Trop J Nat Prod Res, January 2026; 10(1): 6906 – 6912 **ISSN 2616-0684 (Print)**
ISSN 2616-0692 (Electronic)

Tropical Journal of Natural Product Research

Available online at https://www.tjnpr.org

Original Research Article

Anticonvulsant Effects of Fresh *Musa paradisiaca* Stem Juice in Pentylenetetrazole (PTZ)-Challenged Wistar Rats

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ARTICLE INFO

Article history:
Received 15 August 2025
Revised 29 October 2025
Accepted 08 November 2025
Published online 01 February 2026

ABSTRACT

This study aims to evaluate the antiseizure effect of *Musa paradisiaca* stem juice (MSJ). A pentylenetetrazole (PTZ) seizure model involving 36 adult male Wistar rats, randomly distributed into six groups (n = 6) was used in this study. Group 1 - normal control, group 2 - positive control, and group 3 (4 mg/kg b.wt. diazepam, p.o.). Groups 4, 5, and 6 received 50, 75, and 100% v/v MSJ, p.o., respectively. The PTZ (85 mg/kg b.wt., i.p.) was administered 45 min later, on the 10th day. The rats were monitored for convulsions. The results of the lethality test showed that MSJ is not relatively safe at a very high dose. The phytochemical screening revealed several bioactive compounds, with phenols being the most abundant (9.46 ± 0.03 mg/g), followed by alkaloids (5.54 ± 0.98 mg/g) and flavonoids (4.27 ± 1.23 mg/g). Three notable seizure episodes, 1, 2, and 3, were observed. At 75 and 100% v/v, MSJ significantly ($p < 0.05$) increased the latency periods of episode 1 (tonic and clonic) seizures. A 50% v/v of the juice delayed the onset of episode 2 seizures for more than 10 min, compared to that of the untreated group. The 75% and 100% v/v MSJ-treated groups did not show any seizures during episode 2, as observed in episode 1. The standard and test groups did not experience convulsions during episode 3. The findings of this study demonstrated that fresh MSJ offers promising anticonvulsant activity.

Keywords: *Musa paradisiaca*, seizure episode, phytochemical, convulsion, pentylenetetrazole, anticonvulsant, epilepsy.

Introduction

Over the years, seizure disorders, commonly known as epilepsy, have been a serious medical concern because of the burden of psychosocial stigma it places on individuals, which ruins their relationships, marriages, homes, family ties, etc. This disease is a dreaded neurological disease that produces spontaneous and recurrent seizures that result in a brief lapse of attention, and muscle jerks. [1] These muscle jerks are known as convulsions and are characterized by abnormal body movement resulting from increased muscle tone. According to reports, more than 50 million people worldwide suffer from seizure disorders. Above 80% of them live in sub-Saharan Africa and Asia, with extremely low living standards. [2] This could be as a result of prevalence of predisposing factors including infections of the brain, cranial shocks, and perinatal traumas in these countries. [3] In general, great efforts have been made to provide a panacea for neurological disorders, but the treatment of epilepsy has been limited. Recently, several licensed antiseizure medications (ASMs) have been used, but none has neither

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Citation. Ugwuoke C S, Amah C C , Ugwu C O, Ogugofor O M, Eze H I, Okoro J I, Anosike A C . Anticonvulsant effects of fresh *Musa paradisiaca* stem juice in Pentylenetetrazole (PTZ)-challenged Wistar rats. Trop J Nat Prod Res. 2025; 10(1): 6906 – 6912 https://doi.org/10.26538/tjnpr/v10i1.63

Official Journal of Natural Product Research Group, Faculty of Pharmacy, University of Benin, Benin City, Nigeria.

cured nor relapsed the condition completely. Many of these drugs lead to debilitating side effects like cognitive dysfunction and other intolerant issues. [4, 5] Even the commonest ASMs on the market such as benzodiazepines (e.g. diazepam), are associated with a lack of coordination and sleepiness. [6] Literatures have shown that about 30% of patients continue to experience seizure-related crises, even with the use of ASMs. [7, 8]However, there is a need to develop more biofriendly pharmacological formulations that can overcome these challenges.

Musa paradisiaca L. (Plantain) is a plant that has reportedly been used by some herbalists to manage seizures or convulsions in southeastern Nigeria. These herbalists usually extract juice freshly from the plant stem without adding water or other solvents since there is inherently enough water in the stem. This is administered to people living with epilepsy (PLWE) or those suffering from convulsions. In Enugwu-Ezike, Enugu State, Southeast Nigeria, patients with febrile or infantile convulsions are, sometimes, treated with the mother's early morning urine. Other preventive approaches include the utilization of locally-extracted palm kernel (PK) oil, ripe tomatoes, etc. [9] *M. paradisiacal* plants share several morphological features with *Musa sapientum* (banana), in that they both belong to the same family, 'Musaceae'. Moreover, while *Musa paradisiacal* trees are larger and taller, *Musa sapientum* trees have thicker trunks and leaves. [10] The two plants have been used substitutably to manage seizures, especially

infantile (febrile) convulsions in different communities in the south-eastern region of Nigeria. *Musa paradisiaca* is most commonly used in places like Nsukka (Enugu State), Agulu (Anambra State), and Obowo (Imo State). [9] Traditionally, different parts of the *Musa paradisiaca*, like the leaves, the sap, roots, and flowers, have reportedly been used to manage seizures. For instance, the sap is used to cure epilepsy, dysentery, hysteria, diarrhoea, and the fruit serves as food; the leaf extract is used for healing wound, cuts and insect bites; the leaves can trigger abortion; whereas a cold infusion of the root is used to treat venereal diseases and anaemia. [11] The fruit has reportedly been used as a " man power" (aphrodisiac), an anti-scurvy (antiscorbutic), and a diuretic agent.[12] A recent literature on *Musa paradisiaca* have revealed the presence of phytoconstituents like flavonoids, phenolic compounds, and others such as tannins, alkaloids, and saponins.[12, 13] A more recent study on epilepsy revealed that *Musa paradisiacal* stem juice (MSJ) has a positive therapeutic effect on epilepsy by altering some biochemical parameters like γ-amminobutyric acid and glutamate levels, γ-amminobutyrate transaminase (GABA-T) activity, and the brain histology.[9]
To date, no study has documented or reported the anticonvulsant effects of fresh MSJ on PTZ-challenged rats. The present study aims to bridge this gap by providing scientific justification as a potential lead in the management of seizure disorders or convulsions.

Materials and methods

Materials
Plant material
Freshly-harvested samples of *Musa paradisiaca* L. stems were utilized for this study. They were obtained from a farm located at Uwani Akpotoro Obimo (Obeke village) in Nsukka Local Government Area of Enugu State in south-eastern part of Nigeria at about 8: 00 hours on 13th February, 2022. Mr. Alfred Ozioko, the chief taxonomist of the International Centre for Ethnomedicine and Drug Development (InterCEED) (located at No. 110 Aku Road, Box 3138 Nsukka, Enugu State), identified and authenticated the plant specimen. The specimen (Voucher No.: InterCEDD/16058) was deposited to the Department of Plant Science and Biotechnology (PSB)'s herbarium unit at the University of Nigeria, Nsukka (UNN), for future reference.

Experimental animals
Seventy-two (72) animals were included in the experiment, 36 adult nonpregnant female mice (18-26 g) and 36 adult male Wistar rats (120-220 g). Toxicity studies were done using mice, while anticonvulsant studies were performed using rats. The experimental animals were obtained from the animal house of the Department of Pharmacology and Toxicology, UNN. The acclimatization of animals were done for seven days using polyethylene cages maintained at 25 ± 2ºC at room temperature with 55% humidity and a 12 h dark cycle. They were provided with a free access to standard pellets (Guinea Feeds Plc, Nigeria) and clean water *ad libitum*. All experiments involving the animals were carried out following the Guide for the Care and Use of Laboratory Animals provided by the National Research Council and approved by the Faculty of Biological Sciences' Ethics Committee on the Use of Laboratory Animals, UNN (Ref. No: UNN-FBS-EC-1090).

Methods
Preparation of M. paradisiaca L. stem juice
A freshly-collected sample of *M. paradisiaca* L. stem was sliced and washed free of dirt particles. It was further crushed into smaller pieces using a plastic pestle and mortar. The juice was filtered out and diluted into different concentrations with distilled water. The extraction was done daily, and the MSJ was administered to the rats freshly prepared throughout the 10-day experimental period. In accordance with the dosing method of Onyenekwe *et al.* [12], a dose of 100% (v/v) was prepared from MSJ (100 ml); 75% (v/v) was prepared from MSJ (75 ml) made up to 100 ml with distilled water; 50% (v/v) was prepared from MSJ (50 ml) made up to 100 ml with distilled water; and 25% (v/v) was prepared from MSJ (25 ml) made up to 100 ml with distilled water in a volumetric flask. At these concentrations, the experimental rats were fed on the basis of their body weights (Table 1).

Qualitative phytochemical analysis of M. paradisiaca L. stem juice
The preliminary qualitative phytochemical analysis of MSJ was carried out via a standard method described by Trease and Evans. [14] The MSJ was tested for the presence of flavonoids, alkaloids, phenol, saponins, tannins, terpenoids, and steroids.

Quantitative phytochemical analysis of M. paradisiaca stem juice
The following phytoconstituents detected in MSJ which includes alkaloids, flavonoids, phenol, saponins, tannins, steroids and terpenoids, were quantified using standard procedures as described by Harbone [15], Soni and Sosa [16], and Ladan *et al*. [17]

Toxicity and lethality (LD_{50}) study
The median lethal dose (LD_{50}) of MSJ was determined in mice via Karber's modified arithmetic method as described by Aliu and Nwude. [18] Thirty-six (36) nonpregnant female mice were used for this study, and they were divided into six groups of six animals each. Groups 1, 2, 3, 4, 5, and 6 were given different doses of the juice (5, 15, 25, 50, 75, and 100% v/v, respectively) via oral intubation for 7 days. The mice were monitored for 7 days for toxicity and mortality signs.
This was achieved via the arithmetic below:
$LD50 = LD100 - \sum(\mathrm{Md} \times \mathrm{Dd})/n$
n = total number of mice per group
Dd = differences between two successive doses of MSJ administered
Md = average number of dead mice in two successive doses
LD_{50} = Lethal dose causing 50% death in all test animals
LD100 = Lethal dose causing 100% death of all test animals

Experimental design (anticonvulsant study)
A PTZ (pentylenetetrazole)-induced seizure model was used in this study according to Gupta *et al*. [19] involving Wistar rats (n = 36), randomly divided into six groups of 6 rats each (n = 6). The animals were given freshly-prepared MSJ via oral intubation. Group 1 received normal saline (p. o.) and served as the normal control, whereas group 2 was untreated. Group 3 (i.e., standard control) received diazepam (4 mg/kg b. w., p. o.); Groups 4, 5, and 6 received 50, 75, and 100% (v/v) MSJ, respectively. A 10-day treatment period was observed before seizure induction with PTZ. The actual volume (in ml) of MSJ given to each rat according to their body weight (in grams) was evaluated by dividing the weight of each rat by 1 kg (i.e., 1000 g) body weight (b. wt.) of MSJ, and multiplying with 5 ml (OECD standardized minimum volume of drug that an experimental animal can receive). [19, 20]

Mathematically,

$$\textbf{Actual volume (ml)} = \frac{\boldsymbol{Bodyweight\ (g)}}{\boldsymbol{1{,}000g}} \times \mathbf{5}\ \boldsymbol{ml}$$

For example, for a rat weighing 137 g in group IV (50% v/v), the actual volume of MSJ that the rat received was determined as follows:

Since 1,000 g = 1 kg body weight

A rat weighing 137 g will receive $= \frac{137g}{1{,}000g}$, multiplied by the OECD standard volume, which is 5 ml. This gives $\frac{137\ g}{1{,}000g} \times \mathbf{5}\ \boldsymbol{ml}$= 0.69 ml, implying that the rat weighing 137 g received 0.69 ml of MSJ from a 50% v/v concentrate. The calculations were carried out for all the rats within each group, as summarized in Table 1

Induction procedure
Seizure was induced in the Wistar rats on the last day (i.e. on day 10) of treatment. All the experimental groups were injected with PTZ (85 mg/kg b. w., i. p.) 45 min after treatment with MSJ, except those in group 1. 21 The animals were closely observed for signs of seizures.
The experimental protocol was as follows:
Group 1: Normal control (normal saline only)
Group 2: Positive control (normal saline + PTZ)

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

Group 3: Standard control (4 mg/kg diazepam + PTZ)
Group 4: 50% (v/v) MSJ + PTZ
Group 5: 75% (v/v) MSJ + PTZ
Group 6: 100% (v/v) MSJ + PTZ

Evaluation of antiseizure activity
Seizure sign were observed at different time intervals (episodes). Tonic and clonic seizure latencies as well as durations were noted using a stopwatch in accordance with the methods of Gupta *et al.* [21] Tonic seizures were recorded on the basis of the stiffness of the muscles, whereas clonic seizures were on the basis of the involuntary twitching/jerking movements of the rats' muscles.

Justification for the use of crude stem juice
The use of crude MSJ was to mimic traditional usage, where herbalists and indigenous communities often use stem juice without processing (fractionation and extraction processes).

Statistical analysis
One-way ANOVA with repeated measures was used to analyse the data followed by multiple comparisons by Post-hoc test using SPSS version 21 (IBM, SPSS Inc.). The results are expressed as mean ± SDs, and a p-value < 0.05 was considered significant.

Results and Discussion

Phytochemical screening of MSJ

Plants serve as a factory for certain metabolites which play important pharmacological roles when consumed by animals such as alkaloids, phenols, flavonoids, tannins, saponins, steroids, etc. These compounds are found in diverse concentrations in different plants. In this study, the preliminary phytochemical screening of MSJ revealed the presence of flavonoids, alkaloids, phenols, tannins, saponins, and steroids, with no terpenoids (Table 2). In terms of the relative abundance, phenols were relatively highly abundant (9.46 ± 0.03 mg/g), flavonoids, alkaloids, and tannins were present in moderate concentrations – (5.54 ± 0.98, 4.27 ± 1.23 and 3.64 ± 0.02 mg/g, respectively). The high phenolic compounds found in MSJ could be responsible for its anticonvulsant activities. This aligns with earlier studies in which phenolic compounds like flavonoids and other phenolics have demonstrated anticonvulsive effects. [22, 23, 24, 25] Saponins and steroids were found at low concentrations (1.27 ± 0.01 and 0.84 ± 0.03 mg/g, respectively) agreeing with other studies that reported anticonvulsant activities of some of the bioactive compounds found in MSJ at moderate and trace amounts including tannins, alkaloids, saponins and steroids. [25, 26, 27] Flavonoids, being an important class of compounds in nature, play an important role in modulating the treatment of neurodegenerative disorders. This is reportedly due their phenolic nature which enables them to alter cellular oxidation within the nervous system. [28, 29] Some researchers have also argued that flavonoids possess central nervous system activities, and a strong binding affinity for $GABA_A$ receptors which may underlie its anticonvulsant effects. [30]

Table 1: Actual volume of stem juice administered on the basis of body weight following OECD guidelines

Group IV (50% v/v)						
Body weight (g)	137	208	121	183	146	157
Volume administered (ml)	0.69	1.04	0.61	0.92	0.73	0.79
Group IV (75% v/v)						
Body weight (g)	120	132	180	130	162	210
Volume administered (ml)	0.60	0.67	0.90	0.65	0.81	1.05
Group IV (100% v/v)						
Body weight (g)	142	173	182	200	122	208
Volume administered (ml)	0.71	0.87	0.91	1.00	0.61	1.04

Table 2: Phytochemical screening of MSJ

S/N	Phytoconstituents	Relative Abundance	Amount (mg/g)
1	Alkaloids	++	5.54 ± 0.98
2	Flavonoids	++	4.27 ± 1.23
3	Phenol	+++	9.46 ± 0.03
4	Saponins	+	1.27 ± 0.01
5	Tannins	++	3.64 ± 0.02
6	Steroids	+	0.84 ± 0.03
7	Terpenoids	ND	-

The values are presented as the mean ± SDs.
Key: Low Concentration (+); Moderate Concentration (++); High Concentration (+++); Not detected (ND)

Table 3: Results of the toxicity test of MSJ

Group	No. of Animal (n)	Dose (% v/v)	Dose Diff. (Dd) (% v/v)	No. of Death Each Day							Total Death in 7 days	Mean Death (Md)	Dd × Md
				Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7			
1	6	5	10	0	0	0	0	0	0	0	0	0	0
2	6	15	10	0	0	0	0	0	0	0	0	0	0
3	6	25	25	0	0	0	0	0	0	0	0	0	0
4	6	50	25	0	0	0	0	0	0	0	0	0	0
5	6	75	25	0	0	0	0	0	1	0	1	0.5	12.5
6	6	100	25	0	0	0	0	0	1	1	2	1.5	37.5
Sum (∑)												=	50

ISSN 2616-0684 (Print)
ISSN 2616-0692 (Electronic)

$$LD50 = LD100 - \sum(Md \times Dd)/n = 150 - \sum(50)/6 = 50 - 8.33 = 41.67\% \text{ v/v}$$

Determination of toxicity

A dose-dependent toxicity effect of MSJ were observed in this study (Table 3), where no mortality or behavioural changes were observed in groups 1-4, which received 5, 15, 25, and 50% v/v of the juice, except in groups 5 and 6, where only one and two mice died, respectively. This showed that MSJ is relatively safe, but continuous or prolonged administration at high dose could be lethal. The calculated mean lethal dose (LD50) of 41.67% (v/v) confirms this. Moreover, no signs of convulsion were observed in the mice used for the toxicity studies, indicating that it is does not induce convulsions. The results of the histological examination carried out in earlier study by Ugwuoke *et al*. [9] confirmed the safety of MSJ, where no necrosis was found in the brain tissues of rats fed with three graded doses (50, 75, and 100% v/v) of MSJ. Furthermore, this study agrees, to some extent, with the work of Onyenekwe *et al*. [12] who investigated the phytoconstituents of *Musa paradisiaca* L. stem extrude and their effects on rats' haematological parameters, where all four (4) graded doses (25, 50, 75, and 100% v/v) were found to be safe among the tested animals. At present, no literature has reported, or documented any form of lethality on any part of the *M. Paradisiacal*, further suggesting its safety.

Episode 1 anticonvulsant effect of MSJ on PTZ-induced seizures

PTZ, an agonist of GABA, induces convulsions by blocking the binding of GABA (an inhibitory neurotransmitter) to its receptor on the synapse, favouring glutamate (an excitatory neurotransmitter) binding to its receptor, thereby resulting to uncontrollable neuronal misfiring or excitation. [31] Tonic seizure is seizure event (episode) that occurs within 20 seconds where the muscle tone is increased or the limbs become stiff as a result of increased tension. [32] Clonic seizure events involve uncontrollable jerking movements of the muscles on the limbs. [32] Latency to seizure events is the time different between when a PTZ was administered to the animal and when seizures manifested, while seizure duration is the time which seizure event lasted. [33] The longer the latency to the manifestation of seizure, the lesser the animal is likely to have seizure, and the shorter the latency, the more the animal is predisposed to seizures.

Table 4: Episode 1 anticonvulsant effect of MSJ on PTZ-induced seizures

Groups	Tonic seizure latency (min)	Clonic seizure onset (min)	Clonic seizure duration (min)	Status of animals after Episode 1
1	-	-	-	Alive/Active
2	4.96 ± 1.19^{a}	5.44 ± 1.28^{a}	1.31 ± 0.77^{a}	Alive/Active
3	7.46 ± 5.86^{a}	$8.11 \pm 6.71^{a, b}$	0.65 ± 0.54^{a}	Alive/Active
4	$10.44 \pm 1.23^{a, b}$	$11.26 \pm 1.38^{a, b}$	0.64 ± 0.36^{a}	Alive/Active
5	21.93 ± 8.60^{c}	23.62 ± 9.64^{c}	0.89 ± 0.58^{a}	Alive/Active
6	$15.22 \pm 2.61^{b, c}$	$16.07 \pm 2.67^{b, c}$	0.64 ± 0.52^{a}	Alive/Active

The data are expressed as the means ± standard deviations (n = 6). Means with different superscripts down the column are significantly ($p < 0.05$) different.

Group 1: Normal control (normal saline only)
Group 2: Untreated Control (normal saline + PTZ)
Group 3: Standard control (4 mg/kg b.w. diazepam) + PTZ
Group 4: 50% (v/v) MSJ + PTZ
Group 5: 75% (v/v) MSJ + PTZ
Group 6: 100% (v/v) NSJ + PTZ

Table 5: Episode 2 anticonvulsant effect of MSJ on PTZ-induced seizures

Groups	Latency of clonic seizures (min)	Duration of clonic seizures (min)	Status of Animals
1	-	-	Alive/Active
2	12.90 ± 0.92^{b}	0.67 ± 0.40^{b}	Alive/Weak
3	12.72 ± 8.75^{b}	$0.36 \pm 0.18^{a, b}$	Alive/Active
4	25.82 ± 1.04^{a}	$0.23 \pm 0.18^{a, b}$	Alive/Active
5	NC	NC	Alive/Active
6	NC	NC	Alive/Active

The data are expressed as the means ± standard deviations (n = 6). Means with different letters as superscripts down the column are significantly ($p < 0.05$) different; NC: no convulsion

Group 1: Normal control (normal saline only)
Group 2: Untreated Control (normal saline + PTZ)
Group 3: Standard control (4 mg/kg b.w. diazepam) + PTZ
Group 4: 50% (v/v) MSJ + PTZ
Group 5: 75% (v/v) MSJ + PTZ
Group 6: 100% (v/v) MSJ + PTZ

Table 6: Episode 3 anticonvulsant effects of MSJ on PTZ-induced seizures

Groups	Onset of clonic seizure (min)	Duration of clonic seizure (min)	Status of Animals
1	-	-	Alive/Active
2	19.41 ± 1.21	1.32 ± 0.77	Alive/very weak
3	NC	NC	Alive/Active
4	NC	NC	Alive/Active
5	NC	NC	Alive/Active
6	NC	NC	Alive/Active

The data are expressed as the means± standard deviations (n = 6). Means with different letters as superscripts down the column are significantly ($p < 0.05$) different; NC: no convulsion

Group 1: Normal control (normal saline only)
Group 2: Untreated Control (normal saline + PTZ)
Group 3: Standard control (4 mg/kg b.w. diazepam) + PTZ
Group 4: 50% (v/v) MSJ + PTZ
Group 5: 75% (v/v) MSJ + PTZ
Group 6: 100% (v/v) MSJ + PTZ

Base on this study, 50, 75, and 100% v/v MSJ increased the latency of tonic and clonic seizures induced by PTZ; and reduced the duration of clonic seizure (Table 4). Also, from the result of this study latency times for tonic seizures in groups 5 and 6 (21.93 ± 8.60 min and 15.22 ± 2.61 min, respectively) were significantly ($p < 0.05$) longer in the 75 and 100% (v/v) MSJ-treated groups, compared with those in group 2 (4.96 ± 1.19 min). The dose-dependent increase in the latency periods of tonic/clonic seizures in the test groups (4 and 5), as observed in episode 1, is an indication of the anticonvulsant potential of MSJ, whereas the deviation observed in group six may be an aberration resulting from external factors such as human error. Similar findings were reported by Dare *et al*. [34] who observed a dose-dependent rise in the latency period of seizures induced by PTZ in Wistar rats after treatments with kaurenoic acid isolated from *Annona senegalensis* leaves. Also, from the result, the latency period of clonic seizures (11.26 ± 1.38 min) in group 4 was significantly ($P < 0.05$) higher (23.62 ± 9.64 and 16.07 ± 2.67 min, respectively) compared with those of groups 5 and 6, which received 75% and 100% v/v MSJ respectively. This agrees with the results obtained by Rehab *et al*. [35] in which there was a delayed onset of seizure in rats given 500 mg/kg b.w. of both *Cichorium intybus* and *Taaraxacum serotinum*. According to Wang *et al*. [36], a notable ameliorative effect was demonstrated by *Amomum tsaoko* fruit extract on PTZ-induced tonic and clonic convulsions. However, the increment observed in the tonic seizure latency period could be due to the presences of bioactive compounds such as phenolics or flavonoids in MSJ stimulate GABAergic neurotransmission, thereby resulting in a hyperpolarizing effect in the rat brain.

A previous study reviewed the calming or sedative effects of MSJ owing to its ability to increase the levels of GABA (an inhibitory neurotransmitter) compared with the levels of glutamate (an excitatory neurotransmitter) in the brains of experimental rats. [9] The significant increment in the tonic seizure latencies seen in groups 5 and 6 implies that MSJ manifested a greater calming effect on the central nervous system than diazepam at the dose used in this study. [37] The clonic seizures duration was slightly reduced as a result of the administration of MSJ. This study revealed that 75 and 100% (v/v) MSJ led to a marked increase in the latency time of clonic seizures. This implies that the stem juice might have some levels of protection against glutamate-mediated excitotoxicity of the central nervous system as shown by Kaushik *et al.* [38] on the ethanolic extract of *Bacopa monniera* in different models of convulsion. These results further provided additional evidence that MSJ has great antiseizure potentialities.

Episode 2 anticonvulsant effect of MSJ on PTZ-induced seizures

Another level of seizure events were observed in this study where 50% v/v of MSJ significantly ($p < 0.05$) increased the latency time (25.82 ± 1.04 min) of clonic seizures in group 4 when compared to that of group 2 (12.90 ± 0.92 min). Similarly, 50% (v/v) MSJ significantly ($p < 0.05$) increased the latency period of group 4(25.82 ± 1.04 min) when compared with that of group 3 (12.72 ± 8.75 min). This revealed that only group 2 (untreated) and group 3 (standard group) as well as the group administered with a low dose of MSJ (group 4), experienced seizures, suggesting that high doses of stem juice exert better anticonvulsant effects. This finding aligns with the observed increase in the latency period of clonic convulsions induced with PTZ in mice following oral doses of *Otostegia limbata L* extract. [39] In this episode, no clonic seizures were observed at 75 and 100% (v/v), which implies that at a relatively high dose, convulsion was inhibited completely by MSJ. All convulsive rats in each group were alive and also active during this episode, with the exception of those of the untreated group, which displayed some levels of feebleness, showing the extent of a possible neurotoxicity induced by PTZ.

Episode 3 anticonvulsant effects of MSJ on PTZ-induced seizures

The last seizure event (episode 3) shows that only group 2 (untreated) experienced clonic seizures (Table 6). Group 3 and test groups (groups 4 - 6) did not experienced any sign of seizures. Rats in the untreated group survived, but showed persistent weakness after the episode. Based on these findings, it could be noted that fresh MSJ possessed anticonvulsant activities similar to diazepam. The persistent weakness noticed in the rats of the untreated groups could be an indication of the extent to which PTZ has damaged the rat's neuronal cells, as shown in a previous brain histological study by Ugwuoke *et al.*[9] Similarly, it was observed that *n*-hexane and *n*-butanol residual aqueous (RAF)

fractions of *Ipomoea asarifolia* leaves showed a strong anticonvulsant effect against seizures induced by PTZ in mice; which was reported to be as a result of their high flavonoid content. [40] In this episode, the fact that all experimental rats in each of the groups were alive and active with the exception of those in group 2 which rarely survived, but appeared very weak after this episode, is a testament that the MSJ possess antiseizure potential. This study would have benefited from being more extensive, but a lack of adequate resources was a limiting factor. Moreover, the anticonvulsant activity of MSJ should be investigated using other important models of seizure like the Maximal electroshock (MES), strychnine, as well as isoniazid (INH).

Conclusion

The findings revealed that MSJ offers promising anticonvulsant activity because of its ability to significantly delay seizure onset and shorten its duration, thereby offering potential as a natural seizure management remedy. The stem juice demonstrated dose-dependent efficacy, in which higher doses resulted in stronger anticonvulsant effects, suggesting a controllable way to optimize its effectiveness and personalize treatment. This study provides scientific validation for its use traditionally. Further studies involving extraction, isolation, and characterization are require on fresh MSJ to ascertain the exact bioactive compound responsible for its anticonvulsant activity.

Conflict of Interest

The authors declare no conflict of interest.

Authors' Declaration

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

Acknowledgements

The authors acknowledge Prof. Sabinus Oscar O. Eze, (HOD Biochemistry, UNN), as well as Prof. P. E Joshua, (the former PG programme coordinator, Biochemistry, UNN). for supplying the technical support and the facilities used in this work.

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