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STUDIES ON ANTI-INFLAMMATORY AND ANALGESIC ACTIVITY OF *FICUS NERVOSA HEYNE EX ROTH* IN EXPERIMENTAL MODELS

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ABSTRACT

Ficus nervosa Heyne ex Roth is a medium sized evergreen tree belongs to *Moraceae* family. The petroleum ether extract of *Ficus nervosa* (PEFN) leaves was investigated for the evaluation of anti- inflammatory and analgesic activity. Acute toxicity studies were performed as per OECD-423 guidelines. Toxicity signs and symptoms were not observed. For the antiinflammatory activities, carrageenan induced paw edema and cotton pellet induced granuloma at the dose of 200 and 400 mg/kg, *p.o*. Analgesic activity was carried out by tail immersion method in mice. The activity may be due to the presence of steroids in the extract. The extract exhibited significant analgesic and anti- inflammatory activity, which supports the traditional utilization of the plant. This study suggested that, *Ficus nervosa* possess anti- inflammatory properties and analgesic activities.

Key words: *Ficus nervosa*, anti- inflammatory, analgesic, edema, granuloma.

INTRODUCTION

Most clinically important medicines belong to steroidal or non-steroidal anti-inflammatory chemical therapeutics for treatment of inflammation-related diseases. Though these have potent activity, long-term administration is required for treatment of chronic disease. Furthermore, these drugs have various and severe adverse effects. Therefore, naturally originated agents with very little side-effects are required to substitute chemical therapeutics.

Ficus nervosa Heyne ex Roth belongs to the family *Moraceae.* It is a medium sized evergreen tree in evergreen forests up to 400-1600 m (Anonymous 2, Anonymous1). Aerial roots are absent; leaves are coriacuous, glabrous on both sides, oblanceolate to oblong 8-20 cm long, entire margin, narrowed at base.

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Ficus nervosa, traditionally used for pain and inflammation in and around thirumal hills. (Madhava Chetty *et al*., 2008; Anonymous 1). Bark is brown mottled white, wood is white in colour and soft (Gamble, 1967). Therefore, the present study to evaluate the anti-inflammatory and analgesic activity of leaves of *Ficus nervosa*.

MATERIALS AND METHODS

Plant Materials

The *Ficus nervosa* leaves were collected in the month of September, 2009 from Thirumala hills in Chittoor district of Andhra Pradesh, India. The leaves were identified and authenticated by Dr. K. Madhava Chetty, Assistant Professor, Department of Botany, Sri Venkateswara University, Tirupathi.

Preparation of Extract

The leaves of the plant were collected and dried under shade and then powdered with a mechanical grinder. The powder was passed through sieve no.40.

Then the powder was extracted with petroleum ether in a Soxhlet extraction apparatus.

Phytochemical Screening

The PEFN was tested for the presence of saponins, alkaloids, glycosides, steroids, triterpenoids, flavonoids, tannins, reducing sugars by qualitative and quantitative methods (Gokhale *et al.,* 2004)

Animals

Male Wister rats weighing 160-200gm were used for the study of anti- inflammatory activity. Wister rats of either sex (19-32mg) were used for the study of analgesic activity. They were maintained under standard environmental conditions and were fed with standard pellet diet with water ad libitum.

Preparation of the drug for the experimental study

Petroleum ether extract of *Ficus nervosa* was administered in the form of suspension with 2% tween 80 solution and the standard drug dissolved in water was used for the study.

Acute Toxicity Studies

Acute oral toxicity studies were performed as per OECD-423 guidelines. Male Wister mice were used for the study. The animals were divided into six groups containing six animals in each group. The extract was administered orally at the doses from 200- 2000mg/kg. There were no signs of toxicity and mortality was observed up to 2000mg/kg.

Anti- inflammatory activity
Carrageenan induced rat paw edema

The animals were divided into 4 groups each group contained 6 animals. Animals were weighed and marked for identification. Group I: Control, received 2% tween 80 solution, Group II & III treated with PEFN 200 & 400mg/kg, p.o. respectively. Group IV: treated with Indomethacin-10mg/kg, mg/kg, p.o. After 30min of this treatment, 0.1ml of 1% carrageenan in saline was injected into the sub plantar region of the left hind paw of each rat for induce edema to all groups (Winter *et al*., 1962).

After carrageenan injection, calculated the paw volume using Plethysmometer (immersing the paw in mercury cell) by volume displacement method. The paw volume was measured initially and at intervals of 30, 60, 120, 180min. The percentage inhibition of paw volume in drug treated group was compared with control group. The percentage inhibition of paw edema was calculated by using the following formula;

$$\text{Percentage of edema inhibition} = [(V_c - V_t) / V_c] \times 100$$

Vc- Volume of edema in control group
Vt- volume of edema in treated group

Cotton pellet granuloma

The rats are divided into 4 groups, 6 animals in each group. The cotton pellet granuloma model investigated the proliferation phase of inflammation. All groups animals were anaesthetized with diethyl ether. The 20mg of sterile cotton pellets were inserted in each axilla of rats by making small subcutaneous incision. The incisions are sutured with sterile catgut (Crunkhon *et al*., 1971). Group I: Control, received 2% tween 80 solution, Group II & III treated with PEFN 200 & 400mg/kg, p.o, Group IV: treated with Indomethacin-10mg/kg, mg/kg, p.o. for seven days. On 8^{th} day the animals were sacrificed with excess anaesthesia and cotton pellets were removed surgically and separated from extraneous tissues. The pellets were weighted and dried at 70°C for 6 hour and weighted again. The dry weight of the pellets was taken and granuloma formation was measured. The percentage inhibition of granuloma was calculated by using the following formula;

$$\text{Percentage inhibition} = [(Wc - Wd) / Wc] \times 100$$

Wc = Pellet weight in control group
Wd = Pellet weight in drug treated group

Analgesic activity
Tail immersion method

The mice were divided into 4 groups, 6 animals in each group. Mice were weighed and 3-4cm. area of the tail was marked and immersed in the thermo- statically maintained water bath at 51^0c. The withdrawal time of the tail from the hot water in seconds was noted as the reaction time. The maximum cut off time for immersion was 150 seconds to avoid the injury of the tail tissue. Then control group was treated with vehicle, standard group was treated with Indomethacin 10mg/kg and test groups were treated with 200 and 400 mg/kg orally. The initial readings were taken immediately before the administration of the test and standard drugs and at then 60, 90, 120, 150 min after the administration. Tail withdrawal time difference after drug administration was used to indicate the analgesia produced by standard and test drugs (Luiz *et al., 1988)*

RESULTS

Phytochemical Screening

General qualitative and quantitative tests showed, petroleum ether extract of *Ficus nervosa* revealed the presence of steroids.

Effect of the PEFN on carrageenan induced paw edema

The PEFN showed 35.41% inhibits the paw edema at the dose of 200mg/kg and 41.66% inhibition at the dose of 400mg/kg. After 3hr the drug treatment in carrageenan induced paw edema, where as the standard drug showed 43.75% of inhibition.

Effect of PEFN on cotton pellet induced granuloma

In chronic model i.e., cotton pellet granuloma the PEFN showed decreased formation of granuloma tissue of 30.75% at the dose of 200mg/kg, 41.69% at 400mg/kg, where as standard showed 42.90% at the dose of 10mg/kg.

Effect of PEFN in mouse tail immersion method

The PEFN exhibited analgesic activity at the dose 200 and 400mg/kg. The duration as well as the intensity of analgesia produced by *Ficus nervosa* was dose dependent. The analgesic activity was almost comparable to that produced by Indomethacin.

Table 1. Effect of the PEFN on carrageenan induced paw edema

Group	Treatment	Paw edema volume (ml)					Percentage of inhibition
		0min	30min	60min	120min	180min	
I	Control (2% tween 80)	0.27±0.01	0.30±0.01	0.37±0.01	0.4±0.01	0.48±0.01	_
II	PEFN (200mg/kg, p.o.)	0.27±0.02	0.32±0.01	0.37±0.01	0.34±0.00***	0.31±0.01***	35.41
III	PEFN (400 mg/kg, p.o.)	0.29±0.01	0.32±0.01	0.36±0.01	0.32±0.01***	0.28±0.01***	41.66
IV	Indomethacin (10 mg/kg, p.o.)	0.28±0.02	0.33±0.02	0.35±0.01	0.32±0.01***	0.27±0.01***	43.75

n=6, values are expressed as mean ± SEM, *** P < 0.01 when compared with control.

Table 2. Effect of PEFN on cotton pellet induced granuloma

Group	Treatment	Weight of cotton pellet		Percentage of inhibition
		Before	After	
I	Control (2% tween 80)	20±0.00	41.16±1.01	_
II	PEFN (200mg/kg, p.o.)	20±0.00	28.5±0.76***	30.75
III	PEFN (400 mg/kg, p.o.)	20±0.00	24±0.58***	41.69
IV	Indomethacin (10 mg/kg, p.o.)	20±0.00	23.5±0.56***	42.90

n=6, values are expressed as mean ± SEM, *** P < 0.01 when compared with control.

Table 3. Effect of PEFN in mouse tail immersion method

Group	Treatment	Tail withdrawing in sec				
		Before	After			
			60min	90min	120min	150min
I	Control (2% tween 80)	1.5±0.42	1.83±0.30	1.17±0.31	1±0.36	0.7±0.21
II	PEFN (200mg/kg, p.o.)	1.5±0.42	5±0.25***	5.5±0.22***	4.83±0.16***	4.33±0.21***
III	PEFN (400 mg/kg, p.o.)	1.5±0.43	5.5±0.22***	6.5±0.25***	5.66±0.21***	4.33±0.21***
IV	Indomethacin (10 mg/kg, p.o.)	1.83±0.48	6.33±0.42***	7.5±0.34***	5.76±0.17***	4.16±0.30***

n=6, values are expressed as mean ± SEM, *** $P < 0.01$ when compared with control.

DISCUSSION AND CONCLUSION

Carrageenan-induced edema has been commonly used as an experimental animal model for acute inflammation and is believed to be biphasic. The early phase (1–2 h) of the carrageenan model is mainly mediated by histamine, serotonin and increased synthesis of prostaglandins in the damaged tissues surroundings. The late phase is sustained by prostaglandin release and mediated by bradykinin, leukotrienes, polymorphonuclear cells and prostaglandins produced by tissue macrophages (Brito and Antonio, 1998).The result obtained from the carrageenan-induced paw oedema shows that paw oedema was markedly inhibited by the oral administration of the PEFN, thus indicating that the PEFN can inhibit acute inflammatory process and that the extract is orally active. This is because carrageenan-induced paw oedema is an acute model of inflammation (DiRosa, 1972) and has been reported to be active in detecting orally active anti-inflammatory drugs (DiRosa *et al*., 1971).

Similarly in the cotton pellet granuloma model of inflammation the PEFN inhibited the granuloma formation significantly ($P < 0.05$) indicating that the PEFN can also inhibit chronic inflammatory process as is typified by the cotton pellet method (Ismail *et al*., 1997). Non-steroidal anti-inflammatory drugs (NSAID's) act in a manner that the sensitization of pain receptors by prostaglandins at the inflammation site is inhibited (Dhara *et al*., 2000). *Ficus nervosa* also producing same effect like indomethacin in tail immersion method.

The use of plant extracts with medicinal properties may be an alternative in the treatment of different pathologies. The search for pharmacological activities of plant extracts may turn possible the design of less expensive therapies with minor adverse effects. In this paper, the analgesic and anti-inflammatory activity of extracts from *Ficus nervosa* stems was demonstrated in animal models even when used by oral route. Results also indicate that extracts possess low toxicity and could be had a suggested use in the management of pain disorders.

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