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Pharmacological Evaluation of Anti-pyretic Activities of *Averrhoa carambola* Fruit Extract

Raj Kumar Singh Bharti*1, Shivam2, Amit Kumar3, Neha Rahi4 and Sushil Kumar5
[1-5]School of Pharmaceutical Sciences, IFTM University, Lodhipur Rajput, Moradabad-244102, Uttar Pradesh, India
***Corresponding Author's** Email: rajroy.ars@gmail.com

ABSTRACT
This experimental study was done to investigate antipyretic activity of fruit extract of Averrhoa carambola in Swiss-Albino mice. Averrhoa carambola has a multitude of remedies for several diseases. As the treatment of fever was one such remedy, we found that not much work has been done on the antipyretic effect of these plants. So we worked on antipyretic activity Averrhoa carambola. Medicinal plant Averrhoa carambola is the part and parcel of human society to combat against different diseases from the dawn of human civilization. According to World Health Organization, approximately 80% population of the developing countries are facing difficulties to afford synthetic drugs and are relying on traditional medicines mainly of plant origin in order to maintain their primary health care needs. The extracts of the plant was evaluated for the different pharmacological activities. Antipyretic agents and the lack of enough scientific data to support the claims made in ancient literature prompted the present study. For antipyretic tests, healthy Swiss-Albino mice of either sex weighing 30-40 g were used for the test; mice, aged 5-6 weeks, were randomly selected and divided into four groups with five animals in each group. Yeast induced pyrexia in rats at the doses of 400 and 200 mg/kg. When studied on yeast induced pyrexia, ethanol and methanol fractions significantly lowered the rectal temperature time dependently in a manner similar to standard drug paracetamol and distinctly more significant after second hour. These findings suggest that the extracts of Averrhoa carambola possess significant peripherally acting antipyretic property.
Key words: Anti-pyretic Fruits and Plant Averrhoa carambola

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INTRODUCTION

Fever is a complex physiologic response triggered by infectious or aseptic stimuli. Elevations in body temperature occur when concentrations of prostaglandin E_2 (PGE_2) increase within certain areas of the brain. These elevations alter the firing rate of neurons that control thermoregulation in the hypothalamus [1]**.** Fever also related with inflammation and pain, prostaglandins chemical mediator which mediates body temperature, pain and inflammation [2]**.** Fever or pyrexia is may be due to infection, inflammation, tissue damage, graft rejection, and any disease states [3]. Pyrexia is one of the most common medical signs. Antipyretics are the agents which reduce the elevated body temperature. Fever refers to the body's temperature that is higher than the normal range due to an increase in set-point temperature in the hypothalamus [4]. It is a common sign in medicine that shows body temperature elevation above the standard range of 36.5–37.5_C [5,6]. Increased prostaglandin E2 (PGE2) biosynthesis in the hypothalamic pre-optic region alters the neuron firing rate, leading to fever induction [7]. Anti-pyretic drugs inhibit the expression of COX-2, leading to the reduction in the PGE2 biosynthesis, which is the major fever mediator [8]. Anti-pyretic drugs have an inhibitory activity on prostaglandin biosynthesis but do influence body temperature if the elevation is caused by an increase in ambient body temperature or body exercise [9]. *Averrhoa carambola* is a species of tree in the family Oxalidaceae native to tropical Southeast Asia [10]. it has a number of common names, including carambola, star fruit and five-corner [11]. It is a small tree or shrub that grows 5 to 12 m (16 to 39 ft) tall, with rose to red-purple flowers. The flowers are small and bell-shaped, with five petals that have whitish edges. The flowers are often produced year round under tropical conditions. The tree is cultivated in tropical and semitropical regions for its edible fruits[12, 13].. The collected fruits were washed, cut into small pieces and dried in the sun for about a week. *Averrhoa carambola* plant has many medicinal uses. In Brazil, the *Averrhoa carambola* is recommended as diuretic in kidney and bladder complaints [14]. The dried fruit is also used in fever; it is cooling and possesses

antiscorbutic properties. It is considered as one of the best Indian cooling medicines Fruits and its fruit juice are used as antioxidant and astringent [15,16].

MATERIAL AND METHODS

Identification, collection and authentication of plant material

The plant material fruits of *Averrhoa carambola* were taxonomically identified collected and authenticated by qualified botanist. The stem collection was done in the month of April. Plant authentication was done by a team of botanist under supervision of Dr. Ashok Kumar, Head of Botany Department, IFTM University, Moradabad, (UP) India. Collected fruits were dried in shade at room temperature for 20-25 days. The air dried part of *Averrhoa carambola* was reduced to coarse powder. The dry powder of fruits was subjected to successive solvent extraction procedure using various solvents Petroleum ether, ethanol and methanol in the increasing order of polarity. The solvent were evaporated under reduced pressure to obtain a semisolid mass and then vacuum dried to yield solid residues. The dried extracts were stored in air tight container until the time of use.

Drying

The fruits collected were washed under running tap water and were blotted dry. The fruits were then cut into small pieces and kept for drying in oven at temperature 40 ± 2º C for five days.

The dried fruits were ground into powder and passed through sieve No. 100 and used for further experimental purpose.

Preparation of Aqueous Slurry

The aqueous slurry of *A. carambola* fruit powder (ASAC) was prepared in water and used for the dosing purpose (1000 mg powder/kg body weight/ day).

Phytochemical Screening

Extracts obtained from different solvent was subjected to various chemical tests for determination of phytoconstituents presents in them [18].

EXPERIMENTAL ANIMALS

Animals will be fasted prior to test drug administration. For mice food was withdrawn 4 hours prior to drug administration. Following the period of fasting animals was weighed and then the test substance administered in a single dose of 2000 mg/kg to animals by oral gavages. After the test drug administration, food was withheld for next 3-4 hours. Following administration, the individually animals were closely observation for next 4 hours to see any clinical symptom, any change in behavior or mortality. After 6 hours of test administration the animals weighed again recorded. A careful clinical examination was made once in each day for next 14 days. Dosing continues depending on the fixed-time interval outcomes of all the animals up to that time. The testing stops when one of the following stopping criteria first is method: (a) 3 consecutive animals survive at the upper bound; (b) 5 reversals occur in any 6 consecutive animals tested; (c) At least 4 animals have followed the first reversal and the specified likelihood-ratios exceed the critical value. At last, the 10% of maximum dose will be considered safe to carry out the research work [19].

Toxicity Study- Acute oral toxicity Study (LD_{50}): Acute oral toxicity is the adverse effects occurring within a short time of oral administration of a single dose of a substance or multiple doses given within 24 hours.

Observation Period: Animal will be closely observed for next 14 days after administration of test drug

Animals

Wister albino rats of either sex of body weight (100-150g) were used in the present study. Animals were procured from the animal house of the I.F.T.M. University, Moradabad and maintained on a natural day–night cycle (12hr dark: 12hrs light) at room temperature of about 24-26°C, with free access to standard food pellets and water *ad libitum*. Animals were acclimatized for at least ten days before exposure to behavioral experiments. Experiments were carried out between 10:00-17:00 hours. The experimental protocol was approved by the Institutional Animal Ethics Committee, I.F.T.M. University and Moradabad.

Ethical Approval

The study protocol was approved by Animal Ethics committee *Department of Pharmacology, School of Pharmaceutical Sciences, IFTM University, Lodhipur Rajput, Moradabad-244102, Uttar Pradesh, India*

Grouping of Animals

Four groups of animals were used for the study. First group always served as vehicle or control group in all the causes. The second group of animals received the standard drug (Paracetamol). Other two groups of animals received the ethanolic extract in suspension using Carboxymethyl cellulose (0.5% CMC) as the suspending agent, at the required doses.

- Group I- Control group.
- Group II- Standard drug group.

- Group III- Test group treated with low dose (EEAS)
- Group IV- Test group treated with high dose (MEAS).

Pharmacological Studies

Antipyretic Activity

Animals were treated with test and standard drugs for 7 successive days once a day and test was performed on 7th day after 60 min administration of test and standard drugs per oral. On 6th day pyrexia was induced with brewer's yeast and after 18 hr (7th day) temperature was noted down.

Grouping and treatment of animals;

Group I - Received Vehicle (0.5% CMC in distilled water 10ml/kg,po).
Group II - Received standard drugs (Diclofenac sod.10 mg/kg,p.o).
Group III - Received EEAS (400 mg/kg, p.o.)
Group IV - Received EEAS (200 mg/kg, p.o.)
Group V - Received MEAS (400 mg/kg, p.o.)
Group VI - Received MEAS (200 mg/kg, po.)

Yeast induced pyrexia was used to evaluate the antipyretic activity of the test compounds. The body temperature of each rat was recorded by measuring the rectal temperature at predetermined time intervals. Fever was induced by induced by injecting 15% suspension of brewer's yeast (saccharomyces crevice) following a standard method. The rats were allowed to remain quite in the case for some time. The mister probe was inserted 3-4 cm deep in to the rectal after fastening the tail recorded the basal rectal temperature. The animal where then given a subcutaneous injection of 10ml/kg of 15%w/v brewer's yeast suspended in 0.5%w/v CMC solution and the animal where returned to their housing case. 19 hr after yeast injection, the rats where again restrained in individual case to record their rectal temperature. Immediately the test compounds and standard, where administered orally at their respected doses. Rectal temperature of all the rats was recorded at 19 hr immediately before the administration of test compound, vehicle and paracetamol (150mg/kg, i.p) and again at 1 hr intervals up to three hr after the administration [20].

Statistical analysis

All the values were expressed as Mean ± S.E.M. the results were analyzed statistically by one-way ANOVA followed by Dunett's multiple comparison test, $P<0.05$ was considered significant when compared the control group.

RESULTS

Anti-pyretic activity for EEAS

Brewer's yeast-induced pyrexia test

Effect of EEAS on Brewer's yeast induced pyrexia test

In this test EEAS (200 mg/kg) produced significant effect after 1 hr, administration and after 2hrs, 3 hrs and 4 hrs produced moderate and more significant effect respectively. EEAS (400 mg/kg) produced moderate significant effects after 1 hr and more significant after 2 hr, 3 hr and 4 hr of drug administration. The EEAS (200 and 400mg/kg) and Diclofenac sodium (10mg/kg) decreased the rectal temperature at different time interval after 1hr, 2hrs, 3 hrs, and 4 hrs administration of the drug. The standard drug Diclofenac (10 mg/kg) showed more significant effect when compared to the control group as the results are shown in table no 1.

Effect of EEAS on Brewer's yeast induced pyrexia test

Table 1: Effect of EEAS on Brewer's yeast induced pyrexia test

S. No	Treatment group	Dose (mg/kg)	Initial Temp. (^{0}C).	Temp. After 19 hrs of yeast admin.	Rectal temperature after yeast administration			
					1 hr	2 hr	3 hr	4 hr
1.	Control	10 ml/kg	37.33± 0.19	39.23± 0.24	39.18± 0.18	39.21± 0.28	39.40± 0.16	39.96±0.10
2.	Std	10	36.88±0.39^{ns}	38.36±0.34	38.01±0.24	37.71±0.21*	37.88±0.25*	37.21±0.12***
3.	EEAS	200	37.18±0.27^{ns}	37.95±0.31	38.20±0.2*	37.91±0.32*	38.00±0.20*	37.73±0.31***
4.	EEAS	400	37.38±0.30^{ns}	38.76±0.1^{ns}	37.98±0.2**	37.68±0.29*	37.50±0.22*	37.50±0.18***

All values are expressed as Mean ± SEM, test employed ANOVA one way followed by Dunett's test (n=6); significant different from the control at *($P<0.05$), ** ($P<0.01$), *** ($P<0.001$) and ns (non –significant) when compared to control group.

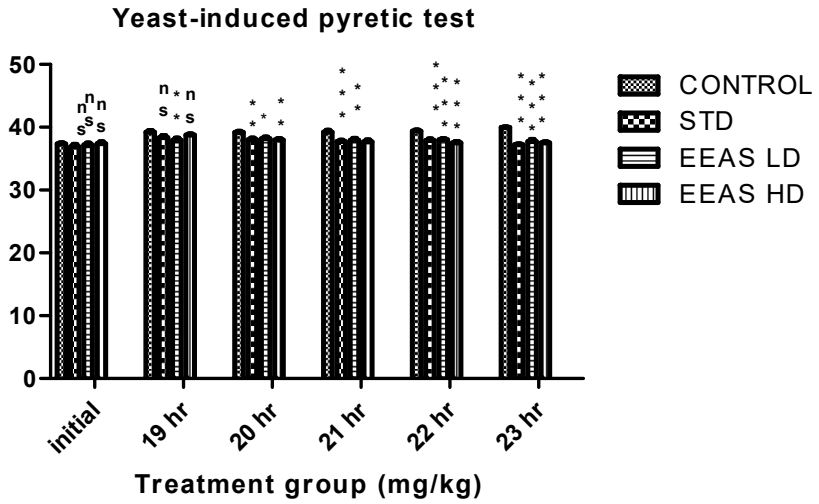

Figure1: Effect of EEAS on Brewer's yeast induced pyrexia test

Anti-pyretic activity (MEAS)

Brewer's yeast induced pyrexia test

Effect of MEAS on Brewer's yeast induced pyrexia test

In this test MEAS (200 mg/kg) produced more significant effect after 4 hr administration and after 2 hr and 3 hr produced moderate significant effects whereas after 1 hr produced non-significant effect.. MEAS (400 mg/kg) produced significant effect after 2 hr, moderate significant effect after 1 hrs where as more significant effects after 3 hrs and 4 hrs of drug administration. The MEAS (200 and 400 mg/kg) and Diclofenac sodium (10 mg/kg) decreased the rectal temperature at different time interval after 1 hrs, 2 hrs, 3 hrs and 4 hrs administration of the drug. The standard drug Diclofenac (10 mg/kg) showed more significant effect after 4 hr and 2 hrs, 3 hrs produced moderate significant where as 1 hr produced non-significant effect when compared to the control group as the results are shown in table no 2.

Table 2: Effect of MEAS on Brewer's yeast induced pyrexia test

S.N	Treatment group	Dose (mg/kg)	Initial Temp. (^{0}C).	Temp. after 19 hr of yeast admin.	Rectal temperature after yeast administration			
					1 hr	2 hr	3 hr	4 hr
1.	Control	10 ml/kg	37.33± 0.19	39.23± 0.24	39.18± 0.18	39.21± 0.28	39.40± 0.16	39.96±0.10
2.	Std	10	36.88±0.39^{ns}	38.36±0.34	38.01±0.24	37.71±0.21*	37.88±0.25*	37.21±0.12*
3.	MEAS	200	38.01±0.36^{ns}	39.36±0.29	38.65±0.30	38.30±0.21^{ns}	37.90±0.26*	37.56±0.30*
4.	MEAS	400	37.25±0.17^{ns}	36.90±0.69	37.50±0.70*	37.91±0.16*	37.16±0.36*	37.30±0.15*

All values are expressed as Mean ± SEM, test employed ANOVA one way followed by Dunett's test (n=6); significant different from the control at *(P<0.05), ** (P<0.01), *** (P<0.001) and ns (non–significant) when compared to control group.

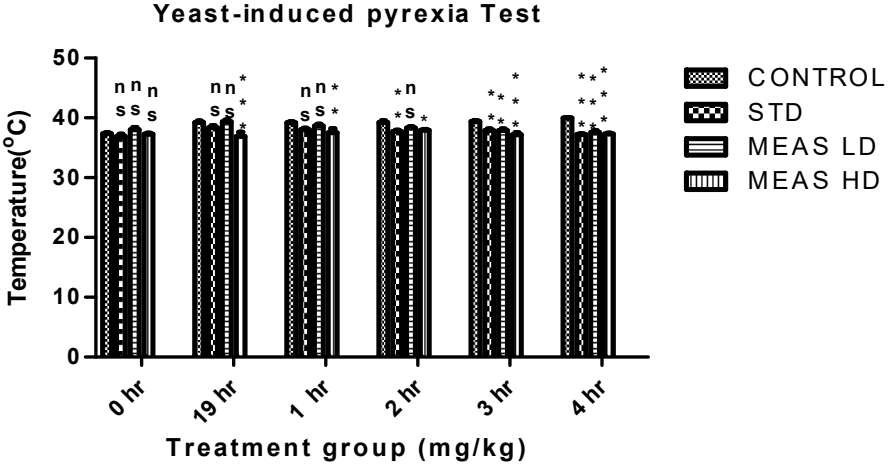

Figure.2 Effect of EEAS in Brewer's yeast induced pyrexia test

DISCUSSION

In the present learning, an effort was to study antipyretic latent of EEAS and MEAS (200mg/kg and 400mg/kg). The ethanolic and methanolic extract of *Averrhoa carambola* (EEAS and MEAS) were also evaluated in the Brewer's yeast induced pyrexia test for its antipyretic activity. Fever is defined as the elevation of core body temperature above normal; in normal adults, the average oral temperature is 37.6°C (98.6°F) [21]. Pyrexia is caused as a result of infection, tissue damage, inflammation, graft rejection, malignancy or due to microbial infections such as bacteria or viruses triggered the body's defense mechanisms. Normally, the infected tissue initiates the synthesis of pro-inflammatory mediator viz., prostaglandin E2 (PGE2) [22]. The results in the present study showed that the EEAS and MEAS possessed the significant anti-pyretic effect in yeast-promotion of the body fever in rats where as fewer actual when compared Paracetamol [23].

CONCLUSION

The results obtained from the in-vivo animal studies indicate that the extract of *Averrhoa carambola* (EEAS and MEAS Fruit Extract) possesses considerable antipyretic activities but is less potent than the reference drugs. However, further studies are required to elucidate the exact mechanism of the antipyretic activities as well as establish their efficacy and safety for clinical purpose. Traditional medication has a profile to the extent in drug upgrading from an herbal stream is concerned. *Averrhoa carambola* consists of several pharmacological activities that have been scientifically proved by using in-vitro. Furthermore, *Averrhoa carambola* natural plant (fruits) advised to acts as a lead compound for the improvement of economical, effective, and nontoxic immunomodulatory marketers for the medication of fever and different non-communicable illnesses too.

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