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Antipyretic and antinociceptive activity of *Diospyros lotus* L. in animals

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PEER REVIEW

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Comments

This is a valuable research work for investigation of safe, effective and potent antipyretic and analgesic phytomedicines. In the present research work, the authors reported the antipyretic and analgesic effect of the said plant. The antipyretic effect has been tested using brewer's yeast induced fever and acetic acid induced writhing for pain. Both of these animal paradigms are recommended and well established.
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ABSTRACT

Objective: To evaluate pharmacologically the traditional use of *Diospyros lotus* as antipyretic and antinociceptive in various animal models.

Methods: *In vivo* experimental models were used in this study. Antipyretic activity of extract/fractions was evaluated in brewer's yeast induced hyperthermic mice while antinociceptive activity was studied in acetic acid induced writhing test at 50 and 100 mg/kg *i.p.*

Results: The crude extract strongly ameliorated the induced pyrexia during various assessment times. Upon fractionation, the antipyretic effects were strongly augmented by the chloroform and ethyl acetate fractions of the plant. However, hexane and butanol fractions were insignificant in their effect as antipyretic. The extract showed marked inhibition on the noxious simulation induced by post acetic acid injection. The effect was strongly supported by other fraction expect hexane.

Conclusions: In short, our study scientifically validated the traditional use of the plant as antipyretic.

KEYWORDS

Diospyros lotus, Ebenaceae, Antipyretic, Antinociceptive activities

1. Introduction

Plants are richest source of bioactive secondary metabolites in a most effective way and with specific selectivity[1,2]. From the start of human being development, men were using different medicinal plants as traditional medicines for their health care. Plants have the ability to produce several valuable classes of chemical constituents which showed interesting biological action[3,4]. *Diospyros* is the most important genus which contains more than 500 species. The distinguishing features of the *Diospyros* species are trees, rarely shrubs, leaves alternate flowers green, white or yellow, few to many, axillary cymes or the pistillate solitary, corolla campanulate, urceolate or tubular, the lobes 3-7 (usually 4-5), stamens four to many mostly with 4-8 staminodia in pistillate flowers, ovary 4-16

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celled; fruit is a large juicy 1-10 seeded berry and the sap wood is white and soft and heartwood is black and hard. The genus *Diospyros* is of more economic importance with many species yield edible fruits and valuable timbers. The best fruit yielding species is the *kaki* or Japanese persimmon (*Diospyros kaki*) has been cultivated in Japan for many centuries. The *kaki* fruits, a large orange-red berries, are very astringent until fully ripe, at which time the tannin content is completely transformed into insoluble crystals. The juice is then sweet and palatable. The other important fruit yielding species are *Diospyros virginiana, Diospyros ebenaster, Diospyros lotus* (*D. lotus*) L., *Diospyros mespiliformis* (*D. mespiliformis*) and *Diospyros melanoxylon*.

D. lotus is a deciduous tree, growing in China and Asia. *D. Lotus* has been cultivated for its edible fruits. The fruit of *D. lotus* is used as a sedative, astringent, nutritive, antiseptic, antidiabetic, antitumor, astringent, laxative, nutritive, antipyretic and for the treatment of constipation[3]. *D. lotus* fruits are used for the treatment of diarrhea, dry coughs and hypertension.

Phytochemical studies have been previously carried out on many *Diospyros* species and have revealed the widespread presence of naphthoquinones and naphthalene derivatives, dimeric naphthoquinones and lupine triterpenes[5]. Chemical investigation of the fruits led to the *D. lotus* identification of some fatty acids, sugars phenolic compounds and non-volatile acids[5,6]. The aim of the current project deals with the antipyretic and antinociceptive activity of crude extract of *D. lotus* in experimental animals.

2. Materials and methods

2.1. Plant material

Roots of *D. lotus* were collected from Toormang Razagram, Dir, KPK, Pakistan, in May 2009. The sample was authenticated by Dr. Abdur Rashid, taxonomist, and Botany Department, University of Peshawar Pakistan. A voucher specimen (Bot/649) has been deposited at the herbarium, Department of Botany, University of Peshawar Pakistan.

2.2. Extraction and isolation

Shade-dried roots of *D. lotus* (14 kg) was powdered and then kept at room temperature in MeOH for 6 d with continuous stirring by simple percolation. After this period, the extracts were concentrated by evaporating solvents using rotary vacuum evaporator under reduced pressure at temperature 45 °C. This process was repeated four times until the extraction was completed and finally 202 g of dark red residue of roots and 155 g of barks was obtained. The MeOH extract of roots was suspended in water and successively partitioned with hexane, $CHCl_3$, EtOAc and BuOH according to standard protocol[7].

BALB/c mice were used in various experiments. They were fed with standard laboratory food and water *ad libitum*. Animals were kept under standard condition of temperature and light. Before the start of experiment, animals were acclimatized with laboratory conditions. The rulings of the institute of Laboratory Animal Resources, Commission on Life Sciences, National Research Council were maintained during all the experiments performed.

2.3. Antipyretic test (yeast induced pyrexia)

The antipyretic activity was determined in BALB/c mice (25-30 g) of either sex[8]. The animals were divided in five groups (n=5). All groups were fasted overnight and allowed free accesses drinking water. Group one received saline as control group and second group received paracetamol as standard drug while the remaining groups received 50 and 100 mg/kg of extract/fractions. Normal temperature was recorded using digital thermometer and then pyrexia was induced in all minces by injecting 20% aqueous suspension of brewer's yeast (10 mL/kg *s.c*). After 24 h, rectal temperature was recorded and corresponding groups were injected with above doses. Rectal temperature was recorded periodically at 1.5, 3 and 5 h of drugs administration.

2.4. Acetic acid induced writhing test

BALB/c mice of either sex (n=6) weighing 25-30 g were used[9]. All animals were withdrawn from food 2 h before the start of experiment. All animals were divided in various groups. Group I was injected with normal saline intraperitoneally as control while group II was injected with standard drug diclofenac sodium (10 mg/kg body weight) and the remaining groups were injected with 50 and 100 mg/kg *i.p.* of methanolic extract and its various solvent fractions. After 30 min of saline, diclofenac sodium and various extract, the animals were treated *i.p.* with 1% acetic acid. The writhing was counted after 5 min of acetic acid injection. The number of abdominal constrictions (writhes) was counted for 10 min.

2.5. Statistical analysis

Results are expressed as mean±SEM. One-way ANOVA was used for comparison test of significant differences among groups followed by Dunnet's multiple comparison post test. A level of significance (P<0.05) was considered for each test.