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Original Research Paper

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ANALGESIC ACTIVITY OF ETHANOL EXTRACT OF STEM BARK EXTRACT OF ZYZIPHUS XYLOPYRUS BY USING TAIL FLICK LATENCY MODEL IN RATS

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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 Tail Flick Latency model in rats.
Settings and Design: This was a longitudinal study done on 30 no. Wistar rats done in post graduate Department of Pharmacology, VIMSAR, Burla
Methods and Material: Tail Flick Latency model
Statistical analysis used: One way ANOVA followed by Dunnett's test.
Results: EEZX 200 and 400 mg/kg showed significant increase in tail flick latency parameters.
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:

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. 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 analgesic activity was done by

a)Tail flick latency : in Wistar rats : with tramadol as the standard drug.

Evaluation of Analgesic activity of Ziziphus xylopyrus

Animals : Wistar albino rats – 30 numbers
Drugs/Chemicals:
1.Tramadol
2.EEZX
3.0.5% Tween 80

Apparatus : Analgesiometer (digital)

Principle :

The tail flick latency test uses radiant heat as the source of pain in the animal. An electrically heated nichrome wire is placed 1/8 th inch below the tail of rat, at 2.5 cm measured distally from the root of tail. The reaction time from the onset of application of heat to the flicking of the tail is recorded as the tail flick latency (pain threshold). The maximum reaction time is kept around is 10 sec to avoid thermal injury. A drug is said to possess analgesic activity if tail flick latency is significantly increased from pre- drug values.

Procedure :

The tail flick latency method as described by D'Amour FE (1941) was followed in this study.

The rat was placed in the rat holder with its tail protruding out. The base of the protruding tail was placed on the nichrome wire of the analgesiometer. A current of 6 amp was applied through the analgesiometer to heat up the nichrome wire. The time taken from the application of heat to the flicking of tail was recorded. The cut- off reaction time was fixed at 10 sec to avoid tissue damage. The rats which showed a TFL of 5 to 6 sec at baseline were included in the study. The rats were divided into 5 groups of 6 animals each and were administered with test and control drugs orally through intra gastric tube. Post drug TFL was assessed at interval of 30 min, 1 hr, 2 hr and 3 hr.

Table No-1

Drug Administration plan for Tail Flick Latency Test.

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

% Analgesia (MPE) = (TL – BL / ML – BL) × 100
Where MPE – Maximum possible effect, ML – Maximum latency (10 sec), TL –Tail Latency, BL – Basal latency

Statistical Analysis :

The mean and standard error of mean of increase/decrease in reaction time(as index of analgesia) were calculated and analysed statistically by using one way ANOVA followed by Dunnett's test.

RESULTS:

In this test, effects of doses of Ziziphus xylopyrus (EEZX) were compared with that of standard drug tramadol and control drug (0.5%Tween 80) on tail flick latency test in rats.The results obtained shown in Table 2.

Table No. 2 Effect of Ziziphus xylopyrus on Tail Flick Latency in Rats

Gr	Drug	Dosage and route	TFL in sec (Mean ±SEM)				
			Basal	30min	1 hr	2 hr	3 hr
I	Tween 80 (0.5%)	10 ml/kg Per oral	3.41±0.08	4 ±0.08	3.12±0.08	3.69 ± 0.04	3.53 ±0.06
II	Tramadol	10 mg/kg Per oral	3.65±0.06	8.13±0.05*#@	8.3 ± 0.05*#@	8.51± 0.05*#@	8.38±0.05*#@
III	EEZX	100 mg/kg Per oral	3.19 ± 0.02	3.10 ± 0.02	3.25 ± 0.06	3.27 ± 0.04	3.21 ± 0.06
IV	EEZX	200 mg/kg Per oral	3.56 ± 0.10	6.05 ± 0.05*	6.20 ± 0.07*	6.44 ± 0.05*	6.28 ± 0.04*
V	EEZX	400 mg/kg Per oral	3.85 ± 0.04	7.71 ± 0.04*#	7.76 ± 0.03*#	7.84 ± 0.05*#	7.86 ± 0.03*#

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. The basal latency (predrug TFL) in all groups was comparable.
2. EEZX 200 and 400 mg/kg showed significant increase in TFL, in comparison with predrug TFL value from 30 min to 3 hour of observation.
3. Tramadol 10 mg/kg showed similar effect.
4. The effect shown by the test drugs i.e. EEZX 200 and 400 mg/kg was comparable with that of standard tramadol 10 mg/kg.
5. The effect shown by EEZX 400 mg/kg was significantly higher than EEZX 200 mg/kg implying a dose dependent response.
6. EEZX 100 mg/kg did not show any significant increase in TFL.

Table No. 3 Percentage Maximum Possible Effect (% analgesia) of Ziziphus xylopyrus on Tail Flick Latency in Rats

Gr	Drug	Dose and route	Percentage maximum possible effect (% analgesia)			
			30 min	1 hr	2 hr	3 hr
I	Tramadol	10 mg/kg Per oral	70.55	73.22	76.53	74.48
II	EEZX	200 mg/kg Per oral	38.66	40.99	44.72	42.23
III	EEZX	400 mg/kg Per oral	62.76	63.57	64.87	65.20

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

1. The effect shown by EEZX 400 mg/kg was significantly higher than EEZX 200 mg/kg implying a dose dependent response.
2. The effect shown by the test drugs i.e. EEZX 200 and 4oo mg/kg was comparable with that of tramadol 10 mg/kg

DISCUSSION:

In Tail Flick Latency test, 200 and 400 mg/kg dose of EEZX showed significant analgesic effect from 30 min to 3 hours of observation time as evident by the increased latency of tail flick of the rats as compared to that in control group. The peak effect was observed at 2 hours with all the drugs. These effects were comparable with that of standard drug tramadol 10 mg/kg. The effect shown by EEZX 400 mg/kg was significantly higher than EEZX 200 mg/kg suggesting a dose dependent analgesic effect. Percentage analgesia was found to be 44.72 and 65.2 for EEZX 200 and 400 mg/kg dose respectively during their peak effect while that of tramadol was 76.53. In this test, 100 mg/kg of EEZX did not show any significant analgesic activity. The test drug in different doses increase the pain threshold significantly during the period of observation and this suggest that EEZX is able to modulate central pain pathways. Pain is centrally modulated via a number of complex processes including opioids, dopaminergic descending nor adrenergic and serotonergic system. (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. (2,8,9)

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. (3,4,9)

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.

REFERENCES:

1. Jena BK, Rath B, Kar S, Mahanta S, Tripathy M, Nayak AK, Wound healing potential of Ziziphus xylopyrus Willd .(Rhamnaceae) stem bark ethanol extract using in vitro and vivo model. Journal of drug delivery and therapeutics 2012; 2: 41- 46.
2. Mishra U S, Murthy P N and Panda S K, Analgesic and anti-inflammatory activities of of an Indian medicinal plant Ziziphus xylopyrus stem bark in an experimental animal models, Elixir Pharmacy 2012; 44: 65- 70.
3. Sudhakar Reddy C, Reddy K N, Murthy E N, Raju V S. Traditional medicinal plants in Seshachalam hills, Andhra Pradesh. India J Med Plant Res, 2009;

3(5): 408 – 412.
4. Rani LS, Devi BK, Soris PT, Maruthupandian A, Mohan VR. Ehnomedicinal plants used by Kanikkars of Agasthiarmalai Biosspere Reserve Western Ghats. J Ecobotech 2011; 16- 25.
5. Rao BR, Sunitha S. Medicinal plant resources of Rudrakod sacred grove in Nallamalais, Andhra Pradesh, India. J Biodivers 2011; 2(2) 75-89.
6. Jagtap SD, Deokule SS, Bhosle SV. Some unique ethnomedicinal uses of plants used by the Korku tribe of Amaravati district of Maharastra, India. J Ethnopharmacol 2006; 107: 463-469.
7. Dhanpal R, Ratna JV, Gupta M, Surathchandrian I, Ovarian antisteroidogenic effect of three ethnomedicinal plants in prepubertal female mice. Int J Biol Pharma Res 2012; 3(1):30-36.
8. D' A Mour F E, Smith D L. A method for determining loss of pain sensation. Pharmacol Exp Ther, 1941; 72: 74 – 79.
9. Colliar H O J, Dinneen L C, Johnson C A, Schneider C. The abdominal constriction response and its suppression by analgesic drugs in the mouse. Br J Pharmaco Chemother, 1968; 32: 295 – 310.