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Investigation of Analgesic Potential of *Ficus carica* Fruits in Experimental Animals

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Abstract

The aim of work was to investigation of analgesic potential of *Ficus carica* fruits in experimental animals. *Ficus carica* possess Hepatoprotective, anticancer, antibacterial, antifungal, hypoglycemic, antispasmodic and antioxidant property. The plant *Ficus carica* contains phytochemicals like Anthocyanin, Scopoletin which possesses analgesic activity. Traditionally, *Ficus carica* is used as analgesic but no scientific investigation has been done for this activity hence this plant has been selected for the present study. *Ficus carica* (Family-moraceae) is commonly known as "FIG" traditionally used in Inflammation and Chest pain. The purpose of this study was evaluated the analgesic activity of ethanolic extract of *Ficus carica* fruits in experimental animal models. The extract was prepared by maceration method. Analgesic potency and acticvity was assessed with the help of tail immersion and tail-flick (to determine the central action) and GAA (glacial acetic acid) writhing test (to determine the peripheral action). Fruit extract at a dose of 200mg/kg and 400mg/kg was administered orally. Pentazocin (10mg/kg) was used as standard drug. The fruit extract exhibited significant (P>0.05) analgesic activity in comparison to control. Thus it can be concluded that ethanolic extract of *Ficus carica* fruits possesses analgesic activity and could provide the use of this plant in pain management.

Keyword: - Ficus carica plant and fruit, Pentazocin, Pharmacological action, Therapeutic activities.

INTRODUCTION

Kingdom – Plantae
Division – Magnoliphyta
Class – Maghnoliosida
Family – Moraceae
Order – Urticales
Genus – Ficus
Species – carica
Use part of plant – Whole plant, specially fruits

Many synthetic NSAIDs are available in the markets which are used as analgesic, antipyretic and antiinflammatory drugs. Due to many severe adverse effects of analgesic like: peptic ulcer, precipitation of asthma, hepatotoxicity, hypertension, bleeding etc. some drugs are banned in India as well as in other countries. Recently Nimesulide banned by the regulatory authorities all over the world. Rofecoxib, Voldecoxib had withdrawal from Social market for increasing cardiovascular risk. The use various synthetic preparations can be replaced with herbal preparation because of their minimal or less side effects.

Vernacular Names

Vernacular name are as in English- common fig tree, Hindi – Angir, Sanskrit- angira, Bengali- angir, Kannadanjura, Tamil- tenatti, telugu- anjuru, Marathi- anjra, Punjabi- fagari.

Distribution

Figs are distributed in Asia with southwest region and eastern region with Mediterranean, from turkey, Spain, Portugal, U.S.A. India, Chile, Persia, Japan, China, and Arabia. Cultivation in India in few states such as Pune (Maharastra) and Bellary and Anantpur district (South India). In Uttar Pradesh, Punjab and Musore, it is mostly grown scattered in gardens or in homeyards.

Morphology

Tree of Ficus carica L. is usually 15-20 feet long, with branches have the trunk diameter approx 7 feet (rarely). The latex is milky white in color and contains ficin, ficin is a enzyme (protein digesting). The leaves of the plant are broaded, nearly 3 to 5 lobed or ovate, rough at above and pubescent below. Fruits are auxiliary, usually pear shaped, variable in size and color. Although considered a fruit, the fig is actually a flower inverted into it. The ripe fig is sweet in taste and juicy. Before ripening fig is gummy with latex.

Chemical constituents

Phytochemicals are the chemicals produced by plants. Literature survey indicated that presence of flavonoids, coumarins, sterols, anthocyanins,and triterpenoids, etc, mostly in plant parts. Dried seeds of fig contain oleic acid, linolenic acid, linoleie acid, palmitic acid, arachidic acid, stearic acid.

Leaves contain bergapten, 4',5'-dihydropsoralen, rutin, 24 methylenecycloartanol umbelliferone, marmesin, stigmasterol, ficusogenin, B-sitosterol, psoralen V-taraxasterol ester and tyrosine moisture, lupeol, protein, fat,

The latex contains 6- 0-linoleyl-B-D-glucosyl-B-sitosterol, 6-0-Oleyl-B-D-glucosyl-ß- sitosterol, 6-0-palmitoyl-B-D- glucosyl-B- sitosterol, caoutchouc, resin, albumin, cerin, sugar and malic acid, rennin, proteolytic enzymes, diastase, esterase, lipase, catalase, and peroxidase.

Fruits of fig contain cyanidin-3-Orhamnoglucoside, and cyanidin-3-0-glucoside, saturated fat, sodium, protein, insoluble sugars, Vit.-A and C, calcium and iron. Roots of fig plant contain bergapten, psoralen. Vitamin B, and B are also found in figs D- glucans have been found as common polyners of the fungal cell wall, they consist of a mixture of linear (1 6)-B-D- glucan with various (1-6) branched oligosaccharides chains.

Pharmacological activity

Figs tree (Ficus) are an understudied now a days in pharmacognosy in several centuries, European and eastern medical writings poultices of figs for tumors treatment for anatural swellings, infection or, alternatively, cancer. Its pharmacological gastroprotective, antioxidant, antibacterial, anti-inflammatory, actions include antispasmodic, antidiarrheal, antitumor, vulnerary, anticancer, immunobalancing/immunoharmonizing, antispasmodic, and nutritive. Nowadays we know that even single pure chemicals can exert pleiotropic effects (Having multiple effects) on genes. This mcans that the compound can induce or suppress a gene to transcribe proteins and that this efect can reverberate downward to affect multiple human organs and multiple physiological systems. If such a multiple or pleiotropic effect is possible from a pure chemical, how much more so, then, is the potential for multiple physiological targeting from a mixture of different compounds.

Table no.1 Therapeutic uses of plant *Ficus carica*

Sr. No.	Part of Plant	Therapeutic uses
1.	Fruit	Leprosy, nose bleeding, antipyretic, aphrodisiac, lithontripic, paralysis, emollient, demulcent, laxative, inflammation, liver disease, chest pain, piles.
2.	Roots	Tonic, Leucoderma, Ringworm infection
3.	Latex	Expectorants, diuretic, anthelmintic, anaemia.
4.	Leaves	Anti-diabetic, Vermifuge, Dermatitis, Phototoxicity in animals.
5.	Seeds	As edible oil, Lubricant.

MATERIAL AND METHODS

The collection of Plant parts

The aerial part of the roots from Ficus (Family-Moraceae) plant were collected in the month of June 2012 from Lucknow, U.P.. The plant material was authenticated by Division of Taxonomy, National Botanical Research Institute, Lucknow, UP, India (NBRI). and voucher specimen was deposited for future reference (Authentication no. NBRI/CIF/318/2012).

Extraction of Plant Material

The shade dried aerial roots part collected and will be subjected for size reduction to coarse powder. The coarse powders were macerated with ethanol (70%) for 72 hrs at room temperature. The liquid phase was decanted and filtered through cotton wool/ muslin cloth Thereafter, the ethanolic extract was evaporated to dryness using the evaporator temperature 60°C. The dried extract gave a yield of 14 % (w/w) and was stored in the packed container until for future use

Animals

Swiss mice weighing 20-30 g of either gender were procured. They were housed maintained by the standard conditions (25±2°C with the relative humidity 30-35%) and used 12 hrs light then 12 hrs dark maintain this cycles respectively. Animals (mice) were provided with std rodent pellet diet and had free excess to water The protocol was approved by IAE (Institutional Animal Ethics Committee) (Approval no.UIP/CPCSEA/J-2013/02).

Drugs and Chemicals

All the chemicals used in the study were of analytical grade: Pentazocin (Novartis Pharmaceuticals), Methanol (SD Fine, Mumbai), Gum acacia (SD Fine, Mumbai), and Acetic acid.

RESULTS

1. Acetic acid induced writhing response

As shown in Table 2 intraperitoneal injection of acetic acid elicited the writhing syndrome in control mice with 59 writhes counted in 15min. Ficus carica produced a significant dose- dependent ($P<0.05$) reduction in the number of writhes with peak effect (51.69% inhibition) produced at the highest dose of 400mg/kg in acute study where as chronic study shown in table 3 produced a significant dose-dependent ($P<0.05$) reduction in the number of writhes with peak effect (48.29% inhibition) at higher dose. This effect comparable and not significantly different ($P>0.05$) from that produced by 10mg/kg pentazocin (56.21%) in acute and in chronic (51.84%). The greatest nociceptive effect was produced.

Table No. 2 Effect of Ficus carica in acetic acid induced writhing responses in acute study

Treatment	Dose (mg/kg)	Total number of writhes (mean±SED)	% Inhibition
Control (Normal saline)	10 mg/kg	59±0.47	-
Standard (Pentazocine)	10 mg/kg	25.833±0.24***	56.21%
Test 1 (Ficus carica extract at lower dose)	200 mg/kg	51.666±0.36***	12.43%
Test 2 (Ficus carica extract at higher dose)	400 mg/kg	28.5±0.31***	51.69%

Values are expressed as mean±SEM***P<0.001 significant as compared to control (one way ANOVA followed by tukey's multiple comparison test)

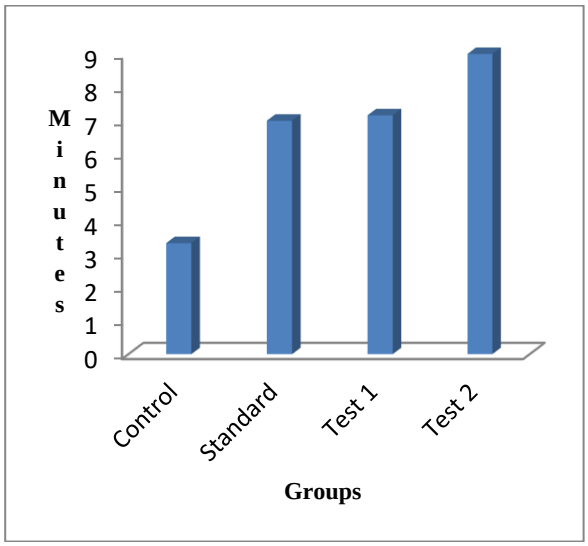

Fig. No.- 1 Effect of Ficus carica in acetic acid induced writhing responses in acute study

Table No.- 3 Effect of Ficus carica in acetic acid induced writhing responses in chronic study

Treatment	Dose (mg/kg)	Total number of writhes (mean±SED)	% Inhibition
Control (Normal saline)	10 mg/kg	58.83±0.43	-
Standard (Pentazocine)	10 mg/kg	28.33±0.36***	51.84%
Test 1 (Ficus carica extract at lower dose)	200 mg/kg	46.83±0.38***	20.77%
Test 2 (Ficus carica extract at higher dose)	400 mg/kg	30.66±0.47***	48.29%

Values are exressed as mean±SEM***P<0.001 significant as compared to control (one way ANOVA followed by tukey's multiple comparison test)

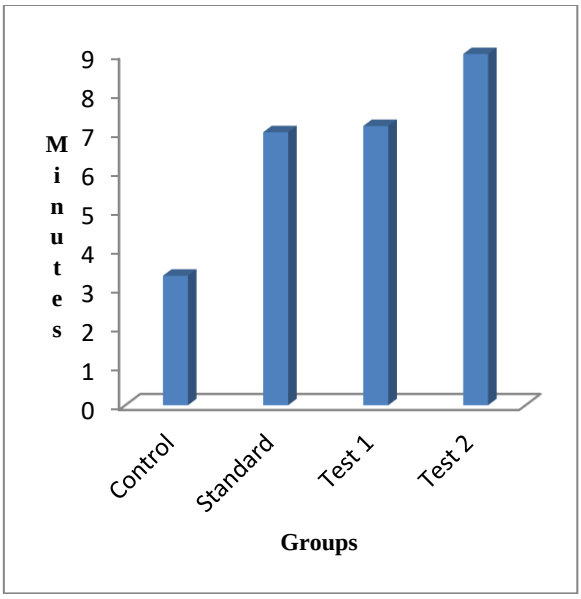

Fig. No.-2 Effect of Ficus carica in acetic acid induced writhing responses in chronic study

2. Tail flick method

In tail flick method, the increase in latency period after 1.5 hr significantly different ($p<0.05$) compared to control values within the same drug treated groups. The extract and Pentazocine caused significant increase ($P<0.05$) in the percent reaction time the percentage increase in reaction time is dose dependent. At all the specific time the percentage of tail flick elongation time differed significantly ($P<0.05$) between the extract and Pentazocine at the both doses of plant extract, being greater for Pentazocine. At the peak of activity 200mg/kg and 400mg/kg extract showed 45.12% and 61.34%. Percentage of tail flick elongation time respectively. Whilst Pentazocine gave 74.52% elongation of tail flick time (table 4).

Table No.-4 Effect of Ficus carica in tail flick method in chronic study

Treatment	Dose (mg/kg)	Total number of writhes (mean±SED)	% Inhibition
Control (Normal saline)	10 mg/kg	3.63±0.14	-
Standard (Pentazocine)	10 mg/kg	7.33±0.11***	74.52%
Test 1 (Ficus carica extract at lower dose)	200 mg/kg	5.66±0.15***	45.12%
Test 2 (Ficus carica extract at higher dose)	400 mg/kg	6.26±0.15***	61.34%

Values are expressed as mean±SEM***P<0.001 significant as compared to control (one way ANOVA followed by tukey's multiple comparison test)

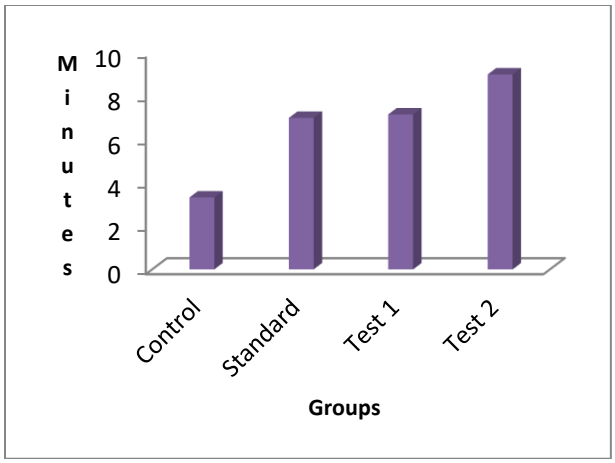

Fig. No.- 3 Effect of Ficus carica in tail flick method in chronic study

Whereas in acute study the extract and Pentazocine caused significant increase (P<0.05) in the percent reaction time. At the peak of activity 200mg/kg and 400mg/kg extract showed 45.12% and 61.34% of tail flick elongation time respectively. Whilst Pentazocine gave 74.52% elongation of tail flick time (Table 5).

Table No.- 5 Effect of Ficus carica in tail flick method in acute study

Treatment	Dose (mg/kg)	Total number of writhes (mean±SED)	% Inhibition
Control (Normal saline)	10 mg/kg	3.63±0.73	-
Standard (Pentazocine)	10 mg/kg	6.78±0.87	86.77%
Test 1 (Ficus carica extract at lower dose)	200 mg/kg	4.43±0.75	22.03%
Test 2 (Ficus carica extract at higher dose)	400 mg/kg	5.46±0.73	50.41%

Values are expressed as mean±SEM P<0.05 significant as compared to control (one way ANOVA followed by tukey's multiple comparison test)

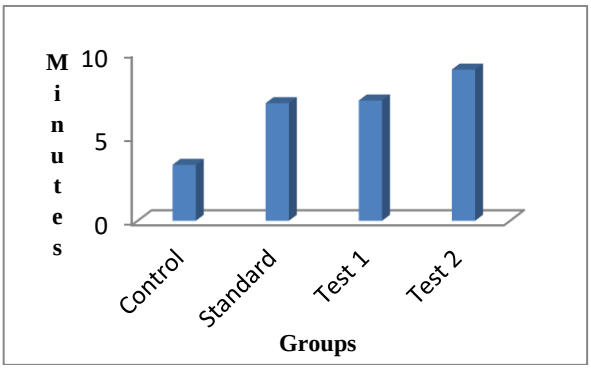

Fig.No.- 4 Effect of Ficus carica in tail flick method in acute study

3 Tail immersion method

In tail immersion method, the increase in latency period after 1 hr significantly different (p<0.01) compared to control values within the same drug treated groups. The extract and Pentazocine caused significant increase (P<0.05) in the percent reaction time. the percentage increase in reaction time is dose dependent. At all the specific time percentage of tail immersion elongation with time differed significantly (P<0.01) between the extract and Pentazocine at the both doses of plant extract, being greater for Pentazocine. At the peak of activity 200mg/kg and 400mg/kg extract showed 52.10% and 61.10%. Percentage of tail flick elongation time respectively. Whilst, The pentazocine gave 52.10% elongation of tail flick time (table-6).

Table No.- 6 Effect of Ficus carica in tail immersion method in acute study

Treatment	Dose (mg/kg)	Total number of writhes (mean±SED)	% Inhibition
Control (Normal saline)	10 mg/kg	3.5±0.42	-
Standard (Pentazocine)	10 mg/kg	7.33±0.42***	52.10%
Test 1 (Ficus carica extract at lower dose)	200 mg/kg	7.33±0.42***	52.10%
Test 2 (Ficus carica extract at higher dose)	400 mg/kg	9±0.57***	61.10%

Values are expressed as mean±SEM ***P<0.05 significant as compared to control (one way ANOVA followed by tukey's multiple comparison test)

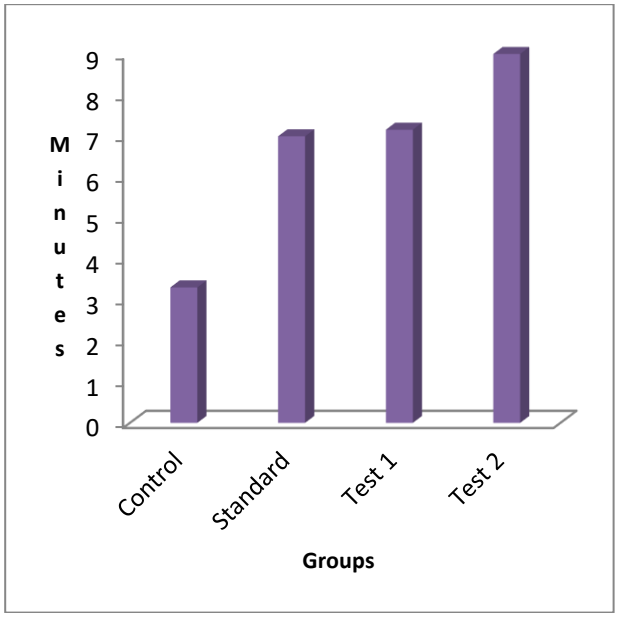

Fig. no.- 5 Effect of Ficus carica in tail immersion method in acute study

Table No. - 7 Effect of Ficus carica in tail immersion method in chronic study

Treatment	Dose (mg/kg)	Total number of writhes (mean±SED)	% Inhibition
Control (Normal saline)	10 mg/kg	3.33±0.42	-
Standard (Pentazocine)	10 mg/kg	7±0.51***	52.40%
Test 1 (Ficus carica extract at lower dose)	200 mg/kg	7.16±0.65***	53.40%
Test 2 (Ficus carica extract at higher dose)	400 mg/kg	9±0.57***	63%

Values are expressed as mean±SEM ***P<0.05 significant as compared to control (one way ANOVA followed by tukey's multiple comparison test)

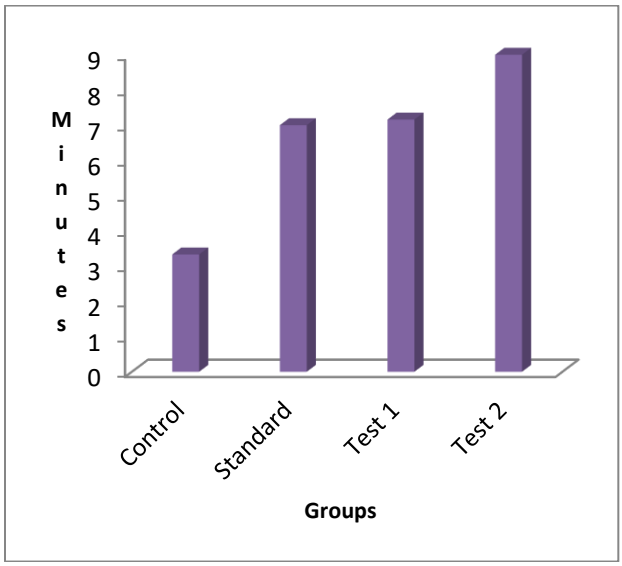

Fig. No.- 6 Effect of Ficus carica in tail immersion method in chronic study

DISCUSSION

Pentazocine is a benzomorphine derivative with mixed opioid antagonist or/and agonist actions. It alters the perception of the response for pain and that produces generalized C.N.S. (Brain) depression via binding with the opiate receptors in CNS and acting as the partial agonist and antagonist. The Tail-flick model is the method for measuring centrally mediated analgesic activity. The tail flick method which is used thermal induced nociception that indicates narcotic involvement and which is more sensitive for the opioids μ receptors. The ability of the extract to prolong the reaction latency to thermally induced pain in mice further suggested central analgesic activity. Anthocyanin and scopoletin presence of flavonoids may be contributory to the analgesic activities of Ficus carica. The tail immersion method is useful in elucidating the centrally mediated that antinociceptive activity, which is focused mainly on the changes on spinal cord level. The significant increase in pain threshold produced by Ficus carica in model suggested that involvement of central pain pathways. Pain is centrally treated the several complex processes including dopaminergic, opiate, serotonergic and noradrenergic systems. The results obtained in this study indicate that different parts.

CONCLUSION

Ficus carica possesses analgesic activity, which are mediated via peripheral and central inhibitory mechanisms. This could provide a rationale for the use of this plant in the treatment of fever, pain with inflammatory conditions in the many medicine.

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