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Neuropharmacological Evaluation of the Ethanol Roots Extract of *Securidacalonge pedunculata* (Polygalaceae) in Mice

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ABSTRACT

The present study examines the neuropharmacological activity of the ethanol root extract of *Securidacalonge pedunculata* Fres (Polygalaceae) using the Open Field and Apomorphine induced stereotypic test in mice. The oral LD_{50} value was evaluated in mice. Preliminary phytochemical screening of the extract was also conducted. The extract significantly inhibited apomorphine induced stereotypic behaviour, decreased the frequency of line crossing, grooming frequency and rearing against the wall in the open field. Acute toxicity test showed an oral LD_{50} value of 922 mg/kg per body weight in mice which is slightly toxic. Phytochemical analysis revealed the presence of carbohydrates; tannins, steroids, alkaloids, flavonoids and cardiac glycosides. These findings suggest that the roots of *S. longepedunculata* possess psychoactive substances with potential antipsychotic properties.

INTRODUCTION

Mental diseases including schizophrenia, anxiety and depression are considered to be a leading global healthcare burden amounting to 12.3 % of the global burden of disease which is expected to rise further in the near future[1]. Approximately 450 million people suffer from a mental or behavioral disorder[2], with only a small portion of them receiving the most basic treatment. However, because of the limited efficacy of current drugs, the need for newer, better-tolerated and more efficacious treatments remains high.

Therefore, in the search for safer, more specific and cheaper therapies for the management of mental disorders, medicinal plant research, worldwide, has progressed constantly, demonstrating the pharmacological effectiveness of many medicinal plants in different animal models.[3]

Securidacalonge pedunculata Fres (Polygalaceae) is a semi-deciduous shrub or small tree that grows to 12 m tall, with an often flattened or slightly fluted bole. It is spiny and much branched, with an open, rather straggly looking crown. The hatchet like appearance of the fruit is referred to in the generic name, while the specific name, 'longepedunculata', refers to the long, slender stalks of the flowers. It is commonly known as *sanya* in Hausa, *ipeta* in Yoruba and *ezeogwu* in Ibo.

It is used for the management of a wide range of ailments. The root bark of *S. longepedunculata* is used for the management and control of coughs, headache, constipation, wound, sore throat, rheumatisms, and gout[4]. Extract of the root bark of *S. longepedunculata* exhibited neuromuscular blocking and negative inotropic and chronotropic cardiac effects[5], and also demonstrated spasmolytic activity on vascular and extravascular smooth muscles in experimental animals[6]. The antisnake venom activity of the aqueous root extract was earlier reported[7,8]. The root powder exhibited insecticidal activity against a number of insects infesting stored grains[9]. Atawodi *et a.,l*[10] reported that the methanol extract of *Securidacalonge pedunculata* has some *in vitro* trypanocidal activities while methyl salicylate reportedly present in the volatile constituent is said to be responsible for the plant biocide effect against stored grain insects[11].

Pharmacological screening of root bark extracts of *S. longepedunculata* revealed that the root bark possesses potent anti-inflammatory effect in the topical and systemic models of acute

inflammation[12]. Antimicrobial activity was observed, particularly from the aqueous root extract[13].

In Northern Nigeria, the plant is employed in traditional medicine principally for its psychotropic properties. A cold infusion is prepared by submerging the roots and leaves in enough quantity of water to soak overnight. The infusion is usually taken orally the following day and then used to bathe. The infusion can be taken singly or in combination with other medicinal plants such as *Annona senegalensis, Syzygium guineense, Piliostigma thonningii and Terminalia avicennioides.*

This study seeks to evaluate the possible antipsychotic, anxiolytic, antidepressant effect and other possible central nervous system activity of this plant in mice.

MATERIALS AND METHODS

Collection and Identification of plant

Fresh root of *Securidacalonge pedunculata* plant was collected by Mr. A.A Maidori of the Pharmacology Department, Faculty of Pharmaceutical Sciences, University of Jos, in the month of April 2012 from Fanshanu, Toro local government area, Bauchi state, Nigeria. The plant was identified and authenticated by Mr. J.J Azila, of the Herbarium Unit, Federal College of Forestry, Jos, Nigeria. A voucher specimen with number 900141 was deposited at the herbarium unit of the Department of Biological Science, Ahmadu Bello University, Zaria, for future reference.

Preparation of Plant and Extraction process

The plant material was cleaned, cut into pieces and air dried in the shade for 2 weeks and milled into a coarse powder with the aid of a mortar and pestle. 200 g of the powdered plant material was macerated in 70% ethanol for 72 hours with occasional shaking. The extract was then filtered through Whatman No 1 filter paper. The marcerate was concentrated (dried in the oven at a temperature of about 40^0C *in vacuo* to give a dry solid residue of the extract. The resultant extract was weighted, stored in a refrigerator and the percentage yield calculated. Known weight of the extract was dissolved in distilled water at an appropriate concentration for oral administration when required. The percentage yield was calculated to be 10.04%w/w.

Animals

Albino mice (18-30g) of either sex were used for the study. The animals were obtained from the Animal House Unit, Department of Pharmacology, University of Jos and the Nigerian Institute of Trypanosomiasis Research (NITR) animal house, Jos, Nigeria. The animals were housed in cages and maintained under standard environmental conditions (26^0C) with access to food and clean drinkable water. The animals were deprived of food the night before the experiment and during the experiment. This was done to ensure that food does not interfere with the absorption of the drug.

Acute toxicity test

The acute toxicity and lethality test of the ethanol extracts of the plant was studied in mice using the method described by Lorke[14].

Apomorphine–Induced Stereotypic Behaviour

The mice were randomly divided into four groups (n = 5) to receive oral administration of the ethanol extract, (200 mg/kg, 400 mg/kg) while the control groups received either Chlorpromazine (2 mg/kg i.p) or Normal saline (10 ml/kg p.o). After 30-60mins, Stereotypic behaviour was induced by injection of Apomorphine (2 mg/kg i.p) in all groups.

Signs of stereotypic behaviour, which include mainly sniffing and gnawing, were observed and scored as follows: Absence of stereotypy= 0; occasional sniffing = 1; occasional gnawing = 2; frequent gnawing = 3; continuous gnawing = 4; gnawing intensively and staying at the same spot = 5.

Open Field Test

Briefly, mice (18 - 30 g) selected at random were divided into groups (n = 5) to receive oral administration of the extract, (200 mg/kg, 400 mg/kg). The control groups received either diazepam (2 mg/kg i.p) or normal saline (10 ml/kg p.o). Thirty to sixty minutes after treatment, each mouse was placed in the centre square of the open field. Horizontal (number of squares crossed) and vertical (number of rearing) activity was recorded manually for 5 min. Behavioural parameters recorded include line crossing, centre square entries, rearing (in the air and against the wall) and stereotypy as shown by frequency and duration of grooming.

The apparatus was thoroughly cleaned between tests with a tissue paper moistened with 10% ethanol to minimize olfactory cues between trials[15].

Statistical Analysis

All the results were expressed as Mean ± SEM. Data were analyzed using one way analysis of variance (ANOVA) followed by Newman Keul's post hoc test in Graph Pad prism software version 5.04 package, $p < 0.05$ was considered as significant.

RESULTS

Acute toxicity test and Phytochemical screening

Acute toxicity (LD_{50}) test[14] which was carried out using albino mice showed *Securidacalonge pedunculata* to be non-toxic up to an oral dose of 922mg/kg body weight. The Phytochemical analysis of *Securidacalonge pedunculata* root revealed the presence of the alkaloids, steroids, tannins, carbohydrates, flavonoids and cardiac glycosides.

The Open Field test

The extract at a dose of 200 mg/kg and 400 mg/kg caused a very significant dose dependent decrease ($p<0.001$) in the number of line crossed when compared to the normal saline treated group. Results from diazepam treated mice were similar. At a dose of 400 mg/kg, the extract caused a significant decrease ($p<0.05$) in rearing against the wall when compared to the vehicle treated group ($p<0.05$). Results from diazepam treated group showed a very significant decrease ($p<0.01$) in rearing against the wall when compared to the normal saline treated group. The frequency of grooming also decreased significantly ($p<0.05$) after administration of *Securidacalonge pedunculata* root extract at a dose of 200 mg/kg compared to vehicle treated group. Similar results were obtained for diazepam treated group.

TABLE 1: Effect of Ethanol Extract of *Securidacalonge pedunculata* Root on Mice in the Open Field

Treatment	Dose(mg/kg)	Locomotors Activity	
		Line crossing	Centre square entries
Normal saline	10ml/kg	65.80±6.36	0.60±0.25
SL Extract	200mg/kg	36.40±1.97***	1.80±1.07
	400mg/kg	26.40±3.23***	0.60±0.40
Diazepam	2mg/kg	36.20±4.65***	1.40±0.40

*Values are presented as mean ± SEM (n = 5); * p <0.05, ** p <0.01,***p<0.001. Newman Keul's post hoc test as compared to control, (SL= S. longepedunculata)*

TABLE 2: Effect of Ethanol Extract of *Securidacalonge pedunculata* Root On Mice In The Open Field

Treatment	Exploratory activity		Grooming			
	Rearing in the air	Rearing against the wall	Frequency	Duration(s)	Defecation	Urination
Normal saline	3.40±1.25	22.60±7.00	5.60±1.36	67.80±19.03	1.40±0.40	0.40±0.25
SL Extract	2.60±1.21	25.00±2.35	1.80±0.92*	25.60±13.10	0.80±0.58	0.60±0.40
	2.40±1.50	8.80±3.40*	3.00±1.00	23.00±8.57	1.00±0.45	0.40±0.25
Diazepam	0.40±0.25	2.20±1.96**	1.40±0.68*	4.20±1.96*	2.20±1.32	0.00±0.00

*Values are presented as mean ± SEM (n = 5); * p <0.05, ** p <0.01,***p<0.001. Newman Keul's post hoc test as compared to control, (SL= S. longepedunculata)*

The Apomorphine Induced Stereotypic Test

The extract at a dose of 400 mg/kg p.o significantly (p<0.05) attenuated apomorphine induced stereotypic behaviour in mice (Table 3).

Table 3: Effect of *Securidacalonge pedunculata* ethanol root extract on apomorphine-induced stereotype behaviour in mice

Treatment	Dose (mg/kg)	Stereotypic Behaviour Score (min)			
		0	10	20	30
Normal Saline	10	3.55±0.16	3.43±0.22	3.39±0.33	3.42±0.23
SL Extract	200	3.29±0.34	3.19±0.35	3.15±0.27	$^{+++}$2.87±0.40
SL Extract	400	2.85±0.65	2.95±0.42	3.12±0.30	$^{++}$1.95±0.44*
Chlorpromazine	2	0.00±0.00	0.00±0.00	0.00±0.00	0.20±0.20

Values are presented as mean ± SEM (n = 5); * p <0.05, Newman Keul's post hoc test as compared to vehicle control. (SL= *S. longepedunculata*). *****Significantly different from the control at p<0.05.++ p<0.01, +++ p<0.001 as compared to the Chlorpromazine treated group.

DISCUSSION

The median lethal dose serves a great purpose as a first pointer to the safety or toxic potential of a substance whose toxicity profile is not yet known[16]. The oral LD_{50} value of the extract is estimated to be 922 mg/kg body weight. Pharmacologically, a median lethal dose; LD_{50} (Oral) value of 922 mg/kg obtained is an indication that the plant is slightly toxic to the experimental model (albino mice) used. This is in accordance with toxicity classification/scale of toxic substances[17].

The result of the phytochemical screening of the extract revealed the presence of alkaloids, cardiac glycosides, carbohydrates, flavonoids, steroids and tannins which may be responsible for the neuroleptic potential of the extract. This is in conformity with reports from previous study[18]. Earlier reports suggest that plants containing flavonoids, saponins and tannins possess activity against many CNS disorders[19].

The open field model provides simultaneous measures of locomotion, exploration and anxiety. It also measures sedative[20], as well as non- specific effects of drug on locomotor activity[21].

It examines anxiety related behaviour characterized by the normal version of the animal to an open, brightly lit area[22, 23]. Animals are afraid of the aversive center and as such spend more time in the protective corners. Anxiolytics reduce this natural aversion and promote exploration such that the time spent in the center is increased. Anxiogenics increase the

animal's natural aversion and as such increase the time spent by animals in the more protective corners compared to the center[22].

In the Open field test, treatment with the extract at a dose of 400 mg/kg showed anxiolytic activity given that there was a significant decrease in rearing against the wall when compared to the saline treated group. A significant decrease was also observed in the number of line crossed at a dose of 200 mg/kg and 400 mg/kg. Similar findings from other studies have also confirmed the anxiolytic property of the extract[24]. In a novel environment as in the open field, anxious rodents exhibited thigmotaxic behaviour, which is a spontaneous preference for periphery/walls of the open field to the central parts.

Thus, the animals exhibited reduced thigmotaxic behaviour as shown by reduced preference for walls of the open field which is consistent with central depressant activity. Decrease in spontaneous motor activity such as locomotor activity (horizontal activity) and rearing (vertical activity) results from reduced excitability of the central nervous system and sedation[25,26]. The decrease in line crossing is indicative of a possible sedative effect.

The administration of *S. longepedunculata* extracts at a dose of 200 mg/kg ($p<0.05$), produced a significant decrease in grooming frequency comparable to the diazepam treated group. No significant difference was observed for defecation and urination. The validity of defecation as a measure of anxiety has been questioned. Hall describes defecation and urination as indices of anxiety in rodents. He argues that the animal will have reduced locomotion in a novel environment but the autonomic nervous system will be activated which will increase defecation in this noxious area[27].

However, Bindra and Thompson[28] argued that there is no significant relationship between fearfulness and urination and defecation as measured in the open field test. Nevertheless, Bindra and Thompson[28] agree that defecation and urination in a novel environment are signs of emotionality, which is not to be equated with fearfulness or timidity. [28]

The ethanol extract of *Securidacalonge pedunculata* root reduced stereotypic behaviour induced by apomorphine at a higher dose of 400mg/kg. This effect is an indication of neuroleptic and antidopaminergic potential of this extract. Apomorphine induces a stereotyped behaviour in rats and mice characterized by licking, sniffing and gnawing in a repetitive, compulsive manner which is an indication of striatal dopaminergic stimulation[29].

Compounds which prevent apomorphine induced stereotypy antagonize D_2 receptors in the nigostriatal system [29].

Therefore, inhibition of apomorphine induced stereotypic behaviour suggests interference with central dopaminergic transmission by the extract.

Securidacalonge pedunculata sedative and anticonvulsant properties were earlier reported by Adeyemi *et al*[24]. The therapeutic benefits of traditional remedies might depend upon a combination of constituents. Saponins have been shown to have profound CNS activities[4, 30]. Flavonoids, alkaloids and tannins have also been shown to possess anticonvulsant, anxiolytic and sedative property[31,32,33]. Flavonoids are natural active compounds that tend to bind to benzodiazepines $GABA_A$ receptors and they act pharmacologically as partial agonists. Some semi-synthetic flavones derivatives are much more potent than diazepam *in vivo* [33,34].It is therefore likely that the flavonoids, tannins, and alkaloids contents of this plant might be contributing to the pharmacological effect of the extract.

CONCLUSION

The results obtained provide evidence that the ethanol root extract of *Securidacalonge pedunculata* may contain psychoactive principles that may be relevant to the management of Psychiatric Disorders.

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