ORIGINAL ARTICLE

Anticonvulsant potential of *Anisomeles malabarica* leaves against experimentally induced convulsions in rats

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Anisomeles malabarica (AM) R.Br. (Lamiaceae) is an aromatic perennial herb, the leaves of which are traditionally used to treat convulsions in southern India. The present study has been designed to investigate the anticonvulsant potential of chloroform, ethyl acetate and methanol extracts of leaves of AM against pentylenetetrazole (PTZ) and maximal electroshock (MES) induced convulsions. All the three extracts were administered (i.e. 100, 200, 400 mg/kg, p.o.) for 7 days and at the end of the treatment convulsions were induced experimentally. Diazepam and phenytoin (1 mg/kg, i.p. and 25 mg/kg, i.p., respectively) were used as reference anticonvulsant drugs against experimentally induced convulsions. High doses (400 mg/kg, p.o.) of chloroform and ethyl acetate extracts both significantly decreased the extent of MES- and PTZ-induced convulsions. On the other hand, ethyl acetate extract at lowest and medium selected doses (i.e. 100 mg/kg, p.o. and 200 mg/kg, p.o., respectively, for 7 days) had also significantly attenuated PTZ-induced convulsions. However, methanol extract at any of the doses used (i.e. 100, 200 and 400 mg/kg, p.o.) did not show any significant effect on PTZ- and MES-induced convulsions. None of the extracts at doses used in the present study have altered locomotor activity and motor coordination. Hence, it may be concluded that chloroform and ethyl acetate extracts of AM leaves are effective against PTZ- and MES induced-convulsions in rats.

Key words: *Anisomeles malabarica* leaves, chloroform extract and ethyl acetate extract, convulsions, maximal electroshock, pentylenetetrazole

INTRODUCTION

Epilepsy is the second most common neurological disorder which affects an estimated 7 million people in India and 50 million people worldwide, i.e. approximately 1–2% of the world population.[1,2] Although several antiepileptic drugs (AEDs) are available to treat epilepsy, the treatment of epilepsy is still far from adequate.[3]

Plants may serve as the alternative sources for the development of new anticonvulsant agents. *Anisomeles malabarica* (AM) (Lamiaceae) is an aromatic, densely pubescent, perennial herb, 1.2–2.0 m in height. It is commonly found in Western Ghats from Maharashtra to Karnataka, Andhra Pradesh, Kerala and Tamil Nadu in India.[4] The plant is reported to possess antiperiodic, diaphoretic, emmenagogue properties.[4,5] Ethnobotanically, the leaves of the AM are used against convulsions, in dyspepsia, intermittent fever, colic, boils, tetanus.[4,6-8] Anticonvulsant property of AM needs further exploration. Therefore, the present study has been designed to investigate the antiepileptic potential of leaves of AM against pentylenetetrazole (PTZ) and maximal electroshock (MES) induced convulsions in rats.

MATERIALS AND METHODS

Collection and Identification of Plant Material

Air-dried leaves of AM were collected from local areas of Tirupati in the month of August 2008 and were dentified by Dr. K. Madhava Chetty (Asst. Professor, Department of Botany, Sri Venkateswara University, Tirupati, Andhra Pradesh, India) for its authenticity and a specimen of the plant material was also deposited at Department of Botany, Sri Venkateswara University for further reference.

Preparation of Extracts

Coarsely powdered leaves (500 g) were defatted with petroleum ether (40–60°C) (at 52°C for 36 hours) and the dried marc was further extracted with chloroform (at 65°C for 48 hours) followed by ethyl acetate (at 80°C for 36 hours) and methanol (at 68°C for 48 hours) using Soxhlet's extractor. The three extracts (chloroform, ethyl acetate and methanol) obtained were dried by removing the solvents using rotary evaporator (Medica Instrument, Mumbai, India). The dried extracts so obtained were placed in a vacuum desiccator and used for further studies.

Phytochemical Screening

All the three extracts were screened for their various

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phytoconstituents using standard procedures.[9,10]

Animals

The experimental protocol used in this study was approved by the Institutional Animal Ethical Committee. Adult male Wistar rats (200–250 g) were obtained from the Animal house, ISF college of Pharmacy, Moga, and housed in groups of two to three animals per cage and maintained at an ambient temperature of 25 ± 1°C with a relative humidity of 50 ± 10% and a 12:12 dark:light cycle. The experiments were carried out during 10:00 AM–1:00 PM . Animals had free access to food and water. The experiments were conducted according to the guidelines of the Committee for the Purpose of Supervision and Control of Experiments on Animals (CPCSEA), Government of India, and approved by Institutional Animal Ethics Committee. Overall, 8% mortality was observed in this study.

Drugs and Chemicals

All the standard chemicals used for the study were freshly prepared and of analytical grade. PTZ was purchased from Himedia Laboratories, Mumbai, India, phenytoin (PHT) from Sun Pharmaceuticals Ltd., Mumbai (India), diazepam (DZP) and Tween 80 from Ranbaxy laboratories, Gurgaon (India).

Drug Administration

PHT (25 mg/kg, i.p.) and DZP (1 mg/kg, i.p.) were dissolved in normal saline and administered once on the 7th day, 1 hour before the induction of seizures by MES and PTZ models, respectively.[1,11,12] The dried extracts of chloroform, ethyl acetate and methanol were suspended in 10% aqueous Tween 80 and administered orally using intra-gastric cannula for 7 days and tested for anticonvulsant activity 1 hour after the last dose.

Induction of Experimental Convulsions

MES model

The development of generalised tonic-clonic seizures has been reported to be induced by applying current (150 mA, 0.2 second) through corneal electrodes using electroconvulsiometer (INCO, Ambala, India). Different parameters observed in MES model were extensor, extensor/flexion ratio, clonus and stupor.[11,13,14] Changes in the time duration and absence or presence of different phases were taken as the measures of effectiveness of the different extracts and the standard drug.

PTZ model

The absence seizures were produced by the single dose administration of PTZ (50 mg/kg, i.p.), a gamma aminobutyric acid (GABA) antagonist.[1,11,15] Various parameters observed in PTZ model for 1 hour of PTZ administration were onset of jerks, number of jerks, latency to clonus, forelimb tonus with hind limb clonus and duration of clonic convulsions.[11,16-18] Changes in the time duration and absence or presence of different phases were taken as the measures of effectiveness of the different extracts and the standard drug.

Assessment of Locomotor Activity

Locomotor activity was evaluated after 7 days of treatment with different extracts but before inducing convulsions by PTZ and MES. The locomotor activity is an index of wakefulness (alertness) of mental ability and assessed in this study to assess the sedative effect of the extracts. The locomotor activity was assessed by using digital actophotometer (INCO, Ambala, India). Each animal was observed over a period of 5 minutes in a square (30 cm) closed arena equipped with infrared light-sensitive photocells and values expressed as counts per 5 minutes. The beams in actophotometer cut by the animal were taken as a measure of movements. The apparatus was placed in a darkened, sound-attenuated and ventilated testing room.[19,20]

Assessment of Rotarod Test

Rotarod activity was evaluated after 7 days of treatment with different extracts but before inducing convulsions by PTZ and MES. Rats which were able to remain on the rotating rod, with a speed of 10 rpm for 5 minutes or more were selected and divided into different groups, each containing six animals. The animals were placed on the rotarod after 30 minutes of drug administration and the latency to fall from the rotarod was noticed.[12]

Experimental Protocol

The animals were randomly divided into 24 groups and each group consisted of six animals.

Maximal electroshock model

Group I (maximal electroshock control): Generalised tonic-clonic convulsions were induced by applying the current (150 mA, 0.2 second) to cornea with corneal electrodes using electroconvulsiometer.

Group II (vehicle control): Aqueous Tween 80 (10% v/v, p.o.) was administered to rats for 7 days and electric shock was given on the 7th day.

Group III (PHT control): Rats were administered PHT standard drug (25 mg/kg, p.o.) once and electric current was given.

Group IV (low dose chloroform extract): Rats were administered chloroform extract (100 mg/kg, p.o.) of AM for 7 days and electric shock was given on the 7th day.

Group V (medium dose chloroform extract): Rats were administered chloroform extract (200 mg/kg, p.o.) of AM for 7 days and electric shock was given on the 7th day.

Group VI (high dose chloroform extract): Rats were

administered chloroform extract (400 mg/kg, p.o.) of AM for 7 days and electric shock was given on the 7th day.
Group VII (low dose ethyl acetate extract): Rats were administered ethyl acetate extract (100 mg/kg, p.o.) of AM for 7 days and electric shock was given on the 7th day.
Group VIII (medium dose ethyl acetate extract): Rats were administered ethyl acetate extract (200 mg/kg, p.o.) of AM for 7 days and electric shock was given on the 7th day.
Group IX (high dose ethyl acetate extract): Rats were administered ethyl acetate extract (400 mg/kg, p.o.) of AM for 7 days and electric shock was given on the 7th day.
Group X (methanol extract): Rats were administered methanol extract (100 mg/kg, p.o.) of AM for 7 days and electric shock was given on the 7th day.
Group XI (methanol extract): Rats were administered methanol extract (200 mg/kg, p.o.) of AM for 7 days and electric shock was given on the 7th day.
Group XII (methanol extract): Rats were administered methanol extract (400 mg/kg, p.o.) of AM for 7 days and electric shock was given on the 7th day.

Pentylenetetrazole model
Group I (PTZ control): Generalised absence seizures were induced by administering PTZ (50 mg/kg, i.p.).
Group II (vehicle control): Aqueous Tween 80 (10% v/v, p.o.) was administered for 7 days and PTZ was given on the 7th day.
Group III (DZP control): Rats were administered DZP standard drug (1 mg/kg, p.o.) once and PTZ was given.
Group IV (chloroform extract): Rats were administered chloroform extract (100 mg/kg, p.o.) of AM for 7 days and PTZ was given on the 7th day.
Group V (chloroform extract): Rats were administered chloroform extract (200 mg/kg, p.o.) of AM for 7 days and PTZ was given on the 7th day.
Group VI (chloroform extract): Rats were administered chloroform extract (400 mg/kg, p.o.) of AM for 7 days and PTZ was given on the 7th day.
Group VII (ethyl acetate extract): Rats were administered ethyl acetate extract (100 mg/kg, p.o.) of AM for 7 days and PTZ was given on the 7th day.
Group VIII (ethyl acetate extract): Rats were administered ethyl acetate extract (200 mg/kg, p.o.) of AM for 7 days and PTZ was given on the 7th day.
Group IX (ethyl acetate extract): Rats were administered ethyl acetate extract (400 mg/kg, p.o.) of AM for 7 days and PTZ was given on the 7th day.
Group X (methanol extract): Rats were administered methanol extract (100 mg/kg, p.o.) of AM for 7 days and PTZ was given on the 7th day.
Group XI (methanol extract): Rats were administered methanol extract (200 mg/kg, p.o.) of AM for 7 days and PTZ was given on the 7th day.
Group XII (methanol extract): Rats were administered methanol extract (400 mg/kg, p.o.) of AM for 7 days and PTZ was given on the 7th day.

Statistical Analysis
In this study, the behavioural assessment data were analysed using one-way analysis of variance (ANOVA) followed by Tukey's test and the results were expressed as mean ± SD. $P < 0.05$ was considered statistically significant.

RESULTS

Phytochemical Screening
Preliminary phytochemical screening revealed the presence of triterpenoids and flavonoids in chloroform extract and ethyl acetate extracts, respectively, whereas methanol extract showed the presence of carbohydrates and amino acids.

Anticonvulsant Screening
Administration of vehicle (aqueous Tween 80, 10% v/v, p.o.) for 7 days did not produce any significant effect on MES- and PTZ-induced convulsions when compared with age-matched naive rats.

Effect of various extracts on maximal electric shock induced convulsions
The administration of high dose of chloroform extract (400 mg/kg, p.o) and ethyl acetate extract (400 mg/kg, p.o.) significantly ($P < 0.05$) decreased extensor phase, extensor/flexion ratio and stupor phase induced by electrical stimulation when compared with MES control. In addition, both the extracts (400 mg/kg, p.o.) significantly ($P < 0.05$) reduced clonus phase when compared with PHT standard control. On the other hand, treatment with chloroform extract (200 mg/kg, p.o.) significantly ($P < 0.05$) reduced extensor phase without affecting extensor/flexion ratio, clonus phase and stupor phase. However, administration of low dose of chloroform extract (100 mg/kg, p.o.), ethyl acetate extract (100 and 200 mg/kg, p.o.) and all the doses of methanol extract (100, 200 and 400 mg/kg, p.o.) did not produce any significant effect on extensor phase, extensor/flexion ratio, clonus phase and stupor phase [Tables 1–3].

Effect of different extracts at different doses on pentylenetetrazole-induced convulsions
The administration of high dose of chloroform extract (400 mg/kg, p.o.) and ethyl acetate extract (400 mg/kg, p.o.) significantly ($P < 0.05$) increased latency to jerks and clonus and decreased the number of jerks, forelimb tonus with hind limb clonus and duration of clonus, whereas treatment with chloroform and ethyl acetate extracts (200 mg/kg, p.o.) significantly ($P < 0.05$) reduced the number of jerks and forelimb tonus with hind limb clonus phases when compared with PTZ control. In addition, ethyl acetate extract (200 mg/kg, p.o.) significantly ($P < 0.05$) increased

Table 1: Effect of chloroform extract at different doses on MES-induced convulsions

Groups	Extensor (sec.)	Extensor/Flexion ratio (sec.)	G7onus (sec.)	Stupor (sec.)
MES control	11.67±1.47	3.30±0.90	43.75±6.84	276.90±79.81
VEH control	10.67±1.52	3.23±0.61	42.67±6.42	223.30±42.52
Chloroform extract (100 mg/kg)	8.83±1.89	2.50±1.15	37.22±6.94	181.70±43.11
Chloroform extract (200 mg/kg)	6.73±0.64*	1.80±0.50	34.67±5.13	187.20±31.62
Chloroform extract (400 mg/kg)	3.00±1.00*†	0.90±0.36*	20.00±2.00P	116.00±28.16*
PHT control	1.33±0.57*	0.83±0.28*	40.80±3.65	122.80±28.77*

Results are expressed as mean ± SD, *P < 0.05 vs. MES control; †P < 0.05 vs. chloroform extract 200 mg/kg; ‡P < 0.05 vs. PHT treated

Table 2: Effect of ethyl acetate extract at different doses on MES-induced convulsion

Groups	Extensor (sec.)	Extensor/Flexion ratio (sec.)	Clones (sec.)	Stupor (sec.)
IVES control	11.67±1.47	3.30±0.90	43.75±6.84	276.90±79.81
VEH control	10.67±1.52	3.23±0.61	42.67±6.42	223.30±42.52
Ethyl acetate extract (100 mglkg)	9.00±2.64	2.16±0.25	43.00±7.55	17430±26.01
Ethyl acetate extract (200 mg/kg)	8.33±1.52	1.73±0.32	36.67±9.71	160.00±23.07
Ethyl acetate extract (400 mg/kg)	2.66±1.55*†	1.03±0.25*	19.00±5.56*1	112.00±34.0*
PHT control	1.33±0.57*	0.83±0.28*	40.80±3.65	122.80±28.77*

Results are expressed as mean ± SD, *P < 0.05 vs. MES control; †P < 0.05 vs. ethyl acetate extract 200 mg/kg; ‡P < 0.05 vs. PHT treated

Table 3: Effect of methanol extract at different doses on electric shock induced convulsions

Groups	Extensor (sec.)	Extensor/Flexion ratio (sec.)	Clones (sec.)	Stupor (sec.)
MES control	11.67±1.47	3.30±0.90	43.75±6.84	276.90±79.81
VEH control	10.67±1.52	3.23±0.61	42.67±6.42	223.30±42.52
Methanol extract (100mg/kg)	9.33±2.51	2.16±0.87	44.33±11.02	217.00±76.92
Methanol extract (200mg/kg)	8.00±2.64	2.36±0.85	37.67± 0.07	201.70±38.84
Methanol extract (400mg/kg)	7.66±1.52	2.66±0.57	43.67±10.60	186.00±55.34
PHT control	1.33±0.57*	0.83±0.28*	40.80±3.65	122.80±28.77*

Results are expressed as mean ± SD, *P < 0.05 vs. MES control

the onset of jerks and significantly decreased the duration of clonus phase. However, both chloroform and ethyl acetate extracts (200 mg/kg, p.o.) failed to increase latency to clonus when compared with PTZ control. In addition, administration of chloroform extract (100 mg/kg, p.o.) and methanol extract at (100, 200 and 400 mg/kg, p.o.) did not produce any significant effect on latency to jerks, number of jerks, forelimb tonus with hind limb clonus, latency to clonus and duration of clonus. However, ethyl acetate extract (100 mg/kg, p.o.) markedly (P < 0.05) decreased forelimb tonus with hind limb clonus and duration of clonus [Tables 4–6].

Effect of different extracts at different doses on locomotor and rotarod tests

Administration of chloroform extract, ethyl acetate and methanol extracts at doses employed in the present study (i.e. 100, 200 mg/kg, p.o.) did not produce any significant effect on locomotor activity and motor coordination or grip strength significantly. However, chloroform and ethyl acetate extracts at maximum dose (400 mg/kg, p.o.) slightly decreased the locomotor activity and grip strength but the effect was not as significant as compared to that of normal control [Table 7].

DISCUSSION

The data obtained in this study for the first time demonstrated that both chloroform and ethyl acetate extracts of AM had significantly inhibited the MES-induced generalised tonic-clonic convulsions and PTZ-induced absence seizures. Further, it was observed that ethyl acetate extract had shown

Table 4: Effect of chloroform extract at different doses on PTZ-induced convulsions

Groups	Onset of jerks (sec.)	Number of jerks (sec.)	ForeUemb tones wishhmdtimb donus (ser.)	Latency to clonus (sec.)	Duration of donus (min.)
PTZ control	53.33±7.63	42.67±6.42	21.33±5.13	148.00±29.82	34.00±8.54
VEH control	62.33±13.50	37.67±7.50	22.00±3.00	103.70±16.90	41.67±12.58
Chloroform extract (100 mg/kg)	68.33±15.31	34.00±5.56	11.67±3.78	118.30±16.80	20.67±10.07
Chloroform extract (200 mglkg)	103.00±15.72	23.67±5.68*	6.66±2.88*	218.00±26.21	13.00±4.58
Chlorof irm extract (400 mg(kg)	144.70±14.50*	6.66±2.08*†	3.00±1.00*	320.00±78.73*	6.33±1.52*
DZPcontrol	188.30±32.53*	6.00±2.00*	1.33±0.57`	325.30±27.47`	6.33±2.08*

Results are expressed as mean ± SD, *P < 0.05 vs. PTZ control; †P < 0.05 vs. chloroform extract 200 mg/kg

Table 5: Effect of ethyl acetate extract at different doses on PTZ-induced convulsions

Groups	Onset of jerks (sec.)	Number of jerks (sec.)	Forelimb tons with bindtimb danns (sec.)	Latency to clones (sec.)	Duration of dons (min.)
PTZcontral	53.33±7.63	42.67±6.42	21.33±5.13	148.00±29.82	34-00±8-54
VEHcontfol	62.33±13.50	37.67±7.50	22.00±3.00	103.70±16.80	41.67±12.58
Ethyl acetate extract (100mg/kg)	90.33±10.02	36.67±12.22	5.66 ±2.08*	111.00±32.51	15.00± 5.00*
Ethyl acetateextract (200mg(kg)	120.00±18.68*	23.00±5.56*	2.66±1.52*	173.70±47.88	9.00±2.00*
Ethyl acetateextraet (400mgfkg)	173.30±25.17*	6.66±2.08*	1.66±0.57*	290.70±70.57*	3.00±1.00*
DZPcontrol	188.30±32.53*	6.00±2.00*	1.33±0.57*	325.30±27.47*	6.33±2.08*

Results are expressed as mean ± SD, *P < 0.05 vs. PTZ control

Table 6: Effect of methanol extract at different doses on PTZ-induced convulsions

Groups	Onset of jerks (sec.)	Number of jerks (sew)	Forelimb tons with bmdtimb nouns (set.)	Latency to donus (sec.)	Duration of dons (min.)
PTZcontral	53.33±7.63	42.67±6.42	21.33±5.13	148.00±29.82	34_00±8_54
VEHcontfal	62.33±13.50	37.67±7.50	22.00±3.00	103.70±16.80	41.67±12.58
Methanolextract (100mg/kJ	56.33±13.01	33.33±6.11	21.00±7.55	95.33±22.19	26.00±6.55
Methanolextract (200mg/kg)	72.00±24.02	44.67±6.42	19.67±2.51	94.33±11.02	27.33±15.57
Methanolextract (400mg/kg)	77.33±13.58	31.00±3.60	16.67±2.30	147.70±31.56	26.00±10.58
DZPcontrol	188.30±32.53*	6.00±2.00*	1.33±0.57`	325.30±27.47`	6.33±2.08*

Results are expressed as mean ± SD, *P < 0.05 vs. PTZ control

to be effective even at a lowest dose against PTZ-induced convulsions, suggesting that ethyl acetate extract may be more effective in inhibiting PTZ-induced absence seizure than MES-induced convulsions. The traditional system of medicine is slow acting as compared to the modern synthetic drugs as it involved the administration of crude preparations. Therefore, the anticonvulsant potential of AM was examined following daily administration for 7 days.

PTZ- and MES-induced seizure models are the most commonly used preliminary screening tests for finding the anticonvulsant potential of drugs. MES model is a characteristic model for the assessment of generalised tonic-clonic seizures, whereas PTZ model is considered to be a predictor of generalised absence seizures.

PHT, reported to act by blocking voltage-dependent Na^+ channels, was employed as a standard drug to prevent MES-induced generalised tonic-clonic seizures.[21,22] Further, anticonvulsant effects of chloroform and ethyl acetate extracts were found to be similar to the beneficial effects of PHT on extensor phase in the MES test, whereas PHT increases the severity of the clonus phase, which is consistent with previous findings suggesting that PHT worsens clonus phase in MES-induced convulsions.[23,24] Interestingly, it has been observed in the present study that both the extracts significantly reduced duration and severity of clonus phase in comparison with PHT. A decrease in extensor/flexion ratio is documented to be an index of increase in seizure threshold.[14] Treatment with both chloroform and ethyl acetate extracts has shown a decrease in extensor/

Table 7: Effect of different extracts at different doses on locomotor and rotarod tests

Groups	Locomotor activity Counts/5 min.	Rotarod activity (sec.)
Normal control	194.70±14.29	258.30±55.43
VEH control	181.70-±66.21	229.00±64.09
Chloroform extract (100 mgl/kg)	182.30±33.95	231.70±53.45
Chloroform extract (200 mgl/kg)	158.70±15.37	241.70±28.15
Chloroform extract (400 mg/kg)	136.30±28.04	170.00±55.22
Ethyl acetate extract (100 mg/kg)	160.0±46.87	199.30±65.77
Ethyl acetate extract (200 mg/kg)	134.30±37.31	208.30±22.90
Ethyl acetate extract (400 mg/kg)	127.00±29.61	178.70±34.00
Methanol extract (100 mg/kg)	191.30±55.72	236.70±62.77
Methanol extract (200 mg/kg)	187.00±37.59	219.30±30.99
Methanol extract (400 mg/kg)	152.30±33.84	226.00±76.62
DZP control (1 mg/kg)	86.33±9.07*	115.30±23.46*
PUT control (25 mg/kg)	104.00±6.00=	126.70±32.53=

Results are expressed as mean ± SD, *P < 0.05 vs. normal control

flexion ratio. Hence, both the extracts are responsible for the anticonvulsant property in the present study.

GABA is a major inhibitory neurotransmitter and the enhancement and inhibition of GABA neurotransmission has shown to attenuate and enhance, respectively, the convulsion.[25,26] DZP, a benzodiazepine, is reported to prevent PTZ-induced absence seizures by enhancing $GABA^A$ receptor-mediated inhibitory neurotransmission.[21] Hence, in the present investigation, DZP has been employed as a standard drug in PTZ model. In addition, N-Methyl-D-Aspartic acid (NMDA) receptor activation has also been implicated to mediate the occurrence of PTZ-induced seizures.[21,27,28] Further, NMDA receptor antagonists such as agmatine, ketamine, diazocilpine and 2-amino-5-phosphonovaleric acid (APV) have been reported to be effective against PTZ-induced convulsions.[29-31] However, the acceptability of NMDA receptor antagonists as antiepileptic drugs is limited as they are often associated with intolerable side effects, mainly impairment of motor co-ordination.[31-34] Hence, the observed ameliorative effect of chloroform and ethyl acetate extracts against PTZ-induced convulsions may be due to potentiation of GABAergic system or by inhibition of glutamatergic excitation via blockage of NMDA receptor. Further, ethyl acetate extract was found to be more beneficial as compared to chloroform extract when assessed in terms of PTZ-induced convulsions. Hence, it seems that chloroform and ethyl acetate extracts possess multiple mechanisms for anticonvulsant action. In contrast, the methanol extract failed to prevent convulsions induced by PTZ and MES models. DZP and PHT have been reported to depress the locomotion and enhance muscle relaxation.[35,36] Interestingly, it was observed in this study that both chloroform and ethyl acetate extracts did not alter locomotor and rotarod activity even at maximum effective dose. Various chemical constituents of plant origin such as terpenoids, particularly triterpenoids and flavonoids, are reported to have anticonvulsant property in various animal models of epilepsy like PTZ, MES, electrical kindling, etc.[37-40] Moreover, previous studies have shown that flavonoids may cause facilitation of GABAergic system, as they are structurally similar to benzodiazepines like molecules present in CNS.[40] The results obtained by preliminary phytochemical screening carried out in the present study showed the presence of triterpenoid and flavonoids in chloroform and ethyl acetate extracts, respectively.

Hence, it may be concluded on the basis of results obtained in this study that chloroform and ethyl acetate extracts inhibit convulsions induced by PTZ and MES models of epilepsy without affecting locomotor activity and motor coordination. The observed anticonvulsant activity may be due to potentiation of GABAergic neurotransmission and/or increase in neuronal seizure threshold by decreased Na^+ channel activity, which may be attributed to the phytoconstituents present in the extracts.

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