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# ANALGESIC ACTIVITY OF ETHANOL EXTRACT OF STEM BARK EXTRACT OF ZYZIPHUS XYLOPYRUS BY USING ACETIC ACID INDUCED WRITHING MODEL IN MICE

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## ABSTRACT

**Context:** Zizyphus xylopyrus (Retz.) is found throughout North- Western India, Pakistan and China.
**Aims:** to study Analgesic activity of ethanol extract of stem bark extract of Zyziphus xylopyrus by using Acetic acid induced Writhing model in mice.
**Settings and Design:** This was a longitudinal study done on 30 no. swiss albino mice done in post graduate Department of Pharmacology, VIMSAR, Burla
**Methods and Material:** Acetic acid induced writhing model.
**Statistical analysis used:** One way ANOVA followed by Dunnett's test.
**Results:** EEZX 200 and 400 mg/kg showed significant decrease in number of writhes in Acetic acid induced Writhing model
**Conclusions:** These results suggest that EEZX at 200 & 400 mg/kg doses possesses significant analgesic effect, however more studies are recommended.

**KEYWORDS :** Carrageenan, inflammation, Analgesic

## INTRODUCTION:

Writhing test is a chemical method used to induce pain of peripheral origin by injection of irritant principles like phenylquinone, acetic acid in mice. Writhings generated by parenteral administration of acetic acid in mice, are due to profound pain of endogenous nature which recur for a prolonged period of time. 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.(1)

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)

One of the most common reasons an individual seeks the advice of a physician is because he or she is in pain. Pain was called by Sherrington, "the physical adjunct of an imperative protective reflex." An analgesic is a medicine that relieves pain. These drugs can be 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 analgesic 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 analgesic 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. swiss albino mice done in post graduate Department of Pharmacology, VIMSAR, Burla after obtaining due permission from the Institutional Animal Ethics Committee,VIMSAR, Burla. Evaluation of **analgesic activity** was done by Acetic acid induced writhing : in Swiss albino mice : with aspirin as the standard drug.

### Evaluation of Analgesic activity of Ziziphus xylopyrus

### Acetic Acid Induced Writhing Test

Animals: Swiss albino mice , 30 numbers
Drugs/Chemicals:

1. Aspirin
2. EEZX
3. 0.5% Tween 80
4. 0.6% Acetic acid

**Apparatus :**
Bell Jar

**Principle :** The abdominal contraction is induced by intraperitoneal injection of acetic acid (0.6%) and the number of abdominal contractions (writhing) is counted over a period of 10 minutes commencing 10 min after the injection of acetic acid. The syndrome is characterized by abdominal torsion, drawing up of limb to the abdominal area and periodic arching of the back to rub the abdominal wall on the glazed surface on which it is kept. The number of writhes in test group animals was compared with those of standard and control group. A drug said to possess analgesic activity if the number of writhes in the test group is significantly decreased from that of control group.

Procedure: The analgesic activity of EEZX was studied in albino mice using acetic acid induced writhing method described by Collier et al., (1968).

Animal were pretreated either with the test drugs, standard drug and vehicle/solvent (control) drug 30 min before intraperitoneal injection of acetic acid (0.6%). After acetic acid injection, the mice were placed in separate bell shaped transparent glass jars and number of abdominal constriction (writhes) were counted over a period of 10 minutes commencing 10 min after injection of acetic acid. The difference in the number of writhes in test group was compared with those in the standard and control groups.

**Table No - 1**
**Drug Administration plan for Acetic acid Induced Writhing Test**

| Group | Treatment | Dose(mg/kg) | Route of administration |
|---|---|---|---|
| 1 | 0.5% Tween 80 | 10 ml/kg | Per oral |
| 2 | Aspirin | 20 | Per oral |
| 3 | EEZX | 100 | Per oral |
| 4 | EEZX | 200 | Per oral |
| 5 | EEZX | 400 | Per oral |

The percentage inhibition was calculated by using formula
% Inhibition = [(Wc –Wt) / Wc] x 100

Where Wc – No of writhes in control group, Wt – No of writhes in test group Statistical Analysis: The mean and standard error of mean of increase/decrease in reaction time were calculated and analysed statistically by one way ANOVA followed by Dunnett's test.

## RESULTS:

The analgesic effect of EEZX was evaluated with the help of acetic Acid induced writhing test. The number of writhes in mice were recorded for both the drugs and were compared with that of control (0.5%Tween 80) and standard (aspirin).

The results obtained are shown in the Table 2.

**Table No. 2**
**Effect of Ziziphus xylopyrus on Acetic acid induced Writhing in Mice**

| Group | Drug& Dose (mg/kg) | Dose and route | No of Writhes Mean ± SEM | %Protection |
|---|---|---|---|---|
| I | Control (0.5%Tween 80) | 10 ml/kg Per oral | 28.83 ± 1.01 | - |
| II | Aspirin | 20 mg/kg Per oral | 6.83 ± 0.30*#@ | 76.3 |
| III | EEZX | 100 mg/kg Per oral | 28.67 ± 0.71 | 0.5 |
| IV | EEZX | 200 mg/kg Per oral | 17.33 ±0.33* | 39.88 |
| V | EEZX | 400 mg/kg Per oral | 10.83 ± 0.47*# | 62.43 |

Data were analysed by one way ANOVA followed by Dunnett's Test. Each value is expressed as Mean ± SEM. n=6. * is p value <0.001 compared to control, # is p value <0.05 compared to EEZX 200, @ is p value <0.05 compared to EEZX 400

1. On comparison with control, EEZX 200 and 400 mg/kg dose showed significant reduction in number of writhes in mice. Aspirin showed similar effect.
2. The effect shown by the test drugs i.e. EEZX 200 and 400 mg/kg was comparable to that of standard aspirin 20 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 change in number of writhes in mice as compared to control.

## DISCUSSION:

In Acetic acid induced writhing test in mice, the two higher doses of EEZX i.e. 200 and 400 mg/kg exhibited significant analgesic effect as compared to those of control and EEZX 100 mg/kg as evident by the no. of writhes. However, percentage analgesia seen with EEZX 200 and 400 mg/kg were 39.88 and 62.43 respectively which were comparable to that of aspirin (76.3). Here also dose dependent analgesic effect of EEZX was observed. In this test drug 100 mg/kg EEZX did not show significant analgesic activity. These effects corroborate with the findings of Mishra U S et al, 2012. (2,8,9)

The abdominal constriction response induced by acetic acid is a sensitive procedure to screen analgesics acting peripherally rather than centrally. This response is thought to involve local peritoneal receptors. PGE2 & PGF2 levels are increase in the peritoneal fluid of mice, injected with intraperitoneal acetic acid. (2,8)

Analgesic activity of EEZX was evaluated by Tail Flick method and Acetic acid induced writhing method to assess the effect of drugs on central and peripheral mechanism of pain respectively. These models are essentially based on acute and short lasting noxious stimuli of thermal or chemical nature. These are well established methods for the evaluation of potential analgesic properties of various drugs. The results of our study indicate that EEZX possesses significant analgesic activity acting by both central and peripheral mechanisms of pain. The abdominal constriction response induced by acetic acid is thought to involve a peripheral mechanism of action involving local peritoneal receptors while the tail flick response indicates involvement of higher centres modulating the pain pathway.The mechanism underlying the analgesic activity of these drugs could be due to diminished production of PGE2.The extract could be interfering with both central(opioid and cholinergic pathways) and peripheral (COX-2)pathways in eliciting the analgesic effects.(2,9)

These results suggest that EEZX at 200 & 400 mg/kg doses possesses significant analgesic effect. However, these positive results have to be seen in the context of limitations of the study, which are: the study was conducted in only in single animal model each of acute and sub-acute models of inflammation, single animal model of pain and single animal model of pyrexia.The study has to be carried out in other animal as well as in in-vitro models of inflammation, pain and fever before these activities can be documented beyond any doubt.

EEZX showed analgesic activity in this models of pain.

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