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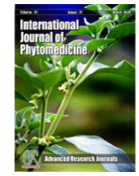

Original Research Article

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Neuropharmacological and biological activities of *Fumaria indica*

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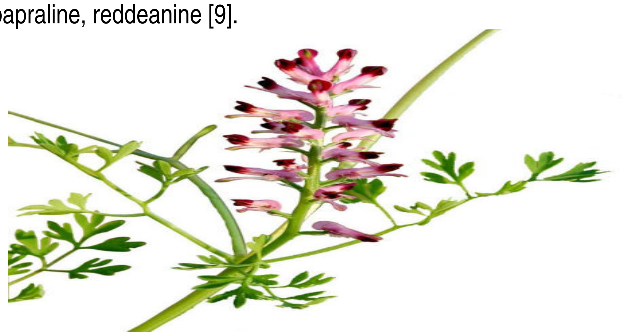
Abstract

Crude extract of *Fumaria indica* was assessed for neuro-pharmacological, analgesic antimicrobial and cytotoxic activities. It decreases muscle tone as indicated by swimming induced depression test (2.41/6 min, 2.56/6 min; at the dose of 500 and 300 mg/kg respectively), it also produces dose dependant (200, 300, 500 mg/kg) increase in traction time and reduces exploratory behaviour therefore, has significant muscle relaxant and anxiolytic effect (p 0.05) as compared to standard drugs diazepam and imipramine. The results of analgesic activity (writhing and hot plate test) were highly significant as the mean number of writhes for drug treated animals was reduced (62.7% at 500 mg/kg) as compared to the control group and reference drug aspirin. The present study also revealed that the extract of *F. indica* has potential to inhibit the growth against different pathogenic bacteria and fungi *in vivo*. Over all the *F. indica* has significant CNS depressant action with moderate analgesic and antifungal effects.

Keywords:zzzzzzzzzzzzzzzzzzzzzzzzzzzzzzzzzzxcxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxxx xxxxxxxxxxxxxxxxxxxxxxxxxxxx

Introduction

Fumaria indica Linn is locally known as "Pitpapra" or "Shahtrah", Traditionally it was used as anthelmintic, alterative, antidyspeptic, blood purifier, cholagogue, diaphoretic, diuretic, laxative, stomachic, sedative, tonic [1, 2.] *F. indica* also possesses antipyretic, antidiarrhoeal, antifungal and hypoglycemic properties [3-5]. It is a smooth muscles relaxant and has hydrocholeretic, by stimulating bile excretion, and hepatoprotective effects [6]. Phytochemical investigation revealed the presence of alkaloids, *viz*. protopine [7], parfumine, cryptopine, copticine, fumariline [8], fumaramine, fumaritine, paprafumicin, paprarine, papracinine, papraline, reddeanine [9].



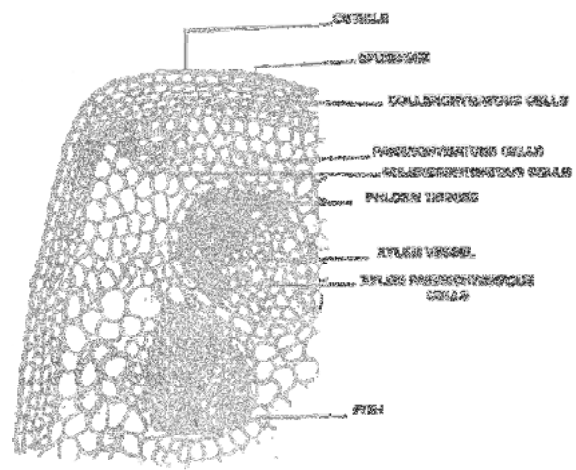


Figure 1: a) Aerial portion of *Fumaria indica,* b) Transverse section of *Fumaria indica* Stem × 60 showing tubular stem, branches and leaves 10.

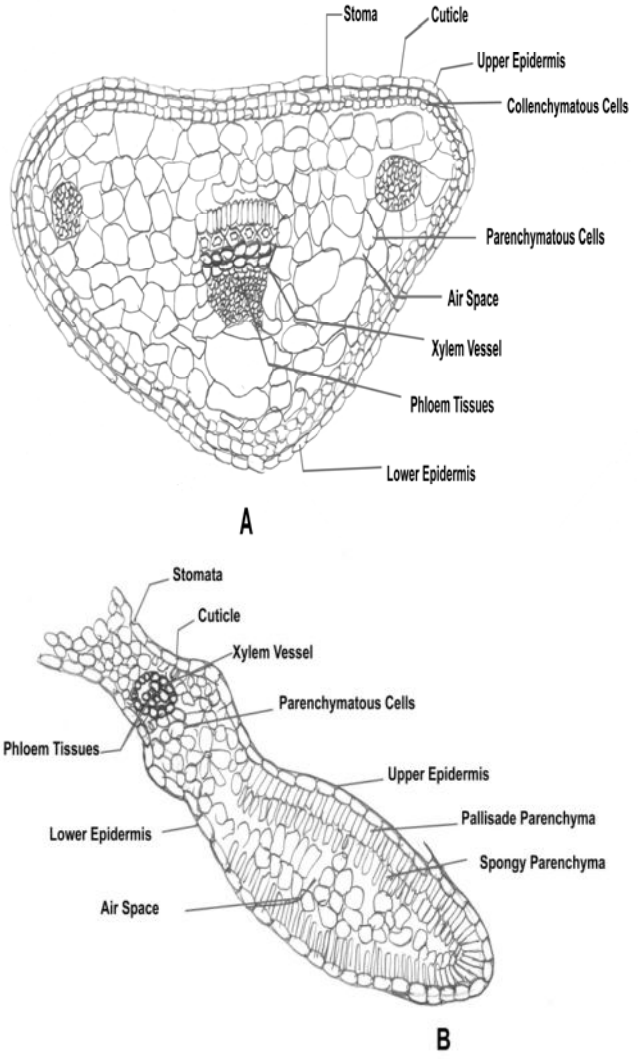
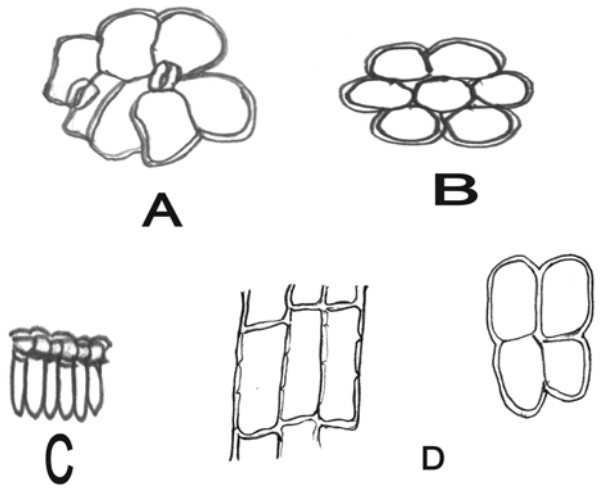


Figure 2 A. Transverse section of Leaf petiole × 80, B. A portion of Leaf lamina × 60 [10].



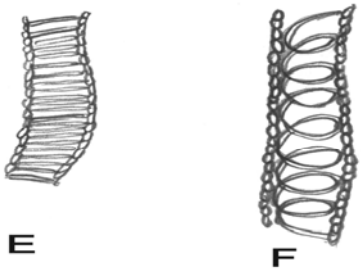


Figure 3: Powdered drug of *Fumaria indica* Stem × 250 A: Epidermis with thin Cuticle, B: Collenchymatous cells, C: Sclerenchymatous cells, D: Parenchymatous cells, E: Annular vessel, F: Spiral vessel [10]

Despite comprehensive work carried out on exploring medicinal activities of this herb, there is no reference in literature to the neuropharmacological aspects of whole plant extract, and the traditionally used medicine are more effective because of less side effect and low cost so it was considered worthwhile to study the neuropharmacology and some other related biological aspects of *F. indica* [11].

Materials and methods

Preparation of crude extract and Chemicals

Dried whole plant of *F. indica* Linn. (5 Kg) was collected from local market Karachi, Pakistan. The plant material was cleaned, and coarsely ground. The powdered material was soaked in 80 % methanol for 15 days with occasional shaking [12]. The filtrate was evaporated on a rotary vacuum evaporator under reduced pressure. Acetylsalicylic acid (Aspirin, 300 mg tablets) and Diazepam (Diazepam, 5 mg tablets) were used as a standard medicine.

FTIR and HPLC Analysis

FTIR and HPLC analysis were performed on crude extract of *F. indica* according to the methods described by [13]. FTIR analysis was performed on Spectrum One and for HPLC spectra Agilent 1100 series was used at 254 nm with flow rate 20 ml/min.

Experimental animals: the animals

Albino rats and mice (male and female) were purchased from H.E.J. Research Institute of Chemistry, Karachi, Pakistan. Mice weighing 24-30 gram and rats 190-220 grams were used for analgesic, anti-inflammatory and behavioural activities. Animals were kept in home cages (five animals in each group) and acclimatize at 30˚C ± 1˚C with access to food and water.

Assessment of neuropharmacological activity (open field, head dip, rearing, traction and swimming test)

Animals were divided in to four groups (each group comprised of 05 animals) for each test. G-A: control, G-B and C received 300 mg/kg and 500 mg/kg crude extract of *F. indica* orally, G-D: animals treated with standard drugs. In CNS activities 2 mg/kg Diazepam was used as reference drug. The observations were made after thirty to forty minutes of oral drug administration. Test and reference drugs were dissolved in distilled water. G-A group received only normal saline. All CNS activities were performed in quiet and calm room.

The apparatus of open field is specifically designed. It consists of 76×76 cm^2 with 42 cm high opaque walls. The floor is divided by lines into 25 equal squares. Animals were placed in the center of this apparatus and counted the number f squares travelled in 30 minutes [14]. Square shaped Head dip box having three holes in each side was used in head dip test. The number of head dips by the animal through these holes in specified time was counted for 30 min. [15]. For rearing activity 1000 ml glass beaker was used which was lined with white paper on bottom. The animals were kept in the beaker and observed their exploratory activity in term of up and down movements for 30 minutes [16]. During this activity mice were trained on iron rod in such a manner so that they can walk easily from one corner to another corner. The time taken by each mice to travel rod was recorded [15, 16]. Swimming induced depression test was carried out according to Porsolt *et al.,* 1978[17]. In this test mice were placed in water, they quickly starts to move their front and hind paws. This activity was performed for six minutes for each MIC and the movements of paws were recorded by stop watch.

Analgesic activity

This activity was performed by using hot plate and writhing test method. Briefly the mice were divided in to four groups. In this test G-D received aspirin 300 mg/kg as a reference standard drug [18]. The reaction time was noted during hot plate test by flicking hind or front paw when mice was placed on hot plate (51±º1). In writhing test after the injection of acetic acid (0.6%) according to body weight. The stretching of body (writhes) were counted for 30 minutes.

Antimicrobial activity

The crude extract of *F. indica* was evaluated for antibacterial and antifungal bioassay. This activity was performed by disc diffusion method against different bacteria and fungi [19].

Insecticidal activity

Rapid toxicity test was performed by using insecticidal activity. This simple technique was used according to the described method [20].

Statistical analysis

statistical analysis was performed according to the method of Alcaraz & Jimenez, 1989[21]. The results were expressed as mean ± SEM. Dunnett's t-test was used to evaluate the significance of results at P 0.05.

Results

The spectral result of HPLC analysis was presented in Figure. 1. It gives 12 peaks with the retention time of 1.97, 3.343, 4.157, 4.560, 5.291, 6.109, 9.111, 11.568, 17.933, 26.630, 47.896. The FTIR finger print of *F. indica* was given in Figure. 2.

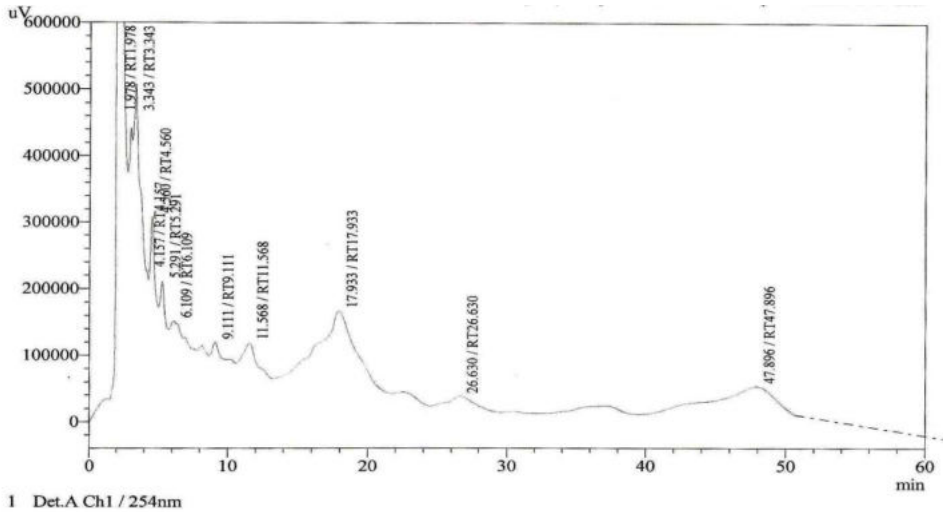


Figure. 1. HPLC spectra of *F. indica*

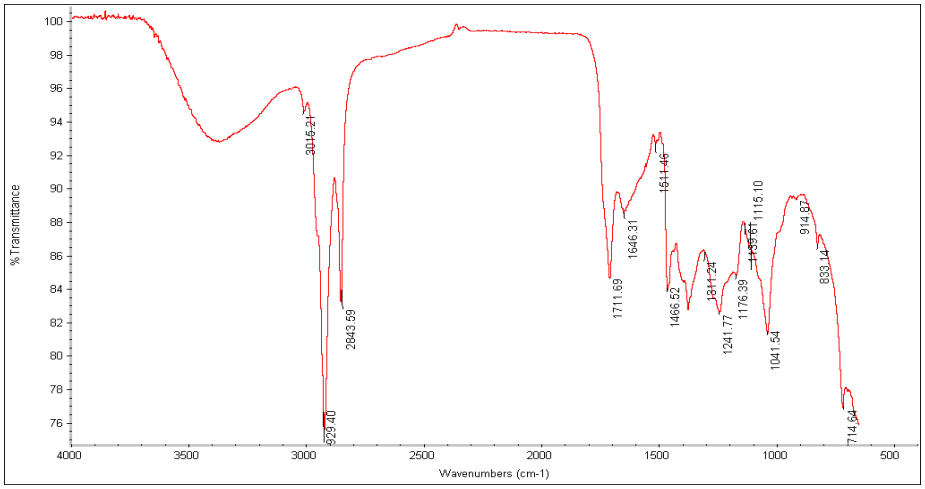


Figure. 2. FTIR finger print of *F. indica*

Assessment of neuropharmacological activity

In all neuropharmacological tests Diazepam as 2 mg/kg was used as the reference compound. Crude extract of *F. indica* was tested in two doses as 300 mg/kg and 500 mg/kg orally. The control group was treated with 0.5 ml saline orally.

Open field test, Head dip test, Rearing test, Traction test, Swimming induced depression test: In open field activity the mean number of squares crossed by the rats with all the four paws was 159.8 for control group, 121 and 115, 91 for 200, 300 mg/kg and 500 mg/kg of crude extract of *F. indica* respectively and 31 for diazepam. The results are more significant at 500 mg/kg oral dose of *F. indica* (Table 1).

Exploratory activity (head dip) was significantly affected and was dose related. Drug treated animals showed passive mood and decreased activity (Table 1).

Like open field and head dip test the activity was also decreased in rearing test. Diazepam showed an average of 14 rearing activities whereas with 200, 300 mg/kg and 500 mg/kg oral doses of crude extract the mean number of rearing activity was 22, 15.1 and 12.7 respectively. Time taken to travel iron rod was significantly increased, which shows muscle relaxant activity of *F. indica* (Table 1). The mean activity time in water tub of animals treated with *F. indica* (2.34, 2.56 and 2.41min. for 200, 300 and 500 mg/kg, 2.1 min. for diazepam. These findings indicate that *F. indica* possesses mild sedative, anxiolytic and muscle relaxant effect (Table 1).

Analgesic, Insecticidal and Antimicrobial activity

In acetic acid induced writhing test acetyl salicylic acid (Aspirin) as 300 mg/kg orally was used as a reference compound. The crude extract of *F. indica* showed significant dose related inhibition of number of writhes and increase in flicking time (Tables 2a and 2b). The results were highly significant (62.7%; 500 mg/kg, % of inhibition of writhes) and comparable with aspirin (69.2%). Table 3 showed that *F. indica* has mild insecticidal activity (50% mortality at 100 mg). The anti-bacterial and anti-fungal results given in Table 4. It gives maximum inhibitory zone against *S. aureus* (13mm) and *T. rubrum* (14mm).

Table 1. Assesment of neuropharmacological activities *Fumaria indica*

Dose mg/kg orally	Mean number of observation ± SEM					
	Open field	Head dip	Cage cross	Rearing test	Mobility time (min)	Traction test (sec)
Control 0.5ml	159.8±4.6	34±3.75	35.7±1.54	39.17±0.93	3.45±1.12	22 ±0.05
CE500	91±3.85*	15±2.56**	15±2.56*	12.7±1.51**	2.41±1.45	28± 0.07
CE300	115±2.34	20±2.24*	17± 2.58	15.1± 0.51*	2.56±1.03	50±0.02
CE200	121±2.34	18± 1.14	20±1.71	22±1.52	2.34±1.01*	33±1.13
Diazepam2	31±2.12**	05±0.09**	09±1.12**	14±1.12	2.1±1.3*	180±3.12**

* significant, ** highly significant at $P < 0.05$

Table 2a. Acetic acid induced writhing test

Dose(mg/kg)	Mean No. of writhes	% of inhibition
Control 0.5ml saline	131±3.38	-
CE500	48.9±2.16	62.7**
CE300	55±1.96	58.0*
CE200	72.8±3.36	44.4
Aspirin 300	40.4±1.27	69.2**

* significant, ** highly significant at P < 0.05 with ± S.E.M

Table 2b. Hot plate activity of crude extract of *Fumaria indica*

Group	Variation flicking time			
Control	0.19±0.014	>0.22	>0.22	>0.22
500	0.19±0.04	0.35±0.05*	0.41±0.06**	0.45±0.01**
300	0.20±0.03	0.31±0.02*	0.36±0.04*	0.33±0.04
200	0.19±0.06	0.32±0.04	0.30±0.04	0.28±0.07
Aspirin	0.18±0.02	0.39±0.03*	0.44±0.04**	0.33±0.08*

* significant, ** highly significant at P < 0.05 with ± S.E.M

Table 3. Insecticidal activity of *Fumaria indica*

Dose mg/ml	No. of survivor	Immobility time	% of Mortality
Positive control	0	-	100
Negative control	10	-	0
1	10	-	0
5	10	-	0
10	10	-	0
25	10	-	0
50	10	-	0
75	08	50± 0.65(min)	20
100	05	35±1.32 (min)	50

Positive control: Coopex (Permethrin) standard drug) = 235.9µg/cm^2, Negative control: Distlle water

Table 4. Antimicrobial activity of *Fumaria indica*

Micro-organism	Zone of inhibition in mm						
	Disc size: 7mm, mg/disc Ampicillin (1), Amphoteracin B (2)						
	1	5	10	25	50	1	2
S.typhi	7	7	9	7	8	18	NA
E. Coli	7	7	10	8	10	21	NA
S. flexr	8	8	10	9	10	14	NA
P. aerug	8	10	11	11	11	14	NA
S. aureus	9	11	12	12	13	20	NA
C. albican	7	7	7	8	12	NA	15
A. parasiticus	7	8	9	9	12	NA	12
T. rubrum	7	8	8	12	14	NA	13

Abbreviations: *S. Aureus., Staphylococcus aureus, P. aerug., Pseudomonas aeruginosa, S. Typhi., Salmonella Typhi, S. Flex.,, Shigella flexneri, E. Coli., Escherichia coli, T. rub., Trichophyton rubrum, ; C. alb., Candida albicans; A. Parasiticus., Aspergillus Parasiticus*

Discussion

The literature survey reveals *Fumaria indica* is an important medicinal plant. It has various important constituents, which are useful for the treatment of many diseases. Phytochemical investigation revealed the presence of alkaloids such as protopine, coptisine, fumariline, papaverine, papracinine, paprazine, parfumine, papraine, lastourvilline, narlumicine, narlumidine, fumoficinaline, fumaranine, fumaritine, adlumidine, and paprafumicine. In present study HPLC and FTIR finger prints provides a useful technique for the identity of crude extract of *F. indica*.

The CNS depressant activity could be helpful to decrease anxiety and panic state in the patient. It decreased open field, head dip and rearing activities, indicated the reduction in locomotion and exploratory behavior. The sedative effect of drugs can be evaluated by measurement of spontaneous motor activities and forced induce swimming test in laboratory animal model [22]. The CNS depressant activity of the *F. indica* was also exhibited by the traction test as the time taken to travel the iron rod by drug-treated animals was increased. The crude extract of *F. indica* was decreased muscle tone of animal by swimming induced depression test. These findings were also supported by the previous reports on isolated compounds from *F. indica* by Pandey [23]. Over all The CNS depressant effect of extract of *F. indica* could be helpful to decrease anxiety and panic state.

Analgesic activities were significant at 300 mg/kg and 500 mg/kg doses, which were comparable with the reference drug aspirin. The acetic acid iduced writhing test is normally used to study the peripheral analgesic effects of drugs and useful for evaluating mild analgesic non-steroidal anti-inflammatory compounds [24]. The observed activity may be because of interfering the synthesis or release of those endogenous substances or desensitization of the nerve fibers involved in pain transmission pathway [25]. The anti-inflammatory and analgesic activities are also proved by the report that protopine significantly inhibited exudative phase of dextran inflammation at 100 mg/kg and that of serotonin inflammation at 50 mg/kg doses, and fumoficinaline at 50 mg/kg was effective only against serotonin inflammation. Both alkaloids decreased vascular permeability to the same extent at 50 mg/kg doses [26].

Antibacterial and antifungal results indicated that the *S. aureus* were the most sensitive bacterial strain with zone of inhibition 13 mm and *T. Rubrum* exhibited strong anti fungal activity with zone of inhibiton 14 mm at 50 mg/disc concentration .In general, extract of *F. indica* found to be more sensitive against fungi. The crude extract also had some insecticidal potential at 75 and 100 mg doses.

Conclusion

From this study it can be concluded that the crude extract of *F. indica* has significant CNS depressant, analgesic, antibacterial and antifungal effect. Therefore, it has potential for the treatment of various CNS disorders as well as effectively used for infectious diseases.

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