International Journal of Pharmaceutics & Drug Research
ISSN: 2347-6346
Available online at http://ijpdr.com

Original Research Article

EVALUATE BIOACTIVE CONSTITUENTS AND ANTIPYRETIC POTENTIAL OF HYDROALCOHOLIC EXTRACTS OF *FOENICULUM VULGARE*

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***Article History:**

Received: 12/02/2021
Revised: 21/02/2021
Accepted: 17/03/2021

ABSTRACT

Medicinal plants are assuming greater importance in the primary health care of individuals and communities in many developing countries. Indian medicinal plants and their derivatives have been an invaluable source of therapeutic agents to treat various disorders. Herbal products are often perceived as safe because they are "natural". *Foeniculum vulgare* Mill. (Apiaceae family) commonly known as fennel, is one of the widespread annual or perennial plants with aromatic odor. *Foeniculum vulgare* (Apiaceae) is a popular plant with valuable medicinal and culinary importance. It is mostly used in the treatment of ailments associated with digestive and respiratory systems, so our aim of the study is extraction, phytochemical screening and anti- antipyretic activity of *Foeniculum vulgare* seeds extract. The Antipyretic effect of Hydroalcoholic extract of seeds of *Foeniculum vulgare* significantly lowered the temperature in yeast induced pyrexia. The lowering of temperature was almost in a similar manner to that of reference drug, paracetamol, suggesting that the plant have antipyretic property which can be assumed to be mediated through interference of prostaglandin synthesis and inhibition of cytokines release. The conclusion of the study demonstrated that Hydroalcoholic extract of leaves of *Foeniculum vulgare* displayed antipyretic property.

Key words: *Foeniculum vulgare*, yeast induced pyrexia, hydroalcoholic extract.

INTRODUCTION:

In India nearly 15000 plant species are used as a source of medicine. Many of the ancestor plants are highly endangered and urgently need to be maintained in their native habitats. Unless we preserve genetic material for propagation from these species now, many will be extinct before we can protect and restore habitats for their long term recovery. Surveying, monitoring and collecting material for propagation from populations of these species are the primary activities of individual. The viable plant material, living plant collections and long term seed storage can be preserved in order to maximize their potential for future use in our restoration efforts. To ensure accurate accession records, especially necessary for future restoration work, collection of highly accurate GPS location data for individual plants and populations is essential, as is creation of high quality species distribution and survey maps. Land owners and government agencies that are willing to

implement plant restoration programs on their properties may also benefit from government.

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 infectious agent or damaged tissue cannot survive (Chattopadhyay *et al*., 2005). Normally the infected or damaged tissue initiates the enhanced formation of proinflammatory mediator's (Cytokines like interleukin 1β, α, β and TNF- α), which increase the synthesis of prostaglandin E2 (PG E2) near peptic hypothalamus area and thereby triggering the hypothalamus to elevate the body temperature (Spacer and Breder, 1994).

As the temperature regulatory system is governed by a nervous feedback mechanism, so when body temperature becomes very high, it dilate the blood vessels and increasing sweating to reduce the temperature; but when the body temperature become very low hypothalamus protect the internal temperature by vasoconstriction. High fever often increases faster disease progression by increasing tissue catabolism, dehydration and existing complaints, as found in HIV (Veugelers *et al* 1997). Drugs having anti-inflammatory activity generally possess antipyretic activity (e.g) non-steroidal anti-inflammatory drugs (NSAIDs). It has been suggested that prostaglandin (PGE) mediates pyrogen fever; the ability of NSAIDs, to inhibit prostaglandin synthesis could help to explain their antipyretic activity.

Fever is one of the most common presenting signs of illness in office-based primary care pediatric practice, accounting for 19% to 30% of visits (Eskerud *et al*., 1992; Baucher *et al*., 2001). Infants and young children are particularly susceptible to fever because of their small body size, high ratio of body surface area to weight, and low amount of subcutaneous fat. Although most experts consider fever a beneficial physiologic response to the infectious process, it can lead to patient irritability and stress as well as high parental anxiety (Guton *et al*., 1997). Therefore, physicians usually prefer to prescribe antipyretic agents in addition to nonpharmacologic, physical fever-reducing modalities (Baraff *et al*., 1993).

Pyrexia or Fever is defined as an elevation of body temperature. It is a response due to tissue damage, inflammation, malignancy or graft rejection. Cytokines, interleukin, interferon and Tumor Necrosis Factor α (TNF- α) are formed in large amount under this condition, which increase PGE2 which in turn triggers hypothalamus to elevate body temperature (Rajani *et al* 2011). Fever is associated with symptoms of sickness behavior which consist of lethargy, depression, anorexia, sleepiness, & inability to concentrate. This increase in set point triggers increased muscle tone & shivering. However antipyretic medication can be effective at lowering the temperature which may include the affected person's comfort (Duraisankar *et al* 2012).

According to Ayurveda, pyrexia originates from a combination of indigestion, seasonal variations and significant alterations in daily routine (Gupta *et al*.,2008). Due to poor hygiene practices and malnutrition, children in developing countries frequently suffer from various forms of infections which present as fevers. These fevers are often accompanied by

aches and pains which all lead to morbidity and mortality (Ighodaro *et al*., 2009).

Antipyretics are drugs which can reduce elevated body temperature. Regulation of body temperature requires a delicate balance between production and loss of heat, and the hypothalamus which regulate the set point of body temperature. Drugs like paracetamol do not influence body temperature when elevated by factors such as exercise or increase in ambient temperature (Gomathi *et al*., 2011).

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 antipyretic effect by suppressing TNF-α (Adesokan *et al*., 2008) and its related compounds also exhibit inhibition of arachidonic acid peroxidation, which results in reduction of prostaglandin levels thus reducing the fever and pain (Taiwe *et al*., 2011).

Medicinal plants are assuming greater importance in the primary health care of individuals and communities in many developing countries. Indian medicinal plants and their derivatives have been an invaluable source of therapeutic agents to treat various disorders. Herbal products are often perceived as safe because they are "natural". *Foeniculum vulgare* Mill. (Apiaceae family) commonly known as fennel, is one of the widespread annual or perennial plants with aromatic odor. *Foeniculum vulgare* (Apiaceae) is a popular plant with valuable medicinal and culinary importance. It is mostly used in the treatment of ailments associated with digestive and respiratory systems So our aim of the study is extraction, phytochemical screening and anti-antipyretic activity of *Foeniculum vulgare* seeds extract.

MATERIAL AND METHODS

Material

Yeast was used in present study.

Methods

Extraction procedure

Following procedure was adopted for the preparation of hydroalcoholic extract from the shade dried and powdered herbs (Mukherjee, 2007).

Extraction by maceration process

60.1 gm dried powdered seeds of *Foeniculum vulgare* has been extracted with hydroalcoholic solvent (methanol: water; 70:30) using maceration process for 48 hrs, filtered and dried using vaccum evaporator at 40^0C.

Determination of percentage yield

The percentage yield of each extract was calculated by using following formula:

$$\text{Percentage yield} = \frac{\text{Weight of Extract}}{\text{Weight of powder drug Taken}} \times 100$$

Phytochemical Screening

The chemical tests were performed for testing different chemical groups present in extracts (Kokate, 1994).

Total Phenolic content estimation

Principle: The total phenolic content of the extract was determined by the modified Folin-Ciocalteu method.

Preparation of Standard: 10 mg Gallic acid was dissolved in 10 ml methanol, various aliquots of 5- 25µg/ml was prepared in methanol

Preparation of Extract: 10mg of dried extract of plant material was extracted with 10 ml methanol and filter. 2 ml (1mg/ml) of this extract was for the estimation of Phenol.

Procedure: 2 ml of each extract or standard was mixed with 1 ml of Folin-Ciocalteu reagent (previously diluted with distilled water 1:10 v/v) and 1 ml (7.5g/l) of sodium carbonate. The mixture was vortexed for 15s and allowed to stand for 15min at 40°C for colour development. The absorbance was measured at 765 nm using a spectrophotometer.

Total flavonoids content estimation

Principle: Determination of total flavonoids content was based on aluminium chloride method (Olufunmiso *et al.,* 2011).

Preparation of standard: 10 mg quercetin was dissolved in 10 ml methanol, and various aliquots of 5- 25µg/ml were prepared in methanol.

Preparation of extract: 10mg of dried extract of plant material was extracted with 10 ml methanol and filter. 3 ml (1mg/ml) of this extract was for the estimation of flavonoid.

Procedure: 1 ml of 2% $AlCl_3$ methanolic solution was added to 3 ml of extract or standard and allowed to stand for 15 min at room temperature; absorbance was measured at 420 nm.

***In Vivo* antipyretic activity**

Animals

Wistar rats (150–200 g) were group housed (n= 6) under a standard 12 h light/dark cycle and controlled conditions of temperature and humidity (25±2 °C, 55–65%). Rats received standard rodent chow and water *ad libitum*. Rats were acclimatized to laboratory conditions for 7 days before carrying out the experiments. All the experiments were carried in a noise-free room between 08.00 to 15.00 h. Separate group (n=6) of rats was used for each set of experiments. The animal studies were approved by the Institutional Animal Ethics Committee (IAEC), constituted for the purpose of control and supervision of experimental animals by Ministry of Environment and Forests, Government of India, New Delhi, India.

Toxicity study

Preliminary experiments were carried out on rats (n=6). Hydroalcoholic extract of seeds of *Foeniculum vulgare* were administered orally in different doses to find out the range of doses which cause zero and 100 % mortality of animals. Acute oral toxicity was conducted according to the method of Organisation for Economic Co-operation and Development (OECD) (OECD, 2001). Animals were kept fasting providing only water, extract were given p.o. in doses of 500, 1000 and 2000 mg/kg/p.o. administered orally for 4 days of different groups of rats (n=6) and the animals were kept under observation for mortality as well as any behavioral changes for evaluation of a possible antipyretic activity.

Yeast induced hyperthermia in Rats

The antipyretic activity was evaluated with fever induced by Brewer's yeast following the established method in rats with some modifications (Tomazetti *et al.,* 2005). At zero hour, the basal rectal temperature of each rat was recorded using clinical digital thermometer. Pyrexia was induced by subcutaneous injection of 15% w/v suspension of Brewer's yeast in distilled water at a dose of 10 mL/kg body weight. After 18 hr of Brewer's yeast injection the rise in rectal temperature was recorded and only animals showing an increase in temperature of at least 0.6°C (or

1°F) were selected for the study. The animals were randomly divided into six groups, each group containing five rats.

Group I received 1% Tween-80 in normal saline orally.

Group II was given standard drug paracetamol at the dose of 100 mg/kg per orally.

Groups III received Hydroalcoholic extract of seeds of *Foeniculum vulgare* at oral dose of 200 mg/kg.

Groups IV received Hydroalcoholic extract of seeds of *Foeniculum vulgare* at oral dose of 400 mg/kg.

After the treatment, the temperature of all the rats in each group was recorded at 0 hr, 1 hr, 2 hr, 3 hr, and 4 hr.

Statistical Analysis

All analysis was performed using graph pad prism for Windows. All statistical analysis is expressed as mean ± standard error of the mean (SEM). Data were analyzed by one way ANOVA, where applicable $p<0.05$ was considered statistically significant, compared with vehicle followed by Dunnett's test.

RESULTS AND DISCUSSION

Antipyretic effects of Hydroalcoholic extract of seeds of *Foeniculum vulgare* on rectal temperature are presented in Table 7. The subcutaneous injection of yeast markedly increased the rectal temperature and the mean increment recorded was 1.24–2°F after 18 hr of administration. The extract and paracetamol treatment groups showed significant effect on rectal temperature with significant reduction of temperature over period of time from 1 hr to 4 hr. The Hydroalcoholic extract of seeds of *Foeniculum vulgare* at the dose of 400 mg/kg and 200 mg/kg body weight significantly attenuated hyperthermia in rats in 1 hr observation and lowering of temperature was even more significant from 2 hr to 4 hr observation period in comparison to control. Standard drug paracetamol also significantly inhibited pyrexia in early and latter hours of observation time intervals. The different treatment Hydroalcoholic extract of seeds of *Foeniculum vulgare* and paracetamol lowered the rectal temperature in time dependent manner.

Yeast induced fever, which represents pathogenic fever, presents an economical and reliable method for assessing new antipyretics. The presence of proteins in yeast is linked to fever via inflammatory reaction in this method. Further, the production of proinflammatory cytokines such as interleukin-1β (IL-1β) and IL-6, interferon-α (IFN-α), and tumor necrosis factor-α (TNF-α) and prostaglandins like PGE2 and PGI2 are responsible for elevating the body temperature by acting on brain. Antipyretics such as paracetamol used in management of fever act through several ways by reducing levels of prostaglandins acting on cyclooxygenase enzymes, enhancing antipyretic message within brain and stimulating anti-inflammatory signals at injury site. The Antipyretic effect of Hydroalcoholic extract of seeds of *Foeniculum vulgare* significantly lowered the temperature in yeast induced pyrexia. The lowering of temperature was almost in a similar manner to that of reference drug, paracetamol, suggesting that the plant have antipyretic property which can be assumed to be mediated through interference of prostaglandin synthesis and inhibition of cytokines release (Veale *et al.*, 1977). The conclusion of the study demonstrated that Hydroalcoholic extract of leaves of *Foeniculum vulgare* displayed antipyretic property.

Table 1: % Yield of hydroalcoholic extract of *Foeniculum vulgare*

S. No.	Part	% Yield (W/W)
1.	Seeds	5.25

Table 2: Phytochemical screening of hydroalcoholic extract of *Foeniculum vulgare*

S. No.	Constituents	Hydroalcoholic extract
1.	**Alkaloids** Dragendroff's test Hager's test	 -ve -ve
3.	**Flavonoids** Lead acetate Alkaline test	 +ve +ve
4.	**Phenolics** $Fecl_3$	 +ve
5.	**Proteins** **And Amino acids** Xanthoproteic test	 +ve
6.	**Carbohydrates** Fehling's test	 +ve
7.	**Saponins** Foam test	 +ve
8.	**Diterpenes** Copper acetate test	 +ve

Table 3: Total Phenolic and Total flavonoid content of extract of *Foeniculum vulgare*

S. No.	Extract	Total Phenol (GAE) (mg/100mg)	Total flavonoid (QE) (mg/100mg)
1.	**Hydroalcoholic extract**	0.125	0.956

Table 4: Antipyretic effect of Hydroalcoholic extract of leaves of *Foeniculum vulgare* in yeast induced pyrexia in rats

Treatment	Dose (mg/kg)	Basal temp. °F	Rectal temperature (°F)				
			0 hour (after 18 hr)	1 hr	2 hr	3 hr	4 hr
Control	15% w/v suspension of Brewer's yeast (10 mL/kg)	99.0	100.5 ± 0.3	100.7 ±0.1	100.7 ± 0.1	100.6± 0.1	100.6 ± 0.1
Paracetamol	100 mg/kg	98.50	100.5 ± 0.3	99.8 ± 0.1	100.5 ± 0.3	99.8 ± 0.1	100.5± 0.3
Hydroalcoholic seeds extract *Foeniculum vulgare*	200mg/kg	98.50	99.7 ± 0.2	99.5 ± 0.2	99.7 ± 0.2	99.5 ± 0.2	99.7 ± 0.2
Hydroalcoholic seeds extract Foeniculum vulgare	400mg/kg	98.40	99.6 ± 0.1	99.5± 0.2	99.0 ± 0.2	98.7 ± 0.2	98.3 ± 0.2

Values are expressed as mean ± SD. $^{*}P < 0.05$-significant compared to formalin treated group.

CONCLUSION

The Antipyretic effect of Hydroalcoholic extract of seeds of *Foeniculum vulgare* significantly lowered the temperature in yeast induced pyrexia. The lowering of temperature was almost in a similar manner to that of reference drug, paracetamol, suggesting that the plant have antipyretic property which can be assumed to be mediated through interference of prostaglandin synthesis and inhibition of cytokines release. The conclusion of the study demonstrated that Hydroalcoholic extract of leaves of *Foeniculum vulgare* displayed antipyretic property.

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