



**Evaluation of neuropharmacological activity of *Fumaria officinalis* Linn. by study of muscle relaxants activity on experimental animals**

<sup>1\*</sup>Uday Raj Sharma, <sup>2</sup>Divakar Goli, <sup>1</sup>Surendra V, <sup>3</sup>Anirbandeep Bose

<sup>1\*</sup>Department of Biotechnology, Acharya Nagarjuna University, Nagarjuna Nagar, Guntur-522 510 India, Email: [Sharma.uday1@gmail.com](mailto:Sharma.uday1@gmail.com)

<sup>2</sup>Department of Biotechnology, Acharya & B M Reddy College of Pharmacy, Soladevanahalli, Hesaraghatta, Bangalore- 560 107, India

<sup>3</sup>Department of Pharmaceutics, Acharya & B M Reddy College of Pharmacy, Soladevanahalli, Hesaraghatta, Bangalore- 560 107, India.

### Abstract

The present study evaluated some neuropharmacological activities of ethanolic extract of *Fumaria officinalis* linn. (*Fumaraciae*) in experimental animal models. *Fumaria officinalis* (FO) (at 100,200 and 500 mg/kg body weight, i.p.) was evaluated for muscle relaxants activity by using Rota rod, Traction test and fall off time is, muscle relaxants are recorded. The results of the present study revealed significant ( $p < 0.001$ ) and dose dependent muscle relaxant and sedative potentiating effects of FO, demonstrating its depressant action on the central nervous system (CNS). From the present study, it can be concluded that the ethanolic extract of *Fumaria officinalis* possessed prominent depressant action on the CNS, as manifested by the important neuropharmacological activities in experimental animals. The present study also showed that 200 and 500mg/ kg body weight posses more significant muscle relaxants activity.

**Key words:** *Fumaria officinalis* Linn, CNS Depressant, Muscle Relaxant, Neuropharmacological activity

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**Corresponding Author:** \* Uday Raj Sharma, Department of Biotechnology, Acharya Nagarjuna University, Nagarjuna Nagar, Guntur-522 510 India, Email: [Sharma.uday1@gmail.com](mailto:Sharma.uday1@gmail.com)

## **1. Introduction**

Modern scientific medical research has investigated the use of ethanolic extracts of FO in treating migraines and epilepsy where relaxation of various muscles takes place. This study was performed to study muscle relaxant activity. [1].

*Fumaria officinalis* Linn. (*Fumaraciae*) is one of the ingredients in a polyherbal formulation, that is known to promote physical and mental health and improve immune power of the organism so that the body can tolerate any nature of stress [2,3]. One such plant, possessing anti convulsion activity is *Fumaria officinalis* Linn. Aerial part of this plant has been used in India as anti convulsion. Hence in the present study we have selected this plant to scientifically evaluate muscle relaxant activity. It has been reported to possess laxative, diuretic, antispasmodic, chronic eczema and antileprotic, blood purification [4,5].

The aim of the present study was, therefore, to evaluate the muscle relaxant activity of the ethanolic extract of *Fumaria officinalis* (EEFO) in experimental animal models, with a view to providing a pharmacological justification (or otherwise) for the ethno medical use of the plants in some rural communities of India. So the study is done to evaluate its muscle relaxant action of ethanolic extracts of FO.

## **2. Materials & Methods**

**Plant Material:** Aerial parts of the plant of *Fumaria officinalis* Linn. were collected from the Nilgiri Hills, Tamil Nadu. The plants were authenticated by Dr. Rajan, (Field Botanist, Central Council for Research in Homeopathy, Govt. of India, Ooty). The voucher specimen (Ref No: 05/P.colog/2007- 2008) of the plant material has been deposited in the Department of Pharmacology. The plants were dried in shade at 4 to 5 days at 25 °C, reduced to fine powder to particle size no 40. Around 1kg of herb of *Fumaria officinalis* was subjected to continuous Soxhlet extraction with Petroleum ether (50-60 °C) for 32 h. The same marc was successively extracted with Chloroform (60 - 70 °C) and Ethanol (72 - 82 °C) for 24 h. The extracts were concentrated on water bath (50 °C). After concentrated preparation, the dried powder extract was stored at 4 °C. The yield of the petroleum extract, chloroform extract and ethanolic extract were found to be 4% (w/w), 2.6% (w/w) and 9.8% (w/w) respectively. Ethanolic extract was used for the experimental study.

**Animals:** Wistar Albino rats (150 - 200 g) and Albino mice (20 - 25g) of either sex procured from Bioneed's animal house, Dhavaspet, Tumkur, were used for the study. The animals were kept in polypropylene cages and maintained at a temperature of  $26 \pm 2$  °C. They were fed with standard diet supplied by Pranav Agro Industries Ltd. Sangli. The study has got the approval (Ref: IAEC/PP/05/2007-2008) from the Institutional Animal Ethical Committee (IAEC). All the animal experiments are conducted in accordance with the guidelines of the CPCSEA (Reg No. 997/c/06/CPCSEA) guide for care and use of laboratory animals. After procuring the animals were acclimatized for 10 days under standard husbandry conditions as: Relative humidity 45 - 55%, and 12 h light and dark cycle.

**Preliminary Phytochemical Screening:** The preliminary phytochemical screening was carried out on the petroleum ether, chloroform, and ethanolic extracts of leaves of *Fumaria officinalis* for qualitative identification. Tests for common phytochemicals were carried out by standard methods described in practical Pharmacognosy [6, 7].

**Acute Toxicity Study:** The albino mice of 20– 25 g body weight of either sex were selected to find out the acute toxicity study of ethanolic extract of *Fumaria officinalis* leaves. The dose of 5, 50, 300 and 2000 mg/kg were selected based on the fixed dose (OCED Guideline No. 420) method of CPCSEA. The extract was administered by intraperitoneally. The animals were continuously observed for 24 h to detect changes in autonomic or behavioral responses. Mortality in each group was observed for 7 days[8].

#### **Evaluation of muscle relaxant activity:**

##### **Rota rod test (motor coordination)**

The animals were trained to maintain balance for 3 min on the horizontal rotating rod (diameter 32 mm rotating at the speed of 5 r.p.m.). Only those rats which could balance themselves were selected for the study. Each mouse was placed individually on the rota rod and the total number of falls within 3 min was noted, which was considered as the basal reading. Subsequently, the animals were divided into five groups, each group consisting of six animals.

Then, the first groups received 10ml/kg normal saline (i.p) and II, III and IV group received the FO at the doses of 100, 200 and 500 mg/kg body weight i.p., respectively. The fifth group (which served as reference) received 10mg/ kg b.w., ip, Diazepam. 30 min later were placed on the rod at interval of 30 min and 1 h. If animal failed more than once to remain on the rod for 3 min, the test was considered to be positive i.e. motor incoordination was present (Kulkarni and Joseph, 1997) [9].

##### **Traction test**

The method of Rudzic *et al.*, (1973) was used. The force paws of a mouse were placed on a small twisted wire rigidly supported above a laboratory bench top. Normal mice grasped the wire with the force paws and when allowed to hang free, placed at least hind foot on the wire within 5 sec. inability to place at least one hind foot marked failure in the traction test.

Then, the first groups received 10ml/kg normal saline (i.p) and II, III and IV group received the FO at the doses of 100, 200 and 500 mg/kg body weight i.p., respectively. The fifth group (which served as reference) received 10mg/ kg b.w., ip, Diazepam. Previously screened mice (n = 06) were exposed to the traction test after 30 and 60 min of treatment. Each animal was hung by their hind legs from the wire and the time of hanging was recorded for 5s after the administration of *Fumaria officinalis* extracts (in different dose) or diazepam (10 mg/kg, i.p.) or vehicle to control group. Failure to hang for less than 5s was considered as the presence of muscle relaxant activity and vice versa [10,11]

##### **Statistical analysis**

All the values are expressed as mean  $\pm$  SEM. Statistical differences between means were determined by one-way ANOVA followed by Dunnett's post hoc test.  $p < 0.05$  was considered as significant.

### **3. Results:**

#### **Preliminary Phytochemical Screening:**

Preliminary Phytochemical investigations of different extracts of leaves of *Fumaria officinalis* Linn. were studied. The petroleum ether extract contains phytosterols, saponins and fixed oils. The chloroform extract contains proteins. The ethanolic extract contains carbohydrates, saponins, flavonoids, phytosterols, tannins and phenolic compounds.

#### **Acute Toxicity Study:**

In the acute toxicity study ethanolic extract of leaves *Fumaria officinalis* were found to be toxic (2/3 mice died) at a dose of 2000 mg/ kg, intraperitoneally. Hence, LD50 cut off value of ethanolic extract was

fixed as 2000 mg/kg body weight. So, that 1/20th, 1/10th and 1/4th of the LD50 cut off value that is, 100, 200 and 500 mg/ kg body weight were selected as screening dose for muscle relaxants activity.

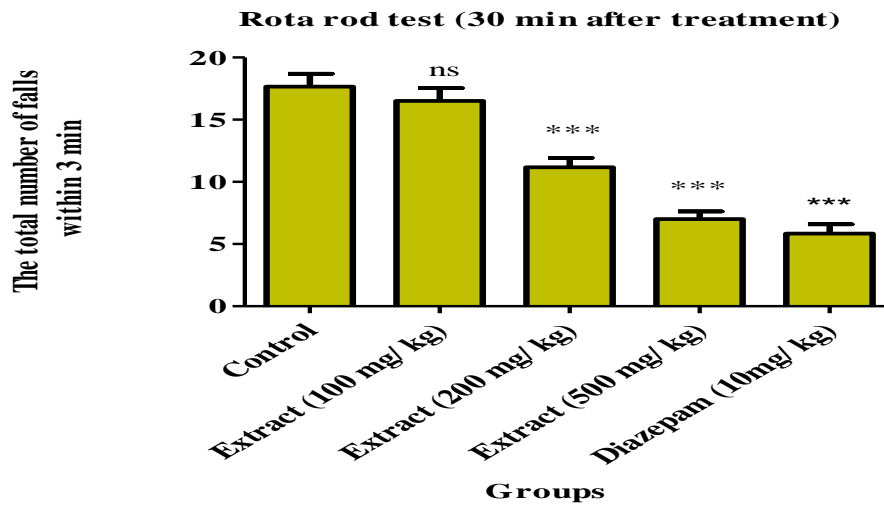
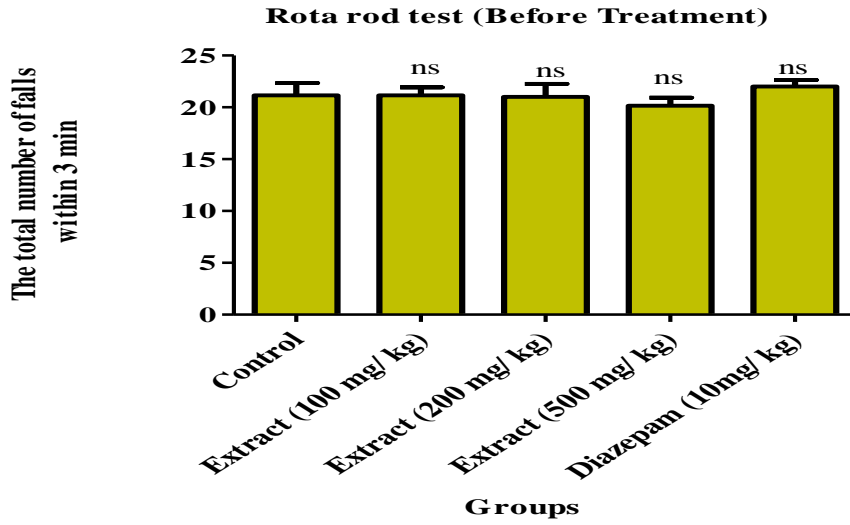
**Rotorod test:** In this test, EEFO (200 and 500mg/kg) both significantly reduced the time spent by the animals on revolving rod when compared to Control (P<0.05). The standard drug (diazepam) also showed significant effect when compared to control (P<0.01), (Table I). The result indicates that ethanolic extract of FO possess a significant skeletal muscle relaxant activity in experimental animals.

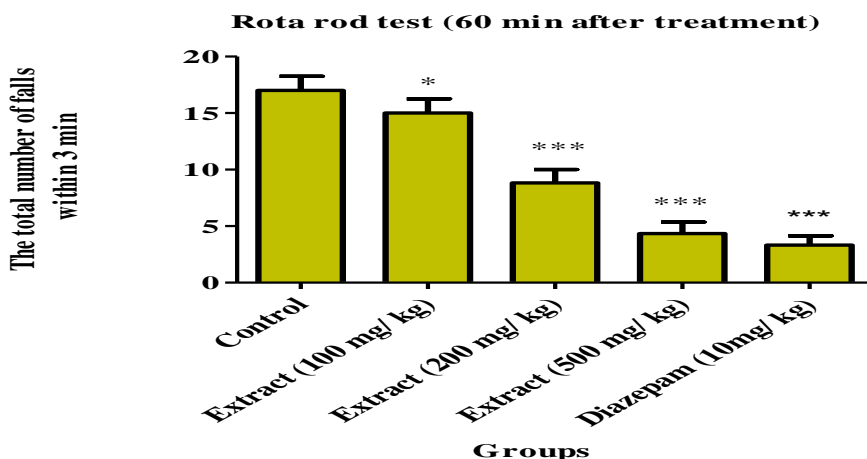
**Traction Test:** In this test, EEFO (200 and 500mg/kg) both significantly decreases the muscle co-ordination activity of mice compared with Control (p< 0.05). (Table II). The standard drug (diazepam) also showed significant effect when compared to control (P<0.01), (Table II). The result indicates that ethanolic extract of FO possess a significant skeletal muscle relaxant activity in experimental animals. At dose of 200 and 500 mg/kg it showed highly significant skeletal muscle relaxant activity at 30min and 60 min of duration.

**Table I: Effect of *Fumaria officinalis* on muscle relaxant activity in mice fall off time (seconds)**

Groups	Before Treatment	After Treatment		% Decrease in fall off time	
		30Min	60Min	After 30Min	After 60 Min
Control 10ml/kg normal saline (i.p)	21.167±0.477 3	17.667±0.4 216	17.000±0.516 4	16.118±3.725	19.340±3.612
Extract Treated 100mg/kg of <i>Fumaria officinalis</i>	21.167±0.307 3 <sup>ns</sup>	16.500±0.4 282 <sup>ns</sup>	15.000±0.516 4*	19.137±2.758 <sup>ns</sup>	29.088±2.507 *
Extract Treated 200mg/kg of <i>Fumaria officinalis</i>	21.000±0.516 4 <sup>ns</sup>	11.167±0.3 073**	8.833±0.4773 **	45.778±2.534**	58.042±1.596 **
Extract Treated 500mg/kg of <i>Fumaria officinalis</i>	20.167±0.307 3 <sup>ns</sup>	7.000±0.25 82**	4.333±0.4216 **	70.087±3.623**	78.433±2.198 **
Standard: Diazepam - 10 mg/kg b. wt.	21.667±0.421 6 <sup>ns</sup>	5.833±0.30 73**	3.333±0.3333 **	73.530±1.137**	84.902±1.410 **

\* Values are Mean ± SEM, (n = 6 in each group). Figures in parenthesis are percent protection as compared to Control group and all values were significantly different (P< 0.01). Experimental groups were compared with Carrageenan control: \*P<0.05 and \*\*P<0.05,\*\*\*P<0.001



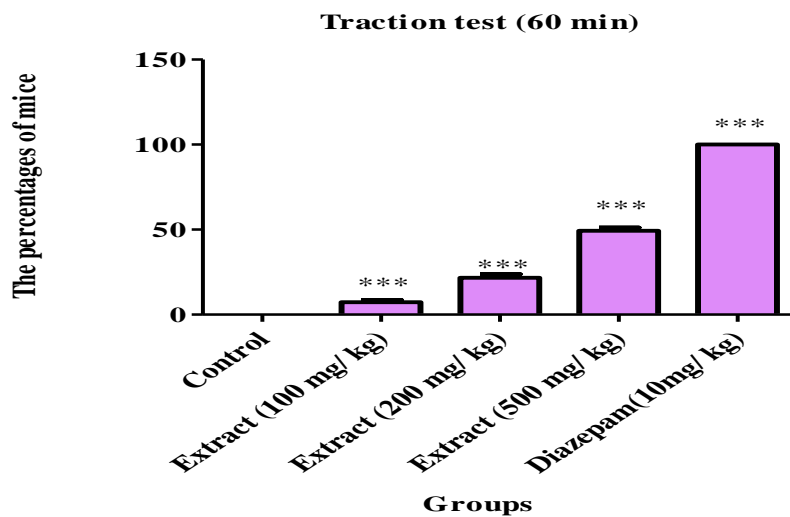
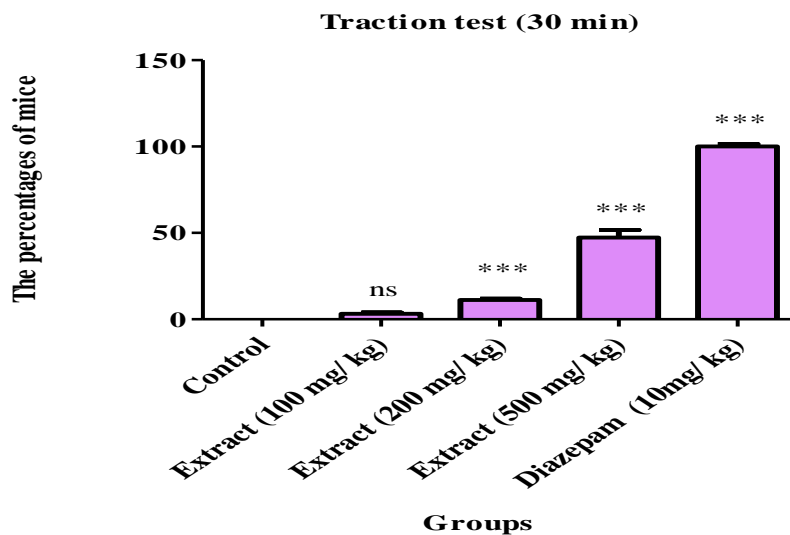


Percent effect of ethanol extract of *Fumaria officinalis* in Rota Rod test.

**Table II: Effect of *Fumaria officinalis* on motor co-ordination**

Groups	Traction test (%)	
	30 Min	60 Min
Control 10ml/kg normal saline (i.p)	0.000±0.000	0±000
Extract Treated 100mg/kg of <i>Fumaria officinalis</i>	3.167±0.3073 <sup>ns</sup>	0.4944 <sup>**</sup>
Extract Treated 200mg/kg of <i>Fumaria officinalis</i>	11.167± 0.3073 <sup>**</sup>	21.667±0.8819 <sup>**</sup>
Extract Treated 500mg/kg of <i>Fumaria officinalis</i>	47.333± 0.1.801 <sup>**</sup>	49.333±0.7601 <sup>**</sup>
Standard: Diazepam - 10 mg/kg b. wt.	100.00± 0.5774 <sup>**</sup>	100±0.00 <sup>**</sup>

\* Values are Mean ± SEM, (n = 6 in each group). Figures in parenthesis are percent protection as compared to Control group and all values were significantly different (P< 0.01). Experimental groups were compared with Carrageenan control: \*P<0.05 and \*\*P<0.05,\*\*\*P<0.001



Percent effect of ethanol extract of *Fumaria officinalis* in traction test.

#### 4. Discussion:

The methanolic extract of *Fumaria officinalis* Linn. was pharmacologically screened for its muscle relaxant study. The result indicates that ethanolic extract of FO possess a significant skeletal muscle relaxant activity in experimental animals. At dose of 200 and 500 mg/kg it showed highly significant skeletal muscle relaxant activity at 30min of duration.

Gamma-aminobutyric acid (GABA) is the major inhibitory neurotransmitter in the central nervous system. Different anxiolytic, muscle relaxant, sedative-hypnotic drugs are elucidation their action through GABA<sub>A</sub>, therefore it is possible that ethanolic extract of *Fumaria officinalis* may act by potentiating GABAergic inhibition in the CNS via membrane hyperpolarization which leads to a decrease in the firing



rate of critical vacuum neurons in the brain or may be due to direct activation of GABA receptor by the extract [12]. Many researchers showed that plant flavonoids, saponins and tannins are useful in many CNS disorders [13]. Earlier investigation on phytoconstituents and plants suggests that many flavonoids and neuroactive steroids were found to be ligands for the GABAA receptors in the central nervous system; which led to the assumption that they can act as benzodiazepine like molecules. Phytochemical investigations also showed the presence of glycoside, flavonoids, saponins and tannins in the extract, so might be these phytoconstituents are responsible for its CNS depressant activity. Therefore, this plant merits further attention. Search on the most active principle as well as elucidation of the exact mechanism of its action is needed. Thus, we conclude that ethanolic extract of *Fumaria officinalis* possess CNS depressant activity and studies are mandatory to establish the precise nature of active constituents as well mechanism of action. This study has established the central nervous system depressant properties of *Fumaria officinalis* [14, 15].

The muscle relaxant effect was observed even with the dose of (200 and 500mg/ kg, body weight) of ethanolic extract of *FO* which showed decrease in the time on the bar as detected by the rotarod test. In this case Diazepam at a dose of 10mg/kg body weight showed a significant lack in motor coordination and muscle relaxant activity in animals treated with the extract[16]. The muscle relaxation and reduced motor activity effects of EEFO could be due to the interaction of flavonoids (chemical constituent of the plant) with the GABA/benzodiazepine receptor complex in brain [17, 18].

## 5. CONCLUSION:

In the present study, the effect of ethanolic extract of *Fumaria officinalis* on muscle relaxation and motor coordination has been evaluated. The result indicated that the ethanolic extract of *Fumaria officinalis* influence the muscle coordination as evidenced in the responses on Rotarod. As the comparison is done with centrally acting benzodiazepine group of drug diazepam, it is assumed that the muscle relaxation and reduced motor activity effects of EEFO could be due to the interaction of flavonoids of the plant with the GABA/benzodiazepine receptor complex in brain . The muscle relaxation property has to be further evaluated which could be used as centrally acting muscle relaxant like Diazepam.

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**Corresponding Author:** \* Uday Raj Sharma, Department of Biotechnology, Acharya Nagarjuna University, Nagarjuna Nagar, Guntur-522 510 India, Email: [Sharma.uday1@gmail.com](mailto:Sharma.uday1@gmail.com)