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Anti-Pyretic potential of *Artocarpus Heterophyllus Lam* leaves on tab vaccine-induced pyrexia

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Abstract
Ethanopharmacological relevances: *Artocarpus heterophyllus* leaves has been traditionally used in Ayurveda system of medicine to treat fever.
Aim of the study: The study investigates on methanolic extract of *Artocarpus heterophyllus* leaves for antipyretic potential in wistar rats.
Materials and methods: Fever was induced by administration of Typhoid, Para-typhoid A and B vaccine, diluted in 1/15 th part of saline, intra peritonially. The hyperexia in rats was measured using thermometer. Methanolic extract of *Artocarpus heterophyllus* leaves of dose 100, 200 and 400 mg per kg^{-1} body weight was administered to animals.
Results and discussion: Methanolic extract of *Artocarpus heterophyllus* leaves of dose 400mg per kg^{-1} body weight produced significant reduction in elevated body temperature compared to that of standard Paracetamol 150 mg per kg^{-1} body weight. The obtained values are expressed as mean±SEM values.
Conclusion: Our results provides information regarding safety and effectiveness of *Artocarpus heterophyllus* leaves extract in treatment of fever.

Keywords: Artocarpus heterophyllus, antipyretic activity, hyperexia, Typhoid, Para-typhoid A and B Vaccine

1. Introduction
Artocarpus *heterophyllus Lam*, [1] commonly known as jack fruit tree and belonging to the family Moraceae. The roots, barks, fruits and leaves are attributed with diverse medicinal properties and are used in various traditional and folk systems of medicine. It is native to Southeast Asia and is believed to have orginated in the southwestern rain forests of the Western Ghats in the Indian subcontinent [2]. The common English name "jack fruit" was used by physician and naturalist Garcia de Orta in his book Coloquios dos simples drogas da India.
The jackfruit has played a significant role in Indian agriculture system for centuries. Archeological findings have revealed that jackfruit was cultivated in India 3000 to 6000 years ago. [3] The morphology of tree varies The jackfruit tree is well suited to tropical lowlands and its fruit is the largest tree-borne fruit, reaching as much as 35 kg (80 lb) in weight, 90 cm (35 in) in length, and 50 cm (20 in) in diameter [4]. Jack fruit is known as National fruit of Bangladesh and also used in India due to its availability in summer seasons where the food is scarce. It requires a soil which is well drained but moist, with a pH of 4.3 to 8.0 and with medium soil fertility. The optimum temperature is 19 to 29° C, altitude at approximately 1600 meters above sea level and the annual rain fall between 1000 and 2400 mm. It requires a soil which is well drained but moist, with a pH of 4.3 to 8.0 and with medium soil fertility.

2. Materials and Methods
2.1 Animal Care and Handling
The experiment was carried out on wistar rats of 4 months, of both sexes, weighing 170-220 gm. They were provided from Mahaveer pvt ltd. The animals were acclimatized to the standard laboratory conditions in cross ventilated animal house at temperature 25±2°C relative humidity 44 –56% and light and dark cycles of 12:12 hours, fed with standard pallet diet and water *ad libitum* during experiment. The experiment was approved by the institutional ethics committee and as per CPCSEA guidelines (Approval no.1196/a/08/CPCSEA).

2.2 Chemicals
Paracetamol and Typhoid vaccine were purchased from Apollo medical store, Visakhapatnam. All other chemicals used for this study were of analytical grade.

2.3 Pyrexia Induced in Rats by Typhoid Vaccine
The room temperature was maintained at 30ºC. Only animals with a body temperature of at least 38ºC (Max) were taken into the test. Typhoid-Paratyphoid A, B vaccine (0.3 ml) was injected I.P. of rats of each group. Standard paracetamol (I.V.) was injected 30 minutes before administration of Typhoid-Paratyphoid A, B vaccine. The rectal temperature of each animal was recorded initial and at the interval of 30 minute after treatment using treatment using tele thermometer up to 3 hours.

2.4 Acute Toxicity study

Table 1: Acute Toxicity Study (CPCSEA guidelines)

Treatments	Dose (mg/kg)	No. of animals used	No of death	% Death
A heterophyllus leaf extract	2000	5	0	0

In the LD50 value determination, we observed that the Leaf extract was safe to use in animals and showed no mortality upto 2000 mg/kg body weight. Therefore 2000 mg/kg dose was considered as a safe dose. 1/5 th (400 mg/kg body wt.), 1/10th (200 mg/kg body w.t) and 1/20th (100mg/kg body w.t) of that was selected for all in vivo experiments as maximal dose.

2.5 Experimental Design

In the experiment, a total of 30 rats were used. The rats were divided into 5 groups comprising of 6 animals in each group as follows:

Group: Control

Group I: Rats received Paracetamol (150mg/k.) only 1 day around 1 hr before measurement of body temperature by the help of digital tele thermometer.

Group II: Rats received Methanol Extract of *A. heterophyllus* (100mg/kg p.o.)

Group IV: Rats received Methanol Extract of *A. heterophyllus*, (200mg/kg p.o.)

Group V: Mice received Methanol Extract of *A. heterophyllus* (400mg/kg p.o)

2.6 Experimental Animals

Wistar albino rats of either sex weighing between 80-120 gms were arranged in five groups of five each. The normal rectal temperature and its hourly variation were recorded at the beginning of the experiment using a digital tele thermometer13, 14. Animals were fasted for 24 hours before giving the drugs, but water freely permitted, pyrexia was induced by the administration of TAB vaccine. The vaccine was given intra peritonially in a dilution of 1/15 in normal saline to all animals. After two hours of the administration of TAB Vaccine, the rectal- temperature of each rat was taken and found to be fairly stabilized. [5]

1. The first group of rats were given the vehicle (0.1% Sodium CMC).
2. The second group was given paracetamol 100mg/kg body weight orally which was used as reference standard drug.
3. The third group was given plant extract orally at a dose of 100mg/kg body weight
4. The fourth group was given the plant extract orally at a dose of 200mg/kg body weight.
5. The fifth group was administered with plant extract 400mg/kgbody weight orally. The rectal temperature of rats were taken using an electronic digital tele thermometer. The results were evaluated by one way ANOVA.

3. Results

Table 2

S. No	Treatment	Normal body temp	Body temp after administration of vaccine	Body temp after drug administration						
				0 hr	0.5 hr	1 hr	1.5 hr	2 hr	2.5 hr	3 hr
1	Control	98.4	102.1	102	101.9	101.8	101.6	101.4	101.2	101
2	Standard	98.5	102.4	102.3	101.9	101.2	100.5	99.9	99.2	98.4
3	Test1	98.4	102.3	102.3	101.	101.2	100.6	99.8***	99.2***	98..6***
4	Test2	98.5	102.2	102.2	101.6	101.0	100.4	99.68***	99.0	98.4***
5	Test3	98.6	102.4	102.4	101.8	101.1	100.5	99.7***	99.1***	98.5***

Values are expressed as MEAN±SEM when p*<0.05,p**<0.001,p***<0.0001 significant when compared with standard

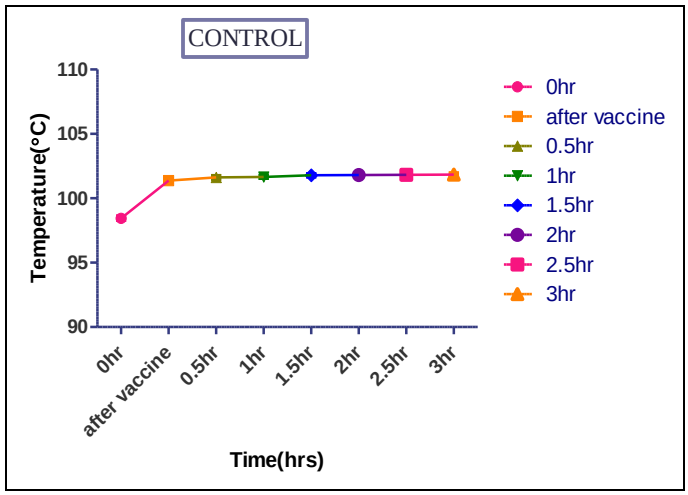

Fig 1

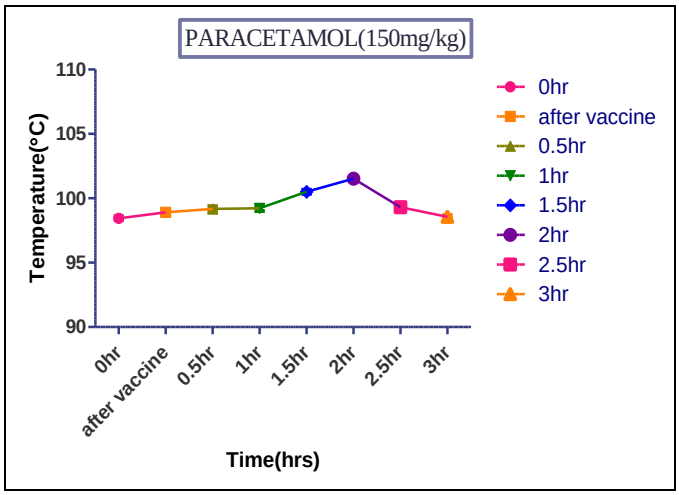

Fig 2

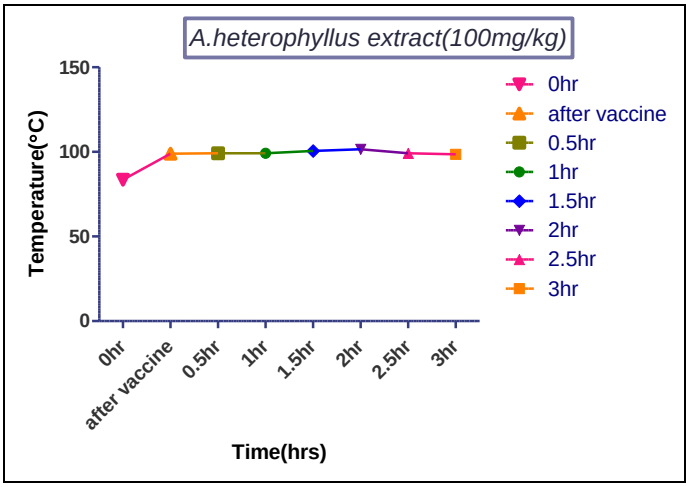

Fig 3

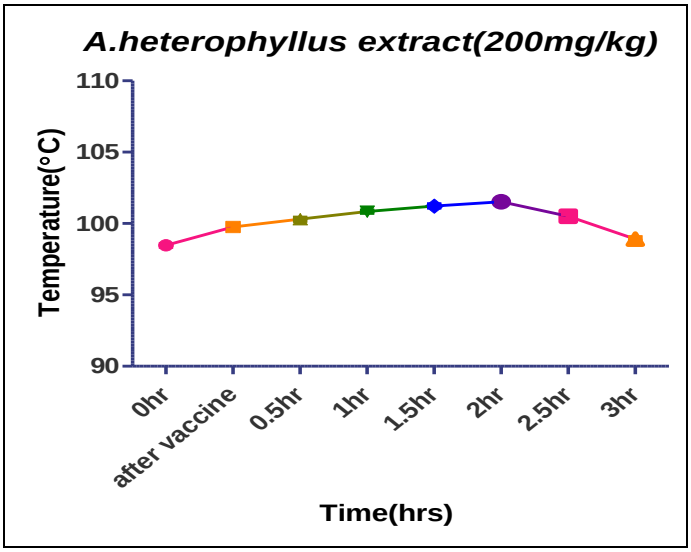

Fig 4

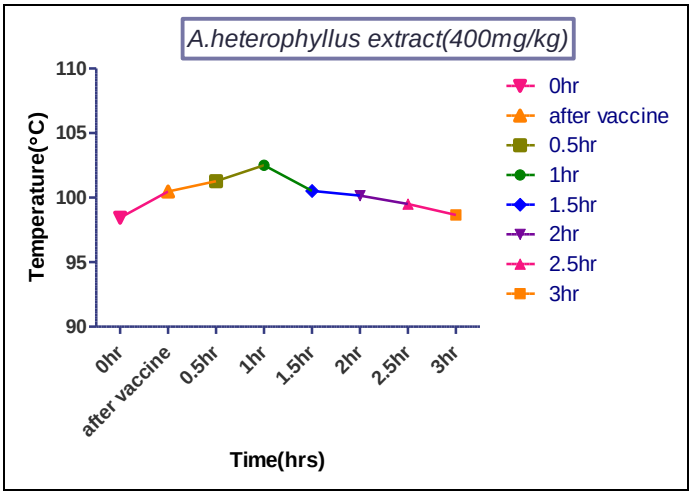

Fig 5

4. Discussion

Antipyretics are the agents which reduce the elevated body temperature. Regulation of body temperature requires a delicate balance between production and loss of heat, and the hypothalamus regulates the set point at which body temperature is maintained. In fever this set point elevates and a drug like paracetamol does not influence body temperature when it is elevated by the factors such as exercise or increase in ambient temperature. Experimental studies reveals that extracts of *Artocarpus heterophyllus* (at dose 400mg/kg) produced an antipyretic action by decreasing the body temperature in the model of fever in rats.

4.1 Conflicts of interest

Conflicts of interest are none

5. References

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