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Research Article

ANTIPYRETIC STUDY OF METHANOLIC BARK EXTRACT OF *PLUMERIARUBRA,* LINN. IN VARIOUS PYREXIA INDUCED MODELS

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ABSTRACT

To provide pharmacological evidence of *plumeria rubra* as antipyretic agent in practice many parts of Pakistan. Antipyretic effect of methanolic extract of the bark of *plumeria rubra* was investigated.on yeast , dinitrophenol and E-coli induced model. Intraperitoneal administration of yeast, dinitrophenol and E-coli in albino rabbits leads to pyrexia. Intraperitoneal administration of methanolic extract of the bark of *plumeria rubra* at a dose 100mg/kg body weight were shown significantly reduce the elevated body temperature of rabbit in yeast induced model which was compared with aspirin (Standard Drug) and solvent used. In dinitrophenol induced pyrexia, mixture of verapamil (2mg/kg) and *Plumeria rubra* (50mg/kg), while in In E-coli induced pyrexia, mixture of Ciproflaxacin (10mg/kg) and *Plumeria rubra* (50mg/kg), significantly reduced the elevated temperature in all models as compared to the standard drug Aspirin.

Keywords: *Plumeria rubra*, Bark extract, Antipyretic activity, Dinitrophenol, E-coli, Verapamil, Yeast.

INTRODUCTION

Plumeria rubra, Linn. belongs to the Apocynaceae family and have trees and shrub containing secretory cells . It is also known as Lal champa in Hindi and True Frangipani in English. The plants from this genus are widely grown in the tropical and subtropical regions all over the world

Plumeria rubra, Linn.is native of tropical America and is cultivated in various parts of North America, West Indies, Malay Archipelago, Cochin China, Jamaica, Brazil and Guiana. It is an easily growing plant. *Plumeria* is a common ornamental in Yards and other planned landscapes. It is easily to growing in hot, dry areas and is found in Hawaii from sea level to 2000 ft elevation. It has moderate wind resistance and salt tolerance. The trees reach maturity (full size) in about five year. Some ornamental species are grown in the warmer regions of the world. About eight species are reported from India, but owing to the overlapping of characters in some species; it become difficult to fix their identity. In India; however, it has been used as an abortifacient

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(Kirtikar and Basu, 1935).

Various scientific evaluations have been conducted to verify the traditional uses of this plant in the folk medicine. The flowers are aromatic. The essential oils from the flowers used for perfumery and aromatherapy purposes. The Leaves of *P. rubra* are used in ulcers, leprosy, inflammations and rubefacient

A decoction of the bark has been used for the treatment of venerial disease and also used in the indigenous system of medicine for the treatment of rheumatism, diarrhoea, leprosy and fever. The root bark cures tumours and rheumatic pains. The bark of the this plant is used as antibacterial agent. (Surendra, et al, 2012)

The decoction of the bark and roots of *Plumeria rubra* is traditionally used to treat Asthma. (Wiart, 2002) We are reporting its antipyretic activity.

MATERIALS AND METHODS

Collection and identification of plant materials:

The bark of the plant having medicinal activity i.e *Plumeria rubra,* Linn. from the residential area of the Bahauddin Zakariya University Multan, Pakistan. The plant material was identified by an expert taxonomist (Prof. Altaf Hussain Dasti) at the institute of Pure and Applied Biology, Bahauddin Zakariya University Multan with voucher No. **P.Fl.565-1.**

Preparation of crude extract:

The plant material was made free from soil and other adulterants and vegetative debris. The dried plant material was grinded to coarse powder with the help of a special herbal grinder. The powdered plant material (1 kg) was subjected to maceration in 70% aqueous-methanol in amber coloured bottle at room temperature for 7 days with occasional vigorous shaking at room temperature and keeping the extract in the dark room. The filtrate was obtained by passing the mixture through a muslin cloth and then through a Whatman qualitative grade 1 filter paper (Williamson, *et al*., 1998). The filtrate was evaporated on a rotary evaporator attached to a vacuum pump at 37°C under reduced pressure to thick paste like consistency. And then the extract obtained was stored at -4°C in air tight jars.

Drugs:

Aspirin as Disprin soluble tablet was purchased from *Reckitt Benckiser* (*Pakistan*) Ltd Verapamil was purchased from Sigma chemicals Company, St. Louis, MO, USA. 2,4 Dinitrophenol was purchased from Roche.(pvt).Ltd.pakistan. And ciprofloxacin was purchased from GSK.

Animals:

The albino rabbits used in these experiments of either sex with the average weight of 1-1.5kg were purchased from local market of Mutlan Pakistan and housed at the animal house of Pharmacy Department, Bahauddin Zakariya University Multan, in plastic cages, maintained at maintained at 23-25°C and were given standard diet and tap water. Food was withdrawn 24 hours prior to the experiments from animals but had free access to water.

The experiment was approved by Ethical commity of animal of Bahauddin Zakariya University Multan with reference# EC-12/9/12.

Preliminary phytochemical analysis:

The aquous methanolic extract was tested qualitatively for the presence of different phytochemical constituents and alkaloids, saponins, tannins, coumarins, flavonoids, sterols and terpenes were found to be methanol extractable constituents of *Plumeria rubra,* Linn.

Evaluation of antipyretic activity of the extract

Yeast-induced pyrexia

Adult albino rabbits fasted for 24 hours but allowed water ad libitum were used for the experiment. They were randomized into 3 groups of 4 rabbits each. At zero hour, the basal temperature of the rabbits was taken using digital clinical thermometer.

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Rabbits were injected yeast at the dose of 0.5 ml/kg body weight, to induce pyrexia. Induction of fever was taken about one to two hours. (Grover, 1990)

Negative control receiving 10ml distill water, positive control group receiving standard drug aspirin, experimental group receiving 100mg/kg Pr.Cr.

2,4–Dinitrophenol (DNP) induced pyrexia

Slightly modifications made in the procedure mentioned by Backhouse et al., (1994). DNP (10 mg/kg) was administered to the rabbits after obtaining the basal rectal temperatures. Hyperthermia developed within 30 min of DNP administration.

Negative control receiving 10ml distill water, positive control group receiving standard drug aspirin, experimental group 1 receiving 100mg/kg Pr.Cr, experimental group 2 receiving verapamil 5mg/kg and group 3 receiving combination of both group 1 and 2 with respective ratio Pr.Cr 50mg/kg + verapamil 2mg/kg.

Rectal temperatures of the animals were obtained at an hour interval for 4hrs.

E-coli induced pyrexia:

Slightly modifications made in the procedure mentioned by Dardi MS, et al., (2005). Pyrexia was induced by a single intravenous injection of E. coli endotoxin (1 microgram/kg i.p.). Negative control receiving 10ml distill water, positive control group receiving standard drug aspirin, experimental group 1 receiving 100mg/kg Pr.Cr, experimental group 2 receiving ciproflaxacin 15mg/kg and group 3 receiving combination of both group 1 and 2 with respective ratio Pr.Cr 50mg/kg + ciproflaxacin 10mg/kg.

Statistical analysis

Data were presented as mean ± standard error (Mean ± SE). Student's t-test was used for comparison between the experimental and control groups. $P < 0.05$ was considered to be statistically significant.

RESULTS

The preliminary phytochemical screening of the methenolic extract showed the presence of plant phytoconstituents such as carbohydrates, alkaloids, glycosides, flavonoids, tannins and saponins were carried out on the powdered bark following standard procedure.

Table 1: Pytochemical analysis of *Plumeria rubra* bark crude extracts (Pr.Cr)

Sr. no	Test	Observations	Result
1	Alkaloid	ppt	Positive
2	Saponins	1cm froth	Positive
3	Tannins	Light purple	Positive
4	Anthraquinones	Pink	Positive
5	Coumarins	Yellow fluorescence	Positive
6	Phenols	Light purple	Positive
7	Flavanoid	Light yellow colour	Positive

Effect of Methanolic crude bark extract of *plumeria rubra* on yeast-induced pyrexia in rabbits.

At a dose of 100 mg/kg body weight, *plumeria rubra* reduced 37.37±0.13C^0 of elevated rectal temperature compared to aspirin 37.44±0.06 C^0 after 3 hours in yeast induced pyrexia rabbits as shown in Table 2. Thus the extract produced significant ($P < 0.05$) antipyretic effect. It was also observed that the solvent has no effect on the reduction of pyrexia of rabbits.

Effect of Methanolic crude bark extract of *plumeria rubra* on 2,4, dinitronitrophenol (DNP)-induced pyrexia in rabbits.

The methanolic extract (100 mg/kg) demonstrated a significant dose-dependent lowering of rectal temperature in DNP-induced pyretic rabbits. The effect was comparable to that of the Calcium

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channel blocking agent verapamil (5mg/kg) and standard drug Aspirin(100 mg/kg) (Table 3). The extract reduced 37.41±0.22 C^0 of elevated rectal temperature compared to verapamil 37.26±0.15 C^0 and aspirin 37.34±0.16 C^0 after 3 hours in 2,4 dinitrophenol induced pyrexia rabbits while the mixture of verapamil and the extract (2mg/kg+50mg/kg) showed significant reduction in the temperature 37.35±0.22 C^0 as shown in Table 3.

Effect of Methanolic crude bark extract of *plumeria rubra* on E-coli induced pyrexia in rabbits.

The methanolic extract produced significant ($P<0.05$) antipyretic effect in E-coli induced pyretic rabbits. At a dose of 100 mg/kg body weight, *plumeria rubra* reduced (37.28±0.08 C^0) of elevated rectal temperate compared to aspirin (37.34±0.12 C^0) and ciproflaxacin (37.31±0.30 C^0), while the combination of both extract and ciprofloxacin reduced the rectal temperature (37.22±0.16 C^0) after 3 hours as shown in Table 4.

DISCUSSION:

On antipyretic activity, the extract inhibited significantly yeast, dinitrophenol and E-coli-induced pyrexia.

Yeast induces pyrexia by increasing the synthesis of prostaglandins (Al-Ghamdi, 2001).

DNP are already reported, induces hyperthermia by uncoupling oxidative

Phosphorylation, as a result of this calcium releases from mitochondrial stores as well as it prevents the calcium reuptake which in result increase the muscle contractility and hyperthermia. (Kumar *et al.,* 2002).

E-coli induces pyrexia by their lipopolysaccharide a vital constituent of cell wall which interns releases interleukin-1 and tumor necrosis factor α. These are responsible for the production of fever causing element prostaglandin E_2. (Steiner AA, et al, 2006).

The probable mechanism could be, antibacterial activity of Pr.Cr.

As antibacterial agents eventually reduces the fever. Pr.Cr possesses good antibacterial activity against E-Coli. So far tested with and without standard antibiotic ciprofloxacin. (Surendra, et al, 2012).

Second possible mechanism could be of Pr.Cr, reducing brain concentration of prostaglandin E_2 especially in the hypothalamus through its action on COX-2 or by increase in the production of the body's own antipyretic substances like arginine and vasopressin (Chandrasekharan, 2002).

The antipyretic potential of Pr.Cr could have been mediated by vasodilatation of superficial blood vessels which interns dissipation of heat following resetting of hypothalamic heat control center (Rang *et al.*, 2007). This action may be due to the phytochemical compounds in this plant.

The phytochemical analysis of this extract showed the presence of alkaloids, monoterpenes, flavonoids and tannins which have been reported to perform antipyretic effect. This study supports the claims of tratditional practice of this durg. (Alam, et al, 2007).

This methanolic extract showed excellent antipyretic effect with and without standard vasodilator Calcium channel blocker verapamil.

The antipyretic property of Pr.Cr depends upon the aforementioned mechanisms or combinations of mechanisms. Till now all the possible mechanisms of antipyretic activity have been reported or studied in detail with their respective standard drugs alone and in combinations. Calcium channel blockade and antimalarial potential of Pr.Cr bark are under investigation in our laboratories.

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Table 2. Antipyretic effect of Pr.Cr on yeast induced pyrexia.

Dose		Rectal Body Temperature (C⁰)			
		0-1 hrs	0-2 hrs	0-3 hrs	0-4 hrs
Control	----	39.98±0.26	40.26±0.25	40.34±0.16	39.85±0.24
Pr.Cr	100mg/kg	40.13±0.12	39.02±0.20	37.86±0.23	37.37±0.13
Aspirin	10mg/kg	40.03±0.10	39.13±0.30	37.91±0.15	37.44±0.06

Table 3. Antipyretic effect of Pr.Cr on dinitrophenol induced pyrexia.

Dose		Rectal Body Temperature (C⁰)			
		0-1 hrs	0-2 hrs	0-3 hrs	0-4 hrs
Control	----	39.12±0.15	39.54±0.21	38.52±0.05	38.15±0.16
Pr.Cr	100mg/kg	40.20±0.12	39.24±0.17	37.95±0.31	37.41±0.22
verapamil	5mg/kg	38.85±0.18	37.92±0.20	37.64±0.24	37.26±0.15
Verapamil+Pr.Cr	2mg/kg+50mg/kg	39.21±0.25	38.36±0.24	37.94±0.28	37.35±0.22
Aspirin	10mg/kg	40.11±0.31	39.51±0.05	37.85±0.13	37.34±0.16

Table 4. Antipyretic effect of Pr.Cr on E-coli induced pyrexia.

Dose		Rectal Body Temperature (C⁰)			
		0-1 hrs	0-2 hrs	0-3 hrs	0-4 hrs
Control	---	38.57±0.15	38.95± 0.13	38.12±0.24	37.86±0.04
Pr.Cr	100mg/kg	40.06±0.28	39.18±0.12	37.94±0.20	37.28±0.08
Ciprofloxacin	15mg/kg	39.12±0.25	38.41±0.34	37.54±0.44	37.31±0.30
ciproflaxacin+Pr.Cr	10mgkg+ 50mg/kg	39.04±0.12	38.2±0.11	37.60±0.31	37.22±0.16
Aspirin	10mg/kg	40.11±0.23	39.23±0.21	37.85±0.24	37.34±0.12

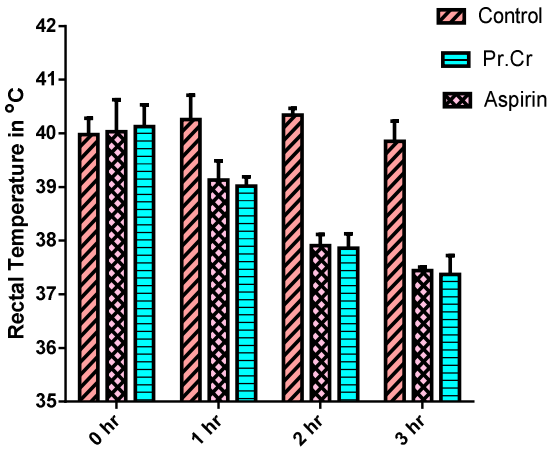

Figure1. Antipyretic activity of *Plumeria rubra*, L bark extract in yeast induced pyrexia.

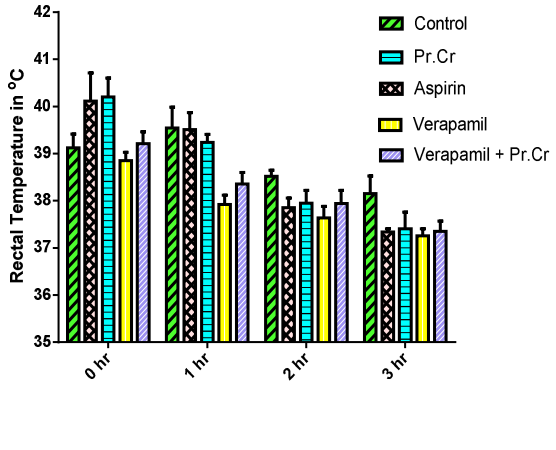

Figure 2. Antipyretic activity of *Plumeria rubra*, L bark extract in Dinitrophenol induced pyrexia.

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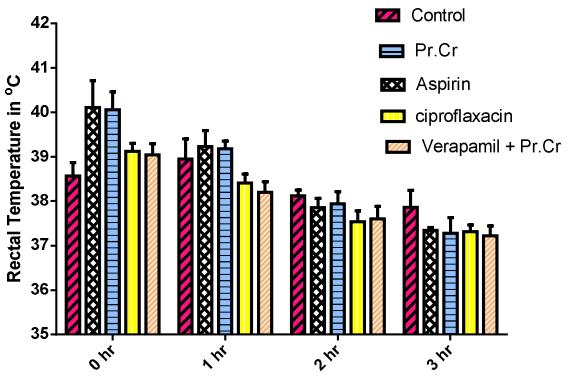

Figure 3. Antipyretic activity of *Plumeria rubra,* L bark extract in E-Coli induced pyrexia.

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