



Research Article

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ANALGESIC ACTIVITY OF ETHANOLIC EXTRACT OF *FICUS GLOMERATA* LEAVES: *IN VIVO* EVALUATION

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ABSTRACT

There are numerous plants which are used in Ayurveda and other traditional system of medicine but their claim is not yet evaluated scientifically in laboratory animals. Present study was intended to evaluate an analgesic activity of a *Ficus glomerata* leaf extract in mice to confirm ethnomedical claim made by traditional health practitioners. Plant was obtained from the natives of Pune district and authenticated at Botanical Survey of India, Pune. Dried leaves of a plant were extracted in ethanol using Soxhlet extractor. Ethanolic extract was evaporated using rota evaporator and stored at cool and dry place. Extract was orally administered in mice (125mg/kg, 250mg/kg and 500mg/kg) and evaluated using hot plate and tail immersion methods. Pentazocine (10 mg/kg) was taken as a standard drug. Significant analgesic activity comparable with standard dose of pentazocine was observed in both the cases. This confirms ethnomedical claim of some workers regarding an analgesic activity of the plant.

Keywords: Analgesic activity, *Ficus glomerata*, Pentazocine, hot plate, tail immersion.

INTRODUCTION

More than 50% population in rural India believes in the traditional alternative systems of a medicine; like Ayurveda, Siddha, Unani and Homoeopathy other than allopathy. In rural India some tribes still totally rely on traditional medicines as modern health practices does not reach adequately. Ayurveda is the system of medicine which use of plants and their herbal products as medicine. Ayurvedic medicine reduces the chance of diseases or they decrease the symptoms or totally cure the diseases or ailments.

Ficus glomerata is found almost in all parts of India as a naturally occurring and eatable fruit bearing plant. The plant is a large deciduous tree distributed all over India from outer Himalayan ranges, Punjab, Maharashtra, Bihar, Orissa, West Bengal, Rajasthan, Deccan and up to South India. Many domestic cattle rely on this plant for their food to different extent and small insect generally found of this plant as a one of the favorite habitat. Fruits of the plant are also used as food by the villagers and tribal. Popularly known as the “Cluster Fig Tree or Goolar Fig (Gular)”, plant is native of Australasia, South-East Asia and the Indian subcontinent. Figs of a tree characteristically and unusually found on the trunk and useful as identification mark. In India the tree and its fruit are called “gular” in the north and “atti” in the south. This tree has height of several meters and characteristically gives milky exudates on the surface abrasion or damage; it is referred as holy plant in the religious literature and generally found in the sagas of god and goddess. This tree is without aerial roots unlike its many family members, leaves are true in nature, quite large in size to cover almost all the plant and make it one of the shadow bearing trees in the summer. Plant is propagated by either using seeds or cuttings of stem or root and requires well-drained

medium to heavy soils for its successful cultivation and grow in all kinds of soil. Natural regeneration is very good from seeds dispersed by animals and birds. Different parts of the plant are already in the medicinal use as a content of several Ayurvedic formulations. In the traditional systems of medicine, the plant is used for various health problems and diseases.

Dried roots are used in dysentery, pectoral complaints, and diabetes, applied in mumps, other inflammatory glandular enlargements and hydrophobia. The bark is highly efficacious in threatened abortion and also recommended in urological disorders, diabetes, hiccup, leprosy, dysentery, asthma and piles. The leaves are good wash for wounds and ulcers. They are useful in dysentery and diarrhea. The infusion of bark and leaves is useful as mouth wash to spongy gums and orally used in dysentery, menorrhagia, glandular swelling, abscess, cervical adenitis, chronic wounds and haemoptysis. Tender leaves are used in bilious affection and also to improve skin complexion. Tender fruits are stomachic, astringent and carminative to bowel, styptic, tonic, useful in the treatment of leucorrhoea, blood disorder, burning sensation, fatigue, urinary discharges, leprosy, menorrhagic epistaxis, intestinal worms dry cough, loss of voice, diseases of kidney and spleen.^{1,2}

Some workers investigated the pharmacological activity of this plant using laboratory animals and proposed the presence of significant hypoglycemic, hypolipidemic, renal anticarcinogenic, antitussive, hepatoprotective, radio protective, antioxidant, wound healing, antiulcer, anti-inflammatory, anthelmintic, antifilarial, antidiarrhoeal, antipyretic, antifungal, antibacterial and larvicidal activity.³⁻⁷

Phytochemical investigation made by many research workers demonstrate the picture of the biochemical

constituents observed in different parts of this plant. As per these investigators, fruit contains glauanol, hentriacontane, β -sitosterol, glauanol acetate, glucose, tiglic acid, esters of taraxasterol, lupeol acetate, friedelin, higher hydrocarbons and other phytosterol. A new tetracyclic triterpene glauanol acetate which is characterized as 13 α , 14 β , 17 β H, 20 α H-lanosta-8, 22-diene-3 β -acetate and racemosic acid were isolated from the leaves. An unusual thermostable aspartic protease was isolated from latex of the plant. The stem bark and fruit showed presence of glauanol acetate.⁸⁻¹⁰

Plant Details

Synonyms

Ficus racemosa L. var. *racemosa*, *Ficus semicostata* F. M. Bailey, *Ficus glomerata* Roxb., *Ficus vesca* F. Muell. *Ficus racemosa* var. *vesca* (Miq.) M. F. Barrett, *Covellia glomerata* (Roxb.) Miq. *Fucus lucescens*, *Ficus racemosa* var. *elo*.¹

Scientific Classification

Kingdom: Plantae
Division: Magnoliophyta
Class: Magnoliopsida
Order: Rosales
Family: Moraceae
Genus: Ficus
Species: *F. glomerata*

MATERIALS AND METHODS

Plant Material Collection and Authentication

Leaves were collected in the month of October from the plants grown in the natural habitat in and around Pune and shade dried for the period of two weeks. Dried parts of the plant were sent to the botanical survey of India, Pune (Vou. No. FIRSUK1) for authentication. After authentication leaves were crushed to make powder using mixer blender and utilized for the process of extraction.^{1,2}

Extraction

Dried powder was soaked in the 95% ethanol and extracted by cold maceration method. Dilute liquid extract was concentrated on rota-evaporator to obtain viscous liquid, which was further dried using sodium sulphide in dessicator to obtain dry powder. An yield of extract was 1.6 % w/w, the color was reddish brown and odour was peculiar.^{11,12}

Animals

Albino Swiss mice of 6-8 weeks of 20-25g body weight of either sex were selected for *in-vivo* evaluation. The animals were acclimatized for seven days in poly propylene cages at 24°C under 12 hours light / dark cycles and feed with standard pellet diet and had free access to water. The experiments were performed in the time period between 1:00 to 5:00 p.m. in pharmacology laboratory of the institute.^{13,14} Animal studies were conducted with prior permission of Institutional Animal Ethics committee (IAEC) with protocol reference number ICP/IAEC/10-11/P-27 for hot plate and ICP/IAEC/10-11/P-28 for tail flick method.

Analgesic Activity

Using Hot plate

Swiss albino mice of either sex were divided into five groups each containing six animals. Thermostat of Eddy's hot plate (Unicon Instruments, Delhi) was adjusted to

55°C and plate was cover till the temperature was stabilized at 55°C (\pm 0.5). Animals were placed on the plate one by one and jumping or paw licking, whichever be the earlier; was taken as a response. Responses were recorded using stop watch (Digital Racer, Delhi) and animals failing to show responses in first 12 seconds were rejected from the study. The latency was recorded at 0, 15, 30, 60 and 90 minute intervals for vehicle, standard and test drug administration. Vehicle was prepared by dissolving 1% Carboxy methyl cellulose in distilled water and administered 10mL orally. Commercially available Pentazocine injection (Talwin; 30mg/mL) were diluted using distilled water and used as standard drug for standard group. Three test groups were injected with 125mg/kg, 250mg/kg and 500mg/kg of EFGL (Ethanolic extract of *Ficus glomerata* leaves) diluted sufficiently in the vehicle without exceeding total volume 0.8mL in each case. The animals were lifted from the plate surface to terminate the test when response by the animals exceeded more than 15 seconds.

Tail immersion method

Swiss albino mice of either sex were divided into five groups, each containing six animals. A water bath (Unicon Instruments, Delhi) was maintained at 51°C (\pm 0.5) using thermostatic setting provided with an instrument. A thick paper was rolled to make a cone with a hole in the bottom. Each animal were taken in cone and allowed to extend tail out through bottom hole. Two centimeter length of a tail was marked using marker pen and dipped to observe the response. Tail flick out of the hot water and body jerk were taken as response. Responses were recorded using stop watch starting from the instant of dipping to the instant of flick. The latency was recorded at 0, 15, 30, 60 and 90 minutes for vehicle, standard and test drug administration. Vehicle was prepared by dissolving 1% Carboxy methyl cellulose in distilled water and administered 1 mL to each animal orally in control group. Commercially available Pentazocine injection was diluted using distilled water and injected i.p. in the standard group. Three test groups were orally given 125mg/kg, 250mg/kg and 500mg/kg of EFGL diluted sufficiently in the vehicle without exceeding total volume 0.8mL in each case.^{13,14}

Experimental design and Biostatistics

All groups were tested simultaneously in both methods of evaluation at identical experimental conditions in parallel experimental design. One way ANOVA were taken as statistical method for testing the significance. All test groups were compared with the vehicle (-ve control) and not with the standard pentazocine; as route of administration was different. Significant difference i.e. error $p < 0.05$ were taken as sufficient level of significance to conclude the existence of alternative hypothesis.¹⁵

RESULTS

Results obtained were studied statistically by calculating standard error of mean (SEM) and % latency with respect to control group for each participating group. Results in case of hot plate are tabulated in Table 1 and illustrated graphically in Chart I, whereas results of tail flick method are given in Table 2 and illustrated graphically in Chart 2.



Figure 1: *Ficus glomerata* tree

Table 1: Hot Plate method Results

Name of the Group	Latency of response in seconds (Mean ± SEM)				% latency with respect to control		
	0 min	15 min	30 min	60 min	15 min	30 min	60 min
Control	3.53±0.31	4.03±0.19	3.95±0.53	4.56±0.35	--	--	--
Standard	3.69±0.37	10.59±0.29	13.92±0.38	12.4±0.27	186	277	236
Test1	3.31±0.23	4.21±0.44	3.89±0.69	3.72±0.22	27.9	17.52	12.38
Test2	3.89±0.67	6.14±0.44	8.78±0.13	7.99±0.30	57.84	126	105.3
Test3	4.54±0.19	10.54±0.20	11.43±0.28	10.75±0.20	132.15	151.7	136.78

Table 2: Tail Flick method Results

Name of the Group	Latency of response in seconds (Mean ± SEM)				% latency with respect to control		
	0 min	15 min	30 min	60 min	15 min	30 min	60 min
Control	2.03±0.35	2.11±0.29	1.69±0.15	2.18±0.16	--	--	--
Standard	2.39±0.20	7.23±0.25	9.07±0.24	7.74±0.32	202.51	279.49	223
Test1	2.56±0.12	2.45±0.21	2.83±0.57	2.38±0.23	-4.29	10.54	-7.03
Test2	2.22±0.16	5.24±0.15	6.01±0.26	4.43±0.22	136	170	99.54
Test3	1.91±0.15	5.82±0.24	7.97±0.34	5.72±0.27	204	317	199

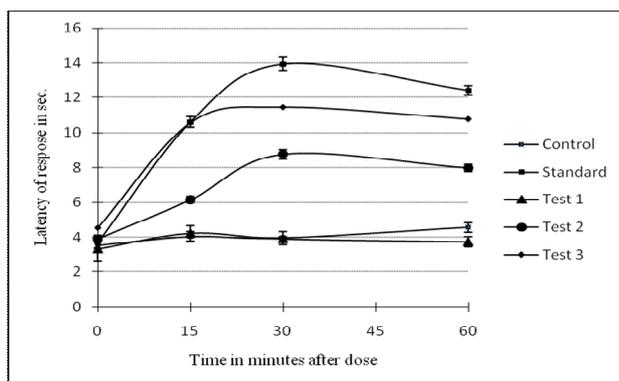


Chart 1: Hot Plate method Results

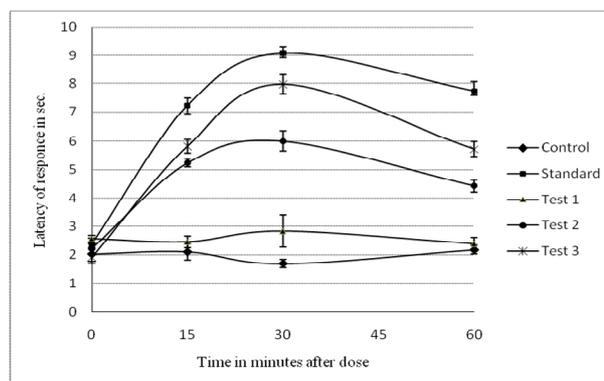


Chart 2: Tail Flick method Results

DISCUSSION

The idea of present invention was generated through the literature study; which was indicating that different morphological parts of this tree like leaves, bark, figs, buds, roots, shoots, wood etc are being used by conventional medical practicers in alternative system of medicine.^{1,2} Mouse is suitable as well as extremely used animal for the purpose of experiments intended to demonstrate analgesic activity and therefore selected for this study. Due to availability of this animal in sufficient quantity; we could use sufficient number of animals to establish a proper degree of significance in the experiment i.e. six animals in each group. Pain sensation was induced by the use of heat in both the methods; which is established, reliable and reproducible technique, if performed with the proper control and caution. Hot plate and water bath were calibrated and tested before the performance, to avoid accidental damage to the animals.

In hot plate experiment, animals those which were not responding to the heat in a particular manner either by paw licking or jumping were excluded from the study. A maximum response observed with highest dose of an extract was less than the response observed with standard dose of pentazocine. There were slow decline in the response in case of extracts as compared to standard indicating longer duration of action shown by the extractives.¹²⁻¹⁴ Tail flick method; in general, has more sensitivity as compared to hot plate method as indicated by lower relative values of standard deviation. Results in case of hot plate and tail flick were similar confirming the analgesic activity shown by the extractives. Here also, there were slow decline in the response as compared to the standard drug indicating longer duration of action; as like in hot plate method.

Response shown in both the experiments was sufficiently clear to demonstrate and reproduce at any place in the laboratory animals. No animal was died in the study and all animals were showing normal behavior in the cage. No acute toxicity was reported during and after study.¹⁵

CONCLUSION

Present work was the systematic, scientific and controlled study with sound experimental design. Ethanolic extract separated alcohol soluble ingredients form the leaves of the plant. One or the more than one ingredient from extract has analgesic activity. Active ingredient(s) when given orally with vehicle; get absorbed in sufficient quantity to produce observable analgesic activity in mice. In each group there were six animals and were treated under reasonably similar conditions in order to record the difference in groups. Animals from the test group particularly test 2 and test 3 shown activities comparable to standard drug injected animals and demonstrate the utility of the extract as analgesic. Observations in case of hot plate have more fluctuations as compared to tail flick method evident from large values of standard deviations. Significant difference were observed in groups when test groups were compared with control group in column wise ANOVA. "There is no significance difference in groups" were assumed null hypothesis and which was rejected successfully at error level 0.05 in both the methods. There is need to separate the extractives by fractionation using different solvents and to perform their qualitative and quantitative analysis. We also recommend further investigation of this activity in other animals and human being to confirm the claim.^{1,2,14,15}

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