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AQUEOUS STEM BARK EXTRACT OF *STEREOSPERMUM KUNTHIANUM* (CHAM, SANDRINE PETIT) PROTECTS AGAINST GENERALIZED SEIZURES IN PENTYLENETETRAZOLE AND ELECTRO-CONVULSIVE MODELS IN RODENTS.

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Abstract

Stereospermum kunthianum, Cham Sandrine Petit (*Bignoniaceae*) known in English as pink jacaranda is used in traditional medicine to treat an array of ailments including febrile convulsions in infants and young children by the rural dwellers in Nigeria. This study examined the anticonvulsant activity of its aqueous stem bark extract (100 – 400mg/kg) against maximal electroshock and pentylenetetrazole-induced seizures in rodents. Phenobarbitone and ethosuximide were used as reference anticonvulsant drugs for comparison. *Stereospermum kunthianum* extract (200 – 400mg/kg, i.p.) remarkably protected (76.9% and 84.6 % respectively) the rats against electroshock-induced seizures. However, the extract (200- 400mg/kg) when administered orally showed a comparatively less effect (33.3% and 55.6% respectively) to the intraperitoneally administered extract in the maximal electroshock test. The extract (100-400mg/kg, i.p.) significantly delayed ($p < 0.05$) the onset of pentylenetetrazole-induced clonic seizures but only slightly prolonged the time of death of the mice. Although the findings in the present study do not provide conclusive evidence, it appears that the aqueous stem bark extract of *Stereospermum kunthianum* produces its antiseizure effect by enhancing GABAergic neurotransmission and/or action in the brain. The results indicate that the aqueous extract possesses anticonvulsant activity in rodents and therefore tend to suggest that the shrub may be used as a natural supplementary remedy in the management, control and/or treatment of childhood convulsions. It can be concluded that the aqueous stem bark extract possesses anticonvulsant activity and therefore lend pharmacological credence to the traditionally claimed use in the treatment of childhood convulsions.

Key words: *Stereospermum kunthianum*, Anticonvulsant activity, maximal Electroshock, pentylenetetra-zole.

Introduction

Seizures are alterations of behaviour due to the disordered, synchronous, and rhythmic firing of populations of brain neurons. In uncontrollable seizures, balance between cerebral excitability and inhibition is tipped towards uncontrollable excitability (McNamara, 2006), manifesting as epileptic episodes. Generalized seizures arise diffusely from the cerebral cortex, with threshold for burst-firing altered through the cortex (Lowenstein, 2004). Many drugs are available for the management of seizures (McNamara, 2006); however, many rural dwellers of the developing countries still depend largely on traditional herbal remedies for the management of seizures. Although there are available scientific reports (Ojewole, 2008; Yemitan and Adeyemi, 2006; Ogbonnia *et al.*, 2003; Aji *et al.*, 2001) to support the folkloric use of some of the herbs used traditionally in the management of seizures, many of them are still without documented scientific evidence of efficacy. *Stereospermum kunthianum* is one of such plants. *Stereospermum kunthianum* (Cham, Sandrine Petit), family Bignoniaceae is a woody shrub of the Sudano-Guinea

savannah regions of Africa and Asia, where the plant parts are used to treat various ailments (Keay *et al.*, 1989; Gill, 1992). Among its traditional medical uses is the use in the management of seizures in infants and young children. We have recently demonstrated the antidiarrhoeal activity of the aqueous extract of *Stereospermum kunthianum* stem bark in in-vivo experimentally –induced diarrhoeal models using mice and rats (Ching *et al.*, 2008). The efficacy of the water extract of *Stereospermum kunthianum* in human complement system fixation *in-vitro* has been reported (Drissa *et al.*, 2002). Antiplasmodial activity of naphthoquinones and one anthraquinone from the lipophilic extract of the root bark of *Stereospermum kunthianum* has also been reported (Onegi *et al.*, 2002). The present study was aimed at investigating the anticonvulsant activity of the aqueous stem bark extract of *Stereospermum kunthianum* in order to establish pharmacological evidence of its folkloric use in the management of childhood convulsions.

Materials and Methods

Plant material

The fresh stem bark of the *Stereospermum kunthianum* was collected in Idi-Okpe, Ogun State, Nigeria in March, 2006. Identification and botanical authentication were done by Mr. Usang Felix Inah of the Forestry Research Institute of Nigeria, Ibadan where a voucher specimen (No. FHI 107277) was deposited for future reference.

Extraction of plant

The stem bark was carefully separated from the woody part, cut into small pieces sun-dried and pulverized using a grinder (Lab. Mill, serial NO. 4745, Christy and Norris Ltd, England). The powdered material (400g) was macerated in 2L of distilled water at an initial temperature of 60°C, allowed to cool and filtered after 24 hrs. The filtrate was evaporated to dryness in an oven set at 40°C until a constant weight was obtained. The yield was 26.4% with reference to the powdered stem bark. The extract obtained was stored in closed containers in the refrigerator until when required for use in experiments reported in our study.

Animals

The animal experiments were carried out according to international guidelines and approved protocols. Wistar rats and Swiss mice of either sex obtained from the Animal House unit of the Department of Pharmacology & Toxicology, Faculty of Pharmacy, University of Benin, Benin City, Nigeria were used. The animals maintained under standard laboratory conditions (12 hrs light and dark cycle) had free access to standard chow (Bendel Feeds and Flour mill Plc. Ewu, Nigeria) and drinking water. The animal experiments were carried out according to international guidelines and approved protocols.

Maximal electroshock (MES)-induced seizures test

The effect of the aqueous stem bark extract of *S. kunthianum* on generalized seizures was evaluated by the maximal electroshock (MES) method as described by Swinyard and Woodhead, (1982). Wistar rats (110 – 160g) fasted overnight but had access to water *ad-libitum* which was only withdrawn during the experiment were randomly allotted to groups of at least six animals per group. The animals were either administered orally or intraperitoneally, distilled water (5ml/kg), extract (100, 200, or 400 mg/kg), or phenobarbitone sodium (30 mg/kg, i.p.). Generalized seizures were induced one hour later with electroshock (Electroshock unit - Ugo Basil, Varese, Italy) through a pair of ear electrodes which delivered an alternating current of constant frequency (60Hz) and 150mA for 0.2sec to elicit tonic hind-limb extension in the animals. Distilled water treated animals receiving this electrical stimulation undergo convulsive seizures pattern having a tonic flexor phase, a tonic extensor phase and clonic phase. An animal was considered to be protected if the characteristic electroshock convulsive seizure pattern was absent. The ratio of animals protected in each group as well as the percentage protected was determined.

Pentylentetrazole (PTZ)-induced seizures test

The method of Swinyard and Woodhead (1982) was used to assess the antiseizure property of the plant extract in mice. Swiss mice (25 – 30g) were divided into five groups of 7 animals each. Distilled water (10ml/kg, i.p.), extract (100, 200, or 400 mg/kg, i.p.), ethosuximide (150 mg/kg, sc.) were administered one hr before induction

of convulsions with pentylenetetrazole (110 mg/kg, i.p.). The animals were observed for 30min especially for hind-limb tonic seizures or convulsions. Hind-limb tonic extensions of the mice were regarded as manifestations of seizures. The ability of the plant extract to prevent the seizures or delay/prolong the latency or onset of the hind-limb extensions was considered as an indication of anticonvulsant activity.

Statistical analysis

Data obtained are presented as means \pm SEM or as percentage protection. Data from distilled water treated animals were used as the control values. The data were analyzed using the Student t-test and statistical significant was considered at $p < 0.05$.

Results

A decoction of *Stereospermum kunthianum* stem bark is taken orally in traditional medical practice for the management of febrile convulsions in infants and young children. Tables 1 and 2 presented the results of the effect of the extract on maximal electroshock-induced seizures in rats. The extract when administered orally at the doses of 100, 200, and 400mg/kg protected the animals against electroshock-induced seizures by 11.1%, 33.3% and 55.6 respectively. Intraperitoneal injection of the extract at the same doses, dose-dependently, remarkably protected the animals against electroshock-induced seizures (Table 2) compared to the orally administered extract. Pretreatment of the rats with the extract intraperitoneally at 200mg/kg and 400mg/kg dose level respectively protected the rats by 76.9 % and 84.6% respectively against electroshock-induced convulsions. Phenobarbitone sodium (30mg/kg) caused 100% protection of the animals against electroshock-induced convulsions. Table 3 shows the effect of the extract on pentylenetetrazole-induced seizures in mice. Pentylenetetrazole (PTZ, 110 mg/kg) produced hind-limb tonic seizures in all the 7 mice used. Aqueous stem bark extract of *Stereospermum kunthianum* caused dose-related and significant ($p < 0.05$) delay of the onset of clonic seizures in the pentylenetetrazole-induced seizures compared to the distilled water pretreated mice. The extract similarly dose-dependently delayed the onset of tonic seizures induced by pentylenetetrazole in mice, which was significant ($p < 0.05$) at the dose of 400mg/kg compared to the distilled water pretreated mice. Pretreatment of the mice with the extract at 100, 200, and 400mg/kg slightly delayed the time to death of the mice compared with the distilled water pretreated mice. The extract (400mg/kg) protected 28.6% of the mice against death by pentylenetetrazole-induced seizures. Ethosuximide remarkably delayed the onset of seizures and significantly ($p < 0.0001$) delayed the time to death of the mice, with 57.1 % of the animals protected against death from pentylenetetrazole-induced seizures (Table 3).

Table 1: Effect of oral administration of aqueous stem bark extract of *Stereospermum kunthianum* on maximal electroshock – induced seizures in rats Each experiment involved at least 6 animals.

Treatment	No. protected /No. used	Protection (%)
Distilled water (5ml/kg,p.o)	0/6	00.0
<i>S. kunthianum</i> (100mg/kg, p.o.)	1/9	11.1
<i>S. kunthianum</i> (200mg/kg, p.o.)	3/9	33.3
<i>S. kunthianum</i> (400mg/kg, p.o.)	5/9	55.6
Phenobarbitone sodium (30mg/kg, i.p.)	6/6	100.0

Protection against seizures is expressed as percentage of the animals which did not convulse.

Table 2: Effect intraperitoneal administration of aqueous stem bark extract of *Stereospermum kunthianum* on maximal electroshock – induced seizures in rats

Treatment	No. protected/No. used	Protection (%)
Distilled water (5ml/kg,i.p)	0/6	00.0
<i>S. kunthianum</i> (100mg/kg, i.p.)	2/14	14.3
<i>S. kunthianum</i> (200mg/kg, i.p.)	10/13	76.9
<i>S. kunthianum</i> (400mg/kg, i.p.)	11/13	84.6
Phenobarbitone sodium (30mg/kg, i.p.)	9/9	100.0

Protection against seizures is presented as percentage of animal which did not convulse .Each experiment involved a minimum of 6 animals.

Table 3: Effect of administration of aqueous stem bark extract of *Stereospermum kunthianum* on pentylenetetrazole – induced seizures in mice

Treatment	Onset of clonic seizures(min)	Onset of tonic seizures(min)	Time of death (min)	Quantal death	Survival (%)
Normal saline (10ml/kg,i.p.)	1.65±0.12	4.44±0.49	8.58±0.74	7/7	0.00
<i>S. kunthianum</i> (100mg/kg,i.p.)	2.38±0.23*	5.50±0.65	10.0±0.78	7/7	0.00
<i>S. kunthianum</i> (200mg/kg,i.p.)	2.75±0.25*	5.79±0.48	11.50±0.61	7/7	0.00
<i>S. kunthianum</i> (400mg/kg, i.p.)	3.0±0.20*	6.33±0.33*	12.0±0.80	5/7	28.6
Ethosuximide (150mg/kg,sc.)	4.67±1.05*	10.0±0.00*	23.0±0.71*	3/7	57.1

Values are mean ±SEM, *P<0.05, significantly different from the distilled water treated animals, Student t – test (n=7)

Discussion

Our findings in the experimentally-induced seizures in the animal models used indicate that *Stereospermum kunthianum* aqueous stem bark extract possesses significant anticonvulsant activity in rodents. This is the first report on the anticonvulsant activity of this plant to the best of our knowledge. Febrile convulsions among infants and young children are a common phenomenon especially in the rural communities (Ojewole, 2008). Although the rural dwellers may not fully understand the etiology of the convulsions, they employ various herbal remedies to prevent, control and treat the convulsions. These remedies are cheap, accessible, and affordable and are generally acceptable in the community (Sofowora, 1993). The results of this study provide evidence in favour of the anticonvulsant activity of *Stereospermum kunthianum*, one of the frequently used plants in this regard. The aqueous stem bark extract of the plant dose-dependently, remarkably protected the animals against electroshock-induced seizures. The extract also caused a significant delay in the onsets of clonic seizures as well as a slight delay in the time of death of the animals in pentylenetetrazole-induced seizures. The ability of *S. kunthianum* to delay onset of seizures in the PTZ test indicates that it has the ability to raise seizure threshold (White et al., 1995). This also indicates its probable effectiveness against absence seizures (McNamara, 2006). Pharmacological agents that enhance GABA-mediated synaptic inhibition suppress seizures in diverse models and glutamate-receptor antagonists also inhibit seizures in diverse models including seizures evoked by electroshock and pentylenetetrazole (McNamara, 2006). The action of the aqueous stem bark extract in this study could be speculated to involve the enhancement of the GABAergic neurotransmission and/ or action in the brain and possible glutamate-receptor antagonist's action since it protects the animals against both electroshock and pentylenetetrazole-induced seizures. Although the present study could not establish the exact mechanism(s) of the antiseizure activity of the extract, it provides evidence for the use of the plant in the management or control of partial or generalized seizures. The results indicate that the aqueous extract possesses anticonvulsant activity in the experimental rodents model used and therefore tend to suggest that the shrub may be used as a natural supplementary remedy in the management of childhood convulsions.

In conclusion the findings of the study indicate that *Stereospermum kunthianum* aqueous stem bark extract possesses anticonvulsant activity and thus lend pharmacological credence to the traditionally claimed and ethno medical use of the plant in the treatment of childhood convulsions in rural communities in Nigeria and other West African countries.

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