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ScienceDirect
Journal of Ethnopharmacology 113 (2007) 111–114
Journal of ETHNO-PHARMACOLOGY
www.elsevier.com/locate/jethpharm

Sedative and anticonvulsant activities of the aqueous root extract of *Sanseviera liberica* Gerome & Labroy (Agavaceae)

Olufunmilayo O. Adeyemi [a,*], Omoniyi K. Yemitan [b], Olayemi O. Adebiyi [a]

[a] *Department of Pharmacology, College of Medicine of the University of Lagos, Idi-Araba, P.M.B. 12003, Lagos, Nigeria*
[b] *Department of Pharmacology, Lagos State University College of Medicine, P.M.B. 21266, Ikeja, Lagos, Nigeria*

Received 3 February 2007; received in revised form 20 March 2007; accepted 1 May 2007
Available online 6 May 2007

Abstract

The central nervous system (CNS) depressant and anticonvulsant activities of the aqueous root extract of *Sanseviera liberica* (ASL) were investigated on various animal models including pentobarbitone sleeping time and hole-board exploratory behaviour for sedation tests, and strychnine, picrotoxin, bicuculline and pentylenetetrazole-induced convulsions in mice. ASL (100–400 mg/kg, p.o.), like chlorpromazine HCl (1 mg/kg, i.m.), produced a dose-dependent prolongation of pentobarbitone sleeping time and suppression of exploratory behaviour. ASL (100 and 200 mg/kg) produced dose-dependent and significant ($P < 0.05$) increases in onset to clonic and tonic convulsions, and at 400 mg/kg, showed complete protection against seizures induced by strychnine, picrotoxin and bicuculline, but not with pentylenetetrazole. ASL up to 10 g/kg, p.o. did not produce death, but i.p. treatment produced mortalities with LD_{50} of 668.3 ± 47.6 mg/kg. Preliminary phytochemical investigations of ASL revealed the presence of carbohydrates, alkaloids, saponins, reducing sugars and oils. The results indicate that ASL has sedative and anticonvulsant activities, therefore, justifying its use in traditional African medicine.

Keywords: *Sanseviera liberica*; Sedative; Anticonvulsant; Strychnine; Picrotoxin; Bicuculline

1. Introduction

There are many classes of anticonvulsants that are of clinical usefulness with good prognosis for controlling seizures in most patients (Cockerel et al., 1995). Despite this, many patients, have seizures that are not adequately managed by the established antiepileptic drugs (AEDs) (Richens and Perucca, 1993). Moreover, the high incidence of detestable adverse effects from the use of AEDs is also a source of widespread concern in patients who use them chronically. These and treatment cost, have made traditional herbs and herbalists very useful and indispensable in the struggle for seizure management and future AED development. There is therefore need for research into medicinal plants with possible anticonvulsant effects, based on folklore use. *Sanseviera liberica* belongs to the family "Agavaceae". It is commonly called African Bowstring or Leopard Lily and is used in traditional medicine for certain ailments. It is numerously found in Australia, the tropic and sub-tropic regions (Wiggins and Porter, 1971) of the world. The root part is used in ethno-medicine in the treatment of fever, headache and cold, as well as analgesic, antibiotic and anti-inflammatory (Watt and Breyer-Brandwiijk, 1962). But widespread claims that the decoction of the root is drunk as a remedy for convulsion, epilepsy and sleep disorder lack documented pharmacological elucidation. This study was therefore carried out to ascertain and regulate the sedative and anticonvulsant claims about the aqueous root extract of *Sanseviera liberica* (ASL).

2. Materials and methods

2.1. Plant materials

Fresh roots of *Sanseviera liberica* were collected from Ibadan, Oyo state, Nigeria, by Mr. Usang Felix Inah, a Superintendent of the Forestry Research Institute of Nigeria (FRIN). It was identified and authenticated at FRIN, where a voucher specimen (FHI 43731) is preserved for reference.

* Corresponding author. Tel.: +234 803 445 9618; fax: +234 1 5851432.
E-mail address: ooadey@yahoo.com (O.O. Adeyemi).

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doi:10.1016/j.jep.2007.05.007

2.2. Extract preparation

Fresh root parts of *Sanseviera liberica* were cut into bits, weighed and rinsed with distilled water. It was boiled in distilled water (100 g in 2.5 L) for 2 h, then covered and left for 24 h for further extraction. Thereafter, it was decanted and filtered with filter paper. The filtrate was dried in the oven at 40 °C. A yield of 12.4% of the evaporated extract was obtained in the process. The extract was freshly dissolved and given in distilled water on each day of experiment for the assays.

2.3. Animals

Young adult albino mice (13–20 g) of both sexes were obtained from the Laboratory Animal Centre, Nigeria Institute of Medical Research (NIMR), Yaba, Lagos, Nigeria. They were fed on *Pfizer* rodent feed and kept under standard light (12 h light/12 h dark) and temperature (25 ± 2 °C) conditions. Ethical approval for animal use was obtained from the Experimental Ethics Committee on Animal Use of the College of Medicine of the University of Lagos, Idi-Araba, Lagos, Nigeria.

2.4. Pentobarbitone induced sleeping time

To groups of mice given oral doses of the extract (100, 200 or 400 mg/kg), pentobarbitone sodium (40 mg/kg, i.p.) was administered 30 min later. The control group received 10 ml/kg normal saline, i.p.15 min before 40 mg/kg, i.p. pentobarbitone. For positive control group, pentobarbitone (40 mg/kg, i.p.) was administered 15 min after chlorpromazine hydrochloride (1 mg/kg, i.m.) (Mujumdar et al., 2000). Onset of sleep was taken as the time when mice accepted the decubitodorsal position for three consecutive trials. Conversely, the duration was considered completed when mice did not accept the decubitodorsal position for three consecutive trials (Yemitan et al., 2001).

2.5. Exploratory activity

This study was carried out by the hole-board method using a white painted wooden board (40 cm × 40 cm) with four equidistant holes (1 cm diameter × 2 cm depth). Each mouse was placed at one corner of the board and the animal moved about and dipped its head into the holes indicating exploratory behaviour. The number of dips in 7.5 min was recorded (File and Wardill, 1975). The test was carried out 30 min after oral treatment with ASL at doses of 100, 200 or 400 mg/kg or chlorpromazine (1 mg/kg, i.m.) to different groups of mice

2.6. Strychnine induced seizures

Mice of either sex were randomly allotted to the different control and test groups. The control mice were administered with strychnine (4 mg/kg, i.m.) 30 min after normal saline (10 ml/kg, p.o.). The positive control group of mice received 4 mg/kg, i.m. strychnine, 15 min after phenobarbitone sodium (40 mg/kg, i.p.) Graded doses (100, 200 or 400 mg/kg, p.o.) of ASL were given to the test groups 30 min before 4 mg/kg, i.m. strychnine. Onset to forelimb cloni and tonic seizures were recorded. Mice that did not convulse 30 min after strychnine administration were considered protected (Yemitan et al., 2001).

2.7. Picrotoxin induced seizures

Mice of either sex were randomly allotted to the different control and test groups. The control mice were administered with picrotoxin (4 mg/kg, i.p.) 30 min after normal saline (10 ml/kg, p.o.). The positive control group of mice received 4 mg/kg, i.p. picrotoxin, 15 min after phenobarbitone sodium (40 mg/kg, i.p.). Graded doses (100, 200 or 400 mg/kg, p.o.) of the extract were given to the test groups 30 min before 4 mg/kg, i.p. picrotoxin. Onset to forelimb cloni and tonic seizures were recorded. Mice that did not convulse 30 min after picrotoxin administration were considered protected (Yemitan et al., 2001).

2.8. Bicuculline induced seizures

Mice of either sex were randomly allotted to the different control and test groups. The control mice were administered with bicuculline (10 mg/kg, s.c.) 30 min after normal saline (10 ml/kg, p.o.). The positive control group of mice received 10 mg/kg, s.c. bicuculline, 15 min after phenobarbitone sodium (40 mg/kg, i.p.) Graded doses (100, 200 or 400 mg/kg, p.o.) of the extract were given to the test groups 30 min before 10 mg/kg, s.c. bicuculline. Onset to forelimb cloni and tonic seizures were recorded. Mice that did not convulse 30 min after bicuculline administration were considered protected.

2.9. Pentylenetetrazole (PTZ)-induced seizures

Mice of either sex were randomly allotted to the different control and test groups. The control mice were administered with pentylenetetrazole (75 mg/kg, i.p.) 30 min after normal saline (10 ml/kg, p.o.). The positive control group of mice received pentylenetetrazole (75 mg/kg, i.p.), 15 min after phenobarbitone sodium (40 mg/kg, i.p.) Graded doses (100, 200 or 400 mg/kg, p.o.) of the extract were given to the test groups 30 min before 75 mg/kg, i.p. pentylenetetrazole. Onset to forelimb cloni, as well as hindlimb extension (tonic convulsion) was recorded. The onset and number of death after showing tonic hindlimb extension were also recorded. Mice that did not convulse 30 min after pentylenetetrazole administration were considered protected.

2.10. Statistical analysis

Results are presented as mean ± S.E.M. Statistical significance between the groups was analyzed by means of an analysis of variance followed by Dunnett's multiple comparison test. P values less than 0.05 were considered significant.

3. Results and discussions

ASL produced significant ($P < 0.05$) and dose-dependent reduction in the onset and prolongation of sleep duration induced

Table 1
Effect of aqueous root extract of *Sanseviera liberica* on pentobarbitone induced sleeping time in mice

Treatment and route	Onset to sleep ± S.E.M. (min)	Sleeping time ± S.E.M. (min)
Control: NS (10 ml/kg, p.o.)	6.7 ± 0.2	46.0 ± 0.3
ASL (100 mg/kg, p.o.)	5.9 ± 0.2*	45.8 ± 0.4
ASL (200 mg/kg, p.o.)	4. 8 ± 0.2*	53.1 ± 0.4*
ASL (400 mg/kg, p.o.)	3. 6 ± 0.2*	66. 6 ± 0.6*
Chlorpromazine (1 mg/kg, i.m.)	3. 9 ± 0.2*	57. 7 ± 0.9*

NS: normal saline; ASL: aqueous root extract of *Sanseviera liberica*.
* Significant $P < 0.05$ compared to control, ANOVA; $n = 6$.

Table 2
Effect of aqueous root extract of *Sanseviera liberica* on exploratory behaviour in mice

Treatment and route	Number of head-dips	
	Pretreatment mean ± S.E.M. (min)	Post treatment mean ± S.E.M. (min)
Control: NS (10 ml/kg, p.o.)	9.5 ± 0.4	9.3 ± 06
ASL (100 mg/kg, p.o.)	8.8 ± 0.5	6.2 ± 0.5*
ASL (200 mg/kg, p.o.)	8. 8 ± 0.5	3. 7 ± 0.5*
ASL (400 mg/kg, p.o.)	9.8 ± 0.4	2. 3 ± 0.2*
Chlorpromazine (1 mg/kg, i.m.)	8. 8 ± 0.5	1. 2 ± 0.3*

Values are mean ± S.E.M. NS: normal saline; ASL: aqueous root extract of *Sanseviera liberica*.
* Significant $P < 0.05$ compared to control, ANOVA; $n = 6$.

by pentobarbitone and the result is comparable to that produced by chlorpromazine (Table 1). Moreover, extract-treated mice showed decreased exploratory activity in a dose-dependent manner, effect comparable to chlorpromazine (4 mg/kg, i.p.) (Table 2). Prolongation of pentobarbitone sleeping time, as well as suppression of exploratory behaviour indicates a central nervous system depressant activity of the extract (File and Wardill, 1975; Mujumdar et al., 2000).

At 100 and 200 mg/kg, ASL produced significant ($P < 0.05$) prolongation of both clonic and tonic seizure latencies, and at 400 mg/kg, complete protection against strychnine (Table 3) and picrotoxin (Table 4) seizures. Strychnine has been demonstrated to have a well defined mechanism of convulsant action reported to be by directly antagonizing the inhibitory spinal cord and brainstem reflexes of glycine (Biggio et al., 1992) and thus increasing spinal reflexes (Rang et al., 2000). Picrotoxin, on the other hand, is a selective non-competitive antagonist of gamma amino butyric acid (GABA) at $GABA_A$ receptor, which have been widely implicated in epilepsy (Rang et al., 2000). GABA is the major inhibiting neurotransmitter in the brain and its inhibition is thought to be an underlying factor in epilepsy (Gale, 1992). Furthermore, at 200 mg/kg of ASL, bicuculline did not prevent clonus, but protected mice against tonic seizures; but complete protection against clonic and tonic seizures was pro-

Table 4
Effect of aqueous root extract of *Sanseviera liberica* on picrotoxin-induced seizure in mice

Treatment and route	Seizure onset ± S.E.M. (min)	
	Clonic	Tonic
Control: NS (10 ml/kg, p.o.)	6.6 ± 0.3	10.0 ± 0.6
ASL (100 mg/kg, p.o.)	7.0 ± 0.2*	10.8 ± 0.3*
ASL (200 mg/kg, p.o.)	15. 6 ± 0.7*	21.9 ± 2.6*
ASL (400 mg/kg, p.o.)	NC	NC
Phenobarbitone (40 mg/kg, i.p.)	NC	NC

Values are mean ± S.E.M. NS: normal saline; ASL: aqueous root extract of *Sanseviera liberica*; NC: no convulsion.
* Significant $P < 0.05$ compared to control, ANOVA; $n = 6$.

Table 3
Effect of aqueous root extract of *Sanseviera liberica* on strychnine-induced seizure in mice

Treatment and route	Seizure onset ± S.E.M. (min)	
	Clonic	Tonic
Control: NS (10 ml/kg, p.o.)	3.4 ± 0.2	5.0 ± 0.3
ASL (100 mg/kg, p.o.)	6.1 ± 0.3*	7.8 ± 0.3*
ASL (200 mg/kg, p.o.)	13. 6 ± 0.2*	15. 0 ± 0.2*
ASL (400 mg/kg, p.o.)	NC	NC
Phenobarbitone (40 mg/kg, i.p.)	NC	NC

Values are mean ± S.E.M. NS: normal saline; ASL: aqueous root extract of *Sanseviera liberica*; NC: no convulsion.
* Significant $P < 0.05$ compared to control, ANOVA; $n = 6$.

Table 5
Effect of aqueous root extract of *Sanseviera liberica* on bicuculline-induced seizure in mice

Treatment and route	Seizure onset ± S.E.M. (min)	
	Clonic	Tonic
Control: NS (10 ml/kg, p.o.)	12.2 ± 0.1	21.3 ± 0.1
ASL (100 mg/kg, p.o.)	13.7 ± 0.2*	28.7 ± 0.2*
ASL (200 mg/kg, p.o.)	22. 6 ± 0.2*	NC
ASL (400 mg/kg, p.o.)	NC	NC
Phenobarbitone (40 mg/kg, i.p.)	NC	NC

Values are mean ± S.E.M. NS: normal saline; ASL: aqueous root extract of *Sanseviera liberica*; NC: no convulsion.
* Significant $P < 0.05$ compared to control, ANOVA; $n = 6$.

Table 6
Effect of aqueous root extract of *Sanseviera liberica* on pentylenetetrazole-induced seizure in mice

Treatment and route	Seizure onset ± S.E.M. (min)		Mortality fraction ± S.E.M.
	Clonic	Tonic	
Control: NS (10 ml/kg, p.o.)	3.5 ± 0.3	7.3 ± 0.7	7/7
ASL (100 mg/kg, p.o.)	3.7 ± 0.2	7.2 ± 0.6	7/7
ASL (200 mg/kg, p.o.)	3.8 ± 0.2	7.4 ± 0.8	4/7*
ASL (400 mg/kg, p.o.)	3.7 ± 0.5	7.9 ± 1.1	0/7*
Phenobarbitone (40 mg/kg, i.p.)	23 ± 2.3*	NC	0/7*

Values are mean ± S.E.M. NS: normal saline; ASL: aqueous root extract of *Sanseviera liberica*; NC: no convulsion.
* Significant $P < 0.05$ compared to control, ANOVA; $n = 7$.

duced by 400 mg/kg of the extract (Table 5). Bicuculline, like picrotoxin acts by blocking the action of GABA, but they differ, being competitive and non-competitive antagonists of $GABA_A$ receptor, respectively (Bloom, 1996; Rang et al., 2000). In the PTZ model, however, ASL did not increase onset to either clonic or tonic seizure, but at higher doses of 200 and 400 mg/kg, like phenobarbitone, it produced dose-related, significant reduction in incidences of mortality following tonic hindlimb tonus (Table 6). Inability of ASL to inhibit clonic seizure in the PTZ test suggest that it may not have the ability to raise seizure threshold (White et al., 1995). Essentially, the effectiveness of a drug against PTZ seizure indicates its probable effectiveness against absence seizures (McNamara, 1989). PTZ has been reported to inhibit chloride conductance by binding to picrotoxin sites of $GABA_A$ receptor complex (Krall et al., 1978). Based on this partial effectiveness, it is difficult to report ASL as having anticonvulsant effect against PTZ seizure; however, ability to reduce mortality after seizure might suggest some potential usefulness of a drug against neurotoxicity which normally causes death following extensive seizures by chemicals.

Based on these results, it is therefore probable that the aqueous root extract of *Sanseviera liberica* has considerable anticonvulsant action that might involve both GABAergic and glycinergic inhibitory mechanism.

Preliminary phytochemical investigations of ASL revealed the presence of carbohydrates, alkaloids, saponins, reducing sugars and oils. The sedative effects of ASL might therefore be due to any one or combination of these phytochemicals. These results provide justification for the traditional use of the root as an orally safe herbal remedy to induce sleep, as well as manage convulsions and epilepsies in traditional African medicine.

References

Bloom, F.E., 1996. Neurotransmission and the central nervous system. In: Goodman and Gilman's The Pharmacological Basis of Therapeutics, 9th ed. McGraw Hill, pp. 267–293.

Biggio, G., Cibin, M., Diana, M., Fadda, F., Ferrara, S.D., Gallimberti, L., Gessa, G.L., Mereu, G.P., Rossetti, Z.L., Serra, M., 1992. Suppression of voluntary alcohol intake in rats and alcoholics by gamma hydrobutyric acid: a non-GABAergic mechanism. Biochemical Psychopharmacologia 47, 281–288.

Cockerel, O.C., Johnson, L., Sander, J.W.A., Hart, Y.M., Shorvon, D.S., 1995. Remission of epilepsy: results from the National General Practice Study of Epilepsy. Lancet 346, 140–144.

File, S.E., Wardill, A.G., 1975. Validity of head dipping as a measure of exploration in a modified hole-board. Psychopharmacologia (Berl.) 44, 53–59.

Gale, K., 1992. Subcortical structures and pathways involved in convulsive seizures generation. Journal of Clinical Neurophysiology 2, 264–277.

Krall, R.L., Penry, J.K., Kuperberg, H.J., Swinyard, E.A., 1978. Antiepileptic drug development. II: anticonvulsant screening. Epilepsia 19, 409–428.

Mujumdar, A.M., Naik, D.G., Waghole, R.J., Kulkarni, D.K., Kumbhojkar, M.S., 2000. Pharmacological studies on *Sterculia foetida* leaves. Pharmaceutical Biology 38, 13–17.

McNamara, J.O., 1989. Development of new pharmacological agents for epilepsy: lessons from the kindling model. Epilepsia 30, S13–S18.

Rang, H.P., Dale, M.M., Ritter, J.M. (Eds.), 2000. Pharmacology, 4th ed. Churchill Livingstone, pp. 604–613.

Richens, A., Perucca, E., 1993. In: Laidlaw, J., Richens, A., Chadwick, D. (Eds.), Textbook of epilepsy. Churchill Livingstone, Edinburgh, pp. 495–559.

Watt, J.M., Breyer-Brandwiijk, M.J., 1962. Medicinal and poisonous plants of south and eastern Africa, 2nd ed., pp. 197–198.

White, S.H., Woodhead, J.H., Franklin, M.R., Swinyard, E.A., Wolf, H.H., 1995. In: Levy, L.H., Mattson, R.H., Meldrum, B.S. (Eds.), Experimental Selection, Quantification and Evaluation of Antiepileptic Drugs, 4th ed. Raven Press Ltd., New York, pp. 99–110 (Chapter 7).

Wiggins, I.L., Porter, D.M. (Eds.), 1971. Flora of the Galapagos Islands. Stanford University Press, Stanford, California, pp. 353–361.

Yemitan, O.K., Ajibade, A.M., Adeyemi, O.O., 2001. Anticonvulsant activity of *Dalbergia saxatilis*. Nigerian Journal of Neuroscience 4, 33–40.