

Anticonvulsant and Neuroprotective Effects of Aqueous Extract of *Emilia sonchifolia* in PTZ and MES Seizure Models

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Abstract

Epilepsy is a major neurological condition and the large percentage of patients report drug-resistant seizures, as well as side effects of the traditional antiepileptic medications. There is a possibility of alternative therapeutic options that have the potential to substitute current treatments and have antioxidant and neuroprotective properties in medicinal plants. This study evaluated the anticonvulsant and antioxidant effects of the aqueous extract of *Emilia sonchifolia* (AEES) using pentylenetetrazole (PTZ)-induced and maximal electroshock (MES)-induced seizure models. A total of 48 experimental animals (Wistar rat and Swiss mouse) were separated into four groups (n = 6) and treated with distilled water (control), AEES (200 and 400 mg/kg respectively), diazepam (5mg/kg). MES was applied to induce electrical and PTZ (70 mg/kg) was applied to induce chemical seizures. The onset, duration and hindlimb tonic extension (HLTE) and mortality were noted. Superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) and malondialdehyde (MDA) were tested on brain homogenates. One-way ANOVA and Tukey-Kramer post hoc test ($p < 0.05$) was used as the statistical test. AEES significantly delayed seizure onset, reduced seizure duration and decreased mortality in the PTZ model in a dose-dependent manner. AEES significantly decreased HLTE period in the course of the observations in the MES model. The use of AEES significantly increased SOD, CAT and GPx activity and decreased the level of MDA relative to controls. the protective and antioxidant effects of 400 mg/kg dose was found to be more protective and similar to diazepam in a variety of parameters.

Keywords: *Emilia sonchifolia*; E pilepsy; Anticonvulsant; Oxidative stress; PTZ; MES; Neuroprotection

1. Introduction

Epilepsy is a debilitating, chronic and neurological disorder that affects about 50 million people globally (Prameswari, 2024). Approximately 30% of patients treated with conventional antiepileptic drugs experience drug-resistant or refractory seizures. (Waris et al., 2024). Also, most of the existing pharmacotherapies are associated with side effects, such as cognitive impairment, complicated drug interactions and teratogenicity, all of which disrupt patient adherence (Costa & Vale, 2024).

Medicinal plants are now of primary importance in finding possible lead compounds because of their high bioactive constituent diversity and ethnopharmacological background (Johannessen et al., 2023). A good example is *Emilia sonchifolia*, a species of Asteraceae that grows in the tropics. Although it is used in the traditional medicine of wounds and diarrhea, its usage in neurology cases is notably considerable (Odelade et al., 2024). Studies have revealed that *Emilia sonchifolia* is a source of alkaloids, flavonoids, phenolic compounds and terpenoids (Jeenoo et al., 2023). These

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metabolites possess antioxidant, anti-inflammatory and neuroprotective properties, which are crucial in addressing the pathophysiological mechanisms underlying seizure propagation and epileptogenesis (Waris et al., 2024).

The analgesic and anti-inflammatory effects of *E. sonchifolia* extracts have already been supported in literature. However, there is paucity in the exploration and a systematic exploration of the anticonvulsant effect of the plant. This study focused on evaluating the anticonvulsant properties of the aqueous extract of *E. sonchifolia* leaves

2. Materials and Methods

2.1. Ethical Clearance

All experimental methods used in this research were formally approved by the Ethics Committee of the Faculty of Basic Medical Sciences, College of Health Sciences, Niger Delta University, Wilberforce Island, Bayelsa State, Nigeria

2.2. Plant Material Collection and Extract Preparation

Emilia sonchifolia plants were collected in Amassoma town, Bayelsa State, Nigeria. The leaves were cleaned with cold water, shade-dried for two weeks and then ground into a powder using an electric blender. For extraction, all the powdered samples (100 g) were soaked in 1 liter of distilled water for 72 hours with occasional stirring. The mixture was filtered using a Whatman filter paper with a 110 mm diameter and the filtered solution was then evaporated at 60 °C in a water bath. Aqueous extracts obtained were stored in labeled containers and stored in a refrigerator until required.

2.3. Drug and Chemicals

The seizure-inducing agent pentylenetetrazole (PTZ) (SIGMA-ALDRICH, Inc, 3050, Spruce Street, St. Louis, MO 63103, USA) and the standard anti-seizure drug diazepam (Juhel Pharmaceuticals Enugu, Nigeria) (used in both experimental models) were used (orally). All other chemicals employed in the study were of analytical quality.

2.4. Experimental Animals

A total of forty-eight animals (twenty-four Swiss mice and twenty-four Wistar rats) were used for this research. The animals were obtained from the animal breeding house of the Pharmacology Department, Niger Delta University. They were acclimatized in the departmental research laboratory for two weeks prior to the experiment. They were placed in regular plastic cages in controlled conditions: 12 hours of light/dark cycle, adequate air circulation and a temperature of 20-25 °C. During this period of acclimatization, they had the unrestricted access to regular chow and clean water.

2.5. PTZ-Induced Seizures Test

Wistar rats were divided into four groups (n=6 per group):

- Group 1 (Control): 10 ml/kg distilled water + 70 mg/kg PTZ
- Group 2 (Test 1): 200 mg/kg *E. sonchifolia* + 70 mg/kg PTZ
- Group 3 (Test 2): 400 mg/kg *E. sonchifolia* + 70 mg/kg PTZ
- Group 4 (Standard): 5 mg/kg diazepam + 70 mg/kg PTZ.

Thirty minutes after these treatments, seizures were triggered by administering pentylenetetrazol (PTZ) at 70 mg/kg. The rats were then monitored for the first 30 minutes to record the time until the first convulsion, signs of Straub's tail, the start of myoclonic jerks and whether any deaths occurred.

2.6. MES-Induced Seizure

Swiss mice were divided into four groups (n=6 per group):

- Group 1 (Control): 10 ml/kg distilled water
- Group 2 (Test 1): 200 mg/kg *E. sonchifolia*
- Group 3 (Test 2): 400 mg/kg *E. sonchifolia*
- Group 4 (Standard): 5 mg/kg diazepam

Thirty minutes after treatment, seizures were induced using an electroconvulsion therapy unit (Electroconvulsive Therapy Unit, Ugobasile Biological Apparatus, 21025, Comerio, VA, Italy. Model No.: 57800-001) that delivered a brief

electrical stimulus (50 mA, 80 Hz for 0.2 seconds) through ear electrodes. To ensure good contact, the electrodes were moistened with saline before being placed on the mice's ears. The current intensity was predetermined in pilot tests to be the level that causes hindlimb tonic extension (HLTE) where the hind legs fully extend without causing death in all control animals. The length of HLTE was recorded and full protection was defined as the total absence of this hindlimb extension.

2.7. Antioxidant Assays

The brain tissue samples were sliced and rinsed with a cold 0.1 mMol Sodium Phosphate buffer, Ph 7.4. Following a standard method, a 10% weight/volume homogenate was made. This mixture was then centrifuged using a refrigerated centrifuge (4 °C) at 1000x g for 10 minutes to remove cell fragments and nuclei. The clear liquid (supernatant) was used immediately to determine oxidative stress parameters (SOD by Misra and Fridovich, 1972; CAT by Beutler, 1989; Paglia and Valentine, 1962).

2.8. Statistical Analysis

The data were statistically analysed using one-way ANOVA with Tukey-Kramer post-hoc testing. Results are presented as mean $\pm$ SD, with statistical significance set at $p < 0.05$.

3. Results

Table 1 Mean onsets of action and durations of action of PTZ-induced seizures in Wistar rats pretreated with Aqueous extract of *Emilia sonchifolia* (AEES)

Groups	Onset of action(s)	Duration of action (s)	Number of deaths
Control (10 ml/kg Distilled water + 70 mg/kg PTZ)	82.46 $\pm$ 5.95 ^d	2737.66 $\pm$ 43.44 ^d	6
Test group 1 (200 mg /kg AEES + 70 mg/kg PTZ)	124.64 $\pm$ 6.82 ^c	1552 $\pm$ 57.8 ^c	2
Test group 2 (400 mg/kg AEES + 70 mg/kg PTZ)	196.84 $\pm$ 7.21 ^b	578.84 $\pm$ 11.95 ^b	0
Standard Group (5 mg/kg Diazepam + 70 mg/kg PTZ)	0.00 $\pm$ 0.00 ^a	0.00 $\pm$ 0.00 ^a	0

The data are presented as the mean $\pm$ standard deviation for a sample size of 6. Different superscripts (a, b, c, d, e) indicate statistical significance ($p < 0.05$) among means within the same column.

Table 2 Mean durations of action of MES-induced seizures in Swiss mice pretreated with Aqueous extract of *Emilia sonchifolia* (AEES)

Groups	30 min	90 min	120 min	Number of deaths
Control (10 ml/kg Distilled water)	42.68 $\pm$ 2.68 ^d	46.67 $\pm$ 4.12 ^d	49.44 $\pm$ 3.80 ^d	4
Test group 1 (200 mg /kg AEES)	28.62 $\pm$ 6.82 ^c	24.52 $\pm$ 2.07 ^c	31.47 $\pm$ 2.90 ^c	1
Test group 2 (400 mg/kg AEES)	9.78 $\pm$ 0.94 ^b	6.38 $\pm$ 0.54 ^b	8.45 $\pm$ 1.20 ^b	1
Standard Group (5 mg/kg Diazepam)	0.00 $\pm$ 0.00 ^a	0.00 $\pm$ 0.00 ^a	0.00 $\pm$ 0.00 ^a	0

The data are presented as the mean $\pm$ standard deviation for a sample size of 6. Different superscripts (a, b, c, d, e) indicate statistical significance ($p < 0.05$) among means within the same column (for each parameter).

Table 3 Mean levels of oxidative stress biomarkers in PTZ-induced seizure Wistar rats pretreated with Aqueous extract of *Emilia sonchifolia* (AEES)

Groups	SOD (U/mg Protein)	Catalase (U/mg Protein)	GPx (U/mg Protein)	MDA (U/mg Protein)
Control (10 ml/kg Distilled water +70 mg/kg PTZ)	2.28 ± 2.10 ^c	1.69 ± 0.75 ^d	1.96 ± 1.15 ^c	4.98 ± 0.02 ^d
Test group 1 (200 mg /kg AEES + 70 mg/kg PTZ)	5.82 ± 0.74 ^b	4.02 ± 0.16 ^c	4.44 ± 0.27 ^b	1.95 ± 0.04 ^c
Test group 2 (400 mg/kg AEES + 70 mg/kg PTZ)	10.89 ± 0.58 ^a	6.38 ± 0.54 ^b	7.98 ± 0.75 ^a	0.1 ± 0.02 ^a
Standard Group (5 mg/kg Diazepam + 70 mg/kg PTZ)	11.08 ± 1.11 ^a	9.44 ± 1.38 ^a	7.08 ± 1.64 ^a	0.95 ± 0.03 ^b

The data are presented as the mean ± standard deviation for a sample size of 6. Different superscripts (a, b, c, d, e) indicate statistical significance ($p < 0.05$) among means within the same column (for each parameter).

Table 4 Mean levels of oxidative stress biomarkers in MES-induced seizure Swiss mice pretreated with Aqueous extract of *Emilia sonchifolia* (AEES)

Groups	SOD (U/mg Protein)	Catalase (U/mg Protein)	GPx (U/mg Protein)	MDA (U/mg Protein)
Control (10 ml/kg Distilled water)	2.08 ± 0.47 ^c	1.65 ± 0.75 ^c	2.28 ± 0.28 ^c	3.94 ± 0.01 ^d
Test group 1 (200 mg /kg AEES)	4.01 ± 0.08 ^b	3.82 ± 0.03 ^b	4.40 ± 0.04 ^b	1.06 ± 0.03 ^c
Test group 2 (400 mg/kg AEES)	6.97 ± 0.18 ^a	5.98 ± 0.12 ^a	6.44 ± 0.06 ^a	0.87 ± 0.21 ^b
Standard Group (5 mg/kg Diazepam)	6.43 ± 0.72 ^a	6.88 ± 0.63 ^a	6.63 ± 0.10 ^a	0.76 ± 0.12 ^a

The data are presented as the mean ± standard deviation for a sample size of 6. Different superscripts (a, b, c, d, e) indicate statistical significance ($p < 0.05$) among means within the same column (for each parameter).

4. Discussion

The present study examined the anticonvulsant and antioxidant effect of aqueous extract of *Emilia sonchifolia* (AEES) on both PTZ and MES-induced seizure models and assessing of the oxidative stress biomarkers in the brain tissue. The results demonstrate a dose-dependent anticonvulsant effect in both models, along with significant enhancement of endogenous antioxidant status by AEES, suggesting a dual neuroprotective mechanism.

Pretreatment with AEES significantly delayed the onset of convulsions and reduced mortality in the PTZ-induced seizure model compared to the control group (Alyami et al., 2020). The 400 mg/kg dose was also more protective, as all mortality and significant differences in seizure duration were avoided as compared to the 200 mg/kg group (Alyami et al., 2020). PTZ is reported to cause seizures mainly by antagonizing the GABA A receptors, which decrease the inhibitory neurotransmission and increases neuron hyperexcitability (Khotimah et al., 2024; Bryson et al., 2023). The delay in seizure onset and decrease in mortality seen in the case of AEES suggest the potential enhancement of GABAergic transmission or excitatory pathways inhibition (Perucca et al., 2023). The full protection of diazepam once again proves the sensitivity of the model (Zhang et al., 2022).

AEES drastically decreased the duration of the hindlimb tonic extension (HLTE) in the widely used MES model, which is effective in assessing agents effective against generalized tonic-clonic seizures (Alyami et al., 2022). The dose of 400 mg/kg yielded significant reduction of seizure duration in all the times of observation and the death rate was lower than

the control (Alyami et al., 2022). The protective action of AEES could signify either the balancing of sodium channel activity or inhibition of excitatory neurotransmission since MES-induced seizures are linked to disrupted neuronal firing through voltage-gated sodium channels and glutamatergic signaling (Kalra 2024).

One of the advantages of this research is the integration of biochemical studies. Oxidative stress and lipid peroxidation revealed by PTZ and MES seizures caused a significant decrease in the level of antioxidant enzymes (SOD, catalase and GPx) and an increase in the level of MDA in control animals (Alyami et al., 2022; Lukawski and Czuczwar, 2023). Both AEES treatment had a strong dose-dependent ability to restore SOD, catalase and GPx activities and lower the level of MDA in both seizure models (Alyami et al., 2022). Notably, the 400 mg/kg dose exhibited antioxidant effects comparable to diazepam across several parameters.

The results suggest that inhibition of oxidative stress can be one of the mechanisms that mediate the anticonvulsant effects of AEES. Oxidative damages are increasingly recognized as one of the major factors in seizure initiation and propagation (Łukawski et al., 2023; Kosmider et al., 2023). The antioxidant and neuroprotective properties of the phytochemical constituents that have already been reported in *E. Sonchifolia* such as flavonoids, phenolics, alkaloids and terpenoids are known (Ezeako et al., 2023; Usman et al., 2025). Other researchers have identified flavonoids to regulate GABAergic transmission and decrease neuronal excitability (Rios et al., 2023), which can be considered as the possible explanation of the pharmacological effects.

The 200 mg/kg dose provided partial protection, significantly reducing seizure duration compared to control, though less effectively than the 400 mg/kg dose (Alyami et al., 2022). This may suggest some form of protection that is not enough to inhibit the spread of the seizures at lower doses. The good dose-response correlation proves the pharmacological appropriateness of the extract.

This research gives experimental evidence about the traditional application of *E. sonchifolia* in neurological conditions (Asaje et al., 2006). A combination of anticonvulsant and antioxidant effects indicate that AEES could have the positive effects of both neurotransmitter and radical scavenging (Firdous et al., 2025).

5. Conclusion

The findings of this research demonstrate that aqueous extract of *Emilia sonchifolia* has substantial anticonvulsant effect on PTZ and MES induced seizure models. The extract also delayed onset of seizures, reduced seizure duration, lowered death rates and enhanced endogenous antioxidant defence mechanisms in a dose-dependent manner.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare no conflict of interest.

Statement of ethical approval

Experimental procedures were all conducted under the Niger Delta University guidelines of care and use of laboratory animals in the biomedical research and approved by the University Animal Ethics Committee.

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