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ANTIDEPRESSANT ACTIVITY OF METHANOL ROOT BARK EXTRACT OF *Securinega virosa* (EX WILLD.) BAILL IN ALBINO MICE

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ABSTRACT
Securinega virosa (S. virosa) is a commonly used medicinal plant in Africa for the management of psychiatric illnesses. Thus, the current study aimed at evaluating the antidepressant activity of the methanol extract of S. virosa in mice. The acute toxicity and phytochemical profiles were also determined. The antidepressant activity of the extract (500, 250 and 125 mg/kg) was assessed using the tail suspension test(TST), forced swim test (FST) and open field test (OFT).The median lethal dose was estimated to be ≤2000 mg/kg. Phytoconstituents like tannins, saponins, flavonoids, alkaloids and cardiac glycosides were found to be present in the crude extract. The methanol root bark extract of S. virosa significantly (p<0.05) decreased duration of immobility and also decreased comotion and exploratory behavior in mice. Results obtained from this study showed that the root bark extract of S. virosa might possess antidepressant activity.
Keywords: Securinega virosa, depression, anxiety, phytochemical

INTRODUCTION

Securinega virosa (*S. virosa*) is one of the most useful medicinal plants found in several African countries (Dalziel, 1936). It is used traditionally in the management of psychiatric illnesses in Northern Nigeria (Neuwinger, 1996). The behavioural (Magaji *et al.,* 2008a; Allen, 2011) and analgesic effects (Magaji *et al*., 2008b) of the methanol root bark extract of *S. virosa* have previously been reported. Depression affects 10-17% of the global population at some point in life, resulting in enormous personal suffering and economic loss (Ronald, 2014). It is associated with high risk of serious physical health problems (Martin and Hilary, 2012), but still remain a neglected problem in palliative care provision across much African countries (Marina et al., 2012). Depression is different from other types of psychiatric disorders like anxieties, thus it should not be confused as each require different treatment modalities (Muhammad et al., 2013; Gadassi and Mor, 2016). Depression unlike anxiety has suicidal tendencies in addition to the mode alterations. Depression has affected around 300 million individuals across the globe (Calvo-Perxas *et al*., 2016; Brent, 2016; Filho *et al*., 2016), and it keep rising outrageously in every community including Nigeria. Factors such as family history, genetic components, life style, environment and diseases were directly or indirectly linked depression (Kimberel *et al*., 2016, Ridout *et al*., 2016). However, with all these devastating characteristics of the disease, current therapies are faced with challenges of poor efficacy and side effects, which made neuro-researchers to look inward and discover novel agents with different characteristics (Khan *et al*., 2018).The present study therefore aimed at evaluating the antidepressant properties of *S. virosa* using forced swim test, tail suspension test and open field test.

MATERIALS AND METHODS

Reagents and Chemicals

Imipramine (Sigma Aldrich USA), Diazepam (Wuhu Kangi Pharma. Co. Ltd), Normal saline (Dana Pharmaceuticals Ltd), Methanol root bark of *Securinega virosa.*

Plant Collection and Preparation

Fresh roots of *S. virosa* were collected in Basawa, a town in Sabon Gari Local Government area of Kaduna State, Nigeria in March 2016. The plant was identified and authenticated by a Botanist in the Herbarium section of Biological Sciences Department, Ahmadu Bello University, Zaria by comparing with a voucher specimen number (918) previously deposited. The root was then washed and bark removed. The root bark was dried under shade with intermittent weighing until constant weight was obtained. It was then coarsely powdered with a mortar and pestle. About 100g of the coarse powder was extracted with 500mls of methanol via Soxhlet extraction over 72hours. The extract was then concentrated and stored in a dessicator until needed for use. Solution of extract was freshly prepared for each experiment.

Phytochemical Analysis

Phytochemical screening was conducted based on standard protocol (Evans, 1996).

Experimental Animals

Swiss Albino mice of either sex (18-22g) were obtained from the Animal House Facility of Department of Pharmacology and Therapeutics, ABU, Zaria. Mice were kept in propylene cages at room temperature, with standard feed and water *ad libitum*. Experimental protocols were approved by the university Animal Handling Ethics Committee. Experiment was conducted in a standard neurobehavioral laboratory between 900h to 1600h.

Acute toxicity studies (LD_{50})

Oral median lethal dose (LD_{50}) of the extract was estimated in mice according to method previously described by Lorke (1983). Briefly, the method was done in two phases, in the first phase, three groups of three mice each were treated per orally with 10, 100 and 1000mg/kg body weight and observed for signs and symptoms of toxicity and death for 24 hours. In the second phase, four groups each containing one mouse was treated with four more specific doses of the extract (1200, 1600, 2900 and 5000 mg/kg). The LD_{50} was determined by calculating the geometric mean of the lowest dose that caused death and the highest dose for which the animal survived (0/1 and 1/1).

Tail Suspension Test

Thirty mice were divided into five groups of six mice each. Group 1 was treated with 10 mL/kg normal saline, groups 2, 3 and 4 were treated with 500, 250 and 125mg/kg of methanol extract of *S. virosa* orally. Group 5 were orally treated with imipramine 10mg/kg respectively. One hour later, mice were suspended on the edge of the shelf 58cm above a table top by adhesive tape placed approximately 1cm from the tip of the tail. The duration immobility was then recorded for a period of 6 minutes (Steru *et al.*, 1985).

Forced Swim Test

Thirty mice were divided into five groups of six mice each. Group 1 was treated with 10 mL/kg normal saline, groups 2,3 and 4 were orally treated with 500, 250 and 125mg/kg of methanol extract of *S. virosa* respectively. One hour later, each mouse was placed in a plexiglass cylinder tank of 40cm height and 18cm width filled with 15cm water at 25℃. The total duration immobility was measured over 5 minutes. A mouse was considered immobile whenever it remained floating passively in the water in a slightly hunched but upright position with its nose just above the surface (Alpermann *et al.*, 1992).

Open Field Test

Thirty mice were divided into five groups with five mice each. Group 1 was treated with 10 mL/kg normal saline. Groups 2, 3, and 4 received 500,250, and 125mg/kg of methanol extract of *S. virosa* respectively. Group 5 received diazepam (15 mg/kg.) One hour later, each mouse was then placed in white wooden open field apparatus (70 x 70 x 35cm, length, breath and height) of which one wall is made of plexiglass. The floor was divided into 16 visible squares (15 x 15 cm)with a central square with the aid of marker and covered with a Plexiglas. One hour after treatment, mice were individually placed at the corner of the apparatus and allowed to explore. Behavior of mice was recorded for 5mins (Rex *etal.*, 1998). Arena was cleaned with 10% ethanol between tests to remove olfactory cues.

Statistical Analysis

Data obtained were analyzed using one-way ANOVA followed by Dunnett's t- test. A *p*value of ≤ 0.05 was considered significant.

RESULT

Phytochemical Analysis

The phytochemical screening of methanol root bark extract of *S. virosa* revealed the presence of steroids, saponins, alkaloids, tannins, carbohydrates and glycosides (Table 1).

Toxicity studies

The oral median LD_{50} was estimated to be greater than2000mg/kg body weight (Table 2).

Antidepressant studies

Tail suspension test

The methanol root bark extract of *S.virosa* significantly ($p \leq 0.05$) decreased the duration of immobility at a dose of 125 mg/kg and500 mg/kg respectively. Similarly, Imipramine significantly ($p \leq 0.001$) decreased the duration of immobility compared to the normal saline treated group (Figure 1).

Forced Swim Test

The methanol root bark extract of *S. virosa* significantly ($p<0.0001$) decreased the duration of immobility at all tested doses. Imipramine (15mg/kg) also significantly ($p \leq 0.0001$) decreases the immobility period as compared to normal saline treated group (Figure 2).

Open Field Test

The methanol root bark extract of *S.virosa* significantly ($p \leq 0.001$ and $p \leq 0.05$) decreased the total number of line crossed at doses of 125mg/kg and 500 mg/kg respectively. Similarly, Diazepam (10mg/kg) significantly ($p \leq 0.001$) decreased the total number of lined crossed(Figure 3).The methanol root bark extract of *S.virosa* significantly ($p< 0.001$) decrease frequency of stretch to attend posture at doses of 125 mg/kg, 250 mg/kg and 500mg/kg when compared with the normal saline treated group. Similarly, diazepam also significantly ($p \leq 0.001$)decreased stretch to attend posture frequency (Figure 4).

Table 1: Phytochemical constituents of the methanol Root Bark Extract of *Securinega virosa*

S/No	Phytoconstituents	Inference
1	Alkaloids	+
2	Flavonoids	+
3	Tannins	+
4	Saponin glycoside	+
5	Cardiac glycoside	+
6	Unsaturated Steroids	+
	and Triterpenes	+
7	Anthraquinones	+
8	Carbohydrates	+

+= present, -=absent

Table 2: LD_{50} Values for Methanol Root Bark Extract of *Securinega virosa* in Mice

LD_{50} Value	Onset of toxicity	Duration of toxicity	Signs of toxicity
≥2000	None	None	None

n=13.

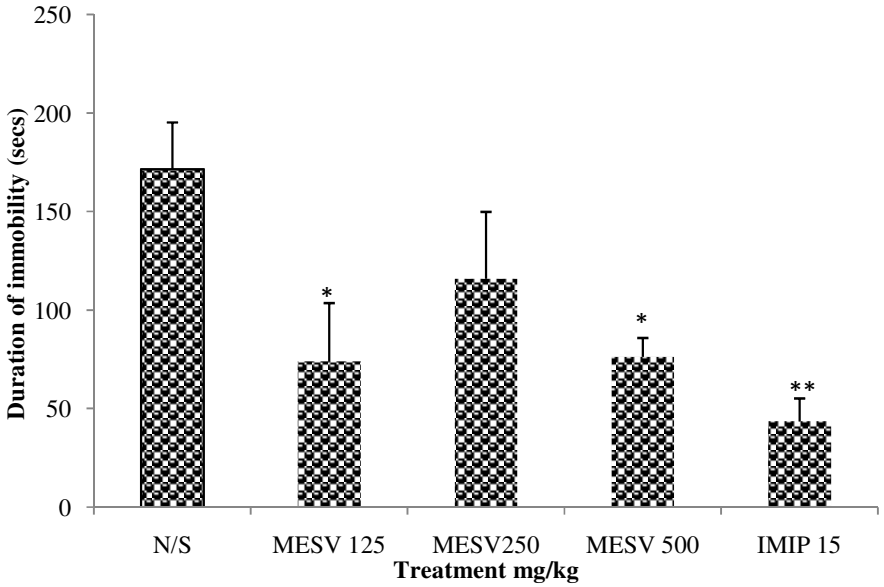

Figure 1: Effect of Methanol Root Bark Extract of *S. virosa* on Duration of Immobility in Mice in the Tail Suspension Test

Data was analyzed using one-way ANOVA followed by Dunnetts t-test and presented as mean±SEM, *= $p \leq 0.05$; **= $p \leq 0.01$are significant statistical difference as compared to normal saline treated group, MESV= Methanol root extract of *S. virosa*, IMIP= Imipramine; n=6,

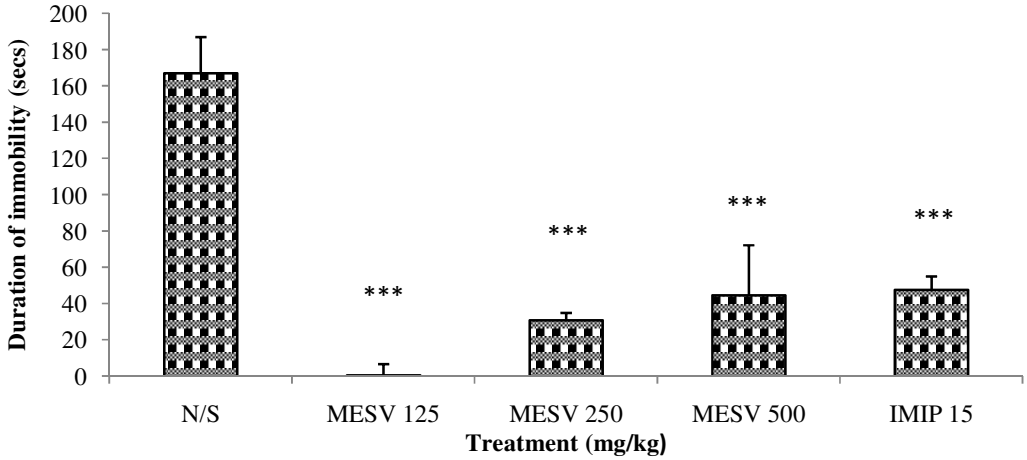

Figure 2: Effect of Methanol Root Bark Extract of *S. virosa* on Duration of Immobility in Mice in the Forced Swim Test

Data was analyzed using one-way ANOVA followed by Bonferoni post hoc and presented as mean ±SEM, ***= P≤0.000 are significant statistical difference as compared to Control group, MESV= Methanol root extract of *S. virosa*, IMIP= Imipramine,n=6

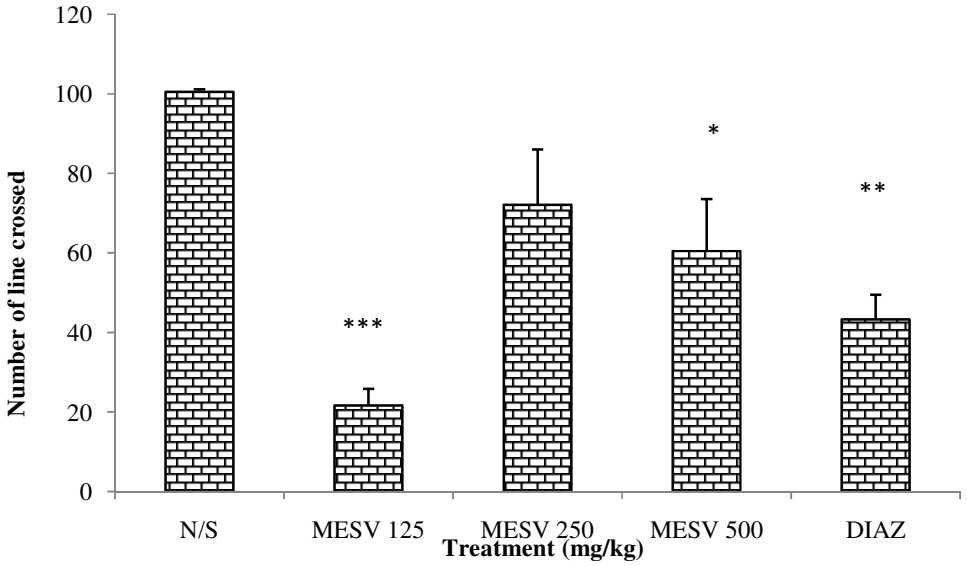

Figure 3: Effect of Methanol Root Bark Extract of *S. Virosa* on the Number of Lines Crossed by Mice in the Open Field Test in Mice

Data was analyzed using one-way ANOVA followed by Dunnett t-test and presented as mean ±SEM, *= $p \leq 0.05$, **= $p \leq 0.01$, ***= $p \leq 0.00$ are significant statistical difference as compared to Control group, MESV= Methanol root extract of *S. virosa*, DIAZ= Diazepam, n=6

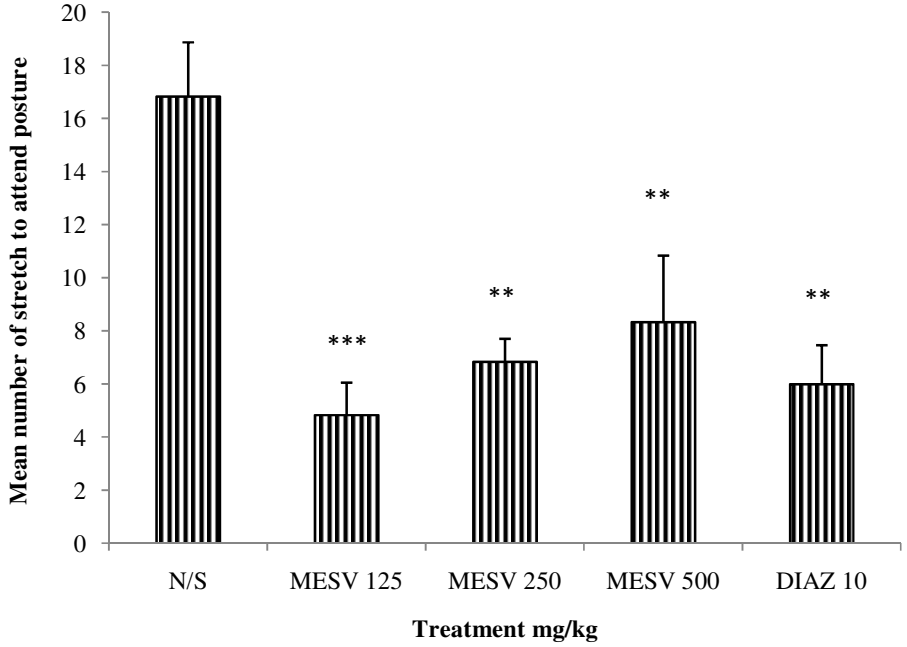

Figure 4: Effect of Methanol Root Bark Extract of *S. Virosa* on Number of Stretch to Attend Posture by Mice in the Open Field Test

Data was analyzed using one-way ANOVA followed by Dunnett's t-test and presented as mean ±SEM, **= $p \leq 0.01$, ***= $p \leq 0.001$ are significant statistical difference as compared to normal saline treated group, MESV= Methanol root extract of *S. virosa*, DIAZ= Diazepam, n=6

DISCUSSION

Securinega virosa is reportedly used as stimulant taken as a broth, the leaf sap is used in cases of epilepsy and with other drugs, the plant is used as tranquilizer in sanity in traditional medicine across the world with Nigeria inclusive (Magaji *et al.,* 2008).

The forced swim test is one of the behavioural tests in rodents utilized to predict clinical efficacy of antidepressants and their possible mechanism of action (Borsini and Meli, 1988). Antidepressant such as serotonin reuptake inhibitors (SSRIS) and tricyclic antidepressant (TCA) reverse the immobility posture and enhance escape attempts behavior. Immobility exhibited by rodents when subject to unavoidable stress such as forced swimming and tail suspension reflect a state of despair or lowered mood, which is thought to reflect depressive episodes in humans (Cryan *et al*., 2005; Everton *et al*., 2018).Rodents when forced to swim in a cylinder from which they cannot escape will after an initial period of vigorous activity, display a characteristic immobile posture which can be readily identified and is said to reflect a state of despair (Kashani *et al*., 2018). The methanol root bark extract of *S. virosa* reverses the immobility and promote the occurrence of escape-related behavior in mice.

Due to the draw backs of false positive or false negative associated with forced swim test (Foyet *et al*., 2014); the tail suspension test was also conducted. In both tests, there was significant reduction of immobility time of mice, and the result was quite comparable to imipramine, the tricyclic antidepressant agent used as standard for the test, indicating that the extract possesses antidepressant activity on the central nervous system.

In order to avoid the false positive response associated with psychostimulants, the effect of extract was tested on locomotion, exploration and anxiety activities in the open field test (Walsh and Cummins, 2001; Yu *et al*, 2007). The extract did not increase spontaneous motor activity in mice, but rather inhibited the locomotor activity. Suggesting that it possesses general CNS depressant potential as previously reported. Putting all the results together, it can be strongly inferred that the antidepressant activity of methanol root extract of *S. virosa*has no relationship with skeletal muscle stimulation. Furthermore, several well-known antidepressants decrease locomotor activity (Brian and Francois, 2015; Yau *et al*., 2017). One of the etiologies of depression is alteration in neurotransmitters function, particularly serotonin, noradrenaline and dopamine (Mayor, 2014; Argyii, 2015; Mannan *et al*., 2015). Therapy with SSRIs has been reported to increase extracellular availability of serotonin (Martin, 2012). Thus, methanol root extract of *S. virosa* may exert its observed antidepressant effect through one or more of the central nervous system neurotransmitters activity on Glutamatergic, GABAergic or Serotonergic pathways. In line with this, researches have previously reported the methanol extract to have antagonized apomorphine induced climbing behavior as well as decreased number of head dips in hole board test in mice (Magaji *et al*., 2008a). This report supported the central depressant activity observed in this study, proposing the involvement of dopaminergic actions on limbic systems and probably GABAergic systems.

Safety and efficacy are factors of great concern when seeking for a novel drug. The LD_{50} of the extract was found be around 2000 mg/kg orally. This is an indications of the plant being slightly toxic as described by Lorke (1983).

The biological or pharmacological actions of plant extracts are known to be due to the presence of specific phytochemical constituents. Antidepressant activities have been linked tosaponins, flavonoids and alkaloids (Haixia *et al*., 2009; Mohit *et al*., 2009).Thus the antidepressant effect exhibited by the plant *S. virosa* may be due to the presence of saponins, tannins and alkaloids found present in the plant.

CONCLUSION

The methanol root bark extract of *S.virosa* showed potentials for antidepressant activity.

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