

Neuropharmacological activity of *Lippia nodiflora* Linn.

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ABSTRACT

Introduction: In the recent years, plants containing flavonoids have gained much more interest in research area, as they are found to be specific ligands for benzodiazepine receptors. **Material and Methods:** In our investigation, we evaluated the neuropharmacological profile of petroleum, chloroform and ethanolic extracts of aerial part of *Lippia nodiflora* Linn. With experimental models using test such as potentiation of diazepam-induced sleeping time, locomotor activity, motor coordination, exploratory behavior pattern, elevated plus maze and maximal electroshock convulsions. Diazepam at doses of 5, 4, and 1 mg/kg served as standard. **Results:** Results showed that the ethanolic extract of *L. nodiflora* at both doses (250 and 500 mg/kg p.o.) and its chloroform extract at a higher dose of 500 mg/kg produced central inhibitory (sedative) effects, anticonvulsant effect and anxiolytic effect in mice. Values were statistically significant ($P < 0.05$ and $P < 0.01$) when compared to the control group. The petroleum ether extract of plant at both dose levels (250 and 500 mg/kg p.o.) did not produce any central effects. **Conclusion:** In conclusion, we can say that the ethanolic and chloroform extracts showed the central inhibitory activity due to the presence of flavonoids and this fact was also supported by the finding that the petroleum ether extract did not show any central effect and flavonoids were not found in it.

Key words: *Lippia nodiflora*, neuropharmacological activity

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INTRODUCTION

Mental, neurological and behavioral disorders are common to all countries and cause immense suffering. People with these disorders are often subjected to social isolation, poor quality of life, and increased mortality. These disorders are the cause of staggering economic and social costs (www.brain_dynamics.net/aboutus.php).^[1] Habituation, dependence and the resulting potential for addiction are the greater disadvantages of the modern synthetic psychopharmacological agents. The abrupt discontinuation of long-term therapy with these drugs leads to serious withdrawal symptoms. Therefore, modern society is now cautiously discovering traditional herbal medicines, particularly those which have been proved to be effective in controlled studies and which in some cases demonstrated even better galenic properties than the conventional medicines. Unique opportunities for research exist in the field of central nervous system (CNS)-active Indian

medicinal plants.^[2]

Lippia nodiflora is a creeping, much branched herb, found in the wet places, almost throughout India, and traditionally used as anodyne, antibacterial, diuretic, etc. Filipinos drink an infusion of the leaves instead of tea.^[3,4] Studies were earlier carried out on anti-inflammatory, analgesic and antipyretic activities and showed an analgesic activity which continued until 3 hours, using eddy's hot plate method.^[5] In previous studies it was shown that *L. nodiflora* contains 15 flavonoids, 3 flavone glycosides, and 12 new flavone sulfates.^[6] Researchers also indicated its gastroprotective,^[7] antifungal,^[8] antibacterial^[9] properties and its excellent effectiveness in cutaneous leishmaniasis.^[10]

No previous scientific information has been found on its neuropharmacological activity to support its use in traditional medicine in neuropharmacological situation. This study investigated its neuropharmacological activity with experimental animal models using potentiation of diazepam-induced sleeping time, spontaneous motor activity (SMA), motor coordination, exploratory behavior pattern, elevated plus maze (EPM) and maximal electroshock induced convulsions in mice.

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MATERIALS AND METHODS

Plant collection

The aerial parts of the plant *L. nodiflora* Linn. were collected locally from the campus of Ultra College of Pharmacy, Madurai. The samples of *L. nodiflora* Linn. were identified and authenticated at the Botanical Survey of India, Coimbatore, where a voucher specimen of the plant was also deposited (voucher No. COIMA3).

Extraction

Fresh leaves of the plant *L. nodiflora* L. (1 kg) were collected from an area in Madurai and the leaves were washed and cut into pieces and air dried. The powdered plant material was extracted using petroleum ether (60–80°C) using a Soxhlet extractor. The marc was further extracted with chloroform and methanol for 72 hours. The extract was filtered and evaporated to dryness under reduced pressure on a rotary evaporator. The yield of petroleum ether, chloroform and ethanolic extracts of *L. nodiflora* L. (LNE) leaves was found to be 3.4, 4.3, and 2.2% w/w, respectively. Before use, the extract was dissolved in tween 80 for administration intraperitoneally (i.p.).

Phytochemical screening

Phytochemical investigation of the extract for the presence of phenolic compounds, flavonoids, tannins, triterpenes, anthocyanins, anthroquinones, and sterols was carried out using the methods previously described by Kokate and Trease and Evans. The presence of alkaloids and saponins was also ascertained.

Animals

Male Swiss albino mice (18–22 g) were used for the study. The animals were housed in colony cages and maintained under standard environmental conditions: 25 ± 2°C temperature, 12:12 hour light:dark cycle, and 45–55% relative humidity, with free access to food and water *ad libitum*. The animals were fasted overnight and during the experiment. All the experiments were carried out during the light period (08.00–16.00 hours). The Institutional Animal Ethical Committee approved the protocol of the study.

LD₅₀ determination

Acute toxicity study was performed according to the OECD-423 guidelines.^[8] Oral acute toxicity was studied in overnight fasted rats provided with water *ad libitum*. Swiss albino mice of either sex (110–160 g) were randomly allocated into groups of five animals per group. The rats were administered distilled water orally (5 ml/kg), control or ethanolic extract (1, 2, 3, 4, 5, 6, 7 or 8 g/kg) of *L. nodiflora*. Besides the number of deaths, other parameters such as agility, muscular tonus, tremors, convulsions, feed and water intake, breathing patterns and presence of

mouth secretions were observed for the first 12 hours and for further 14 days. If mortality was not observed, the procedure was repeated for a higher dose till a maximum dose of 8 g/kg was attained.

Pharmacological evaluation

Potentiation of diazepam-induced sleeping time^[12,13]

Antidepressants at higher doses can be evaluated as they potentiate the sleeping time. Many of the pharmacological testes are based on the potentiation of sleeping time induced by barbiturates or other sedative agents.

The animals were divided into seven groups, each containing six mice. The groupings are as follows:

- Group I: Treatment given with vehicle (2.5% Tween 80) and diazepam 5 mg/kg i.p.
- Group II: Received petroleum ether extract 250 mg/kg p.o. and diazepam 5 mg/kg i.p.
- Group III: Treatment given with petroleum ether extract 500 mg/kg p.o. and diazepam 5 mg/kg.
- Group IV: Received chloroform extract 250 mg/kg p.o. and diazepam 5 mg/kg i.p.
- Group V: Received chloroform extract 500 mg/kg p.o. and diazepam 5 mg/kg.
- Group VI: Received ethanol extract 250 mg/kg p.o. and diazepam 5 mg/kg.
- Group VII: Received ethanol extract 500 mg/kg p.o. and diazepam 5 mg/kg.

Each animal was observed and the onset of sleep and duration of sleep was recorded. Sleeping time in all cases was measured as the time interval between the loss and regaining of righting reflex.

Spontaneous motor activity^[14,15]

SMA was performed using actophotometer (Inco, Ambala, India). The CNS depressant or stimulant property can be evaluated by considering the locomotor activity of the animal after treating with the drug. Mice were grouped of into eight groups consisting of six animals in each and treated with vehicle or plant extracts or received diazepam. The treatment schedule is as follows:

- Group I: Served as control and received vehicle orally (2.5% Tween 80).
- Group II: Served as standard and received diazepam 1 mg/kg i.p.
- Group III: Received petroleum ether extract 250 mg/kg p.o.
- Group IV: Received petroleum ether extract 500 mg/kg p.o.
- Group V: Received chloroform extract 250 mg/kg p.o.
- Group VI: Received chloroform extract 500 mg/kg p.o.
- Group VII: Received ethanol extract 250 mg/kg p.o.
- Group VIII: Received ethanol extract 500 mg/kg p.o.

The locomotor activity for each animal was automatically recorded for 5 min before drug treatment and after the treatment at 30 min intervals for a total of 120 min. Results of the treated groups were compared with those of the control group at each time interval.

Motor coordination^[16,17]

Rotarod (Inco, Ambala, India), a biological research apparatus, is used to evaluate the activity of drugs interfering with motor coordination. The instrument (a horizontal rotating device) was set at a rate of 16 revolutions per minute. Mice were placed on the horizontal rod and those that were able to remain on the rod longer than 3 min were selected for the study. Animals were grouped and treated as per the treatment schedule given in SMA.

Inability to remain on the rod at least for 3 min was considered as a positive test and the time of fall of the mouse was recorded.

Exploratory behavior pattern^[14,18]

The study was carried out using a wooden board measuring 40 × 40 cm with 16 evenly spaced holes. Eight groups of mice containing six in each were used for the study and they were treated as per the treatment schedule given in SMA.

The total head dips before any treatment, 30 min after diazepam treatment and 45 min after the extract treatment were recorded for 5 min by placing the animal on a board with 16 evenly spaced holes. Results were expressed as means for the various treatment groups at different time intervals.

Elevated plus maze^[17,19]

The EPM apparatus consists of two open arms (30 × 5 cm) and two closed arms (30 × 5 × 20 cm) emanating from a common central platform (5 × 5 cm). The two pairs of identical arms were opposite to each other. The entire apparatus was elevated to a height of 50 cm above the floor level.

The animals received the treatment as per the SMA treatment schedule, 45 min before the start of session. At the beginning of the session, a mouse was placed at the center of the maze, its head facing the closed arm. It was allowed to explore the maze for 5 min. The time spent in open arm, percent entries in the open and closed arms, and total entries were recorded. An entry was defined as the presence of all four paws in the arm. The EPM was carefully wiped with 10% ethanol after each trial to eliminate the possible bias due to the odor of the previous animals. The percentage time spent and open arm entries were calculated using the following formulae:

$$\text{Percent time spent in open arm} = \frac{\text{Time in open arm}}{\text{Time in the open arm} + \text{time in closed arm}} \times 100$$

$$\text{Percentage of open arm entries} = \frac{\text{Number of entries in open arm}}{\text{Total arm entries}} \times 100$$

Maximal electroshock induced convulsions^[17,20]

The electroshock assay in mice is used primarily as an indication for compounds which are effective in grand mal epilepsy. Tonic hind limb extensions are evoked by electric stimuli which are suppressed not only by anti-epileptics but also by other centrally acting drugs. Eight groups of mice consisting of six animals in each were used for the study and they were treated as per the treatment schedule given in SMA. The animals received a current of 45 mA for 0.2 seconds duration through electro convulsimeter (Lucknow, U.P) using corneal electrodes, after 60 min of oral administration of plant extract or vehicle or diazepam. The incidence and duration of extensor tonic was noted. A complete abolition of hind limb tonic extension was noted. A complete abolition of hind limb tonic extension was considered as 100% protection.

Statistical analysis

The data obtained were analyzed using one-way analysis of variance (ANOVA) followed by Dunnett's "P" test. P value <0.05 was considered statistically significant. The results were expressed as mean ± SEM and three animals from each group.

RESULTS

Preliminary phytochemical test

The petroleum ether extract of *L. nodiflora* showed the presence of phytosterols only. Chloroform extract showed the presence of alkaloids, phytosterols, and flavonoids. In the ethanolic extract, phytosterols, carbohydrates, tannins and flavonoids were found to be present. The color reactions also indicated the presence of flavonoids in chloroform and ethanolic extracts.

Acute oral toxicity

It was found that administration of various doses of chloroform extract of *L. nodiflora* upto the dose of 5000 mg/kg body weight did not produce any signs of toxicity and mortality.

Potentiation of diazepam-induced sleeping time

The petroleum ether extract of *L. nodiflora* did not show any significant potentiation of sleeping time at both doses levels (250 and 500 mg/kg), while the chloroform extract at 500

mg/kg significantly ($P < 0.01$) potentiated the diazepam-induced sleeping time.

The ethanolic extract increased the duration of sleeping in a dose-dependent manner; both the dose levels of ethanolic extract (250 and 500 mg/kg) potentiated the sleeping time significantly ($P < 0.01$) when compared to vehicle treated group and the effects were dose dependent [Table 1].

Spontaneous motor activity

The petroleum ether extract at 250 and 500 mg/kg and the chloroform extract at 250 mg/kg did not show any decrease in locomotor activity. Chloroform extract at a dose of 500 mg/kg showed significant ($P < 0.01$) decrease in locomotor activity within 60 min, whereas when the mice were treated with ethanol extracts (250 and 500 mg/kg), the locomotion was reduced with increase in the dose compared to control. Diazepam showed significant decrease ($P < 0.01$) in locomotor activity after 30 min of its administration. Results are given in Table 2.

Motor coordination

The petroleum ether extract of the plant *L. nodiflora* did not produce any reduction in motor coordination. Chloroform extract at 500 mg/kg dose showed a significant ($P < 0.01$) reduction in motor coordination within 60 min. It was found that the ethanolic extract (250 and 500 mg/kg) exhibited a marked reduction ($P < 0.01$) in motor coordination in mice and mice were unable to be held on the rotating rod. These effects were dose dependent and observed within 60 min of the extract administration and

persisted for 120 min. Diazepam at a dose of 1 mg/kg showed the same effects within 30 min of administration [Table 3].

Exploratory behavior (head dip test)

The effects of petroleum ether, chloroform and ethanol extracts of *L. nodiflora* at dose levels of 250 and 500 mg/kg on the number of head poking in the head dip apparatus are shown in Table 4. During the test interval of 5 min, the ethanol extract reduced the number of head dipping in a dose-dependent manner. Diazepam, a well-established sedative, also exhibited decrease in number of head dipping. Petroleum ether extract did not show any significant effect on head dipping while the chloroform extract at a dose of 500 mg/kg significantly ($P < 0.01$) reduced the head dipping.

Elevated plus maze

In the EPM, the behavior, as observed, confirmed the anxiolytic activity of diazepam as reported previously. The petroleum ether extract and chloroform extract at 250 mg/kg did not show any significant effect. The chloroform extract at 500 mg/kg significantly ($P < 0.01$) increased the time spent in open arm and percent open arm entries. The ethanolic extract at 250 mg/kg showed a marked increase in the time spent in open arm than effect of extract at 500 mg/kg. The total arm entries and percent open arm entries also were increased significantly in the ethanolic extract of *L. nodiflora* Linn. at doses of 250 and 500 mg/kg ($P < 0.01$). The ethanolic extract at a higher dose of 500 mg/kg showed a significant ($P < 0.01$) decrease in the time spent in the open arm, without any change in

Table 1: Effect of *Lippia nodiflora* Linn. on diazepam-induced sleeping time

Group	Treatment	Onset of action (min)	Duration of action (min)
I	Control (diazepam 5 mg/kg)	6.5 ± 0.28	54.5 ± 1.7
II	Petroleum ether extract (250 mg/kg) + diazepam (5 mg/kg)	7 ± 0.40	52.5 ± 1.5
III	Petroleum ether extract (500 mg/kg) + diazepam (5 mg/kg)	6.5 ± 0.28	55.25 ± 1.7
IV	Chloroform extract (250 mg/kg) + diazepam (5 mg/kg)	6.75 ± 0.47	53.75 ± 1.5
V	Chloroform extract (500 mg/kg) + diazepam (5 mg/kg)	5.5 ± 0.8	67.75 ± 2.6**
VI	Ethanolic extract (250 mg/kg) + diazepam (5 mg/kg)	5.28 ± 0.25	68.75 ± 2.7**
VII	Ethanolic extract (500 mg/kg) + diazepam (5 mg/kg)	4.25 ± 0.25**	94.25 ± 1.2**

Each value represents the mean ± SEM (n = 6), **Values are significantly different at $P < 0.01$

Table 2: Effect of *Lippia nodiflora* Linn. on spontaneous motor activity

Group	Treatment	Experimental mean time (min)				
		0	30	60	90	120
I	Vehicle control	374.75 ± 7.33	352.98 ± 18.23	338.5 ± 17.5	300 ± 4.79	274.25 ± 5.64
II	Diazepam (1 mg/kg)	382.75 ± 11.70	104 ± 4.14**	52.75 ± 4.32**	38 ± 1.87**	18 ± 1.2**
III	Petroleum ether extract (250 mg/kg)	377.5 ± 13.52	354.25 ± 11.88	316.25 ± 22.25	295.75 ± 6.7	266 ± 9.4
IV	Petroleum ether extract (500 mg/kg)	365.5 ± 8.89	333.75 ± 16.14	315.75 ± 7.28	285.75 ± 7.3	257 ± 10.15
V	Chloroform extract (250 mg/kg)	389.75 ± 11.96	363.75 ± 16.80	289 ± 11.74	264.5 ± 5.69	255 ± 11.5
VI	Chloroform extract (500 mg/kg)	372.25 ± 10.34	355.75 ± 16.67	237.5 ± 9.13**	185.25 ± 13.87**	143.5 ± 5.7**
VII	Ethanolic extract (250 mg/kg)	370.75 ± 5.87	343.25 ± 10.70	219 ± 8.35**	136.5 ± 12.08**	84.5 ± 5.3**
VIII	Ethanolic extract (500 mg/kg)	375.25 ± 14.09	332.5 ± 20.25	110 ± 6.32**	68 ± 6.01**	38.25 ± 2.87**

Each value represents the mean ± SEM (n = 6), **Values are significantly different at $P < 0.01$

entries in open arm, entries in closed arm and total entries [Figures 1 and 2].

Maximal electroshock induced convulsions

The ethanolic extract at 250 mg/kg and chloroform extract at 500 mg/kg showed significant ($P < 0.05$) decrease in the duration of hind limb extensor phase. The ethanolic extract at 500 mg/kg and diazepam at 4 mg/kg exhibited significant ($P < 0.01$) decrease in the duration of hind limb extensor phase and the incidence of convulsions in mice also reduced. The petroleum ether extract at both dose

levels did not express any anticonvulsant activity [Table 5].

DISCUSSION

Insomnia, seizures, anxiety and mental health problems, in general, and senile neurological disorders, in particular, are widely prevalent in modern fast-paced life with a multitude of stressful conditions.

It is now becoming exceedingly apparent that the available psychotherapeutics drugs do not properly meet the

Table 3: Effect of *Lippia nodiflora* Linn. on motor coordination

Group	Treatment	Time spent on rods (min)				
		0	30	60	90	120
I	Vehicle control	210 ± 7.38	210.75 ± 3.86	213.75 ± 5.64	208.75 ± 5.39	210.25 ± 5.15
II	Diazepam (1 mg/kg)	207 ± 8.49	18.75 ± 1.49**	20.25 ± 1.79**	49.25 ± 3.56**	73.25 ± 2.28**
III	Petroleum ether extract (250 mg/kg)	213.75 ± 12.57	214.75 ± 6.39	208 ± 8.52	213.5 ± 9.56	219.5 ± 7.00
IV	Petroleum ether extract (500 mg/kg)	201.75 ± 4.66	210.5 ± 4.66	217.75 ± 3.88	206.5 ± 3.52	213 ± 6.17
V	Chloroform extract (250 mg/kg)	208.25 ± 7.34	206 ± 5.93	202 ± 3.08	207.5 ± 2.72	205.25 ± 5.07
VI	Chloroform extract (500 mg/kg)	217.75 ± 5.64	203.75 ± 3.86	69.25 ± 4.27**	100.5 ± 1.79**	140.5 ± 4.52**
VII	Ethanolic extract (250 mg/kg)	208 ± 3.87	197.75 ± 1.79	62.5 ± 3.86**	100.25 ± 1.79**	140.75 ± 3.17**
VIII	Ethanolic extract (500 mg/kg)	218.75 ± 3.35	204.5 ± 3.79	41.75 ± 1.49**	71.5 ± 3.06**	108.25 ± 2.81*

Each value represents the mean ± SEM (n = 6), *Values are significantly different at $P < 0.05$, **Values are significantly different at $P < 0.01$

Table 4: Effect of *Lippia nodiflora* Linn. on exploratory behavior (head dip test)

Group	Treatment	Head dips in 5 min		Percent activity (%)
		Before treatment	After treatment	
I	Vehicle (control)	36.5 ± 2.53	37 ± 2.48	-
II	Diazepam (1 mg/kg)	36.5 ± 1.93	8 ± 0.91	78.08
III	Petroleum ether extract (250 mg/kg)	38 ± 1.2	32.25 ± 1.31	15.13
IV	Petroleum ether extract (500 mg/kg)	34 ± 2.27	33.5 ± 1.55	1.47
V	Chloroform extract (250 mg/kg)	34.75 ± 1.93	30 ± 1.08*	13.66
VI	Chloroform extract (500 mg/kg)	38 ± 2.16	22.25 ± 1.31**	41.44
VII	Ethanolic extract (250 mg/kg)	33.25 ± 3.06	22 ± 1.78**	33.83
VIII	Ethanolic extract (500 mg/kg)	34 ± 2.4	13.25 ± 1.109**	61.02

Each value represents the mean ± SEM (n = 6), *Values are significantly different at $P < 0.05$, **Values are significantly different at $P < 0.01$

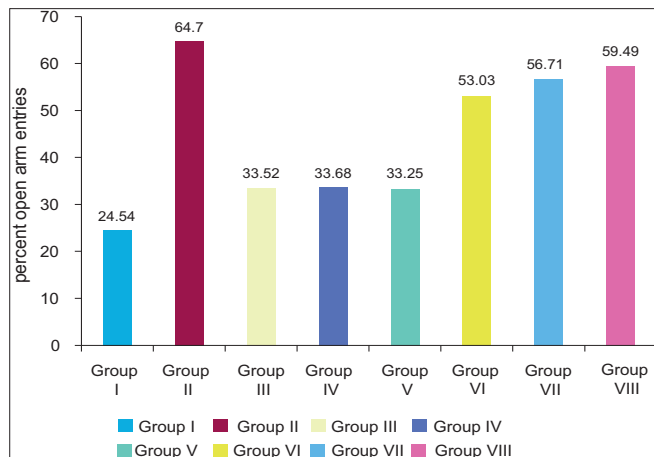


Figure 1: Effect of *Lippia nodiflora* Linn. on percent open arm entries.

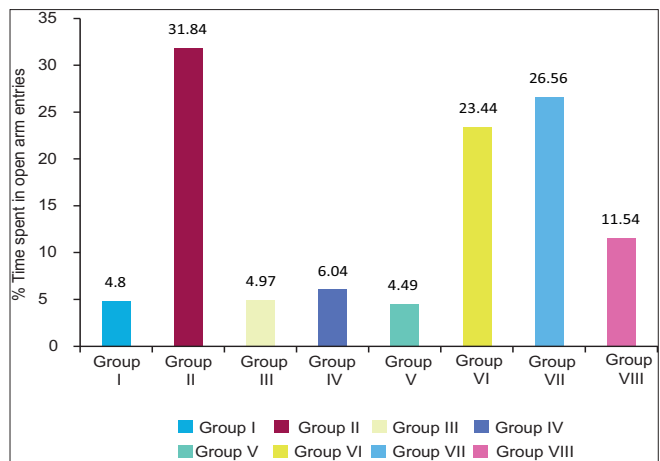


Figure 2: Effect of *Lippia nodiflora* Linn. on percent time spent in open arm.

Table 5: Effect of *Lippia nodiflora* Linn. on maximal electroshock convulsions

Group	Treatment	Duration of tonic hind limb extension (Sec)	Incidence of convulsions
I	Vehicle (control)	15.5 ± 1.32	6/6
II	Diazepam (4 mg/kg)	1.25 ± 0.94**	2/6
III	Petroleum ether extract (250 mg/kg)	14.75 ± 1.10	6/6
IV	Petroleum ether extract (500 mg/kg)	14.25 ± 1.25	6/6
V	Chloroform extract (250 mg/kg)	15.5 ± 1.04	6/6
VI	Chloroform extract (500 mg/kg)	10.5 ± 0.64*	5/6
VII	Ethanol extract (250 mg/kg)	10.25 ± 0.62*	5/6
VIII	Ethanol extract (500 mg/kg)	2.5 ± 1.5**	2/6

Each value represents the mean ± SEM (n = 6), *Values are significantly different at $P < 0.05$, **Values are significantly different at $P < 0.01$

therapeutic demands of a vast majority of patients with mental health problems, and that herbal remedies remain the ultimate therapeutic hope for many such patients in the world. However, till now, very little attention has been paid to develop structurally and/or functionally novel CNS active drugs from psychoactive medicinal plants.

The present study demonstrated that the ethanolic extract of *L. nodiflora* Linn. at both doses and chloroform extract (at 500 mg/kg dose) produced central inhibitory effects in mice. The extracts of *L. nodiflora* significantly reduced spontaneous motor activity in mice. The decrease in spontaneous motor activity gives an indication of the level of excitability of the CNS and this decrease may be closely related to sedation resulting from depression of the CNS.^[16]

The ethanolic extract significantly reduced the motor coordination in mice and prolonged diazepam-induced sleeping time. The prolongation of diazepam-induced sleeping time may be attributed to an action of extracts on the central mechanisms involved in the regulation of sleep. Similar effects were also obtained with chloroform extract at a dose of 500 mg/kg, while the petroleum ether extract did not show any central effect at both the dose levels (250 and 500 mg/kg), thus suggesting that the ethanolic extract at both doses (250 and 500 mg/kg) and chloroform extract at 500 mg/kg dose might be acting as a mild neurosedative. The reduction in motor coordination might also be a result of neuromuscular blockage.^[16]

The chloroform extract at 500 mg/kg dose and the ethanol extract at both dose levels (250 and 500 mg/kg) produced a significant decrease in exploratory behavior pattern as shown by the results on head poking in the head dip test. This decrease in head dipping by plant extracts also reveals their sedative behavior. The chloroform extract at a dose of 500 mg/kg and ethanolic extract at a dose of 250 mg/kg increased the time spent and entries in the open arm. Results suggest that the increase in total arm entries is due to an increase in open arm entries rather than closed arm entries. At 500 mg/kg dose of ethanol extract, it was found that the time spent in open arm

was decreased without any change in open arm entries, closed arm entries and total entries. This prominent effect shown by higher dose of ethanolic extract may be due to the sedative effect of the extract rather than anxiolytic effect. At higher doses, diazepam (20 mg/kg p.o) in rats and chlordismethyldiazepam (benzodiazepine receptor full agonist) at 5 mg/kg i.p. in mice showed a decrease in activity in anxiolytic tests, which was concluded as a sedative effect.^[19]

The chloroform extract at a dose of 500 mg/kg and ethanolic extract at both dose levels (250 mg/kg and 500 mg/kg) inhibited the maximal electroshock induced convulsions. This may also suggest that the anticonvulsant action is mediated by the chloride channel of the GABA/benzodiazepine receptor complex. The petroleum ether extract at both doses and chloroform extract at a lower dose (250 mg/kg) did not show any effect in electroshock induced convulsions.^[20]

Sedation and anxiety are primarily mediated in the CNS by the GABA-A receptor complex, which is also involved in other physiological and neurological disorders such as epilepsy, depression, Parkinson syndrome and Alzheimer's disease. Diverse drugs that are used in these pathologies might modify the phenomena of GABA system at the level of the synthesis of GABA mediators, release or re-uptake or metabolism.^[21]

Many flavonoids were found to be ligands for the GABA_A receptors in the CNS, which led to the hypothesis that they act as benzodiazepine like molecules. This is supported by their behavioral effects in animal models of anxiety, sedation and convulsion. Several experiments with some natural and synthetic flavones and flavanones have shown that they can modulate GABA-generated chloride current, either positively or negatively.^[22]

The preliminary phytochemical studies about the plant extracts indicated that the chloroform and ethanolic extracts contain flavonones, flavones, etc. Literature review also indicates that *L. nodiflora* contains number of

flavonoids, namely, nepetine, jaceosidine, and hispidulin aglycones; hispiduline, jaceosidin, nepetin, hydroxyluteoline and nodiflorein mono and disulfates; lippiflorin A and B glycosides, nodifloretin A and B, nodiflorin A and B and nodifloridin A and B glucosides. Therefore, it may exhibit CNS depressant activity.

However, along with flavonoids, a number of other chemical constituents like alkaloids, resins, sugars, stigmasterol and β -sitosterol are also present in *L. nodiflora*. Therefore, further studies are planned so establish the exact mechanism of CNS depressant, anticonvulsant and anxiolytic activities of chloroform and ethanolic extracts of aerial part of *L. nodiflora* by using agonists and antagonists.

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