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RESEARCH ARTICLE

Anticonvulsant activities of the methanol crude extract and fractions of the leaf *Solanum americanum (S.a.)* in pentylenetetrazole and 4-amino pyridine induced seizure in white albino rats

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Abstract: This research investigated the anticonvulsant effect of the crude extract and fractions of *Solanum americanum's* (S.a.) leaves on seizures induced by pentylenetetrazole (PTZ) and 4-amino pyridinein albino rats to authenticate the use of the leaves in the treatment of epilepsy in South Eastern Nigeria. The leaves of S.a were extracted with methanol and fractionated using n-hexane, ethyl acetate and methanol. The parameters observed were onset of convulsions in minutes, duration of clonic phase in minutes, percentage protection from seizures and mortality. The anticonvulsant tests were carried out using 60 (sixty) white albino rats (weighing 80-136 g) of both sexes, varying concentrations of both methanol extracts and fractions (12.5, 25.0, 50.0, 100 and 200 mg/kg b.w.) were administered to the rats after which convulsion were induced in the rats using 9.0 mg/kg of PTZ and 1.5 mg/kg 4-amino pyridine on different groups (35 and 25) of rats respectively. The results of the various groups were compared with the control group and significance was analyzed by one-way ANOVA. The acute toxicity test was conducted at a dose of 3000 mg/kg. At a peak dose of 200 mg/kg methanol crude extract, hexane and methanol fraction in PTZ model protected the animals from seizure at 89.30%, 100%, 100% but gave 80%, 80% and 60% protection from mortality respectively. Hexane fraction (12.5, 25, 50, 100 and 200 mg/kg) protected the rats against mortality at 20%, 40%, 60%, 60% and 80% respectively, while no anticonvulsant activities were detected in ethyl acetate fraction. Differences among the means and standard deviation was statistically significant at $P < 0.05$. The acute toxicity test showed that the leaf of S.a. is non-toxic. The result obtained substantiated the use of the leaf of *Solanum americanum* ethnobotanically as anticonvulsant.

Keywords: epilepsy, methanol extract, *solanum americanum*, 4-aminopyridine, pentylenetetrazole

1 Introduction

Internationally, some plants have been acclaimed as therapeutic agents [1]. There has been an increasing demand on herbal remedies to ill-health. Epilepsy is explained as an incurable central nervous system disorder with peculiarity of showing immediate manifestation of seizures entirely identified with the loss of sensibility and mobility of the body [2]. Epilepsy is a chronic condition having recurrent seizures triggered from within brain, which occur in the absence of a metabolic-toxic disease [3]. Epileptic seizures are caused by excessive and unusual cortical nerve cell activity in the brain [4,5]. This syndrome has witnessed so much treatment gap. The treatment gap is defined as the percentage of people with active epilepsy requiring treatment but who are not on it. This is estimated at a staggering 75% in low-income countries, 50% in middle-income and only 10% in the high-income countries [6]. This may be attributed to variety of factors such as financial and other peculiar logistical obstacles that can be attributed to under-developed countries like Nigeria. Herbals are the commonest sources of cheap medicals and a lot of herbals have been published as potential sources for the management of epilepsy [7–10]. Several studies have proven that antiepileptic can be gotten from plant origin [11–13].

The purpose of this study is to investigate the antiepileptic properties of the methanol extracts and fractions of the leaf part of *solanum americanum* on pentylenetetrazole and 4-aminopyridine-induced seizure in white albino rats. This study will reduce the incidence of artificial antiepileptic drugs which are bedecked with side health effects [14, 15].

2 Materials and Methods

2.1 Plant materials

Samples of leaves of *Solanum americanum* were harvested on March 5 in 2020 from Akesan Village, Alimosho local government area of Lagos state. Identification of the plant was done by Dr. O.K. Oluwa of the department of Botany, Lagos state university, Ojo. Voucher number Nwabiani 001-005 deposited there. Analytical grade reagents and double distilled water were purchased from MC Donald Scientific emporium.

2.2 Extraction

The leaves of the plant samples were shade dried and powdered. About 400 g of powdered sample was weighed, put in conical flask, 4 litres of methanol were added and plugged with cotton wool. This was allowed for one day at room temperature with continuous stirring. The supernatant was filtered and the solvent was evaporated to get the crude extract. The crude extract was stored in airtight bottles in a refrigerator for subsequent usage [16]. The extraction was done in batches.

2.3 Vacuum liquid chromatography (VLC)

VLC was carried out according to the method described by Ogbuagu [17] with slight modification. Silica gel 100 g of TLC grade 60 H, (Merck Germany) was used as an adsorbent medium for partitioning. The slurry was prepared by mixing the crude extract 46.21 g with 92.4 g silica gel of 60 mesh size 20-250 μm (Merck Germany). The slurry is inserted as a thin layer on top of the adsorbent, the initial solvent 400 ml n-hexane was used, 400 ml of ethyl acetate fraction was eluted and collected. Finally, methanol of 400 ml was suctioned and the methanol eluent collected. This provided three fractions of the plant leaf crude extract. These fractions were dried with rotary evaporator to reduce the solvents, put in an oven temperature of 42^{o}C and further dried in a desiccator which was packed with silica gel packets and activated charcoal. These fractions were used to test for anticonvulsant effect on albino rats.

2.4 Anticonvulsant tests

Anticonvulsant activity of methanol extracts of *Solanum americanum* was studied in rat. Animal models of pentylenetetrazole (PTZ) [18] and 4-aminopyridine induced convulsion were used to evaluate the anticonvulsant effects of the plant's extracts and fractions.

2.4.1 Ethics statement (Ethical approval)

The experimental protocol was approved by College of Medicine, University of Lagos, Health Research Ethics Committee (CMUL HREC Reg. no.: CMUL/ACUREC/11/22/1112). Care of laboratory animals were taken as per OECD-423 guidelines.

2.4.2 Animals

Swiss albino rats of any of the sex weighing between 80-136 g were used. The animals were purchased at Priceless test animal farm at Agbara, Ogun State. The animals were acclimatized to laboratory conditions seven days before the experiment and were fed with standard pellet, water and libitum under standard environmental condition.

2.4.3 Acute toxicity test

Acute toxicity study of the methanol extracts of *S.a.* was carried in adult albino rats according to OECD-423 guidelines [19]. Rats were divided into 3 groups (n = 5) and fasted overnight. Rats of the 1st and 2nd groups received *Solanum americanum* extracts, respectively at a dose of 3000 mg/kg (5 ml/kg) by the oral route. Rats of the 3rd group (control) treated with the vehicle (3% v/v Tween 80 in distilled water) and kept under the same conditions. Each animal was observed for symptoms of toxicity and/or mortalities during the first 30 minutes and periodically during 24 hours, with special attention given during the first 4 h and then every day for 14 days.

2.4.4 Pentylenetetrazol (PTZ) - Induced Seizure Test

This scientific test was carried out according to the method described by Ya'U *et al.* [20] with slight modification. In this study, thirty-five (35) rats were assigned into different groups and unique identifying mark on each animal was placed. The groups are written below:

Group I received 10 ml of distilled water;

Group II received 12.5 mg/kg b.w. of *Solanum americanum*;

Group III received 25 mg/kg b.w. of *Solanum americanum*;
Group IV received 50 mg/kg b.w. of *Solanum americanum*;
Group V received 100 mg/kg b.w. of *Solanum americanum*;
Group VI received 200 mg/kg b.w. of *Solanum americanum*;
Group VII received 200 mg/kg b.w. of Valproic acid (standard drug).

Thirty (30) minutes after treatment, the animals were induced with pentylenetetrazole (9.0 mg/kg b.w.). The onsets of seizure and mortality rate were evaluated [20].

2.4.5 4-aminopyridine-induced Seizure in rats

This scientific test was carried out following the method described by Salahdeen and Yemitan [21]. A total of twenty-five (25) rats were used in this study, unique identifying mark was placed on each animal and the groups are written below:
Group I received 10ml of distilled water;
Group II received 12.5 mg/kg b.w. of *Solanum americanum*;
Group III received 25 mg/kg b.w. of *Solanum americanum*;
Group IV received 50 mg/kg b.w. of *Solanum americanum*;
Group V received 30 mg/kg b.w. of phenobarbitone (standard drug).

Thirty minutes after the administration with the above doses of plant extract of *S.a,* convulsions were induced using 4-aminopyridine (1.5 mg/kg b.w.) subcutaneously and were observed over a period of 30 minutes. Mean onset of seizure and mortality was observed and recorded.

2.4.6 Statistical analysis

The results of the duration of seizures was analyzed using the ordinary one-way ANOVA followed by Dunnett's 't' test. Differences among the means and standard deviation were statistically significant at $P < 0.05$.

3 Results and discussion

The animals were found to be alive at 3000 mg/kg per oral feeding of the methanol extract. After 14 days it was observed that the plant did not produce observable changes in behaviors such as alertness, restlessness, breathing, diarrhea and weakness.

As shown in Table 1, MCE showed anticonvulsant activity against PTZ and 4-aminopyridine induced clonic seizure. The mean onset of seizure time to clonic seizure was significantly increased at all doses of MCE $P < 0.0001$ when compared to control. The extract at dose levels of 12.5 mg/kg b.w.of MCE and 25 mg/kg b.w. of MCE also did not protect the animals against PTZ and 4-aminopyridine induced seizure and mortality. Maximum protection, 40%, 80% and 80% from mortality relative to control was also achieved by MCE 50 mg/kg, MCE 100 mg/kg and MCE 200 mg/kg respectively for PTZ-induced seizure. However, the extract at concentration of 50 mg/kg in 4-aminopyridine protected the animals from mortality at 60%. This supports the work carried out by Ravi et al. that the ethanol's extract of *Solanum nigrum* is anticonvulsants [22]. 34.29% protection from clonic seizure was observed at MCE 50 mg and 40% protection from mortality relative to control was achieved at this dose. VP200, on the other hand, displayed 100% protection from clonic seizure which was greater than all doses of MCE. Studies recorded that anticonvulsant activity of methanol stem bark extract of *Securinega virosa* in mice possessed higher percentage protection (80%) from seizure at the dose of 12.5 mg/kg in PTZ- induced seizure as compared to MCE which did not protect the animals from seizure at the same dose. Although, 50.0 mg/kg *Securinega virosa* gave 20% protection from seizure to the animals while MCE gave 39.13% protection from seizure in 4-aminopyridine chemo-induced seizure [23]. This means that MCE gave a better protection from seizure than *Securinega virosa* at the same dose.

In Table 2, doses of Hf12.5 mg/kg and Hf 25 mg/kg protected the rats 20% and 40% respectively against PTZ-induced seizures. There was a delayed onset of seizures from 5.29±0.05 to 6.31±0.07 and % protection from seizure of the rats from 25.64 to 41.03. Doses of Hf 12.5 mg/kg, Hf 25 mg/kg and Hf 50 mg/kg protected the rats against mortality of 20%, 40% and 60%, respectively. At a dose of 50 mg/kg hexane fraction showed 64.10% protection from seizures and 60% protection from mortality in PTZ- induced seizure while at the same dose4-aminopyridine induced seizure rats have very high percent (83.30%) protection from seizure and very high percent (80%) protection from mortality when compared to the standard drug phenobarbitone. Hexane's fraction has strong anticonvulsant properties. The mean onset of seizure time to clonic seizure was significantly increased at all doses of Hf. Hexane fraction displayed a higher anticonvulsant property than the methanol crude extract and ethylacetate fraction which did not show any anticonvulsant properties.

Table 1 Anticonvulsant effect of Methanol crude extract (MCE) in PTZ and 4-aminopyridine induced seizure in rats

Anticonvulsant Effect	Group by Conc. mg/kg b.w.	Mean onset of seizure (mins)	% protection from seizure	% Protection from mortality
MCE in PTZ induced seizure in rats	Control	2.47 ± 0.31	0.00	0.00
	12.5	7.27 ± 0.38	0.00	0.00
	25	8.61 ± 0.25	0.00	0.00
	50	16.50 ± 0.46	34.29	40.00
	100	16.90 ± 0.76	69.36	80.00
	200	19.08 ± 0.83	89.30	80.00
	200 (VP)	-	100.00	100.00
MCE in 4-aminopyridine induced seizure in rats	Control	8.32 ± 0.10	0.00	0.00
	12.5	9.15 ± 0.07	0.00	0.00
	25	10.68 ± 0.26	13.04	0.00
	50	15.00 ± 0.05	39.13	60.00
	30 (phenobarbitone)	-	100.00	100.00

Note: Values are expressed as Mean ± SD. (n = 5 mice). Compared to CON (control). MCE is methanol crude extract 12.5 mg/kg b.wof MCE, 25 mg/kg b.w. of MCE, 50 mg/kg b.w. of MCE,100 mg/kg b.w. of MCE, 200 mg/kg b.w. of MCE have adjusted *P*-value of < 0.0001. VP: Sodium valproate, CON: group treated with 10 ml/kg distilled water. S.a. is *Solanum americanum.*

Table 2 Anticonvulsant effect of hexane fraction (Hf) in PTZ and 4-aminopyridine induced seizure in rats

Anticonvulsant Effect	Group by Conc. mg/kg b.w.	Mean onset of seizure (mins)	% protection from seizure	% Protection from mortality
Hf in PTZ induced seizure in rats	Control	3.33 ± 0.05	0.00	0.00
	12.5	5.29 ± 0.05	25.64	20.00
	25	6.31 ± 0.07*	41.03	40.00
	50	12.35 ± 0.14*	64.10	60.00
	100	14.25 ± 0.18*	78.40	60.00
	200	-	100.00	80.00
	200(VP)	-	100.00	100.00
Hf in 4-aminopyridine induced seizure in rats	Control	9.23 ± 0.06	0.00	0.00
	12.5	11.29 ± 0.06	0.00	0.00
	25	12.06 ± 0.42	76.70	60.00
	50	13.27 ± 0.15	83.30	80.00
	30 (phenobarbitone)	-	100.00	100.00

Note: Results are expressed as ratio, mean ± SD. n = 5 rats. * indicate significance compared to con group at $p< 0.05$ in between means and standard deviations

Table 3 Anticonvulsant effect of methanol fraction (Mf) in PTZ and 4-aminopyridine induced seizure in rats

Anticonvulsant Effect	Group by Conc. mg/kg b.w.	Mean onset of seizure (mins)	% protection from seizure	% Protection from mortality
Mf in PTZ induced seizure in rats	Control	7.33 ± 0.02	0.00	0.00
	12.5	8.48 ± 0.16	3.33	0.00
	25	10.34 ± 0.10*	13.33	0.00
	50	11.56 ± 0.15*	23.33	20.00
	100	13.76 ± 0.12	76.67	60.00
	200	-	100.00	60.00
	200(VP)	-	100.00	100.00
Mf in 4-aminopyridine induced seizure in rats	Control	11.2 ± 0.66	0.00	0.00
	12.5	11.8 ± 0.11	0.00	0.00
	25	12.68 ± 0.17	0.00	40.00
	50	16.40 ± 0.50	58.33	60.00
	30 (phenobarbitone)	-	100.00	100.00

Note: The results are expressed as ratio, mean ± SD and %, n = 5 rats/group. * indicate significance compared to control group at $P < 0.05$.

Table 3 showed that the methanol fraction gave 23.33% protection from seizure and 20% protection from mortality against the PTZ- induced seizure at a dose of Mf 50 mg/kg bw. Doses of Mf 12.5 mg/kg and Mf 25 mg/kg protected 3.33% and 13.33%, respectively of the rats against PTZ-induced seizure. There was a delayed onset of seizures from 7.33±0.02 to 13.76±0.12 at a dose of 100 mg/kg with 76.67% protection from seizure and 60% protection from mortality. Dose of 200mg/kg protected the animals against seizure and produced 60% protection against

mortality. Also, methanol fraction exhibited 58.33% protection from seizure and 60% protection from mortality against the 4-aminopyridine induced seizure at a dose of Mf 50 mg/kg b.w. This has a significant prolonged onset of seizure from 11.2±0.66 minutes to 16.40±0.50 minutes in rat when compared to control.

Table 4 showed that the plant extract's ethylacetate fraction exhibited zero% protection from seizure. There was 20% protection from mortality against the PTZ induced seizure at a dose of 200 mg/kg b.w and 40% protection from 4-aminopyridine at a dose of 50 mg/kg b.w. [24]. This shows that the plant's anticonvulsant properties are not deposited in the ethylacetate fraction.

Table 4 Anticonvulsant effect of ethylacetate fraction (Ef) in PTZ and 4-aminopyridine induced seizure in rats

Anticonvulsant Effect	Group by Conc. mg/kg b.w.	Mean onset of seizure (mins)	% protection from seizure	% Protection from mortality
Ef in PTZ induced seizure in rats	Control	3.65 ± 0.20	0.00	0.00
	12.5	4.42 ± 0.16	0.00	0.00
	25	4.50 ± 0.32	0.00	0.00
	50	4.20 ± 0.26	0.00	0.00
	100	4.23 ± 0.27	0.00	20.00
	200	4.56 ± 0.24	0.00	20.00
	200(VP)	-	100.00	100.00
Ef in 4-aminopyridine induced seizure in rats	Control	9.16 ± 0.10	0.00	0.00
	12.5	9.38 ± 0.07	0.00	0.00
	25	10.58 ± 0.10	0.00	0.00
	50	10.52 ± 0.20	0.00	40.00
	30 (phenobarbitone)	-	100.00	100.00

Note: The results are expressed as ratio, mean ± SD and %, n = 5 rats/group

4 Conclusion

Data from this study show that *Solanum americanum* significantly increases the time of onset of seizure by minutes and reduces the frequency of convulsions on PTZ and 4-aminopyridine induced seizures. Stoppage of seizures induced by pentelenetetrazole in laboratory animals is the most easily obtainable initial screening test for identifying prospective lead to anticonvulsant drugs [24, 25]. Also, the anticonvulsant properties displayed by *Solanum americanum* authenticated the earlier review of twenty-seven plants of solanum species that the family Solanaceae are anticonvulsant. The findings on the acute oral toxicity shows that the methanol extract of *Solanum americanum* is not toxic and is safe to be used as an herbal remedy for epileptic patients. The research investigation suggests that the polar methanolic extract and the non-polar hexane fraction of the leaf of the plant of *Solanum americanum* has anticonvulsant properties on the absence, myoclonic and clonic seizure chemical models of epilepsy employed in the experiment.

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Conflicts of interest

The authors declare that there was no conflict of interest.

References

[1] Ogirima SAO. Web-based decision support system for prescription in herbal medicine. Journal of Emerging Trends in Engineering and Applied Sciences. 2015, 6(7): 245-254. https://hdl.handle.net/10520/EJC174438

[2] Epilepsy WHO. A manual for medical and clinical officers In Africa. Geneva: World Health Organization, 2002.

[3] Haslam HAR. The nervous system. In: Kliegman R, Behrman R, Jenson H, Stanton B, (Eds). Nelson Textbook of Pediatrics, 18th ed. Philadelphia: Saunders Publishers,2008, 2457-2530.

[4] Fisher RS, Boas W van E, Blume W, et al. Epileptic Seizures and Epilepsy: Definitions Proposed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE). Epilepsia. 2005, 46(4): 470-472. https://doi.org/10.1111/j.0013-9580.2005.66104.x

[5] Sathyanarayana Rao KN, Subbalakshmi NK. An experimental study of the anticonvulsant effect of amlodipine in mice. Singapore Medical Journal. 2010, 51(5): 424.

[6] Meyer AC, Dua T, Ma J, et al. Global disparities in the epilepsy treatment gap: a systematic review. Bulletin of the World Health Organization. 2009, 88(4): 260-266. https://doi.org/10.2471/blt.09.064147

[7] Tanko Y, Eze ED, Jimoh A, et al. Anticonvulsant Activity of Methanol Stem Bark Extract of Securinega Virosa (Euphobiaceae) in Mice. IOSR Journal of Pharmacy and Biological Sciences. 2012, 4(1): 44-47. https://doi.org/10.9790/3008-0414447

[8] Pitchaiah G, Anusha VL, Hemalatha CH, et al. Anxiolytic and anticonvulsant activity of methanolic extract of allium cepa Linn (Onion) bulbs in Swiss albino mice. AkiNik Publications. 2015, 4(2): 131-135.

[9] Hema B, Bhupendra S, Mohamed Saleem TS, et al. Anticonvulsant effect of Drosera burmannii Vahl. International Journal of Applied Research in Natural Products. 2009, 2(3): 1-4.

[10] Yaro AH, Musa AM, Magaji MG, et L. Anticonvulsant potentials of methanol leaf extract of Cissus cornifolia Planch (Vitaceae) in mice and chicks. International Journal of Herbs and Pharmacological Research. 2015, 4(2): 25-32.

[11] Garba K, Hamza AY. Anticonvulsant actions of ethanol stem bark extract of Trichilia roka (Meliaceae) in mice and chicks. The Journal of Phytopharmacology. 2015, 4(4): 231-234. https://doi.org/10.31254/phyto.2015.4409

[12] Sandeep KK, Karunakar K, Jarinabanu T, et al. Antiepileptic activity of ethanolic extract of Biophytum sensitivum (L.) DC. in Animal models.Indian International Journal of Current Research and Academic Review. 2015, 3(7): 23-30.

[13] Agedew T, Nedi T, Umer S, et al. Anticonvulsant activity of 80% methanol leaf extract and solvent fractions of Buddleja polystachya fresen (Buddlejaceae) in mice. Ethiop Pharm Journal. 2021, 36(2): 121-30.

[14] Olesen JB, Abildstrøm SZ, Erdal J, et al. Effects of epilepsy and selected antiepileptic drugs on risk of myocardial infarction, stroke, and death in patients with or without previous stroke: a nationwide cohort study. Pharmacoepidemiology and Drug Safety. 2011, 20(9): 964-971. https://doi.org/10.1002/pds.2186

[15] Renoux C, Dell'Aniello S, Saarela O, et al. Antiepileptic drugs and the risk of ischaemic stroke and myocardial infarction: a population-based cohort study. BMJ Open. 2015, 5(8): e008365. https://doi.org/10.1136/bmjopen-2015-008365

[16] Anjali S, Sheetal S. Phytochemical Analysis and Free Radical Scavenging Potential of Herbal and Medicinal Plant Extracts. Indian Journal of Pharma and Phytochemistry. 2013, 2(4): 22-29.

[17] Ogbuagu AS. Phytochemical and Antimicrobial Screening of Cassia Occidentalis. Ph.D dessertation, Dept of Pure and Industrial chemistry, Nnamdi Azikiwe University, Awka. 2012, 61-70.

[18] While HS, Woodhead JH, Wilcox KS, et al. Discovery and preclinical development of antiepileptic drugs.In: Levy, R.H., Mattson R.H., Meldrum B.S, Perucca, E. antiepileptic drugs. 5th ed. Philadelphia: Lippincott Williams and Wilkins Ltd. 2002, 36-48.

[19] OECD guideline for testing of chemicals: Acute oral toxicity-acute toxic class method. Guideline No. 423, Organization for Economic Co-operation and Dev., 2001, 1-14.

[20] Ya'u J, Yaro AH, Malami S, et al. Anticonvulsant activity of aqueous fraction ofCarissa edulisroot bark. Pharmaceutical Biology. 2015, 53(9): 1329-1338. https://doi.org/10.3109/13880209.2014.981280

[21] Salahdeen HM, Yemitan OK. Neuropharmacological effects of aqueous leaf extract of Bryophyllum pinnatum in mice. African Journal of Biomedical Research. 2009, 9(2): 101-107. https://doi.org/10.4314/ajbr.v9i2.48782

[22] Ravi V, Saleem TS, Maiti PP, et al. Phytochemical and pharmacological evaluation of Solanum nigrum Linn. African Journal of Pharm and Pharmacol. 2009, 3(9): 454-457.

[23] Rasilingam D, Duraisamy S, Subramanian R. Anticonvulsant activity of bioflavonoid gossypin. Bangladesh Journal of Pharmacology. 2008, 4(1): 51-54. https://doi.org/10.3329/bjp.v4i1.1081

[24] Tyagi N, Sharma A, Verma KS, et al. CNS Acting Potential of Natural Products with Special Reference to Family Solanaceae. Systematic Reviews in Pharmacy. 2021, 12(4): 219-223.

[25] Duraisami R, Srinivasan D, Ramaswamy S. Anticonvulsant activity of bioflavonoid gossypin. Bangladesh Journal of Pharmacology. 2009, 4(1): 51-54.