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Short Communication

ANTIPYRETIC ACTIVITY OF ETHANOLIC EXTRACT OF LEAF AND BARK OF *DIOSPYROS VIRGINIANA* IN YEAST INDUCED PYREXIA

S. PRIYA[1], S. NETHAJI[2]

[1]P. G. Department of Biotechnology, S. T. E. T. Women's College, Mannargudi, Tamil Nadu, India, [2]P. G and Research Department of Biochemistry, Marudupandiyar College, Vallam, Thanjavur, Tamil Nadu, India
Email: piri_333@yahoo.co.in

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ABSTRACT

Objective: To evaluate the antipyretic effect of the ethanolic extract of leaf and bark of *Diospyros virginiana* Linn against brewer yeast induced pyrexia model in albino rats of both sexes was investigated.

Methods: The Pyrexia was induced by subcutaneously injecting 20% w/v brewer's yeast suspension (10 ml/kg) into the animals. After the injection, the rectal temperature of each rat was measured. Paracetamol (150 mg/kg) was used as the standard drug.

Results: The results showed that the ethanol extracts of leaf of *Diospyros virginiana* possessed significant antipyretic effect compared to the bark extract.

Conclusion: This study provides evidences for the antipyretic activity of *Diospyros virginiana* which could partly contribute to its ethno medical use.

Keywords: *D. virginiana,* Brewer yeast, Rectal temperature, Paracetamol.

Over the past decade, herbal medicine has become a topic of global importance, making an impact on both world health and international trade. Medicinal plants continue to play a central role in the healthcare system of large proportions of the world's population. This is particularly true in developing countries, where herbal medicine has a long and uninterrupted history of use [1]. Pyrexia or fever is caused as a secondary impact of infection, malignancy or other diseased states. It is the body's natural defense to create an environment where an infectious agent or damaged tissue cannot survive. Normally the infected or damaged tissue initiates the enhanced formation of pro-inflammatory mediator's which increase the synthesis of prostaglandin E_2 (PGE_2) near peptic hypothalamus area and there by triggering the hypothalamus to elevate the body temperature.

Diospyros is a genus of over 700 species of deciduous and ever-green trees, shrubs, and small bushes. *Diospyros virginiana* L is a persimmon species commonly called the American Persimmon from Ebenaceae family [2]. It is a deciduous tree native to China, and the south eastern portion of the United States. The tree grows wild but has been cultivated for its fruit and wood since prehistoric times by Native Americans. The peculiar characteristics of its fruit have made the tree well known [3]. The fruit is a globular berry, with variation in the number of seeds, some-times with eight and sometimes without any. The fruit had the high content of vitamin C and it contained anti-oxidant compounds like vitamin-A, beta-carotene, lycopene, lutein and cryptoxanthin. Fresh fruits also contained healthy amounts of minerals like potassium, manganese, copper, and phosphorus. The fruit had many valuable B-complex vitamins such as folic acid, pyridoxine [4]. The unripe fruit is extremely astringent and it has been beneficial in various forms of disease of the bowels, chronic dysentery and uterine hemorrhage. The ripe fruit has been used medicinally as antiseptic and for the treatment of diphtheria, dropsy, fevers, and thrush. The bark is antiseptic and its infusion was employed to cleanse, stimulant foul and indolent ulcers [5].

Persimmons have been also used to treat bronchitis, catarrh, cough, goiter, hangover and hiccoughs. The bark has been used in intermittent and both it and the unripe fruit have been beneficial in various forms of disease of the bowels, chronic dysentery and uterine hemorrhage which is used in infusion syrup or vinous tincture [6]. The extract/fractions of *Diospyros virginiana* might contain active principles that exhibited inhibitory action on cyclooxygenase. As a result, they produced antipyretic activity by preventing the formation of prostaglandins or by increasing the concentration of body's own antipyretic components. Our finding of the analgesic property of this plant is in accordance with the effect of other species of this genus. This study evaluated the antipyretic activity of leaf and bark ethanolic extracts of *Diospyros virginiana* using experimental models in rats.

D. virginiana belongs to the family *Ebenaceae* was collected from Coonoor, Nilgiris District, Tamil Nadu, India and identified by the special key given Cambell flora [7]. The leaf and bark of *D. virginiana* were washed with sterile distilled water. After, the leaves and bark were shade dried and powdered by using pestle and mortar. 25g of powder was filled in the thimble and extracted successively with ethanol using a Soxhlet extractor for 48 h. The extracts were concentrated using rotary flash evaporator and preserved at 5 °C in airtight bottle until further use. The ethanolic extracts of the plant was diluted with distilled water and was administered orally to mice.

Body weights of the animals were recorded and they were randomly divided into 5 groups of 6 animals each as follows

Group I: Normal control

Group II: Subcutaneous injection of yeast (10 ml/kg)

Group III: Yeast (10 ml/kg)+standard drug paracetamol (150 mg/kg) orally

Group IV: Yeast (10 ml/kg)+leaves extract of *Diospyros virginana* (500 mg/kg) orally

Group V: Yeast (10 ml/kg)+bark extract of *Diospyros virginana* (500 mg/kg) orally

Pyrexia was induced by subcutaneous injection of 20% w/v of brewer's yeast (10 mg/kg) in distilled water. Basal rectal temperature was measured before the injection of depth of 2 cm into the rectum. The rise in rectal temperature was recorded 19h after yeast injection paracetamol 150 mg/kg body weight was used as the standard antipyretic drug. Rectal temperature of animals was noted at regular intervals following the respective treatment. The temperature was measured at 1st, 2nd, 3rd hr after drug administration.

The statistical analysis was done by ANOVA [8] followed by Dunner's test for multiple comparisons P<0.01 was considered significant in the experiment.

Non-steroid anti-inflammatory drugs are among the most commonly prescribed due to their considerable effectiveness in the treatment of pain, inflammation and rheumatic disorders. Since their drugs have toxic effect to the various organs of the body, search for safe herbal remedies with potent antipyretic activity received momentum recently.

Subcutaneous injection of the pyrogenic dose of yeast produced elevated changes in rectal temperature of the rats as shown in the table-1. The *Diospyros virginiana* both extracts caused a dose-dependent decrease in rectal temperature when compared to the control. The ethanolic *Diospyros virginiana* leaf extracts revealed a significant decrease (P<0.05) in temperature between 2 to 5 h after administration. *Diospyros virginiana* bark extract showed the significant decrease (P<0.05) in temperature 3 to 5 h respectively. However, paracetamol (10 mg/kg) used as the reference drug caused a greater reduction in the rectal temperature of the rats at the onset-which was significant different (P<0.05), when compared to both control and control treated groups. The antipyretic effect started as from the 1st h after drug and extract administration and was sustained for 4 h while control showed no antipyretic effect in the entire period of experiment.

Antipyretic activity is a characteristic of drugs or compounds which have an inhibitory effect on prostaglandin-biosynthesis and an indispensible role of prostaglandins in the febrile response has been demonstrated [9]. In the present pharmacological evaluation, the leaf and bark extract of *Diospyros virginiana* was extensively investigated for its antipyretic activity against Brewer's yeast induced pyrexia model in rats. The extracts produced a significant reduction in yeast induced pyrexia in rats dose-dependently and its effect is comparable to that of the standard anti-pyretic drug (paracetamol) used in this study. The ethanolic extract of the both plant leaf and bark at a dose level of 500 mg/kg exhibited competent, potent and comparable results.

Fever is a result of a finely tuned, complex event that involves both the peripheral immune system and the brain, through which a series of inflammatory and metabolic processes are regulated and it is now commonly accepted that prostaglandin E_2 (PGE_2) is the final fever mediator in the brain, specifically in the pre optic area of the anterior hypothalamus [10], thus it may be plausible to conclude that the extract inhibits the synthesis of prostaglandins, albeit to a very little extent. Pyrexia is a result of secondary impact of infection, tissue damage, inflammation, graft rejection, malignancy or other diseased states. 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 within the hypothalamic region [11].

A natural antipyretic agent with reduced or no toxicity is therefore, essential. Since antipyretic activity is commonly mentioned as a characteristic of drugs or compounds, which have an inhibitory activity on prostaglandins biosynthesis, the yeast induced hyperpyrexia in rat model was employed to investigate the antipyretic activity of the extract [12]. Yeast induced pyrexia is called pathogenic fever which is due to the production of prostaglandins (PGE_2) which set the thermoregulatory center at a higher temperature.

Antipyretics have been shown to suppress fever by inhibiting prostaglandin synthetase, resulting in the blockade of the synthesis of prostaglandin in the brain or suppressing the rise of interleukin-1α production subsequent to interferon production. Flavanoids like baicalin have been shown to exert an antipyretic effect by suppressing TNF-α [13] and its related compounds also exhibit inhibition of arachidonic acid peroxidation, which results in reduction of prostaglandin levels thus reducing the fever and pain. The results of present study indicate that the ethanol leaf extracts of *Diospyros virginiana* possesses significant antipyretic effect compared to the effect of bark extract on yeast induced hyperthermia in rats. This may be attributed to the presence of flavonoids and saponins in the extracts which may be involved in inhibition of prostaglandin synthesis. Also, there are several mediators or multiprocessors underlining the pathogenesis of fever. Inhibition of any of these mediators may bring about antipyresis.

The present investigation was promoting *Diospyros virginiana* plant as a promising antipyretic plant species seeking vast multi dimensional future research work up to the molecular level to establish new up-to-date scientific data about this plant species and to elucidate its exact mechanism of an antipyretic effect.

Table 1: Effect of ethanolic extracts of *Diospyros virginiana* on body temperature in yeast induced pyrexia in experimental animals

Groups	Rectal temperature in ° C after 18 h of yeast injection			
	0 h	1h	2h	3h
Group I	37.30±0.7	37.50±0.7	37.70±0.6	37.60±0.4
Group II	40.53±0.11	40.18±0.17	39.21±0.14	39.13±0.16
Group III	40.43±0.19	38.65±0.17	38.46±0.19*	37.66±0.18*
Group IV	40.61±00.14	39.63±0.19	39.13±0.24	38.68±0.12
Group V	40.58±0.11	39.23±0.12	38.01±0.14*	37.71±0.16*

Values are expressed as SEM *P<0.01 Vs control, 6 Number of animals were used in each group.

CONFLICT OF INTERESTS

Declared None.

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