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PROSTAGLANDIN MEDIATED ANTIPYRETIC EFFECTS OF THE AQUEOUS AND ALCOHOLIC EXTRACTS OF THE SEEDS OF *TRIGONELLA FOENUM- GRAECUM* IN ALBINO RAT

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ABSTRACT

Fenugreek, *Trigonella foenum-graecum* L.[Fam. Fabaceae], also known as methi, is indigenous to the Mediterranean region, the Ukraine, India, and China. The medicinal properties of fenugreek is found in the ripe, dry seeds, which have been used for thousands of years in Arabian, Greek, Indian, and Chinese medicine. The present study was undertaken to evaluate the possible antipyretic activity of the aqueous and ethanolic extracts of *Trigonella foenum-graecum* seeds. The methodology used is the antipyretic activity of the aqueous and ethanolic extract at different doses (200mg/kg and 400mg/kg p.o) was evaluated using the Brewer's yeast induced pyrexia model in rats with paracetamol (150mg/kg) as the standard drug. The percentage of antipyretic activity was then calculated. The resulted is Both the extracts at the doses of 200mg/kg and 400 mg/kg significantly ($p < 0.05$) reduced the increased rectal temperature. The extracts started reducing the elevated rectal temperature after the third hour of treatment in a dose dependent manner. At the dose of 400 mg/kg the aqueous and ethanol extract reduced the elevated rectal temperature by 76.19 % and 83.87 % respectively as compared to the reference drug paracetamol (96.52%), after 6 hrs of treatment. Thus both the extracts of *Trigonella foenum-graecum* seed have antipyretic activity, the ethanol extract being slightly more potent than the aqueous extract. So that can conclude the present study shows that *Trigonella foenum-graecum* seeds extracts possess significant antipyretic activity.

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Key Words

Antipyretic, Brewer's yeast, fenugreek, prostaglandin, *Trigonella foenum-graecum*, rectal temperature

INTRODUCTION

Trigonella foenum graecum (TFG) of family fabacea, an annual herb, chiefly cultivated for its seeds, commonly known as fenugreek is a common condiment of our Indian Community. TFG has rich medicinal properties. Its seeds have hypoglycemic and hypolipidaemic activities¹. Medical Papyri from ancient Egyptian tombs reveal that it was used as an antipyretic². Our previous studies have revealed its antinociceptive and anti-inflammatory properties³. Drugs which possess anti-inflammatory and analgesic properties may also exhibit antipyretic effect. Thus this study was carried out with the objective of assessing the possible antipyretic effect of the aqueous and alcoholic extracts of seeds of TFG by yeast induced pyrexia in albino rats.

MATERIALS AND METHODS

Plant material and preparation of extracts: The seeds of TFG were collected from the local market and identified by a pharmacognocist. They were crushed to a coarse powder and extracted with ethanol (70%v/v) and distilled water in a soxhlet's extractor for 24hrs and then air dried. The alcoholic and the aqueous extracts were stored in refrigerator and reconstituted in distilled water just prior to use.

Drugs and chemicals: Paracetamol was obtained as gift sample from Mepro Pharmaceuticals Pvt. Ltd., Surendranagar, Gujarat, India. Double distilled water was employed for reconstitution of the extracts. Both the standard drug and the extracts of TFG were given by oral route.

Animals: Adult Wistar albino rats of either sex weighing 150-200gms were taken, housed in cages at normal room temperature and had access to food and water ad libitum. The animals with constant rectal temperature were selected for the study. They were then divided into 6 groups of 6 rats in each group.

EVALUATION OF ANTIPYRETIC ACTIVITY⁴

Prior to the experiment, the rats were maintained in separate cages for 7 days and the animals with approximately constant rectal temperature were selected for the study. Fever was induced by administration of 15 % w/v aqueous suspension of

Brewer's yeast subcutaneously below the nape of the neck at a dose of 20 ml/kg of body weight. Rectal temperature was determined by introducing a clinical thermometer 1 inch into the rectum and keeping it inside for 1 minute. Only rats that showed an increase in temperature of at least 0.7 °C were used for the study. The rats were then divided into 6 groups of 6 rats in each. The rectal temperature was recorded using a clinical thermometer immediately before and 18 h after Brewer's yeast injection. After 18 h of yeast injection different groups received vehicle (distilled water), aqueous and ethanol extracts (200 and 400 mg/kg body weight) and reference drug (paracetamol, 150 mg/kg body weight) through oral route. The rectal temperature was then periodically recorded at 1hr, 3hr and at 6 hour over an observational period of 6 hours.

Percentage reduction in rectal temperature was calculated considering the total fall in temperature to normal level as 100%.

% reduction =

$$\frac{\text{temp 18 hrs after yeast} - \text{temp after drugs/extract at different hours}}{\text{temperature 18 hrs after yeast} - \text{normal rectal temperature prior to yeast administration}} \times 100$$

temperature 18 hrs after yeast- normal rectal temperature prior to yeast administration

The protocol was approved by the Institutional Ethical Committee.

STATISTICAL ANALYSIS

The values were expressed as mean \pm standard error of mean (SEM). The degree of significance was assessed by Student's 't' test and p values < 0.05 was considered as statistically significant.

OBSERVATIONS AND RESULTS

The mean initial basal rectal temperature in this study ranged from 34.43°C \pm 0.10°C to 34.75°C \pm 0.12°C. The rise in temperature after 18 hrs of induction of fever by yeast was 35.68°C \pm 0.16°C to 36.33°C \pm 0.19°C. Thus in this study the experimental rats showed a mean increase of about 1.25 °C in rectal temperature 18 hours after Brewer's yeast injection. Both the extracts of TFG seeds showed significant (p < 0.05) antipyretic activity and reduction of the elevated rectal temperature from the third hour of treatment and in a dose dependent manner. The initial and final rectal

temperatures ($^{\circ}\text{C}$) after 6 hours, in the groups treated with aqueous extract (400 mg/kg body weight) and ethanol extract (400 mg/kg body weight) were found to be $35.68^{\circ}\text{C} \pm 0.16^{\circ}\text{C}$ and $34.85^{\circ}\text{C} \pm 0.13^{\circ}\text{C}$, $36.20^{\circ}\text{C} \pm 0.29^{\circ}\text{C}$ and $34.95^{\circ}\text{C} \pm 0.25^{\circ}\text{C}$ respectively, compared to $35.71^{\circ}\text{C} \pm 0.19^{\circ}\text{C}$ and $34.60^{\circ}\text{C} \pm 0.15^{\circ}\text{C}$ in the paracetamol (reference drug) treated group. At the dose of 400 mg/kg body weight the aqueous extract and ethanol extract reduced the elevated rectal temperature by 76.19% and 86.20% respectively as compared to 96.52 % by the reference drug paracetamol after 6 hrs. Hence, both the extracts exhibited significant antipyretic activity in a dose dependent manner and that the ethanolic extract of TFG was found to be slightly more potent than the aqueous extract.

DISCUSSION

Fever may be due to infection or may be due to tissue damage, graft rejection and or other disease states. Yeast-induced pyrexia is called pathogenic fever and its etiology involves production of prostaglandins, which set the thermoregulatory centre at a lower temperature⁵. The production of prostaglandins, mainly the most potent pyretic agent, PGE2 appears to be a final pathway responsible for fever production induced by several pyrogens. Antipyretics are the agents that reduce this elevated body temperature. The antipyretic activity is generally exhibited by the nonsteroidal anti-inflammatory drugs, due to their inhibitory effect on prostaglandin biosynthesis in the central nervous system⁶. Both the aqueous and ethanol extracts of TFG exhibited significant ($p < 0.05$) antipyretic activity in

yeast-induced elevation in body temperature in rats in a dose dependent manner and the effects were comparable to the reference antipyretic drug paracetamol. As it is accepted that prostaglandin E2 (PGE2) is the final fever mediator in the brain, specifically in the preoptic area of the anterior hypothalamus⁷, thus it may be plausible to conclude that the observed antipyretic activity of TFG seeds extract possibly inhibits the synthesis of prostaglandins in the central nervous system. The ethanol extract was found to be slightly more potent than the aqueous extract. Phytochemical studies have shown that TFG seeds contain flavonoids and saponins⁸. Some studies report that some flavonoids are predominant inhibitors of either the cyclo-oxygenase or the lipo-oxygenase enzymes involved in the arachidonic acid metabolism pathway^{9,10}. Our previous studies have also shown prostaglandin mediated antinociceptive properties of TFG seeds³. Therefore, the assessed antipyretic activity in the aqueous and alcoholic extracts may be due to presence of the above group of phytoconstituents in TFG seeds which modulates prostaglandins involved therein. Hence these seeds may be potentially useful in the management of febrile conditions in humans, a validation of its traditional use as an anti-pyretic agent.

CONCLUSION

The results provide a scientific basis for the utilization of this herb in traditional medicine. However further studies and tests are needed to explore the exact active principles responsible for the antipyretic activity.

TABLE -1: EFFECT OF TFG SEED EXTRACTS ON BREWER'S YEAST INDUCED PYREXIA IN ALBINO RATS

GROUPS	DOSE	RECTAL TEMPERATURE IN $^{\circ}\text{C}$ AND THE % REDUCTION OF PYREXIA							
		BEFORE YEAST INJECT (A)	18hrs AFTER YEAST (B)	AFTER DRUG/EXTRACT TREATMENT					
				1 HOUR (C ₁)		3 HOUR (C ₃)		6 HOUR (C ₆)	
CONTROL	0.5ml distil water	34.75 ± 0.12	35.81 ± 0.13	35.90 ± 0.13	-	35.91 ± 0.10	-	35.81 ± 0.12	-
PARACETAMOL (STANDARD)	150 mg/kg	34.56 ± 0.17	35.71 ± 0.19	34.68 $\pm 0.13^*$	89.56%	34.58 $\pm 0.17^*$	98.26%	34.60 $\pm 0.15^{**}$	96.52%

AQUEOUS EXTRACT OF TFG SEEDS	200 mg/kg	34.73 ± 0.13	36.33 ± 0.19	36.00 ± 0.18	20.65%	35.75 ± 0.15*	36.25%	35.30 ± 0.14**	63.37%
	400 mg/kg	34.63 ± 0.13	35.68 ± 0.16	35.40 ± 0.12	26.66%	35.16 ± 0.09*	49.52%	34.85 ± 0.13**	76.19%
ETHANOLIC EXTRACT OF TFG SEEDS	200 mg/kg	34.43 ± 0.10	35.83 ± 0.19	35.80 ± 0.22	30.00%	35.40 ± 0.17*	39.09%	34.90 ± 0.19**	84.54%
	400 mg/kg	34.65 ± 0.12	36.20 ± 0.29	36.00 ± 0.29	36.36%	35.23 ± 0.26*	65.58%	34.95 ± 0.25**	86.20%

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