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ANTIPYRETIC ACTIVITY OF *THESPESIA POPULNEA* FRUITS

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ABSTRACT: In the present study, the alcoholic and aqueous extracts of *Thespesia populnea* were investigated for their antipyretic activity. Suspension of subcutaneous administration of brewer's yeast in albino rat leads to pyrexia. Oral administration of extracts at a dose of 500 mg/kg body weight significantly reduced the elevated body temperature of rat. This antipyretic effect has been compared with antipyretic effect of standard paracetamol.

INTRODUCTION: Regulation of body temperature requires a delicate balance between the production and loss of heat; the hypothalamus regulates the set point at which body temperature is maintained. This set point is elevated in fever (from infection, tissue damage, inflammation, graft rejection, or malignancy), as a result of formation of cytokines such as IL-1b, IL-6, interferons, and TNF-a. The cytokines increase synthesis of PGE_2 in circumventricular organs in and adjacent to the preoptic hypothalamic area; PGE_2, in turn, increases cyclic AMP and triggers the hypothalamus to elevate body temperature by promoting an increase in heat generation and a decrease in heat loss.

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Aspirin and NSAIDs suppress this response by inhibiting PGE_2 synthesis but do not influence body temperature when it is elevated by factors such as exercise or in response to ambient temperature. Yeast-induced fever is called pathogenic fever. The production of prostaglandins, particularly PGE_2 appears to be a final pathway responsible for fever production induced by several pyrogens [1].

Pyrexia or fever is caused as a secondary impact of infection, malignancy or other diseased states. It is the body's natural function to create an environment where infectious agents or damaged tissues cannot survive [2].

When body temperature becomes high, the temperature regulatory system, which is governed by a nervous feedback mechanism, dilates the blood vessels and increases sweating to reduce the temperature. When the body temperature becomes low, hypothalamus protects the internal temperature by vasoconstriction.

High fever often increases faster disease progression by increasing tissue catabolism, dehydration, and existing complaints, as found in HIV. Fever is associated with symptoms of sickness behavior which consist of lethargy, depression, anorexia, inability to concentrate. This increase in set point triggers increased muscle tone & shivering. Antipyretic medication can be effective at lowering the temperature which may include the affected person's comfort [3].

Thespesia populnea (L.) Soland ex Correa (Malvaceae) is distributed mainly along the coastal regions throughout India, often planted as avenue tree. Earlier the plant has been studied for its antibacterial, antiviral, wound healing, anticancer [4], antisteroidogenic activity [5] and for dermatitis [6]. Aqueous extracts of fruits of this plant are reported for its wound healing activity [7].

MATERIALS AND METHODS:

Collection of plant material: The fruits of *Thespesia populnea* were collected from Kottayam district in Kerala, India in October 2006 and were authenticated by Mr.K G Sreekumar, Senior Research Officer, Pharmacognosy Unit, Govt Ayurveda Research Institute, Poojapura, Thiruvananthapuram, Kerala. A voucher specimen PC-03/2006 was submitted at Academy Of Pharmaceutical Science, Pariyaram Medical College, Kannur for future reference. Dried fruits were ground to a coarse powder, passed through sieve no 24, stored in airtight container, and used for further extraction.

Preparation of extracts:

Ethanol extract: The shade dried powdered fruits (500g) were exhaustively extracted with 95% ethanol using a Soxhlet apparatus. The extract was concentrated *in vaccuo* to a syrupy consistency. The percentage yield of extract was found to be 4.12 %.

Aqueous extract: The dried powders (24#) 100 gm was taken in a 2000ml conical flask with 500ml of distilled water to which 10ml chloroform were added as a preservative. It was extracted up to 7 days with daily 2 hours stirring with the mechanical stirrer. After 7 days the extract was filtered through the muslin cloth and the marc was pressed and its filtrate dried in hot air oven at 45^0C to a semisolid mass [8]. It was stored in airtight container in a refrigerator below 10^oC. The percentage yield of extract was found to be 6.19%.

Animals: Albino rats (Wistar) weighing 150-200 gm were used in this study. They were procured from animal house, Pariyaram Medical College, Kannur, Kerala. The animals were acclimatized for one week under standard laboratory conditions. They were housed in polypropylene cages and maintained at 27°C ± 2°C under 12 hrs dark / light cycle. They were fed with standard rat feed (Gold Mohr Lipton India Ltd.) and water *ad libitum*. (Ethical clearance for conducting experiments on animals was obtained from the Institutional Animal Ethics Committee (APSC/CPCSEA-01/IAEC/2011).

Antipyretic activity: Rats were given 20 ml/kg (20%) suspension of brewer's yeast subcutaneously. Initial rectal temperature was recorded (Smith and Hambourger, 1935). After 18 hours animals showing an increase of 0.3 – 0.5^{o}C in rectal temperature were selected and allocated into four Groups of six animals each. The test extract (500 mg/kg orally) was administered to the groups II to III. Group I served as control received 0.3 ml normal saline and Group IV served as reference standard (Paracetamol 100 mg/kg p.o.). Rectal temperature was determined by thermal probe Ellab thermistor thermometer 1, 2, 3 and 4 hrs, after test extract/reference drug administration [9].

RESULTS: The photochemical screening of ethyl alcohol extract revealed the presence of carbohydrates, steroids, alkaloids, terpenoids, flavonoids, tannins and poly phenols, while aqueous extract showed presence of carbohydrates, alkaloids, flavonoids, tannins and poly phenols.

The antipyretic activity of the test extract was detetermined by using the yeast provoked elevated rectal temperature with EETP and AETP at doses of 500 mg/kg showed significantly decrease in the yeast provoked elevated rectal temperature. Antipyretic activity of EETP found to be maximal at 4 hr after the treatment. The results are show in **Table 1**.

TABLE 1: ANTIPYRETIC ACTIVITY OF *THESPESIA POPULNEA* ON BREWER'S YEAST-INDUCED PYREXIA IN RATS

Treatment	Dose (mg/kg)	Rectal temperature (^oC) before and after treatment					
		Before treatment		After treatment			
		0h	18h	1h	2h	3h	4h
Control (saline)	5 ml/kg	37.6±0.2	39.2±0.1	39.2±0.1	39.2±0.1	39.2±0.1	39.2±0.1
EETP	500	37.5±0.1	39.7±0.1	38.6±0.1*	38.6±0.1*	38.3±0.1*	38.1±0.1*
AETP	500	37.4±0.1	39.9±0.2	38.8±0.2*	38.8±0.1*	37.9±0.1*	37.6±0.1*
Paracetamol	100	37.6±0.1	39.5±0.2	38.3±0.2*	38.2±0.1*	37.1±0.1*	37.2±0.1*

Values are mean ± S.E.M. (n = 6), *P < 0.001 compared with control group. EETP: Ethanol extract of *T. populnea*. AETP: Aqueous extract of *T. populnea*.

DISCUSSION: Yeast-induced fever is called pathogenic fever. Its etiology includes production of prostaglandins, which set the thermoregulatory center at a higher temperature [10]. Elevation in body temperature occurs when the concentration of prostaglandin E_2 (PGE_2) increases within parts of the brain. Such an elevation contributes to a considerable alteration in the firing rate of neurons that control the thermoregulation process in the hypothalamus. It is now evident that most of the antipyretic drugs exert their action by inhibiting the enzymatic activity of cyclooxygenase and consequently reducing the levels of PGE_2. The present results showed that ethanol extract and aqueous extract of *T. populnea* possesses a significant antipyretic effect in yeast-provoked elevation of body temperature in rats, and its effect was comparable to that of paracetamol (standard drug).

Therefore, inhibition of prostaglandin synthesis could be the possible mechanism of antipyretic action as that of paracetamol [11]. Fever has been recognized as a major sign of diseased condition right from the very beginning of human civilization. The febrile response is coordinated by the central nervous system through endocrine, neurological, immunological and behavioral mechanisms [12].

In addition, there are several mediators or multi processes underlining the pathogenesis of fever. Inhibition of any of these mediators may bring about antipyresis.

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