animals were died. So the LD50 is greater than 2000 mg/kg. (OECD guidelines 2006)

Anti-pyretic activity

Brewer's yeast-induced pyrexia in rats

Requirements

1. Brewer's yeast
2. Digital thermometer
3. Paracetamol

Study design

For this activity rats that showed an increase in temperature of at least 0.7℃ were divided into 5 groups of six animals in each group:

Group I – Negative Control received Vehicle (10ml/kg)
Group II – Positive control received Standard drug (paracetamol 150mg/kg)
Group III – Test group received MEVV (100mg/kg).
Group IV – Test group received MEVV (200mg/kg).
Group V – Test group received MEVV (400mg/kg).

Procedure

Antipyretic activity was measured by slightly modifying the method described by S. Mahesh et al., 2009 and Patra1 A. et al., 2009. Rats were fasted overnight with water *ad libitum* before the experiments. Pyrexia was induced by subcutaneously injecting 20% w/v brewer's yeast suspension (10ml/kg) into the animal's dorsum region (below the nape of the neck). 18h after the injection, the rectal temperature of each rat was measured using a digital thermometer (HICKS, digital thermometer with beeper). Only rats that showed an increase in

temperature of at least 0.7℃ were used for experiments. MEFJ (100mg/kg, 200mg/kg and 400mg/kg b.w.) or paracetamol (150mg/kg b.w.) or vehiclewas administered orally and the temperature was measured at 1, 2, 3, and 4h after treatment.(Paschapur MS et al., 2009; Patra A et al., 2009)

Statistical analysis:

The results are expressed as mean ± SEM of 6 animals. Parametric data were assessed by the method of analysis of one- way ANOVA followed by Dunnett's test. P< 0.05 was considered as statistically significant whereas P>0.05 was considered as non-significant (ns).

Results

Preliminary phytochemical screening: Phytochemical screening revealed the presence of flavonoids, saponins and carbohydrate, Tannins and Phenolic Compounds in methanolic extract.

Acute toxicity:

Methanolic extract did not show any toxicity and mortality up to maximum dose of 2000 mg/kg of body weight. Common side effects such as mild diarrhea, loss of weight and depression were not recorded.

Anti-pyretic activity

The methanolic extract (200, 400mg/kg) of *Flacourtia jangomas*significantly reversed yeast inducedfever at 1, 2, 3 and 4 hr, while at 100mg/kg dose shown significant and non-significant action. The reference drug paracetamol (150mg/kg) also suppressed fever induced by yeast in rats, given in Table 1 and Figure 1.

Table 1:

Effect of MEFJ on Brewer's yeast-induced pyrexia in rats:

Drug	Dose (mg/kg)	Rectal temperature in °C at time (h) -18[a]	0[b]	1	2	3	4
Control	……	36.84±0.08	37.74±0.04 (0.90)[C]	37.81±0.02	37.74±0.03	37.71±0.04	37.73±0.06
Extract	100	36.88±0.12	37.86±0.16 (0.98)[C]	37.64±0.04[NS]	37.52±0.05[*]	37.49±0.05[NS]	37.39±0.08[*]
	200	36.76±0.08	37.81±0.1 (1.05)[C]	37.61±0.06[*]	37.46±0.08[**]	37.21±0.09[**]	36.97±0.1[**]
	400	36.91±0.11	37.82±0.02 (0.91)[C]	37.56±0.06[**]	37.43±0.06[**]	37.05±0.1[**]	36.98±0.07[**]
Paracetamol	150	36.98±0.1	37.87±0.18 (0.89)[C]	37.51±0.06[**]	37.41±0.06[**]	37.01±0.07[**]	36.99±0.1[**]

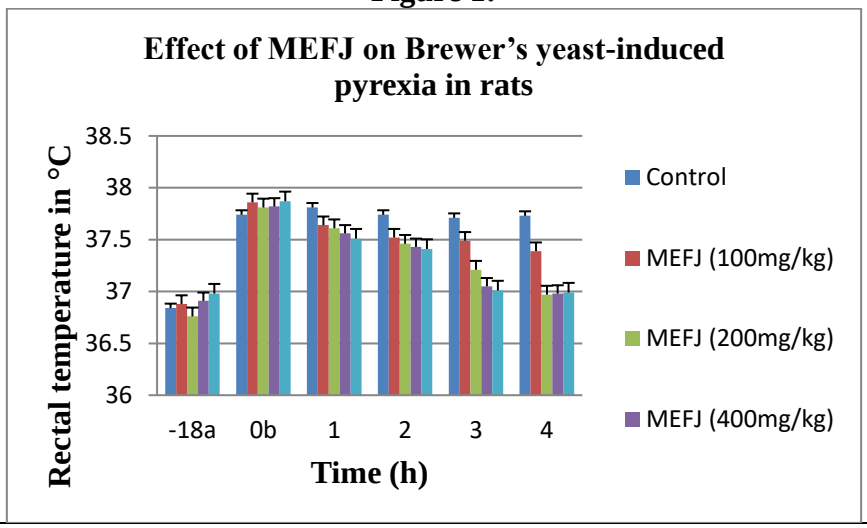
n: six animals in each group; Values are mean + SEM. [NS]P>0.05, *P<0.05, **P<0.01, when compared to control.

a: temperature just before yeast injection

b: temperature just before drug administration

c: change in temperature following yeast injection

Figure 1:



a: temperature just before yeast injection
b: temperature just before drug administration

Discussion

Search for herbal remedies with potent antipyretic activity received momentum recently as the available antipyretics, such as paracetamol, nimesulide etc. have toxic effect to the various organs of the body. (Chattopadhyay D et al., 2005)

It is well known that pyretic activity involves stimulation of the region in the hypothalamus that control body temperature; via prostaglandins synthesized within the central nervous system and that the blood-brain barrier prevents drug molecules or other chemicals from entering the central nervous system. Several investigators have used this method to record pyrexia 15 to 18 hrs, after yeast injection, and then administered the antipyretic drugs to be studied.**(**Sabina EP et al., 2009)

Usually most anti-inflammatory and analgesic drugs possess antipyretic activity. In general,non-steroidal anti-inflammatory drugs produce their antipyretic action through the inhibition of prostaglandin synthetase within the hypothalamus. (Hayare SW et al., 2000)

Therefore, the antipyretic activity of MEFJis probably by inhibition of prostaglandin synthesis in hypothalamus.

Conclusion

The result of the present study concludesthat the MEFJshown significant antipyretic activity. Further investigations are required to isolate the active constituents responsible for this activity and to elucidate the exact mechanisms of action.

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