VOLUME-9, ISSUE-1, JANUARY-2020 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Pharmacology

ANTI-INFLAMMATORY ACTIVITY OF ZYZIPHUS XYLOPYRUS BY USING COTTON PELLET INDUCED GRANULOMA MODEL (SUB-ACUTE INFLAMMATION) IN ALBINO RATS

Dr Gujaram Marandi — Assistant Professor, Pharmacology department, Bhima-Bhoi Medical college and Hospital, Balangir, Odisha

Dr Pravin Dhone* — Professor and Head, Bhima-Bhoi Medical college and Hospital, Balangir, Odisha *Corresponding Author

ABSTRACT

Context: Ziziphus xylopyrus, locally known as 'sider'or 'ber' has been used in various condition but scientific evidence are not available.

Aims: to study anti-inflammatory activity of Zyziphus xylopyrus by using Cotton Pellet induced Granuloma model (sub-acute inflammation) in albino 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: the study was done by Cotton pellet induced granuloma.

Statistical analysis used: One way ANOVA followed by Dunnett's test.

Results: On comparison with basal values, EEZX 200 and 400 mg/kg showed significant reduction in Cotton pellet induced granuloma.

Conclusions: These results suggest that EEZX at 200 & 400 mg/kg doses possesses significant anti-inflammatory activities, however more studies are recommended.

KEYWORDS : Carrageenan, inflammation

INTRODUCTION:

Inflammation, pain and fever are very common clinical phenomena and accompany diverse disease conditions. The drugs currently used to treat them are mainly NSAIDS, glucocorticoids and opioids. However, these drugs produce many adverse reactions especially when used chronically.

India has a centuries old tradition of using medicinal plants and herbal medicines for the alleviation of various ailments. There are about 45000 plant species and among them, several thousands have been claimed to possess medicinal properties.

Ziziphus xylopyrus, locally known as 'sider'or 'ber' is one of such versatile tree species used for food, fodder, medicines and desertification control in arid lands. Ziziphus xylopyrus (Family : Rhamnaceae) commonly known as 'Jujab' in English, 'Kantabaula' in Odia and 'Ghunta' in Hindi is either a large struggling shrub or a small tree armed with spines and found in Odisha, North Western India, UP, Bihar and other parts of India. (1)

As per the ethnomedicinal information, various parts of this plant have been reported to be used traditionally for the treatment of diverse disease conditions like stem bark for stomach-ache and cholera, root bark for bleeding piles, epistaxis, bleeding mouth and skin rash, fruits for diabetes, stomach- ache, urinary spasm, sterility in women and diarrhoea, leaves and flowers for pimples, boils, snake bite and leucoderma, leaves and stem for hysteria, antiseptic and headache, root for asthma, pyorrhoea and seeds for chest pain and diarrhoea. (2,3,4) This plant is also reported to possess antidepressant, antimicrobial, anthelmintic and wound healing activities. (5,6,7) However, there are few scientific studies as regards its anti-inflammatory, analgesic and antipyretic properties.

With this background, the present study was planned to screen the ethanolic extract of stem bark for anti-inflammatory 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 Anti-inflammatory Activity was done in following way.

a)Cotton pellet induced granuloma: model of sub-acute inflammation : in Wistar rats : using diclofenac as standard drug.

Preparation of extracts

The stem bark of Ziziphus xylopyrus plant was collected, cleaned, shade dried and powdered by mechanical grinder. 100 gms of the pulverized stem bark was extracted with petroleum ether and ethanol successively in a soxhlet apparatus. Petroleum ether was used as the initial step of extraction for defatting the plant materials. Then, from this, ethanol extract was separately filtered and concentrated at reduced temperature on a rotatory evaporator. The yield of petroleum ether and ethanol extract was found to be around 3.21 and 15.13 (W/W) respectively. The ethanol extract was found to be soluble in 5% Tween 80.

Experimental animals:-

The healthy adult albino rats weighing between 150-250 gms and Swiss albino mice weighing between 20-30 gms were selected for the study. They were kept in polypropylene cages in temperature regulated rooms with air cooling and 12: 12 hours light and dark cycle, provided with standard laboratory diet and had free access to water. The animals were allowed to get acclimatized to environmental conditions for at least five days before the start of experiment. Food was withdrawn 12 hours before and also during the experimental hours.

Evaluation of Anti-inflammatory activity of Ziziphus Xylopyrus Cotton Pellet induced Granuloma (8,9)

Drugs/Chemicals were used as follows:

Drug Administration plan in Cotton Pellet Granuloma method

Group	Treatment	Dose (mg/kg)	Route of administration
1	0.5% Tween 80	10 ml/kg	Per oral
2	Diclofenac	15	Per oral
3	EEZX	100	Per oral
4	EEZX	200	Per oral
5	EEZX	400	Per oral

Procedure :Cotton pellet induced granuloma in rats was used for producing subacute inflammation by employing the method of Swingle and Shidman et al., (1972).

The cotton pellets each weighing 50 mg were made by rolling of cotton wool and then sterilized by autoclaving. The rats were anesthetized with ether, axilla was shaved and swabbed with 70% (v/v) alcohol. Midline incision of 1 cm was made in the axillary region. A small tunnel was made on either side of incision with the help of small blunt forceps. The animals were divided into five groups (n = 6) and were administered with vehicle/ standard drug/ test substance for 10 days. On 10th day, the pellets were dissected out and the moist pellet were weighed and then dried in an incubator at 69°C until a constant weight was obtained. The granuloma tissue formation (dry weight granuloma) was calculated after deducting the weight of cotton pellet (50 mg) from the constant dry weight of the pellet and this was taken as a measure of granuloma formation. The anti-inflammatory effect was assessed by measuring the inhibition of the granuloma weight in the test groups as compared with the control. The granuloma inhibition percentage for each group was calculated and compared with the control group considered as 100% of inflammatory activity.

The Granuloma tissue formation = Constant dry wt of pellet – Initial wt of cotton pellet (50 mg).

The percentage inhibition was calculated by using formula,
Percentage inhibition = Wc–Wt / Wc x 100
Wc – weight of granuloma in control group
Wt – weight of granuloma in treated group

Statistical Analysis :
The mean and standard error of mean of increase/decrease in weight of granuloma was calculated and analysed statistically by using One way ANOVA followed by Dunnett's test.

RESULTS:

The anti-inflammatory effect of Ziziphus xylopyrus was evaluated in a model of sub-acute inflammation i.e. cotton pellet granuloma method in rats. The increase or decrease in weight of cotton pellet granuloma was determined for EEZX and were compared with that of 0.5% Tween 80 (control) and diclofenac (standard).

Effect of Ziziphus xylopyrus on Cotton Pellet Granuloma in Rats

Group	Drug	Dose and Route	Granuloma weight (in mg) mean ± SEM	% Inhibition
I	Tween 80 (0.5%)	10 ml/kg Per oral	74.50 ± 1.11	-
II	Diclofenac	15 mg/kg Per oral	33.33 ± 0.88*#@	55.26
III	EEZX	100 mg/kg Per oral	74.67 ± 0.88	-
IV	EEZX	200 mg/kg Per oral	50.50 ± 1.25*	32.21
V	EEZX	400 mg/kg Per oral	38.50 ± 0.76*#	48.32

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 weight of cotton pellet in control group, EEZX 200 and 400 mg/kg dose showed significant decrease in weight of cotton pellet. Diclofenac 15 mg/kg also showed similar effect.
2. However, the effect shown by the test drugs i.e. EEZX 200 and 400 mg/kg were comparable with that of diclofenac 15 mg/kg.
3. The effect shown with EEZX 400 mg/kg was significantly higher than EEZX 200 mg/kg depicting a dose dependent response.
4. EEZX 100 mg/kg did not show significant change in weight of cotton pellet as compared to control.

DISCUSSION:

Anti-inflammatory activity was tested in Carrageenan induced rat hind paw edema (acute inflammation) and cotton pellet induced granuloma (sub-acute inflammation). Carrageenan, a sulphated mucopolysaccharide derived from Irish sea moss, has been widely used for the production of experimental model of inflammation by various workers.

In Cotton pellet granuloma test (subacute inflammation), EEZX 200 and 400 mg/kg dose exhibited significant anti-inflammatory activity. The percentage inhibition in the weight of granuloma seen with EEZX 200 and 400 mg/kg were 32.21 and 48.32 respectively which were comparable with that of diclofenac which was 55.26. However, the same were significantly higher as compared to that by the control group. Here also dose dependent anti-inflammatory activity of EEZX was observed. In this study,100mg/kg EEZX did not show any significant anti-inflammatory activity. Our finding corroborate with that of Jena BK *et al* 2012. (8,9)

Cotton pellet granuloma is a model of non-immunological types on inflammation and edema is mainly due to proliferative phase of inflammation. Efficacy of EEZX in this model might be due to an increase in synthesis of collagen and mucoploysaccharides and increase in the number of fibroblasts during granuloma tissue formation.

So our study shows that EEZX possess anti-inflammatory activity in both acute and sub-acute models of inflammation.

These results suggest that EEZX at 200 & 400 mg/kg doses possesses significant anti-inflammatory activities. 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.

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