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Research Article

Time and Dose Dependent Antipyretic Investigations of Ethanolic Leaves and Fruits Extracts of *Prosopis cineraria* L. (Druce)

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Abstract

The aim of this Study was to establish a comparative investigation of Antipyretic activity of ethanolic extract of leaves and fruits of the *Prosopis cineraria* and phytochemical evaluation of ethanolic extracts of these parts. Crude ethanolic plant extracts of leaves and fruits of *Prosopis cineraria* at a dose of 200 and 300 mg/kg of body weight were used to evaluate the antipyretic activity. These extracts were evaluated by inducing brewer's-yeast induced pyrexia in albino rats. Results were presented as Mean ± SEM by using SPSS 12.0. Leaves and fruit extracts of *Prosopis cineraria* decreases hyperpyrexia to a significant level when these results were compared to standard control. The leaves extract shows significant effects in lowering the rectal temperature of rats than fruits extract at 200mg/kg while at dose of 300 mg/kg both leaves and fruit extract reduce pyrexia significantly. The phytochemical evaluation shows that both parts of plant contain saponins, tannins, pholobatannins, flavanoids, alkaloids, steroids and cardiac glycosides. Results indicate that ethanolic leaves and fruit extract of Prosopis cineraria possess significant antipyretic activity at different doses which establishes scientific basis for its traditional uses i.e. in rheumatism.

Keywords: *Prosopis cineraria*, Pyrexia, Paracetamol, brewer's-yeast, albino rats

1. Introduction

Increase in the body temperature above the normal physiological limits is known as pyrexia, which may results due to physiological stress such as seen during ovulation, increased thyroid secretion, excessive exercise, from the lesions to central nervous system, infection by microbes, a host of non-infectious processes as inflammation or due to leukemia (Ahmadiani et al., 2001). During such stress as seen in pyrexia, synthesis of pro-inflammatory mediators is increased. These mediators e.g. cytokines, interleukins results in synthesis of prostaglandins etc. near the hypothalamic region of brain which causes pyretic reaction by shifting the normal equilibrium in hypothalamus to generate more heat etc. (Joseph et al., 2011). As the body temperature rises, through a feedback mechanism, the blood vessels dilate to lower the temperature. When body temperature decreased, then there is vasoconstriction and the body's internal temperature is preserved. Most of antipyretics serve their function through COX-2 inhibition and lowers the body temperature by PgE2 inhibition. Many synthetic antipyretics inhibit the COX-2 irreversibly and selectively but cause damage to hepatocytes, golmerulocytes, cardiac cells and cells of brain cortex. Therefore, it is very important to use the natural antipyretic agents which are non-specific in their action and have least effects on other organs of the body (Khan et al., 2008).

Prosopis cineraria also known as kherji, jandi or ghaf in different locations of the world. The plant is distributed in various Middle East countries and also various states of India like Rajasthan, Gujarat, Haryana, Uttarpradesh and Tamilnadu (Velmurugan et al., 2011). The genus Prosopis belongs to family Leguminosae, sub family Mimosiaceae and contains approximately forty four species (Khatri et al., 2011). Whole plant is useful for the treatment of many diseases e.g., skin diseases, piles, worms, coughs, vertigo

and dyspnoea (Manikandar et al., 2009). The bark of plant is used for the treatment of rheumatism in the Indian province of central Punjab (Verma et al., 2011). The flowers of plant are mixed with sugar and eaten by the pregnant women as a protectant against abortion; the ashes of plant have depilatory action when it is rubbed on the skin (Khatri et al., 2011). Farmers eat ripe dried fruits of plant to get rid of the excessive thirst during summer season. Flowers of plant, when mixed with sugar in water, are used for skin diseases, to prevent boils, as blood purifier and for producing cooling effect. Phytochemical evaluation of plant reveals that it contains ethyl acetate methyl heptacosanoate. In addition, heptacosanoate, β-sitosterol, ursolic acid, gallic acid, luteolin and β-sitosterol, 3-O-β-D-glucopyranoside was also detected in various parts of plant and had been isolated from it (Khan et al., 2008). Some other researcher have also reported a few new chemical constituents from the plant e.g. patulitrin (a glucoside of petuletin), sitosterol (steroid), spicigerine (alkaloid), prosogerine A & B, prosogerin C, and prosogerin E (flavones) (Ukani et al., 2000).

2. Materials and Methods

2.1. Collection of plant material

Leaves and fruits of *Prosopis cieneraria* were collected from the desert of Bahawalpur in the month of April. The *Prosopis cieneraria* leaves and fruit part was authenticated by the Assistant professor of Botany Mr. Saeed Raza Peerzada from the Cholistan Institute of Desert Studies (SIDS) of the Islamia University of Bahawalpur and voucher number of the latter of authentication is 0573-IU. The specimen was deposited at the herbarium of the pharmacy department of the Islamia University of Bahawalpur which is maintained by Dr. Qaiser Jabeen, Associate professor of pharmacology in the department of pharmacy, The Islamia University of Bahawalpur for future reference and voucher number is PC-LE-03-12-036 for leaves and PC-FT-06-12-038 for fruit.

For the preparation of extracts of dried leaves and fruit of *Prosopis cineraria* were used. Paracetamol was taken from the market of Bahawalpur. Ethanol was brought from Merk KgaA Darmstadt, Germany. Distilled water was taken from the Department of pharmacy, IUB, Pakistan. Rotary evaporator brought from Eyela, Co. Ltd. Japan. Refrigerator used was from Dawlance, Pakistan and the results of study were analysed by using SPSS version15.0.

2.2. Animals

Albino rats of either sex weighing 180-200 grams were used for the experiments. The animals were randomly divided in to eight groups and each group contains four rats. Animals had access to lab food and water *ad libitum*.

2.3. Ethical standard

This study was approved by the Board of Advanced Study and Research (BASR), The Islamia University of Bahawalpur, and the institutional ethical committee, Department of Pharmacy, The Islamia University of Bahawalpur, Bahawalpur, Pakistan, in compliance with "Guide for care and use of laboratory animals (1996)". The ethical committee gave a letter of recommendation for using the Albino rats in this study, whose reference no. is Pharm 1857.

2.4. Preparation of crude plant extract

The plant material was washed under fresh running tap water and dried under shade until a constant weight was obtained. The plant material was ground to coarse powder by using pestle and mortar and then using an electric grinder. Then it was macerated in 70% ethanol for three days with occasional stirring. At the end of third day, plant material was first filtered through muslin cloth and then through Whatman qualitative grade 1 filter paper. The filtrate was concentrated under reduced pressure and low temperature by using rotary evaporator. The extract was stored at -20℃ to prevent the deterioration of temperature sensitive components until further used for the phytochemical and pharmacological studies (Jabeen et al., 2009).

2.6. Phytochemical evaluation

The different chemical tests were performed on the extracts of leaves and fruit of *Prosopis cineraria* to screen for various classes of bioactive secondary metabolites such as alkaloids, saponins, tannins, flavonoids, cardiac glycosides and anthraquinones according to the methods described by El-Olemy and

co-workers (1994) and Trease and Evans (2009).

2.7. Antipyretic action

For the determination of antipyretic actions of the crude plant extracts, pyrexia was induced in rats by administration of 20% w/v aqueous suspension of brewer's yeast at a dose of 10 ml/Kg, i.p. injection (Ahmadiani et al., 2001). The animals were then fasted until completion of experiment while they had free access to water. Before administration of brewer's yeast, rectal temperatures were measured with digital clinical thermometer 16 hours earlier that served as normal control. On next day, before the administration of the standard antipyretic drug and extract in the respective groups, temperatures were recorded in fevered rats that serve as positive control (Vane, 1987). Temperatures were recorded at -16 hour, 0 hour, 1 hour, 2 hour, 3 hour and 4 hour. Paracetamol at dose of 150 mg/Kg of the body weight was administered as i.p injection which served as reference control (Sawadogo et al., 2006).

3. Results and Discussion

Preliminary phytochemical analysis reveals that the crude plant extract contains flavanoids, saponins, tannins, phlobatannins, steroids and cardiac glycosides as shown in Table (1).

Table.1 Results of phytochemical analysis of ethanolic extracts of leaves and fruit parts of *Prosopis cineraria.*

No.	Phytochemical tests	Test results
1	Alkaloids	++
2	Saponins	+
3	Tannins	+
4	Flavonoids	+++
5	Cardiac Glycosides	++
6	Anthraquinones	++++

The investigation of the antipyretic effects of crude extract of *Prosopis cineraria* leaves and fruits on the albino rats was done at a dose of 200 and 300 mg/Kg of body weight. Effects were compared to the standard control group to which paracetamol was administered at a dose of 150 mg/Kg of body weight by intra-peritoneal injection. After sixteen hours of administration of Brewer's yeast, rectal temperatures of rats were increased up to 39.8 ± 0.187oC, as indicated by control group. It was found that both leaves and fruits extracts proved to be highly significant antipyretics in their effects after 2 hours of administration of plant extracts. As both extract significantly reduces rectal temperatures of the rats. Leaves extract at 200 and 300 mg/kg dose produces effects however fruits extract shows its effects at 300 mg/kg. While after three hours of extract administration it was found that both leaves and fruits extract at 300 mg/kg produced highly significant results compared with the standard control group that was treated with standard drug paracetamol. It is obvious from Table (2) and Figure (1) and (2).

Table: 2. Antipyretic effects of *Prosopis cineraria* leaves and fruits extracts at various doses on albino rats

Groups	Dose	-16 hr	0 hr.	1 hr.	2hr.	3 hr.	4 hr.
A	-	37.2 ±0.132	37.2 ±0.111	37.2 ± .0854	37.2 ±0.085	37.2 ± 0.0629	37.2 ± 0.0816
B	-	37.4 ±0.225^{ns}	39.8 ±0.187$^{\psi}$	39.7 ±0.187$^{\psi}$	39.6 ±0.081$^{\psi}$	39.3 ± 0.175$^{\psi}$	39.1 ± 0.266$^{\psi}$
C	**150 mg / Kg**	37.1 ±0.0957^{ns}	39.7 ± 0.155^{ns}	37.9 ± 0.160$^{\psi}$	37.5 ±0.155$^{\psi}$	37.3 ± 0.0250$^{\psi}$	37.5 ± 0.108**
D	**200 mg / Kg**	37.3 ±0.308^{ns}	39.0 ± 0.437^{ns}	38.3 ± .463*	38.3 ±0.206$^{\psi}$	37.7 ± 0.225**	37.9 ± 0.119**
E	**300 mg / Kg**	37.2 ±0.119^{ns}	39.6 ± 0.138^{ns}	38.7 ± .346*	37.9 ± 0.263$^{\psi}$	37.4 ± 0.137$^{\psi}$	37.5 ± 0.0408$^{\psi}$
F	**200 mg / Kg**	37.4 ±0.455^{ns}	39.5 ± 0.478^{ns}	38.7 ± .405^{ns}	38.3 ± 0.524*	37.8 ± 0.519*	38.0 ± 0.512^{ns}
G	**300 mg / Kg**	37.1 ±0.0854^{ns}	39.2 ± 0.111*	38.4 ± .155**	38.3 ± 0.524$^{\psi}$	37.4 ± 0.158$^{\psi}$	37.6 ± 0.149**

A=Normal control, B=Diseased control, C=Paracetamol / standard control, D=*Prosopis cineraria* leaves, E=*Prosopis cineraria* leaves, F=*Prosopis cineraria* fruits, G=*Prosopis cineraria* fruits; n = 4. P < 0.05 significant (*), P < 0.01 significant (**), and P < 0.0001 highly significant (ψ), ns = non-significant

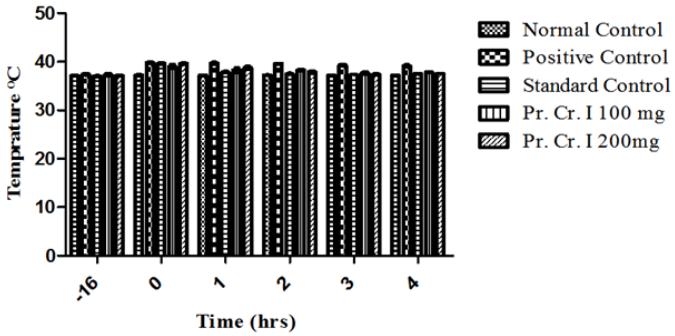

Fig. 1 Effects of *Prosopis cineraria* crude leaves extract on temprature of Albino rats

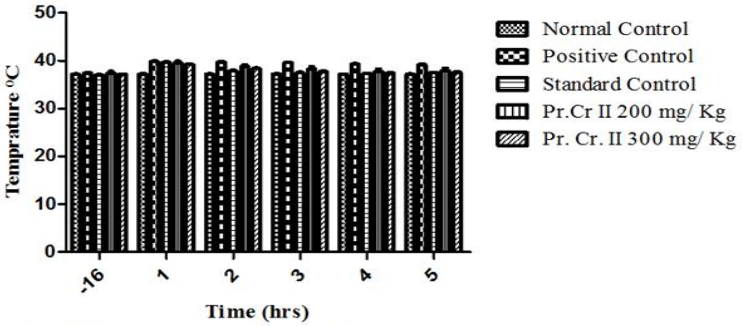

Fig. 2 Effects of *Prosopis cineraria* crude fruits extract on temprature of Albino rats

As modern universal attention in the herbal medicine has led to the development and studies of many remedies which are used by various racial groups of the world (Almeida et al., 2001). The results obtained in this study are in accordance with the previous studies performed on aqueous extract of *Prosopis cineraria* stem bark extract which reduces the pyrexia of albino rats (Josephet al., 2011). Decrease in rectal temperature of rats was dose dependant and comparable to standard drug used during this study (Singh et al., 2010). The ethanolic extract of *Prosopis cineraria* leaves which reduces rectal temperatures of rats, means that leaves must contains such substances which reduces pyrexia (Sunilson et al., 2009). Ethanol and aqueous extracts were evaluated previously for antipyretic effects, showed significant reduction of hyper-pyrexia, this confirms that Aqueous-ethanolic solvent dissolves substances which reduces pyrexia (Berkanet al., 1991, Daud et al., 2006, Singh et al., 2010). We can say that antipyretic effects of *Prosopis cineraria* may also be due to both central and peripheral effects, which are due to presence of psychoactive components that cause central nervous depression. As nervous system depression reduce body temperature both in normal and fevered conditions (Ta ïve et al., 2011). PgE2 are responsible for increasing body temperature by acting on preoptic areas of hypothalamus in brain. So it is one possible mechanism through which these extract inhibit PgE2 in brain and lowers pyrexia (Li et al., 2008). Antipyretic effects observed may be due to single or group of biologically active metabolites of the plant. As phytochemical evaluation reveals that both leaves and fruits extract contains flavanoids, saponins, tannins, phlobatannins, steroids and cardiac glycosides. So these secondary metabolites in *Prosopis cineraria* may also be responsible for this antipyretic activity (Sunilson et al., 2009). Prostaglandins are inhibited by flavanoids, as flavanoids also act as antioxidants which results in decreasing pyrexia (Mutalik et al., 2003, Sharma et al., 2010) and it is known that prostaglandins are involved in raising the body temperature. Therefore flavanoids present in *Prosopis cineraria* cause hypothermia. Alkaloids reduce body temperature but they cause gastric ulcers which suggest that they have same mechanism as that of NSAIDS, alkaloids in this case are one of active constituents that lowers temperature (Esra et al., 2002). It is reported that those plants that acts as antimicrobial agent they reduce pyrexia. In this case fever was produced by Brewer's yeast and was reduced by extracts of plant, as *Prosopis cineraria* also possesses antimicrobial properties, so it is another possible mechanism through which it reduces pyrexia (Velmurugan et al., 2011) but for leaves part of this plant it is need to be explore for antimicrobial property. It is concluded from results that *Prosopis cineraria* contains such active biological constituents which have antipyretic effects. Therefore further evaluation directs to isolation of responsible components which will provide new lead compounds.

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