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# ANTI-PYRETIC ACTIVITY OF ETHANOL EXTRACT OF STEM BARK EXTRACT OF ZYZIPHUS XYLOPYRUS BY USING BREWER'S YEAST INDUCED PYREXIA MODEL IN RATS

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## ABSTRACT

**Context:** Zizyphus xylopyrus (Retz.) is found to have antipyretic activity.
**Aims:** to Anti-pyretic activity of ethanol extract of stem bark extract of Zyziphus xylopyrus by using Brewer's Yeast induced pyrexia model in rats.
**Settings and Design:** This was a longitudinal study done on 30 no. Wistar rats and and swiss albino mice done in post graduate Department of Pharmacology, VIMSAR, Burla
**Methods and Material:** Brewer's Yeast induced pyrexia model in rats.
**Statistical analysis used:** One way ANOVA followed by Dunnett's test.
**Results:** EEZX-200 and 400 mg/kg dose showed significant reduction in rectal temperature. Conclusions: These results suggest that EEZX at 200 & 400 mg/kg doses possesses significant antipyretic effect, however more studies are recommended.

**KEYWORDS :** Carrageenan, inflammation, Analgesic, antipyretic

## INTRODUCTION:

Fever is a complex pathological process that manifests itself as a regulated elevation of body temperature over the normal circadian variations. Although fever may be regarded as a host defense response, it has potentially harmful consequences such as convulsions, dehydration, especially brain damage and seizures usually happen during severe and long-lasting fever in children . Therefore, quite a number of people think that fever is a disease rather than a symptom or sign of illness and it is important to keep the body temperature in the state of homeostasis within the narrow range. As a thermoregulatory manifestation to systemic inflammation, fever has been studied for years. Our understanding of the molecular mechanisms has substantially advanced over the past decade. (1,2,3)

Ziziphus is a genus of about 40 species of spiny shrubs and small trees in the buckthorn family, Rhamnaceae, distributed in the warm-temperate and subtropical regions throughout the world.

Zizyphus xylopyrus (Retz.) is found throughout North- Western India, Pakistan and China. A large, straggling shrub or a small three, armed with spines, up to 4 m. in height7 . Sanskrit : Ghoti, Gotika, Bengali : Kulphal, English : Jujab, Gujrati : Gatbadar, Gatabordi, Hindi : Ghunta, Kakora, Kaathabera, Kannada : Yeranu, Marathi : Ghoti, Bhorghoti, Tamil : Kottai, Mulkottai, Telugu : Gotti, Got, Gotiki.

This has been used in various conditions like stomach- ache, urinary spasm, sterility in women and diarrhoea, leaves and flowers for pimples, boils, snake bite and leucoderma. This has been used psychiatric disorder. It has been used in other economic industry. (3,4,5)

Antipyretic drugs are very commonly used all over the world. They are sold as an over-the-counter (OTC) or prescription drug. (6,7) However they are having various side effect. Zyziphus xylopyrus has been known to have antipyretic effect. In India, traditional medicines play important role, however, there are few literature available.

With this background, the present study was planned to screen the ethanolic extract of stem bark for antipyretic activities as part of exploring the traditional system of medicine for finding useful properties in a scientific manner.

## SUBJECTS AND METHODS:

This was a longitudinal study done on 30 no. Wistar rats done in post graduate Department of Pharmacology, VIMSAR, Burla after obtaining due permission from the Institutional Animal Ethics Committee,VIMSAR, Burla.

### Evaluation of Antipyretic activity

### Brewer's Yeast Induced Pyrexia Test

Animals: - Wistar albino rats – 30 in number
Drugs/Chemicals:

1. Paracetamol
2. EEZX
3. 0.5% Tween 80
4. 15% Brewer's yeast

Principle: The test involves the measurement of rise in body temperature of rats following subcutaneous injection of 15% suspension of Brewer's yeast solution and its decrease or otherwise after administration of vehicle/standard/test drugs. It can be tolerated by rat in a dose not exceeding 10 ml/kg injected subcutaneously within a period, not more than 10 minutes.

### Procedure :

The anti-pyretic activity was studied by using Brewer's yeast induced in albino rats employing the method of Loux et al., (1972). (8,9)

For this study, 10 ml/ kg of 15% aqueous suspension of Brewer's yeast in normal saline was administered subcutaneously after measuring the rectal temperature using digital thermometer. Eighteen hours after the yeast injection, the animals were again placed in individual cages for recording the rectal temperature. The test drug, control drug and standard drug were given 18 hrs after the yeast injection. The rats were restrained for their rectal temperature to be recorded at 0 hr i.e, immediatetly before test drug, vehicle and standard drug administration and again at hourly intervals for next five hours i.e, 1 hr, 2 hr, 3 hr, 4 hr and 5 hr after injection.

**Table No - 1**
**Drug Administration plan for Brewer's Yeast induced Pyrexia method**

| Group | Treatment | Dose(mg/kg) | Route of administration |
|---|---|---|---|
| 1 | 0.5% Tween 80 | 10 ml/kg | Per oral |

| | | | |
|---|---|---|---|
| 2 | Paracetamol | 15 | Per oral |
| 3 | EEZX | 100 | Per oral |
| 4 | EEZX | 200 | Per oral |
| 5 | EEZX | 400 | Per oral |

**Statistical Analysis :**

The mean and standard error of mean of increase/decrease of temperature were calculated and analysed statistically by one way ANOVA test followed by Dunnett's test.

**RESULT-**

In this test, effects of three doses of Ziziphus xylopyrus (EEZX) were compared with that of standard drug paracetamol and control drug (0.5% Tween 80) in mice. The results obtained are shown in Table 12

**Table No. 2 Effect of Ziziphus xylopyrus on Brewer's yeast induced pyrexia in Rats**

| Gr | Drug | Dose and route | Rectal Temp in °C at time (h) | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | 18 hr after yeast inj | 0hr | 1hr | 2hr | 3 hr | 4hr | 5hr |
| I | Control (0.5%Tween 80) | 10 ml/kg Per oral | 36.4±0.03 | 36.5±0.05 | 36.5±0.10 | 36.6±0.04 | 35.8±0.03 | 36.0±0.04 | 35.5±0.02 |
| II | Paracetamol | 15 mg/kg Per oral | 36.4±0.04* | 36.2±0.02 | 36.0±0.08 | 36.0±0.02* | 35.8±0.02** | 35.5±0.1* | 35.6±0.09 |
| III | EEZX | 100 mg/kg Per oral | 36.4±0.02 | 36.5±0.06 | 36.5±0.11 | 36.6±0.04 | 35.8±0.03 | 36.0±0.05 | 35.5±0.03 |
| IV | EEZX | 200 mg/kg Per oral | 35.8±0.04 | 36.2±0.08 | 36.0±0.010*** | 36.9±0.07* | 35.2±0.02** | 36.0±0.14 | 36.3±0.11* |
| V | EEZX | 400 mg/kg Per oral | 35.4±0.02 | 35.5±0.14 | 35.5±0.06* | 35.4±0.02* | 35.8±0.01*** | 35.4±0.11* | 35.2±0.20*** |

Data were analysed by one way ANOVA followed by Dunnett's Test. Each value is expressed as Mean ± SEM. n=6. * is p value <0.05 compared to control, ** is p value <0.01 compared to control, *** is p value <0.001 compared to control.

1. On comparison with control, EEZX-200 and 400 mg/kg dose showed significant reduction in rectal temperature. Paracetamol showed similar effect.
2. The effect shown by the test drugs i.e. EEZX 200 and 400 mg/kg was comparable with that of standard drug paracetamol 15 mg/kg.
3. The effect shown with EEZX 400 mg/kg was significantly higher than EEZX 200 mg/kg implying a dose dependent response.
4. EEZX 100 mg/kg did not show any significant reduction in rectal temperature as compared to control.

**DISCUSSION:**

In this study, anti-pyretic effect of EEZX was evaluated by the method of Brewer's yeast induced pyrexia and the same was compared with that of the standard antipyretic paracetamol.

In this study, EEZX at 200 and 400 mg/kg dose produced significant antipyretic activity as compared to 100 mg/kg. In the first hour, the antipyretic activity of EEZX 200 and 400 mg/kg was significant.EEZX 200 mg/kg caused a highly significant reduction of fever at 3 hr. However, the effect increases significantly at the dose of 400 mg/kg at 1, 2 and 4 hrs. Antipyretic activity with EEZX (200 & 400 mg/kg) was comparable with that of the standard drug paracetamol. However, EEZX 100 mg/kg did not show any significant antipyretic activity. Our results are corroborated by the finding Balakrishnan A et al 2012. (9)

Brewer's yeast induced pyrexia is a reproducible and sensitive model of fever for testing antipyretic effect of various drugs. Antipyretic potential of any drug can be predicted by this method. The test involves the measurement of rise in rectal temperature of rats following the subcutaneous injection of 15% suspension of Brewer's yeast and its decline, if any following administration of test and standard drugs. Yeast induced pyrexia in rats is a suitable and sensitive model for evaluating antipyretic effects of test compounds. Yeast on injection induces both TNF- and prostaglandin synthesis in the body.(8)

Fever is a pathophysiological condition resulting from the interaction of central nervous system and immune system and is a result of injury, infection, tumor and inflammation. The elevation of body temperature during such conditions results from the pyrogen induced upward resetting of thermoregulatory set point. Pyrogens, on injection into experimental animals, induce the production of pro-inflammatory cytokines (e.g., IL-1β, IL-6, IFN-α and TNF) which stimulate release of local PG (produced by the activity of COX) that leads to elevation of body temperature.

Antipyretics such as paracetamol and other NSAIDS reduce fever by suppressing prostaglandin synthesis, resulting in the blockade of the synthesis of prostaglandin in the brain or suppressing the rise of IL-1α production subsequent to interferon production. Flavonoids found in Z. xylopyrus have been shown to exert antipyretic effect by suppressing TNF-α and its related compounds also exhibit inhibition of arachidonic acid peroxidation, which result in reduction of prostaglandin levels thus reducing fever. EEZX might have suppressed production of pyrogenic cytokines such as TNF-α and IL-1β, while lowering the thermoregulatory set-point by blocking COX production of PGE2.

Thus it appears justified to conclude that ethanol extract of stem bark of Ziziphus xylopyrus possesses anti-pyretic activities. All these important preliminary findings can be taken as the basis upon which further studies can be carried out in other animal models to establish these potential beneficial effects beyond doubt. Then phytochemical studies to identify the chemicals responsible for producing these effects need to be done before finally going for clinical studies so that the drugs can be brought from the bench to bedside.

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