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Psycopharmacological Study of Ethanol Leaf Extract of *Solenostemon monostachyus*

Jude E. Okokon[1]*, Koofreh Davies[2], Augustine I. Bassey[3],

1. Department of Pharmacology and Toxicology, Faculty of Pharmacy, University of Uyo, Uyo, Nigeria
2. Department of Physiology, Faculty of Basic Medical Sciences, University of Uyo, Uyo, Nigeria.
3. Department of Clinical Pharmacology and Therapeutics, Faculty of Basic Clinical Sciences, College of Medicine, University of Uyo, Uyo, Nigeria

ABSTRACT

Solenostemon monostachyus P. Beauv (Lamiaceae) is a medicinal plant used traditionally in the treatment of central nervous system (CNS) disorders. The leaf extract was investigated for antidepressant effect on the CNS. The ethanol leaf extract of *S. monostachyus* (75-225 mg/kg) was evaluated for CNS effect in mice using open field test, Tail suspension tests and Forced swimming test models. The extract was found to significantly ($p<0.05$-0.01) increased the frequency of line crossing, rearing and walling activities of mice in open field test and also decreased significantly ($p<0.05$-0.001) duration of immobility time of mice in force swimming and tail suspension tests. The findings of this study show that the leaf extract of *S. monostachyus* has a significant psychotomotor effect with a weak antidepressant activity and this supports its use in ethnomedicine for the treatment of central nervous system disorders.

KEYWORDS: *Solenostemon monostachyus*, antidepressant, CNS

INTRODUCTION

Solenostemon monostachyus P. Beauv (Lamiaceae) is an important herb that is widespread in West and Central Africa. It occurs as an annual weed in anthropogenic habitats and rocky savannahs. It is slightly succulent, aromatic, and grows up to 100 cm tall (Mve-Mba *et al.*, 1994). The aerial parts of the plant are used in various decoctions traditionally by the Ibibios of the Niger Delta of Nigeria to treat stomach ulcer, fever/malaria (Adebayo and Krettli, 2011; Ajibesin *et al.*, 2008), hemorrhoid, and other inflammatory diseases. The decoction of the plant is also used to treat hypertension and as a diuretic (Koffi *et al.*, 2009). Phytoconstituents such as diterpenoids (Toshio *et al.*, 1980), flavonoids, coumarin, and polyphenol (N'guessan *et al.*, 2011) have been isolated. The leaf essential oil of *S. monostachyus* has been reported to contain b-pinene, oct-1-en-3-ol, b-caryophyllene, octan-3-ol, and (*E*,*E*)-a-farnesene (Mve- Mba *et al.*, 1994). The plant has been reported to possess antioxidant (N'guessan *et al.*, 2011; Okoko and Ere, 2012), antihypertensive (Fidele *et al.*, 2012), antimicrobial (Ekundayo and Ezeogu, 2006), antiulcer (Amazu *et al.*, 2015), antidiabetic and hypolipidemic (Okokon *et al.*, 2015), antipyretic and antimalarial (Okokon *et al.*, 2016a), antiinflammatory and antinociceptive (Okokon *et al.*, 2016b), hepatoprotective and nephroprotective (Okokon *et al.*, 2017) activities. We report the antidepressant activity of *S. monostachyus* to provide scientific basis for its use in traditional medicine.

MATERIALS AND METHODS

Plants collection

The plant material *S. monostachyus* (leaves) were collected in compounds in Uruan area, Akwa Ibom State, Nigeria in August, 2018. The plant was identified and authenticated by a taxonomist in the Department of Botany and Ecological Studies, University of Uyo, Uyo, Nigeria. Hebarium specimen was deposited at Department of Pharmacognosy and Natural Medicine Herbarium.

Extraction

The plant parts (leaves) were washed and shade-dried for two weeks. The dried plants' materials were reduced to powder using mortar and pestle. The powdered material was soaked in 50% ethanol. The liquid filtrate was concentrated and evaporated to dryness in vacuo 40˚C using rotary evaporator and stored in a refrigerator at - 4˚C.

Animals

Albino Swiss mice (19 – 28 g) of either sex were obtained from the University of Uyo animal house. They were maintained on standard animal pellets and water *ad libitum*. Permission and approval for animal studies were obtained from the College of Health Sciences Animal Ethics committee, University of Uyo.

*Corresponding author E-mail: judeefiom@yahoo.com Tel.No.+234-8023453678

Determination of median lethal dose (LD_{50})

The median lethal dose (LD_{50}) of the extract was estimated using albino mice by intraperitoneal (i.p) route using the method of Lorke (1983).

This involved intraperitoneal administration of different doses of the extract (100 -1000 mg/kg) to groups of three mice each. The animals were observed for manifestation of physical signs of toxicity such as writhing, decreased motor activity, decreased body/limb tone, decreased respiration and death. The number of deaths in each group within 24 hours was recorded. The LD_{50} was calculated as geometrical means of the maximum dose producing 0% (A) and the minimum dose producing 100% mortality (B).

$$LD_{50}=\sqrt{AB}$$

Evaluation of antidepressant activity

Open field test

Swiss albino mice of either sex were randomly divided into groups of 5 mice each and treated as follows for 5 days before open field test; control (normal saline, 2 mL/kg *p.o.*), imipramine (5.0 mg/kg, *p.o.*) and ethanol leaf extract of *S. monostachyus* (75, 150, 225 mg/kg *p.o.*). The open-field arena was made of acrylic (transparent walls and black floor, 30 × 30 × 15 cm), divided into nine squares of equal areas. The open field was used to evaluate the exploratory activity of the animal (Archer, 1973). The observed parameters were the number of squares crossed (with the four paws) and number of grooming and rearing, recorded for 5 min testing period.

Forced swimming test

Swiss albino mice of either sex were randomly divided into groups of 5 mice each and treated as follows for 5 days before the behavioural test; control (normal saline, 2 mL/kg *p.o.*), imipramine (5.0 mg/kg, *p.o.*) and *S. monostachyus* ethanol leaf extract (75, 150, 225 mg/kg *p.o.*). For assessing antidepressant activities, we employed the method described by Porsolt *et al.,* (1977; 1978). The development of immobility when mice were placed inside an inescapable cylinder filled with water reflects the cessation of persistent escape-directed behavior. Briefly, mice were individually placed in a circular tank (46 cm tall × 20 cm in diameter) filled with tap water (25 ± 1°C) to a depth of 20 cm and left there for 5 min. During this period, the behavior of the animals was recorded by an observer. Mice were considered immobile when remained floating without struggling and making only slight movements necessary to maintain the head above the water.

Tail suspension test (TST)

Mice of either sex were randomly divided into groups of 5 mice each and treated as follows for 5 days before tail suspension test; control (normal saline, 2 mL/kg *p.o.*), imipramine (5.0 mg/kg, *p.o.*) and ethanol leaf extract of *S. monostachyus* (75, 150, and 225 mg/kg, *p.o.*). The total duration of immobility induced by tail suspension was measured according to the methods described by Steru *et al.,* (1985). Briefly, mice both acoustically and visually isolated were suspended 50 cm above the floor by adhesive tape placed approximately 1 cm from the tip of the tail. Immobility time was recorded during a 6 min period. Mice were considered immobile only when they hung passively and were motionless.

Data and statistical analysis

The results were presented as mean and SEM and comparisons among groups for statistical significant differences were done by analysis of variance (ONE WAY ANOVA) followed by Turkey Kramer's multiple comparison tests using GraphPad Prism 5.3 application software. The p-values of less than 0.05 were considered as indicative of significance.

RESULTS

Open field test

Administration of leaf extract of *S. monostachyus* (75-225 mg/kg) for 5 days caused significant ($p<0.05$ - 0.01) non dose-dependent increase in the frequencies of line crossing, rearing and walling activities when compared to control. The standard drugs, imipramine (5 mg/kg), caused a significant ($p<0.001$) increase in the locomotor activity of the mice as evident in the frequency of the line crossing, walling and rearing activities (Table 1).

Table 1: Effect of ethanol leaf extract of *S. monostachyus* on locomotive behavior of mice during open field test.

TREATMENT	DOSE	LINE CROSSING	WALLING	REARING
	mg/kg			
Control normal saline	-	35.25 ±3.53	10.75 ± 1.50	1.25±0.25
Immipramine	5	126.3 ±8.67^{c}	15.66 ± 2.02^{c}	18.0±0.30^{c}
Crude extract	75	83.0±1.52^{c}	15.33 ± 2.60^{c}	14.00±1.70^{c}
	150	81.66 ± 4.05^{c}	17.33 ± 2.84^{c}	21.66±6.33^{c}
	225	72.33 ± 1.45^{a}	14.33±2.33^{a}	18.66±0.56^{c}

Data are expressed as MEAN ± SEM, Significant at [a]p < 0.05, [c]p<0.001, when compared to control. (n=6).

Effect on force swimming test

Administration of the ethanol leaf extract of *S. monostachyus* (75-225 mg/kg) to mice for five days caused considerable decreases in the duration of immobility in mice during force swimming test which was not significant (p>0.05) when compared to control. These decreases were non dose-dependent. The standard drug, imipramine (5 mg/kg) similarly produced a significant (p<0.05) reduction in the immobility time of the mice when compared to control (Table 2).

Table 2:Effect of ethanol leaf extract of *S. monostachyus* on behavior of mice during forced swimming test.

TREATMENT	DOSE	Duration of immobility (min)
	mg/kg	
Control normal saline	-	2.94±0.53
Immipramine	5	1.15±0.18 [a]
Crude extract	75	2.70±0.22
	150	2.66±0.19
	225	2.61±0.23

Data are expressed as MEAN ± SEM, Significant at [a]p < 0.05, when compared to control. (n=6).

Effect on tail suspension test

Administration of the ethanol leaf extract of *S. monostachyus* (75 – 225 mg/kg) to mice for five days decreased immobility duration non dose-dependently during tail suspension test though not significant (p<0.05) when it was compared to control. The standard drug, imipramine (5 mg/kg), exerted a significant (p<0.05) reduction of the immobility time of the mice when compared to control (Table 3).

Table 3: Effect of ethanol leaf extract of *S. monostachyus* on behavior of mice during Tail suspension test.

TREATMENT	DOSE	Duration of immobility(min)
	mg/kg	
Control normal saline	-	2.90 ± 0.07
Immipramine	5	1.02± 0.13 [a]
Crude extract	75	2.25± 0.17
	150	2.08 ± 0.16
	225	2.14±0.07

Data are expressed as MEAN ± SEM, Significant at [a]p< 0.05, when compared to control. (n=6).

DISCUSSION

In this study, evaluation of the effect of ethanol leaf extract of *S. monostachyus* on central nervous system was carried out in mice using different models; Open field test, tail suspension test and force swimming test. The leaf extract (75-225 mg/kg) was found to cause significant dose-dependent increases in the frequency of line crossing, walling and rearing activities of the pretreated mice (Table 1). It also reduced considerably the immobility time of the mice in force swimming. Monitoring of locomotor activity of animals has been used to assess the effect of drug on the CNS. An increased movement is a measure of the level of excitability of the CNS (Ozturk *et al*., 1996), while its decrease may be resulting from depression of the CNS (Kolawole *et al*., 2007). Central nervous system stimulants are known to increase locomotor activity, while agents with depressant activity cause reduction in movements (Yadav *et al.*, 2008). The leaf extract was found to increase significantly line crossing, walling and rearing activities during open field test suggesting stimulatory effect on the CNS. The leaf extract further demonstrated CNS stimulatory effect by its potential to decrease immobility time of mice during force swimming and tail suspension tests. Forced swimming and tail suspension tests are two of the most commonly used animal models of depression for antidepressant screening. In the forced swimming test, the development of immobility when mice are placed into an inescapable cylinder of water reflects the cessation of persistent escape-directed behavior (Lucki, 1997). The tail suspension test is based on the fact that animals subjected to the short-term, inescapable stress of being suspended by their tail, will develop an immobile posture. Various

antidepressants are able to reverse the immobility and promote the occurrence of escape related behavior. Both models of depression are widely used to screen new antidepressants (Porsolt *et al*., 1977, 1978; Steru *et al*., 1985). These tests are quite sensitive to major antidepressant drugs including tricyclics, serotonin-specific reuptake inhibitors, MAO inhibitors, and atypical antidepressant (Porsolt *et al*., 1977; Steru *et al*., 1985; Detke *et al*., 1995). Forced swimming and tail suspension tests represent the behavioural despair model, and are claimed to reproduce a condition similar to human depression (Porsolt *et al*., 1977; Willner, 1984; Steru *et al*., 1985). The tests are based on the observation that animals, following initial escape oriented movements, develop an immobile posture when placed in an inescapable chamber. The immobility is thought to reflect either a failure of persistence in escape-directed behaviour (i.e. behavioural despair) or the development of passive behaviour that disengages the animal from active forms of coping with stressful stimuli (Lucki, 1997). It is well known that clinically effective antidepressants (such as imipramine) typically increase the swimming efforts of the animal seeking a solution to the problem and, therefore, they decrease the duration of immobility in the forced swimming test (Porsolt *et al*., 1977). This was observed in this study. Similarly, the results of this study suggest that the leaf extract exhibited significant antidepressant activity with a strong psychomotor stimulation. The leaf extract has been reported to contain a number of compounds such as diterpenoids (Toshio *et al*., 1980), flavonoids, coumarin, and polyphenol (N'guessan *et al*., 2011). Phytochemical constituents such as flavonoids have been implicated in antidepressant action on the CNS (Hossain *et al*, 2009), while polyphenols especially flavonoids like quercetin and rutin have also been reported to exhibit antidepressant effect (Nolder and Schotz, 2002). These phytochemical constituents may be responsible for the observed activity of the leaf extract in this study.

CONCLUSION

The results of this study show that ethanol leaf extract of *S. monostachyus* possess CNS stimulatory activity which justifies its use in ethnomedicine for the treatment of central nervous system disorders.

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Conflict of interest declaration

The authors declare no conflict of interest

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