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Research article

Antiepileptic effects of antioxidant potent extract from *Urtica dioica* Linn. root on pentylenetetrazole and maximal electroshock induced seizure models

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ABSTRACT

Urtica dioica Linn. (Urticaceae) is a medicinal plant that has shown various therapeutic utilities in folklore medicine along with its use in the treatment of epilepsy. The entire plant has a sensible reservoir of nutritional elements and micronutrients. The purpose of the present study was to investigate the antiepileptic effect of antioxidant potent extract of *Urtica dioica* root on animal models. Antioxidant activity of various solvent extracts i.e. Petroleum ether extract (PEE), Ethyl acetate extract (EAE), Chloroform extract (CE) and Ethanolic extract (EE) were screened by DPPH radical scavenging assay using Ascorbic acid as the standard. Further the most potent antioxidant extract was subjected to antiepileptic activity against MES and PTZ model. The IC_{50} values of different *Urtica dioica* extracts (PEE, CE, EAE, and EE) in antioxidant assay were found to be 167.54 ± 1.97, 134.41 ± 0.82, 88.15 ± 1.39 and 186.38 ± 1.91 μg/ml in DPPH radical scavenging assay, respectively. The EAE has showed the potent antioxidant activity. In experimental study the EAE (100 and 200 mg/kg, p.o) has found to be effective and significant against MES and PTZ induced seizures. The present study also suggested that antioxidant potent extract (EAE) of *Urtica dioica* root has antiepileptic effect against MES and PTZ induced seizures. However, further research studies will investigate the active component(s) of *Urtica dioica* responsible for the observed anticonvulsant effects.

1. Introduction

Epilepsy is defined as the disorder of central nervous system characterized by attacks of disturbed brain activities those results in convulsions and seizure [1]. About 50 million people worldwide are affected by epilepsy [2]. A cascade of biological events like cognitive impedance and oxidative stress are found that results in the advancement of epilepsy linked with recurrent seizures [3, 4]. Epileptic seizure can arise when there is excitation and inhibition imbalance due to a decrease in GABAergic and an increase in glutamatergic transmission [5, 6]. In such condition the role of antiepileptic drugs is through the maintenance of balance between the brain neurotransmitter GABA and glutamate as well as glutamate receptors blockage [7, 8]. Several undesirable effects have been reported time to time with the conventional and newer antiepileptic drugs. Among which cognitive impairment is the one undesired [9, 10]. Hence, at such a time, herbal medicine have shown experimentally promising results in animal models related to epilepsy [11]. Plant based medicines are widely used due to their wide acceptance and therapeutic effects with minimal side effects [11, 12].

Urtica dioica Linn. (*U. dioica*) belonging to family Urticaceae is an annual and perennial plant commonly known as stinging nettle [13]. The vernacular names for this plant are Vrishchhiyaa-shaaka in Sanskrit; Bichu Butti in Hindi and Shisuun/Kandali in folk languages [14]. Traditionally, plant is used in various disorders like menstrual hemorrhage, rheumatic pain, cough, stomachache, liver insufficiency, anemia, eczema, haematuria, nephritis, menorrhagia, epilepsy, jaundice and diarrhea [15, 16]. It is whole plant commonly used as food, medicine, cosmetic, textile production, fodder, biodynamic agriculture and as colouring agent i.e. (E140) in foods and medicines [17]. *U. dioica* is well documented to possess phyto-constituents like steroids, terpenoids, flavonoids specially quercetin, isoquercitrin, astragalin, kaempferol, isorhamnetin and rutin, phenolics i.e. phenylpropanes, scopoletin, caffeic acid and chlorogenic acid, coumarins, polysaccharides, proteins, lectins, vitamins and minerals [16]. It has been reported that the plant have

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immune-stimulatory, anti-carcinogenic, anti-inflammatory, antioxidant, antiallergenic, anti-androgenic, hepatoprotective, hypoglycemic and antiviral activities [13, 14, 15, 16]. On the basis of ethnomedical use of the plant in the treatment of epilepsy [16, 18] and as per reported documented data, plants having flavonoids and coumarins contents are proved for antiepileptic activity [19, 20, 21]. Other previous work on a species of *Urtica* i.e. *Urtica triangularis* has already been proved as anti-epileptic [22]. Therefore, the present study has investigated the possible anticonvulsant potential of *U. dioica* in animal models.

2. Materials and methods

2.1. Chemicals

Pentylenetetrazole (PTZ) (PubChem CID: 5917); L-ascorbic acid (PubChem CID: 54670067); Phenytoin (PHT) (PubChem CID: 1775); Diazepam (DZP) (PubChem CID: 3016); Pentobarbitone sodium (PubChem CID: 23676152); Tween 80 (PubChem CID: 5281955); Rutin (PubChem CID: 5280805); Gallic acid (PubChem CID: 370); DPPH (PubChem CID: 74358), Aluminium chloride (PubChem CID: 24012), Folin-Ciocalteus phenol reagent. The analytical grade chemicals and solvents were used in the study and purchased from Loba Chemie Pvt Ltd, Central Drug House Pvt Ltd, Sigma-Aldrich Corporation, Zydus Healthcare Ltd., Ranbaxy Fine Chemicals Ltd and HiMedia Laboratories Pvt Ltd.

2.2. Experimental animal

Swiss albino mice (20–25gm) and male Wistar albino rats (180–250 g) of either sex were used in the study. Animals were obtained from the Central Animal House, SBSPGI, Balawala, Dehradun, India. Prior to experimentation, animals were acclimatized to laboratory conditions at room temperature. Animals were provided standard laboratory conditions (Room temperature 20 ± 5 °C; humidity (50 ± 5%); 12 h light/dark cycle) with *ad libitum* access to food (standard dry rat pellet diet) and water. All the animals were acclimatized for seven days before the study. The experimental protocol of the study was approved by Institutional Animal Ethics Committee (IAEC) bearing the registration number (vide approved by 273/PO/Re/S/2000/CPCSEA, 24 November 2000) and carried out in accordance with the guidelines of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Government of India.

2.3. Plant material

About a kilogram of fresh roots of the plant was collected from the local area of Balawala, Dehradun in the month of August and authenticated by Dr. Kumar Ambrish from Botanical Survey of India, Dehradun, (Uttarakhand) India, Ref. BSI/NRC/tech./Herb(Ident.)/2018-19/118763/13 December 2018.

2.4. Extraction

The powdered plant material (250g) was extracted by continuous hot extraction process using soxhlet apparatus with petroleum ether (60–80 °C). With rota-evaporator the extract was concentrated and transferred to a pre-weighed china dish followed by drying in a vacuum dessicator. The marc obtained was air dried and further used for extraction with chloroform followed by ethyl acetate and ethanol. For further studies, the dried extracts were placed in desiccators and percentage yield was calculated.

2.5. Preliminary phytochemical screening

The qualitative assays were performed for various solvent extracts of *U. dioica* (PEE, CE, EAE and EE) to test for the presence of phytochemicals as per described standard methods [23, 24].

2.6. In-vitro free radical scavenging activity

2.6.1. DPPH radical scavenging activity

The antioxidant activity of *U. dioica* roots extracts (petroleum ether extract (PEE), chloroform extract (CE), ethyl acetate extract (EAE) and ethanol extract (EE)) were assessed by DPPH radical scavenging ability. For the DPPH assay, the 0.1 mM solution of DPPH in methanol was prepared.1 ml of this solution was transferred to 2 ml of test drug solution at different concentrations (50–250 μg/ml). The resulting mixture was shaken vigorously and allowed to stand at room temperature for 30 min. The absorbance was then measured at 517 nm. Ascorbic acid (STD) was used as standard.

The percentage of scavenging activity was determined by using the following formula:

$$\text{Percentage of Inhibition } (\%) = [(A_c - A_s/A_c)] \times 100$$

Where A_c is the absorbance of reaction mixture without the test sample; A_s is the absorbance of reaction mixture with various concentrations of sample [25].

2.7. Determination of total phenolic content and total flavonoid content

Folin Ciocalteu's method was used for the estimation of total phenolic content and aluminium chloride colorimetric assay for assessing flavonoid content using Gallic acid and Rutin respectively, as standard [26].

2.8. Acute toxicity study

As per the organization for economic co-operation and development (OECD) guidelines, the toxicity of extract was studied. Swiss albino mice of either sex, weighing (20–25 g) were used in the toxicity study. The extract dose of 2000 mg/kg was prepared in water and administered to a group of six animals, as recommended in the guideline. Each animal was observed after every hour for signs of toxicity and abnormality in behavior up to the 48th hour following dose administration. After this, daily observations for toxicity and mortality were made up to the 14th day. The body weights of the animals were recorded every third day. At the end of14th day after dosing, all the mice were sacrificed [27].

2.9. Assessment of antiepileptic activity

2.9.1. Pentylenetetrazole (PTZ) induced seizures

The animals were divided into five groups (n = 06) and Group I animals served as control receiving normal saline, p. o., Group II served as Positive control receiving Diazepam (DZP) (4 mg/kg, i.p.) and Groups III-V animals were administered with the *U. dioica* extract (EAE) at doses of (50, 100 and 200 mg/kg, p. o.). After 30 and 60 min, administration of a single dose of PTZ (50 mg/kg, i.p.) to the rats, which were placed in individual cages (50 × 50 × 40cm) to observe the behaviors of animals for next 30 min. The onset of first myclonic jerks, duration of tonic generalized extensor and duration of generalized clonic seizures were noted [19, 28].

2.9.2. Maximum electro shock (MES) induced seizure

For the MES method, Wistar albino rats (180–250gm) of either sex were used. In MES model the animals were divided into five groups (n = 06) with Group I animals serving as control and received normal saline p. o., Group II served as Positive control and received Phenytoin (PHT) (25 mg/kg, i.p.) and Groups III-V animals were administered with the *U. dioica* extract (EAE) at doses of (50, 100 and 200 mg/kg, p. o.), 60 min prior to electric shock. After 30 and 60 min, current of (150 mA, 0.2 s) was applied through corneal electrodes using Electro convulsiometer (INCO, India) to produce generalized tonic-clonic seizures in all the groups of animals. The extent of tonic hind limb extension (THLE) was observed to assess the antiepileptic activity [19, 28].

2.10. Assessment of sedative activity

2.10.1. Measurement of locomotor activity

The animals of either sex were divided into five groups (n = 06), with six animals in each group. Group I received normal saline, p. o., Group II received standard drug Diazepam (DZP) 4 mg/kg, i.p., Groups III-V were administered *U. dioica* extract (EAE) (50,100 and 200 mg/kg, p. o.). The activity of animals was again observed after 30 min of i.p. and 60 min of p. o. dose respectively by placing them in the actophotometer (INCO, India). The animals were observed for a period of 5min in a square (30 cm) closed arena fitted with infrared light-sensitive photocells. The values were expressed as counts per 5 min [12, 28].

2.10.2. Pentobarbitone sleeping time

The animals were divided into five groups (n = 06), each consisting of six animals. Group I received normal saline, p. o., Group II received standard drug Diazepam (DZP) 4 mg/kg, i.p., Groups III-V groups were administered *U. dioica* extract (EAE) (50, 100 and 200 mg/kg, p. o.). After 30 min of i.p. and 60 min p. o. later, pentobarbitone sodium (20 mg/kg, i.p.) was administered to all the rats. Each animal was observed for the loss of righting reflex (animal is not able to turn back when turned). The parameter for hypnotic effect was the duration between loss and recovery of righting reflex [28].

2.11. Statistical analysis

The data was analyzed by one-way ANOVA followed by multiple comparison Dunnett test using Graph Pad Prism version 5.0. for the behavioral assessment and results were expressed as mean ± SEM. A $p < 0.05$ was considered statistically significant.

3. Results

3.1. Extraction of plant material

Successive solvent extracts of *U. dioica* were subjected for calculating their % yield, color and consistency respectively given in Table 1.

3.2. Preliminary phytochemical screening

U. dioica various solvent extracts reveals the presence of saponins, steroids/terpenoids, phenolics, flavonoids, coumarins and tannins in different extracts. The qualitative preliminary phytochemical screening of *U. dioica* extracts (PEE, CE, EAE and EE) were mentioned in Table 2.

3.3. DPPH radical scavenging activity

The antioxidant activity of *U. dioica* extracts (PEE, CE, EAE and EE) showed DPPH radical scavenging activity with an IC_{50} of 167.54 ± 1.97 μg/ml, 134.41 ± 0.82 μg/ml, 88.15 ± 1.39 μg/ml and 186.38 ± 1.91 μg/ml respectively. Ascorbic acid (STD) (IC_{50} 62.08 ± 1.06 μg/ml) showed an excellent activity. The EAE has shown significant free radical quenching capacity as compared to other extracts (Figure 1).

3.4. Determination of total phenolic content and flavonoid content of antioxidant potent U. dioica extract (EAE)

The total phenols and flavonoids content of *U. dioica* extract (EAE) were found to be 2.23% (w/w) and 1.81 % (w/w) respectively.

3.5. Acute toxicity study

No mortality was seen at a dose of 2,000 mg/kg for the study period of 14 days. However, no any changes in activity like scratching, curved tail, shivering, grooming, excitation, convulsion, fatigue, diarrhoea and falling of hair has been observed.

3.6. Assessment of antiepileptic activity

3.6.1. Pentylenetetrazole (PTZ) induced seizures

The antioxidant potent extract (EAE) at dose (50 mg/kg, p. o.) reduced the duration of both tonic generalized extensor and clonic seizure, but without producing any significant effect on the onset of tonic generalized extensor and clonic seizure; myoclonic jerks, when compared with vehicle control. However, it was seen that EAE significantly increased the onset of both generalized clonic seizure and myoclonic jerks, when given at doses (100 and 200 mg/kg, p. o.) as compared to vehicle control (Table 3).

3.6.2. Maximum electro shock (MES)-induced seizure

The dose administration of antioxidant potent extract EAE (100 and 200 mg/kg, p. o.) has shown significantly reduced the tonic flexion, and Tonic hind limb extensor (THLE) phase as compared to vehicle control. The EAE of *U. dioica* (200 mg/kg, p. o.) produced significant activity in MES seizure (Table 4).

3.7. Assessment of sedative activity

3.7.1. Measurement of locomotor activity

The antioxidant potent extract of *U. dioica* (EAE) in doses of (50–200 mg/kg) has shown significant reduction in locomotor activity in rats when compared with vehicle-treated control animals. The standard diazepam treated group at the dose (4 mg/kg, i.p.) also showed a significantly reduction in locomotor activity in animals (Table 5).

3.7.2. Pentobarbitone sleeping time

The antioxidant potent extract (EAE) at dose (50–200 mg/kg, p. o.) on pre-treatment, dose dependently reduced the pentobarbitone induced sleep latency with significant effects shown at a dose level (200 mg/kg, p. o.). Diazepam (4 mg/kg, i.p.) served as positive control significantly decreased the latency to sleep and also increased the duration of sleep (Table 6).

4. Discussion

The present study demonstrate the anticonvulsant effects of *U. dioica* on generalized tonic clonic seizures induced by pentylenetetrazole (PTZ) and maximal electroshock (MES) in animal model.

Table 1. Percentage extractive value and characterization of *U. dioica* extracts.

Extracts	Colour	Odour	Consistency	Yield (%w/w)
PEE	Pale yellow	Characteristic	Semi-solid	3.72
CE	Greenish brown	Characteristic	Semi-solid	4.08
EAE	Reddish brown	Characteristic	Semi-solid	1.78
EE	Reddish brown	Characteristic	Semi-solid	7.05

PEE- Petroleum ether extract; CE- Chloroform extract; EAE- Ethyl acetate extract; EE- Ethanolic extract.

Table 2. Preliminary phytochemical screening of *U. dioica* different solvent extracts.

Class of constituents	PEE	CE	EAE	EE
Amino acids	-	-	-	+
Proteins	-	-	-	+
Carbohydrates	-	-	-	+
Steroids/Triterpenoids	+	-	-	-
Alkaloids	-	-	-	-
Glycosides	-	-	-	+
Saponins	-	-	-	+
Phenolics	-	+	+	-
Flavonoids	-	-	+	-
Coumarins	+	-	-	-
Tannins	-	-	-	+

PEE- Petroleum ether extract; CE- Chloroform extract; EAE- Ethyl acetate extract; EE- Ethanolic extract; (-) Negative; (+) Positive.

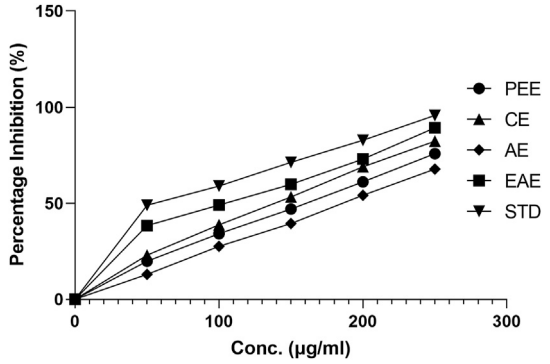

Figure 1. DPPH radical scavenging effect of various solvent extracts of *U. dioica;* Petroleum ether extract (PEE), Chloroform extract (CE), Ethyl acetate extract (EAE), Ethanol extract (EE) and Ascorbic acid (STD).

The acute toxicity studies were performed with EAE which served in the selection of the doses of EAE for further studies. In acute toxicity screening in mice, no deaths were observed after 14 days administration of antioxidant potent extract (EAE) of *U. dioica*.

MES and PTZ are the most commonly used models for the screening of novel antiepileptic drugs. They help to find antiepileptic drugs which could be fruitful in preventing generalized absence epilepsy or partial seizures in human [29, 30]. Prolongation of the inactivation duration of sodium channels, may be the probable mechanism of action of some medicinal plants [31]. In numerous experimental studies it has been stated that excessive free radicals production due to seizure activity has induced brain damage in experimental animals [32, 33, 34, 35]. The *U. dioica* has reported to have potent antioxidant potential in different experimental studies [36]. In the present study, the extract (EAE) of *U. dioica* has showed the potent antioxidant effect (IC_{50} 88.15 ± 1.39 µg/ml) in DPPH radical scavenging assay.

Pentylenetetrazole is a non-competitive antagonist used experimentally that exerts convulsant effects by producing the blocked of chloride ionophore of the $GABA_A$ receptor complex [37]. In addition to the activation of N-methyl-d-aspartate (NMDA) receptor seizure mechanism

Table 3. Effect of antioxidant potent extract (EAE) of *U. dioica* on PTZ-induced seizure.

Groups	Myclonic jerk (s)		Tonic generalized extensor (s)		Generalized clonic seizure (s)	
	Onset	Duration	Onset	Duration	Onset	Duration
Vehicle control	76.79 ± 6.71	42.33 ± 2.53	164.74 ± 3.82	20.61 ± 1.68	287.34 ± 8.37	32.71 ± 2.15
DZP (4 mg/kg, i.p.)	0.0[a]	0.0[a]	0.0[a]	0.0[a]	0.0[a]	0.0[a]
EAE (50 mg/kg, p.o.)	124.79 ± 13.24[a]	18.46 ± 1.73[a]	212.22 ± 11.41[a]	9.83 ± 1.83[a]	386.85 ± 10.19[a]	12.43 ± 2.58[a]
EAE (100 mg/kg, p.o.)	285.67 ± 23.60[a,b]	7.33 ± 1.03[a,b]	338.72 ± 8.76[a,b]	7.03 ± 4.67[a,b]	415.46 ± 4.34[a,b]	8.47 ± 4.85[a,b]
EAE (200 mg/kg, p.o.)	337.9 ± 15.32[a,b,c]	5.46 ± 2.03[a,b,c]	414.40 ± 8.34[a,b,c]	5.08 ± 3.58[a,b,c]	510.22± 6.67[a,b,c]	5.65 ± 3.92[a,b,c]

Results are expressed as mean ± SEM; (n = 6). [a] $p < 0.05$ vs VC; [b] $p < 0.05$ vs EAE 50 mg/kg; [c] $p < 0.05$ vs EAE 100 mg/kg; Statistical analysis done by one-way ANOVA followed by multiple comparisons Dunnett's test.

Table 4. Effect of antioxidant potent extract (EAE) of *U. dioica* on MES-induced convulsions.

Groups	No. of animal showing THLE	Various phases of convulsions (s)				
		Flexion (sec.)	Extension (sec.)	Clonus	Stupor	% Protection against THLE
Vehicle control	6/6	3.16 ± 0.75	9.50 ± 0.54	17.16 ± 0.98	27.37 ± 0.34	0
PHT (25 mg/kg, i.p.)	0/6	1.50 ± 0.54[a]	2.30 ± 0.51[a]	3.50 ± 0.51[a]	10.64 ± 0.23[a]	100[a]
EAE (50 mg/kg, p.o.)	3/6	2.60 ± 0.81[a]	6.50 ± 1.04[a]	9.65 ± 0.89[a]	24.56 ± 0.87[a]	50.00[a]
EAE (100 mg/kg, p.o.)	4/6	2.50 ± 0.54[a,b]	4.80 ± 0.75[a,b]	8.43 ± 0.81[a,b]	20.73 ± 0.45[a,b]	66.66[a,b]
EAE (200 mg/kg, p.o.)	1/6	2.10 ± 0.40[a,b,c]	3.00 ± 0.89[a,b,c]	6.85 ± 0.81[a,b,c]	16.86 ± 0.50[a,b,c]	83.33[a,b,c]

Results are expressed as Mean ± SEM (n = 6); [a] $p < 0.05$ vs VC; [b] $p < 0.05$ vs EAE 50 mg/kg; [c] $p < 0.05$ vs EAE 100 mg/kg; Statistical analysis done by one-way ANOVA followed by multiple comparisons Dunnett's test.

Table 5. Effect of antioxidant potent extract (EAE) of *U. dioica* on locomotor activity.

Groups	Locomotor activity in 10 min (counts)
Vehicle control	212 ± 4.63
DZP control (4 mg/kg, i.p.)	51 ± 7.44[a]
EAE (50 mg/kg, p.o.)	198 ± 4.84[a]
EAE (100 mg/kg, p.o.)	163 ± 5.33[a,b]
EAE (200 mg/kg, p.o.)	98 ± 4.56[a,b,c]

Results are expressed as Mean ± SEM (n = 6); [a] $p < 0.05$ vs VC; [b] $p < 0.05$ vs EAE 50 mg/kg; [c] $p < 0.05$ vs EAE 100 mg/kg; Statistical analysis done by one-way ANOVA followed by multiple comparisons Dunnett's test.

Table 6. Effect of antioxidant potent extract (EAE) of *U. dioica* on Pentobarbitone sleeping time.

Groups	Onset of sleep (min.)	Duration of sleep (min.)
Vehicle control	18.00 ± 3.63	47.11 ± 3.08
DZP control (4 mg/kg, i.p.)	4.80 ± 1.86*	105.00 ± 5.22*
EAE (50 mg/kg, p.o.)	16.22 ± 2.37	129.18 ± 16.23
EAE (100 mg/kg, p.o.)	7.20 ± 2.62	119.93 ± 20.54
EAE (200 mg/kg, p.o.)	4.62 ± 0.97*	110.00 ± 23.11*

Values are expressed as Mean ± SEM (n = 6). Statistical analysis done by one-way ANOVA followed by multiple comparisons Dunnett's test. *P value <0.05 when compared to control.

pentylenetetrazole has also been delineated to produce modulation of potassium and calcium channel conductance [38, 39, 40, 41].

In the present study we have demonstrated the anticonvulsant effect of different doses of antioxidant potent extract of *U. dioica* (EAE) in PTZ and MES models of seizures in experimental animals. EAE at a dose level (200 mg/kg) showed maximum protection against pentylenetetrazole induced seizures in experimental animals. However, EAE (100 mg/kg) exhibited significant increases in latency to myclonic jerks. On the other hand maximal electroshock models have showed significant protection with EAE (200 mg/kg, p. o.) against tonic hind limb extension. The antioxidant potent extract EAE has shown protective effect against PTZ and MES induced seizures exhibiting its potential use in experimental animals.

Phenytoin is a widely used standard control drug in MES model. It acts by blocking the voltage-dependent Na^+ channels [42]. Diazepam is also quite effective and is being widely used for absence seizures due to its facilitating GABAergic activity [29]. However, there is suppression of the locomotor activity seen with Diazepam and others benzodiazepines [43].

The plant extract also produced a significant reduction in pentobarbitone sleeping time test by lowering the sleep latency. This effect might be potentiating the hypnotic effects of pentobarbitone via actions at the $GABA_A$ receptor. The onset of sleep caused by EAE may indicate its CNS depressant potential.

In the present study possible sedative effect of antioxidant potent extract of *U. dioica* (EAE) was screened by using locomotor activity test. The EAE showed inhibition of locomotor activity in this test. The effective doses of EAE (100 and 200 mg/kg) has shown to cause marked decrease in locomotor activity and also impairment of motor coordination, as was observed in diazepam control.

Various experimental observations have clearly shown that flavonoids produce antiepileptic activity through modulating the (GABA) receptor-Cl^- channel complex, due to structural similarity with benzodiazepines [19, 44]. In the present study, the phytochemical screening of the extract revealed the presence of phenolic compounds, flavonoids as active phytoconstituents. However, flavonoids are well reported for their antiepileptic activity [45]. Hence, the results of experiments evidenced antiepileptic effect of antioxidant potent extract of *U. dioica* (EAE) against convulsions. The anticonvulsant effects of EAE with presence of flavonoids might be either due to inhibition of Na^+ channels or potentiating the GABAergic system.

5. Conclusions

In conclusion, the findings of the present study indicate the protective effect of antioxidant potent extract of *Urtica dioica* (EAE) for controlling epilepsy. Therefore, in further research we will attempt to find the phytoconstituent(s) of the EAE of *Urtica dioica* involved and their mechanism of action.

Declarations

Author contribution statement

Aanchal Loshali: Performed the experiments; Analyzed and interpreted the data.

Bhuwan Chandra Joshi: Conceived and designed the study; Analyzed and interpreted the data; Wrote the manuscript.

Ankush Sundriyal: Conceived and designed the study; Analyzed and interpreted the data.

Sushmita Uniyal: Analyzed and interpreted the data; Wrote the paper.

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Data availability statement

Data will be made available on request.

Declaration of interests statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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