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ANALGESIC AND ANTIEMETIC ACTIVITIES OF *FICUS EXASPERATA* VAHL., AND *CLEOME CILIATA* SCHMACH AND THONN.

Misbah Zubair[1], Syed Waseemuddin Ahmed[1], Salman Ahmed[1*], M.Shaiq Ali[2] and Patrricia Akpomedaye Onocha[3]

[1]Department of Pharmacognosy, Faculty of Pharmacy, University of Karachi, Karachi-75270, Pakistan.

[2]H.E.J. Research Institute of Chemistry, International Centre for Chemical & Biological Sciences, University of Karachi, Karachi-75270, Pakistan

[3] Natural products/Medicinal Chemistry Unit, Department of Chemistry, University of Ibadan, Ibadan, Oyo State, Nigeria

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***Correspondence for Author**
Salman Ahmed
Department of Pharmacognosy
Faculty of Pharmacy,
University of Karachi, Karachi
75270, Pakistan.

ABSTRACT

The present investigation is an attempt to evaluate analgesic and antiemetic activities of *Ficus exasperata*; *Cleome ciliata* leaves methanolic extract by using chick emesis model (oral treatment) and acetic acid induced writhing test (intraperitoneal treatment) in mice respectively. The antiemetic activity (150 mg/kg b.w., of extract) was carried out by using chlorpromazine (150mg/kg) as standard antiemetic drug. The analgesic activity (250 mg/kg b.w., of extract) was performed by using aspirin (150mg/kg) as standard analgesic drug. The results showed significant analgesic and antiemetic effects.

KEYWORDS: *Ficus exasperata*; *Cleome ciliata*; antiemetic; analgesic; chick emesis model; acetic acid induced writhing test.

INTRODUCTION

Ficus exasperata Vahl., the sand paper tree (family Moraceae), is a small to medium-sized tree. Leaves are alternate, leathery and ovate-elliptic. Figs are singly or in pairs, orange-red when ripe. It is widely distributed in Africa, Arabian Peninsula, Angola, Ethiopia, India, Mozambique, Sri Lanka, Senegal, Yemen, Zambia and South-eastern Zimbabwe[1,2]. Various

parts of plant are used as abortifacient, analgesic, antiarthritic, antidiarrheal, antidysenteric, diuretic, febrifuge and wound healing. *Ficus exasperata* is used against, cutaneous or subcutaneous parasitic infection, edema, leprosy, ophthalmic and oral infections nasopharyngeal afflictions, rheumatism, gout, kidney disorders, hemorrhoids and venereal diseases. Leaves have been used internally to treat anxiety, arthritis, epilepsy, hypertension, rheumatism[3,4] easing childbirth, treating leprosy[5], sexually transmitted diseases, gastroenteritis, opthalmia, cough and heamorrhoid[6]. Whereas their external use is recommended in asthma, bronchitis, chest pain, emphysema, cardiac arrhythmias, tuberculosis[4,7], fungal infections, ringworm, rheumatism, jaundice and inflammation of the gums. Stem bark is used for the treatment of abscesses, abnormal enlargement of the spleen, eye ailments, hemorrhoids and stomach-ache. It is locally applied on the body for the treatment of malaria[2]. Roots are used to manage asthma[8], eye problems, tuberculosis, venereal diseases and to expel worms[2]. Anti-diabetic, hypotensive, antioxidant, anti-inflammatory, antiarthritic, antinociceptive, anticonvulsant, anxiolytic, antiulcer, antipyretic, antimicrobial, uterotonic[4], pesticidal[9] anthelmintic[10], anti-dysmenorrhea[11], antimalarial[12], diuretic[13], anti-gastroenteritic[14], molluscicidal[15]activities are reported from leaves. Bark demonstrates anti-inflammatory[16] and antioxidant[17] properties. Flavonoids, glycosides, saponins, steroids and tannins are reported from leaves, stem and root[18]. Fruits contain higher proportion of unsaturated fatty acids (linoleic acid and oleic acid) whereas saturated fatty acids detected include stearic acid and palmitic acid[19]. The chemical structures of isolated phytochemicals are mention in Figure 1.

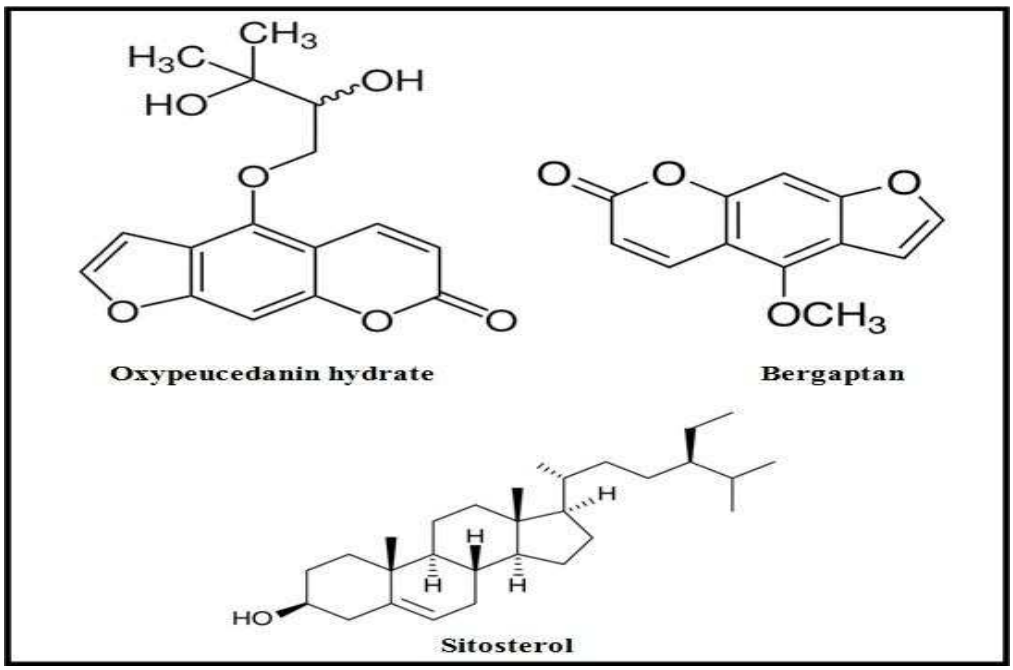

Figure 1: Chemical structure of constituents isolated from *Ficus exasperata* Vahl[16].

Cleome ciliata Schmach and Thonn., the spider plant (family Capparaceae) is a green creeping annual or short-lived perennial herb that spreads like a spider. It is widely distributed in coastal regions of Africa, especially in Nigeria, Uganda, Tanzania and Ghana[20,21]. The plant grows erect to a height of 30 cm., and then falls flat on the ground where it continues to grow and flower[22]. It has a slender leaf stalk with trifoliate leaves; the leaflets are net-veined and elliptical with smooth margin[20]. The flowers are distinctly dimorphous with respect to the ovaries of the mature flower. The normal ovary (fertile) and short ovary (abortive) both types are produced on the same plant[22]. The mature fruit is a capsule and dry dehiscent. Placement of leaves on the plant is spirally alternate and the fruits arise at the axial of the leaves[20]. The seeds are attached along the sutures formed by the two carpels of the fruit and average 50 seeds per pod. They are small and reniform with the embryo curled up with the sharp radical end touching the cotyledons to form a disc-like structure[20-22]. The plant juice is used for earache, convulsions[21] and peptic ulcers[23]. Leaves are anthelminthic and carminative[24] and their sap is externally applied for chronic otitis media[25]. The leaves of the plant possess antibacterial properties. Preliminary phytochemical investigation suggests the presence of alkaloids, flavonoids, glycosides, saponins, steroids, tannins and terpenoids[26]. The present investigation was conducted to evaluate the analgesic and antiemetic activities of *Ficus exasperata* and *Cleome ciliata* leaves extracts. Although the analgesic effect of *Ficus exasperata* leaves extract has been studied earlier by using formalin test[27]. The presented attempt is further justification of analgesic effect by using acetic acid induced writhing test. Antiemetic effect is reported for the first time.

MATERIALS AND METHODS

Collection of Plant material

The leaves of *Cleome ciliata* Schmach and Thonn, and *Ficus exasperata* Vahl, were collected from the forest of Ibadan, Nigeria and identified by Mr. Felix Usang of Forest Research Institute of Nigeria (FRIN). Voucher specimen was deposited at the Herbarium of the Institute.

Preparation of the plant extracts

Fresh plant materials (2 kg each) of leaves of *Cleome ciliata* Schmach and Thonn, and *Ficus exasperata* Vahl, were soaked separately in methanol for a week and the extracts were

condensed to dryness by evaporation using rotary evaporator at 40°C. These concentrated methanol extracts were used for bioassay.

Animals

Young male chicks, 4 days old (32-52 g) and Swiss albino mice (weighing 20-30 g) of both sexes were obtained from Big-bird Poultry Breeders (Pvt) Ltd., and Animal house of Aga Khan University, Karachi, Pakistan respectively. They were housed in plastic cages with saw dust as beddings under temperature 25 ± 2°C; 12 h/12 h light-dark cycle and given food and water *ad libitum*. Permission and approval from animal studies were obtained from Board of Advanced Studies and Research, University of Karachi [BASR. Res. No.09(46)-2006]. Chicks (for antiemetic activity) and mice (for analgesic activity) were randomly divided into four groups.

Drugs and Chemicals

Acetic acid , copper sulfate (Scharlau Chemie S.A. Barcelona, Spain), chlorpromazine (ICN, USA), Dimethyl sulfoxide (DMSO), tween 80 and methanol (Merck, Darmstadt, Germany) were used in the experiment.

Acute toxicity test

Acute toxicity studies demonstrate that the leaves of *Ficus exasperata*[28] and *Cleome ciliata* are safe for administration[26].

Analgesic activity

Mice were randomly divided into four groups of seven animals each. Dose of 250mg/kg of *Cleome ciliata* and *Ficus exasperata* were administered to two groups while the remaining two groups received distilled water 10 ml/kg and aspirin 150 mg/kg respectively, following protocols established by Koster *et al*., (1959)[29] and Salawu *et al*., (2008)[30]. All treatments were administered intraperitoneally, and after 30 min 10 ml/kg of 0.6% acetic acid solution in normal saline were injected intraperitoneally. The numbers of writhes were counted for 15 mins after acetic acid injection. The percentage inhibition was calculated using formula[31]:

$(N – Nt / N) \times 100$

Where

N = Average number of writhes in control group ; Nt= Average number of writhes in test group

Antiemetic activity

The antiemetic activity was determined by following the protocols of Akita *et al.*, 1998[32]. Each chick was set aside in a large beaker for 10 minutes to stabilize. Chlorpromazine and extracts were dissolved in 0.9 % saline containing 5 % DMSO and 1 % tween 80 and administered abdominally at a dose of 150 mg/kg b.w., to the test animal. After 10 minutes copper sulfate was administered orally at 50 mg/kg b.w., to each chick, then the number of retching was observed during the next 10 minutes. The percent inhibition was calculated by the following formula:

Inhibition (%) = [(A-B)/A] x 100

Where

A = Frequency of retching in control group ; B = Frequency of retching in test groups

RESULTS AND DISCUSSION

Ficus exasperata and *Cleome ciliata* significantly decreased the number of writhes when compared to the aspirin treatment and the control (**Table 1 and Figure 2**). *Ficus exasperata* and *Cleome ciliata* in dose of 250 mg/kg body weight reduced the numbers of writhes by 49.78 and 36.87%, respectively. The group of mice treated with aspirin at a dose of 150 mg/kg body weight had 13 writhes compared to the 69.7 writhes of the control group, thus aspirin reduced the writhes by 81.34%. The acetic acid induced writhing method is an effective method to evaluate peripherally active analgesics. The abdominal constriction response induced by acetic acid is a sensitive method to test peripherally acting analgesics[33]. Hyperalgesia, induced by the injection of acetic acid, is characterized by contraction of the abdominal muscle accompanied by body elongation and an extension of the forelimbs. Various peripherally acting analgesic drugs such as ibuprofen, aspirin and indomethacin have been reported to inhibit acetic acid induced writhing in mice[33,34]. Tested extracts of *Ficus exasperata* and *Cleome ciliata* leaves reported effective against acetic acid induced writhing in mice and has been suggested to be a peripherally acting analgesic[35], perhaps via the inhibition of synthesis and release of prostaglandins and other endogenous substances[30]. The mechanism of action may be linked to the inhibition of cyclooxygenases.

Table 1: Effect of *Ficus exasperata* and *Cleome ciliata* on acetic acid induced writhing in mice.

Treatments	Dose (mg/kg i.p.,)	Mean Number of writhes ± S.E.M. (15 mins)	% age inhibition of writhes
Control	-------	69.7±3.44	--------
AS	150	13.0±2.1	81.34

FE	250	35.0±1.3	49.78
CC	250	44.0±0.57	36.87
AS= Aspirin ; FE= *Ficus exasperata* ; CC= *Cleome ciliata* ; S.E.M = Standard Error of Mean, N=7, *p<0.05 vs. control applying unpaired t=test.			

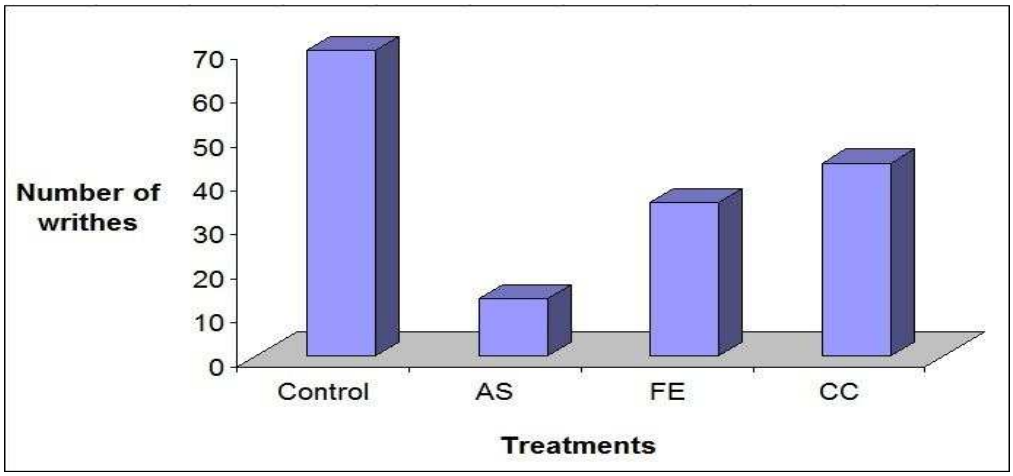

Figure 2: Analgesic effect of *Ficus exasperata* and *Cleome ciliata*

The results of antiemetic effect of methanol extracts of *Ficus exasperata* and *Cleome ciliata* are shown in **table 2 and figure 3**. Leaves extracts of *Ficus exasperata* and *Cleome ciliata* showed 46.21% and 58.20% inhibition of retches. The standard drug chlorpromazine showed 35.23 % inhibition of retches. The methanol extracts of *Ficus exasperata* and *Cleome ciliata* showed significant ($p < 0.05$) anti-emetic effect in young chicks. The protective effect of the extract against copper sulfate induced retching in young chicks is possibly by peripheral action as the oral copper sulfate induces emesis by peripheral action through excitation of visceral afferent nerve fibers of the GIT[36]. It has also been established that the peripheral 5-HT_3[37], 5-HT_4[38] or NK_1[39] receptors are involved in emesis. Therefore, it may be said that the methanol extracts of *Ficus exasperata* and *Cleome ciliata* produced antiemetic activity by receptor antagonism and has peripheral antiemetic action. Moreover, anti-emetic activity by using copper sulfate proposed 5-HT_3[37], 5-HT_4[38] or NK_1[39] receptors antagonism. Therefore it may be said that extracts were able to effectively prevent emesis and has a peripheral anti-emetic action.

Table 2: The anti-emetic effect of *Ficus exasperata* and *Cleome ciliata* on copper sulfate induced emesis in chicks.

Treatments	Number of Retches (Mean ± SEM)	Inhibition (%) of retches
Control	70.10 ± 3.28	-------
CZ	45.40 ± 3.11*	35.23
FE	37.70 ± 3.12*	46.21

CC	29.30±1.92*	58.20
CZ = Chlorpromazine; FE= *Ficus exasperata* ; CC= *Cleome ciliata* ; S.E.M = Standard Error of Mean, N=7, Dose=150 mg/kg p.o., *= $p < 0.05$ significantly different from control value using unpaired student's *t*-test.		

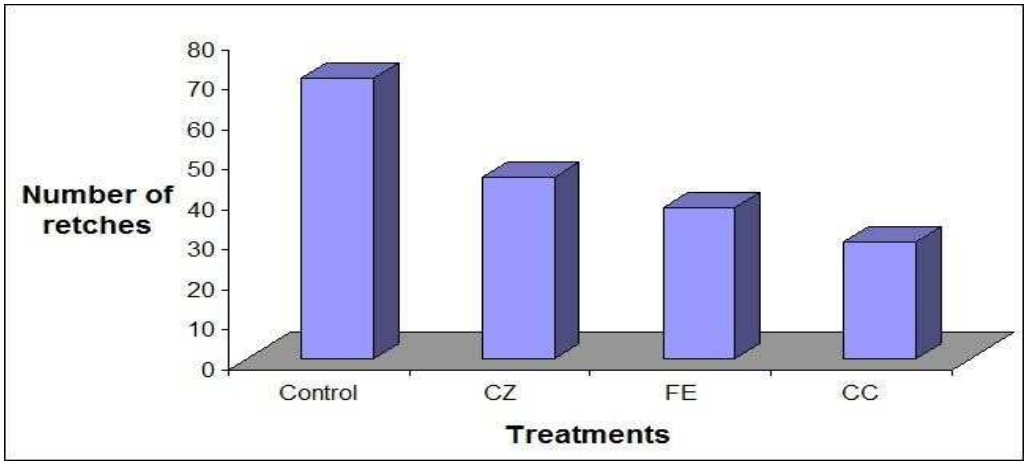

Figure 3: Antiemetic effect of *Ficus exasperata* and *Cleome ciliate*

As mentioned earlier that flavonoids, steroids and terpenoids are reported from *Ficus exasperata*[18] and *Cleome ciliata*[26]. Flavonoids, steroids and terpenoids have analgesic and antiemetic activities[40]. So, it may be implied that the observed analgesic and antiemetic effects were due to the presence of these phytochemicals. However compound targeted activities are further required to justify the responsible analgesic and antiemetic compound(s) and other bioassays to clarify actual mechanism.

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