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Evaluation of Anticonvulsant Activity of Aqueous Leaf Extract of *Telfairia occidentalis* in Mice

Oloruntobi Joshua Imoru[1*], Oyemitan Idris Ajayi[1] and Ilesanmi Olapade Rufus[1]

[1]Department of Pharmacology, Faculty of Pharmacy, Obafemi Awolowo University Ile-Ife, Osun State, Nigeria.

Authors' contributions

This work emanated from the M.Phil. thesis of author OJI. Author OJI conceived and designed the study, performed and managed the literature search and statistical analysis, wrote the protocol and the first draft of the manuscript. Author IOR was the main supervisor while author OIA co-supervised the work. All authors read and approved the final manuscript.

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ABSTRACT

Aims: This work evaluated the anticonvulsant effect of aqueous leaf extract of *Telfairia occidentalis* in Mice. This was to validate the use of *T. occidentalis* in the treatment of sudden attack of convulsions in folkloric medicine.
Study Design: One-factor, two controls - three test groups experimental design.
Place and Duration of Study: Department of Pharmacology, Faculty of Pharmacy, Obafemi Awolowo University, Ile-Ife, Osun State, Nigeria, between October 2012 and January 2013.
Methodology: Anticonvulsant effect of *T. occidentalis* was evaluated using the following animal models of convulsion: strychnine, pentylenetetrazole (PTZ) and maximal electroshock (MES). Five groups of white albino mice (n = 6) were randomly selected. Group 1 was the control (normal saline, 10 ml/kg, i.p.), group 2 was the positive control (diazepam, 1 mg/kg, i.p.), while group 3, 4 and 5 were treated with aqueous leaf extract at 50, 100 and 200 mg/kg, i.p., respectively. All the

**Corresponding author: E-mail: tobiimoru@yahoo.com;*

animals in each group were pre-treated for 30 minutes before administration of PTZ (85 mg/kg, i.p.), strychnine (2 mg/kg, i.p.) or exposure to MES. The latency to convulsion, duration of convulsion and percentage protection from mortality were recorded in each group.
Results: *T. occidentalis* (50, 100 and 200 mg/kg) was not effective in preventing strychnine and PTZ-induced convulsions, and did not prevent Hind Limb Tonic Extension (HLTE) in MES.
Conclusion: Aqueous leaf extract of *Telfairia occidentalis* did not show significant anticonvulsant activity as claimed in folkloric medicine.

Keywords: Telfairia occidentalis; anticonvulsant activity; maximum electroshock; aqueous extract.

1. INTRODUCTION

Telfairia occidentalis (synonym: *Telfairia occidentale*; Family: *Cucurbitaceae*) is a native to the tropical rainforest of West Africa with the largest diversity in Southern Nigeria. Different species of *Telfairia* are also grown as leaf vegetables in other tropical regions of the world including: India, Bangladesh, Sri Lanka and the Caribbean. It is also grown to some extent in South Africa and Latin America [1,2]. *T. occidentalis* is a perennial plant with large fluted fruit. It is dioecious and drought-tolerant. It is a creeping vegetable shrub that spread low across the ground with simple, dark green large lobed leaves that are as wide as 18 cm and long as 35 cm [2-4].

The ethno-social uses of *T. occidentalis* are seen among the Igbos of the Southern part of Nigeria where it is extensively cultivated as vegetable and food crop [5]. The young shoots and leaves of the seeds are cooked and eaten as such or used in preparing soup [2]. The seeds are known to have oil and protein composition of 29% and 30% respectively [6]. The roots are known locally as potent human poison and there are reports of their use as fish and human poisons [7].

Odugbemi and Akinsulire [8] reported that the leaf of *T. occidentalis* is used as blood tonic in the treatment of gastrointestinal disorders and in the treatment of convulsions. Gbile [9], Alada [10], Ukwuoma and Muanya [11] also reported that in folkloric medicine, the fresh leaves are used in the treatment of anaemia, malaria and sudden attack of convulsions.

Minerals such as calcium, potassium, magnesium, iron, sodium and phosphorus are concentrated in the testa, pulp and husk of the plant [12]. The leaves together with the edible shoots contain 80% moisture, 11% crude protein, 25% carbohydrate, 3% oils, 11% ash and as much as 700 ppm of iron [13]. The nutritional content of *T. occidentalis* makes it desirable as dietary supplement for human [13]. The economic and nutritional advantage of *T. occidentalis* plant is its clear agronomic superiority over many plant protein sources [14].

While Tindall [15] reported that leaves of *T. occidentalis* contain oxalates, saponins, glycosides, flavonoids, alkaloids and resins, Ezugwu and Nwodo [16], in their studies on *T. occidentalis* and characterization of fixed oils from the seed, reported that, the leaf and stem of *T. occidentalis* contain tannins, reducing sugar, but absence of glycosides, saponins, alkaloids, flavonoids, sterols and triterpenoids. The root however, was said to contain tannins, reducing sugar, glycosides, saponins, sterols and triterpenoids, but absence of alkaloids and flavonoids.

Review of pharmacological studies on *T. occidentalis* revealed that dietary intake of the leaf could prevent garlic-induced haemolytic anaemia in rats [17]. Similarly, Alada [10] and Ajayi [18] reported increased haematological parameters from aqueous leaf extract of *T. occidentalis* in laboratory animals. Aderibigbe et al. [19], Nwajo et al. [20], and Eseyin et al. [21] reported that extract of *T. occidentalis* was observed to reduce blood glucose level in glucose induced hyperglycaemic, and to also have anti-diabetic effects in streptozotocin and alloxan induced diabetic laboratory animals. Oboh [22] reported that the aqueous extract of *T. occidentalis* has hepatoprotective effect against garlic-induced oxidative stress. Oluwole et al. [23] reported the anti-inflammatory effect of *T. occidentalis* in laboratory animals. *T. occidentalis* seed oil has been reported to ameliorate the effect of quinine induced testicular damage [24]. The seed oil, due to its high phosphorus content was said to be a potent agent in reducing kidney stone disease [25]. The anti-oxidative property of the seed oil was also said to enhance fertility [26]. Low dose of 400 mg/kg body weight of the seed oil could also improve sperm count and testicular histology in rats [27].

Convulsion is a medical condition where body muscles contract and relax rapidly and repeatedly, resulting in an uncontrolled shaking of the body. Because a convulsion is often a symptom of an epileptic seizure, the term convulsion is sometimes used as a synonym for seizure [28-29]. Epileptic seizure, according to the International League Against Epilepsy (ILAE), is a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain. While epilepsy is a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures, and by the neurobiological, cognitive, psychological and social consequences of this condition [30]. 20 – 30% of 50 million persons worldwide who suffer from epilepsy have seizure that are resistant to treatment with the currently available antiepileptic drugs [31]. For this reason, there is obvious need for development of new and more effective antiepileptic drugs. Therefore, numerous compounds are currently in their different stages of preclinical and clinical trials [32,33]. However, many rural dwellers of the developing countries still depend mostly on traditional herbal remedies for the management of seizures. Even though there are scientific reports available to support the folkloric medicinal use of some of the herbs in the management of seizures, many of them are still without documented scientific evidence of efficacy [34-37].

Folkloric medicinal information indicates that *T. occidentalis* is used in the treatment of sudden attack of convulsion. But there is paucity of information generally on the neuropharmaco-logical and specifically on the anticonvulsant profile of this plant. Hence this study was carried out to validate, or otherwise, the folklore claim of *T. occidentalis* of having anticonvulsant activity.

2. MATERIALS AND METHODS

2.1 Plant Material and Preparation of *Vernonia amygdalina* Extract

Fresh leaves of *Telfairia occidentalis* were purchased from Atakunmosa market in Ilesa Town, Ilesa –West Local Government Area of Osun State, Nigeria. On the 17th of August, 2012, and were authenticated by Mr. G. Ibhanesebhor of the Department of Botany, Faculty of Science, Obafemi Awolowo University. The voucher specimen of the leaves of plant was prepared and deposited at the Herbarium Unit of the Department of Botany, Faculty of Science, Obafemi Awolowo University, Ile-Ife, with Voucher No: IFE 16902.

Fresh leaves of *T. occidentalis* were collected, air-dried and milled into powder with the aid of electric grinder. A powdered leaf of *T. occidentalis (*353 g*)* was extracted cold in 7 litres of water with continuous shaking for 48 hours in a mechanical shaker. The mixture was filtered and the filtrate concentrated using a rotary evaporator at a maximum temperature of 45℃ to obtain the crude aqueous extract of the plant. Further drying of the extract was carried out using the freeze-dryer to obtain semi-solid extracts. The total dried aqueous extract obtained from 353 g of leaf of *T. occidentalis* was 90.84 g given 27.90% w/w yield. The semi-solid paste of the aqueous extract of the plant was then stored in the refrigerator at 4℃ until it was needed for use.

2.2 Experimental Animals

White albino mice of both sexes weighing between 23 g and 28 g were obtained from the Animal House, Department of Pharmacology, Faculty of Pharmacy, Obafemi Awolowo University (OAU), Ile-Ife, Osun State. The animals were kept under conducive laboratory conditions and fed with standard animal feed (Grower's mash), and water *ad libitum*. The "principle of laboratory animal care" (National Institute of Health-NIH publication No. 85-23) guidelines and procedures were followed in this study. The Ethical Committee of the Faculty Postgraduate Committee, Faculty of Pharmacy, Obafemi Awolowo University, approved the research work.

2.3 Drugs and Laboratory Materials

Diazepam (Valium® Swipha Nig. Ltd, Nigeria), pentylenetetrazole (PTZ, Sigma Chemicals Co. St. Loius, USA), Strychnine (Sigma Chemicals Co. St. Louis USA). Ugo Basile electroconvulsive machine (Model 57800, Ugo Basile Biological Research Apparatus, Italy), stop watch, weighing balance syringes and needles.

2.4 Administration of Extracts

The aqueous extracts were administered to mice through the intraperitoneal route. The volume of extracts administered intraperitoneally was 10 mL per kg or 0.1 mL per 10 g of body weight

of the animal in all cases. The intraperitoneal route was used in this study because it gives faster and more consistent results and test are readily reproducible. This route is preferred in CNS tests because of the possibility of interference of metabolic processes with the test agents given through the oral route [38].

2.5 Acute Toxicity

The acute toxicity (i.p. LD_{50}) of the aqueous leaf extract of *T. occidentalis* was estimated in 13 white albino mice using standard method of Lorke [39]. Briefly, this includes two phases: The 1st phase uses 3 animals for each dose level 10, 100 and 1000 mg/kg. The mice are kept under the same laboratory conditions and observed for signs of toxicity which include but is not limited to paw-licking, stretching, respiratory distress and mortality for the first critical four hours and after 24 hours the number of death per group is recorded. The result obtained from this test is used as a basis for selecting the subsequent doses in the 2nd phase following a standard table. The 2nd phase involved administering four different doses to one mouse per group and the mice are observed for signs of toxicity for the first critical four hours and thereafter 24 hours for mortality. The intraperitoneal median lethal dose (LD_{50}) was calculated as the geometric mean of doses that caused 0 and 100% mortality respectively. The $LD_{50} = \sqrt{(A \times B)}$, where A = maximum dose that caused 0% mortality and B = minimum dose that caused 100% mortality. The working doses (i.e. treatment doses) used in this experimental work were arrived at by the formula 1/3 x LD_{50}. All treatment doses were below the third of the LD_{50}.

2.6 Anti-convulsant Evaluation of *Telfairia occidentalis*

2.6.1 Pentylenetetrazole-induced convulsion in mice

The method of Swinyard et al. [40], was employed. Thirty mice of both sexes were randomly allotted into five groups of six mice each. The first group received 10 mL normal saline per kg body weight i.p., the second group was given 1.0 mg diazepam per kg body weight i.p., while the third, fourth and fifth groups received 50, 100 and 200 mg extract per kg body weight i.p. respectively. Thirty minutes later, mice in all the groups received 85 mg/kg (i.p.) pentylenetetrazole. Mice were observed for over a period of 30 minutes. Absence of an episode of clonic spasm of at least 5 seconds duration indicated a compound's ability to abolish the effect of pentylenetetrazole on seizure threshold.

2.6.2 Strychnine-induced convulsion in mice

The method of Porter et al. [41] was employed. Thirty mice of both sexes were randomly allotted into five groups of six mice each. The first group received 10 mL normal saline per kg body weight i.p., the second group was given 1.0 mg diazepam per kg body weight i.p., while the third, fourth and fifth groups received 50, 100 and 200 mg extract per kg body weight i.p. respectively. Thirty minutes later, mice in all the groups received 2.0 mg strychnine per kg, i.p. Abolition of tonic extensor jerks of the hind limbs was considered an indicator that the testing materials could prevent strychnine-induced convulsions.

2.6.3 Maximum electroshock-induced convulsion in mice

The method of Swinyard and Kufferberg [42] and Browning [43] was employed. Twenty-five mice of both sexes were randomly allotted into five groups of five mice each. The first group received normal saline 10 mL per kg body weight i.p., the second group received 1.0 mg diazepam per kg body weight i.p., while the third, fourth and fifth groups received 50, 100 and 200 mg extract per kg body weight i.p. Thirty minutes later, maximum electroshock was administered to induced seizure in the mice using Ugo Basile electroconvulsive machine (Model 57800) with an electrode clipped to each ear of the mice. The current, shock duration, frequency and pulse width were set and maintained at 18 mA, 1.0 s, 100 pulse per second and 0.5 ms respectively. Abolition of Hind Limb Tonic Extension (HLTE) was considered as protection from electroshock [41,44].

2.7 Statistical Analysis

Results are expressed as mean ± SEM. Statistical difference for parametric data was determined by one-way analysis of variance (ANOVA) followed by a post hoc test (Student Newman-Keuls Test (SNK)). Percentage protection and mortality were analyzed by non-parametric method (Chi square test). Difference was considered statistically significant with $p < 0.05$ for all comparisons. Computer software Graph pad PRISM® version 3.00 was used for the analysis.

3. RESULTS

3.1 Acute Toxicity

For the first critical four hours during the acute toxicity studies, animals that received higher doses of the aqueous leaf extract of *Telfairia occidentalis* were noticed to be passive and were also seen stretching, while those that received lower doses of extract were seen active when placed back into their home cages. However no death was recorded during the hours. The aqueous leaf extract of *T. occidentalis* was found to have median lethal dose (LD_{50}) in mice of 775 mg/kg i.p.

3.2 Effect of Aqueous Leaf Extract of *T. occidentalis* on Pentylenetetrazole (PTZ)-induced Convulsion in Mice

In the control group of animals, PTZ (85 mg/kg; i.p.) consistently induced tonic-clonic convulsions. There was 100% occurrence of tonic convulsion and mortality. While pretreatment with diazepam (1 mg/kg, i.p.) significantly suppressed both clonic and tonic PTZ convulsions, with 0% mortality, pretreatment with *T. occidentalis* at any of the tested doses did not block both the clonic and the tonic PTZ convulsions. However, while 100% mortality was recorded at 50 mg/kg of extract, 83% mortality was recorded at both 100 and 200 mg/kg of extract (Table 1).

3.3 Effect of Aqueous Leaf Extract of *T. occidentalis* on Strychnine-induced Convulsion in Mice

In the control group of animals, 2 mg/kg, i.p. of strychnine induced tonic-clonic convulsions in all the animals in the group and with 100% mortality. Neither 1 mg/kg of diazepam nor *T. occidentalis* at all the doses tested protected the animals against death. 100% mortality was recorded in all groups of animals. However, 1 mg/kg i.p of diazepam significantly ($F_{4,25}$ = 6.50; P < 0.01) delayed the onset of tonic convulsion induced by strychnine (Table 2).

3.4 Effect of Aqueous Leaf Extract of *T. occidentalis* on Maximum Electroshock-Induced Convulsion in Mice

In the control group, the entire animals exhibited hind limb tonic extension (HLTE) after electroshocks. Pretreatment with 1 mg/kg, i.p. of diazepam and *T. occidentalis* at all tested doses did not abolish HLTE (Table 3).

Table 1. Effects of aqueous leaf extract of *Telfairia occidentalis* on pentylenetetrazole-induced seizures in mice

Group	Dose (mg/kg)	Onset of clonus (min)	Onset of tonus (min)	% mortality
Saline	10 mL/kg	1.11±0.12	7.19±0.51	100.00
Diazepam	1	30.00±0.00*	30.00±0.00*	0.00*
Telfairia occidentalis	50	1.27±0.13	4.99±0.90	100.00
	100	1.10 ±0.12	9.78±4.19	88.33
	200	2.32±1.20	9.88±4.13	88.33

*Data are expressed in mean ± SEM of latencies to clonus and tonus, and percentage mortality (n = 6 per group). Significantly different from control: ANOVA followed by Newman-Keuls Multiple Comparison Test. Chi square test for % mortality. * p < 0.001*

Table 2. Effects of aqueous leaf extract of *Telfairia occidentalis* on strychnine -induced seizure in mice

Group	Dose (mg/kg)	Onset of tonic convulsion (min)	% Mortality
Saline	10 mL/kg	3.01±0.71	100
Diazepam	1	6.65 ±0.51*	100
Telfairia occidentalis	50	3.22±1.00	100
	100	4.03±0.73	100
	200	5.07±0.17	100

*Data are expressed in mean ± SEM of latency to tonic convulsion and percentage of mortality (n = 6 per group). Significantly different from control: ANOVA followed by Newman-Keuls Multiple Comparison Test. * p < 0.01*

Table 3. Effects of aqueous leaf extract of *Telfairia occidentalis* on maximal electroshock induced convulsion in mice

Group	Dose (mg/kg)	Onset of HLTE (sec)
Saline	10 mL/kg	1.90±0.14
Diazepam	1	2.38±0.23
Telfairia occidentalis	50	2.37±0.13
	100	2.21±0.27
	200	2.23±0.16

Data are expressed in mean ± SEM of latency to hind limb tonic extension (HLTE). ANOVA followed by Newman-Keuls Multiple Comparison Test

4. DISCUSSION

The aqueous leaf extracts of *Telfairia occidentalis* was found to have median lethal doses (LD_{50}) of 775 mg/kg, i.p. showing that this plant extract is moderately toxic to the experimental animal model (mice) used in this particular study. Ibrahim et al. [45] had reported a LD_{50} of 288.50 mg/kg, i.p. of ethanolic extract of VA in mice, claiming a relative toxicity to the animal model used in their study. Lorke [39], stated that substances toxic at less than 1 mg/kg are considered highly toxic; And considering that the LD_{50} estimates of these plant extracts are far above this toxicity level thus, these plant extracts are moderately toxic to the experimental animal model (mice) used in this particular study.

The result of anticonvulsant effect of *T. occidentalis* in this study showed that *T. occidentalis* did not possess significant anticonvulsant activities.

T. occidentalis at all doses tested in this study did not prevent convulsions in PTZ and strychnine models; and also did not protect against hind limb tonic extension (HLTE) in the MES model. Anticonvulsant activity in PTZ model identifies compounds that can raise the seizure threshold in the brain [46].

Antiepileptic drugs that are effective in the treatment of generalized tonic-clonic and partial seizures such as phenytoin, carbamazepine, oxcarbazepine and lamotrigine suppress HLTE in MES model [43]. Strychnine is a competitive antagonist of glycine [47], and as such, the absence of anticonvulsant activity in the strychnine-induced convulsion model, suggests that the extract of *T. occidentalis* may not interact with glycine receptors.

Anticonvulsant drugs that are administered in the treatment of epilepsy (which does not necessarily cause convulsions) as well as non-epileptic convulsion disorders act through three main mechanisms: Enhancement of GABA action, inhibition of sodium channel function and inhibition of calcium channel function.

Other mechanisms include inhibition of glutamate release and blockage of glutamate receptors. However, it has been reported that the action of many antiepileptic drugs remains poorly understood [28]. Reports on chemical constituents of plants and their pharmacology suggest that plants containing flavonoids, saponins and tannins possess activity against many CNS disorders [48].

It has also been well reported in literature that flavonoids enhance GABA neurotransmission, and GABA is the main inhibitory neurotransmitter which is suppressed in epilepsy [49]. *T. occidentalis* is rich in these indicated phytochemicals [15,16] and may be exerting its observed anticonvulsant activity as claimed by the folk medicine through the synergistic activities of these various phytochemicals. However, Further study will be needed that will investigate fractions of this extract that are rich in different phytochemicals for their anticonvulsant activities and the possible mode of action.

5. CONCLUSION

It can therefore be concluded, that aqueous leaf extract of *Telfairia occidentalis* did not show significant anticonvulsant activity as claimed in folklore medicine.

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CONSENT

Not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exit.

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