

Research Article

Antidepressant activity of ethanol leaf extract of *Panicum maximum*

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Background: *Panicum maximum* is used in Ibibio ethnomedicine for the treatment of various diseases including central nervous system disorders.

Objective: To investigate the *in vivo* antidepressant activity of *Panicum maximum*.

Methods: The ethanol leaf extract of *Panicum maximum* (48 -144 mg/kg) was investigated for antidepressant activity in Swiss albino mice using open field, force swimming and tail suspension tests.

Results: The extract was found to significantly ($p < 0.05-0.01$) increase the frequency of line crossing, rearing and walling activities of mice in open field test. The extract also decreased significantly ($p < 0.05-0.001$) duration of immobility time of mice in force swimming and tail suspension tests.

Conclusion: The leaf extract of *P. maximum* has antidepressant activity and this supports its use in ethnomedicine for the treatment of central nervous system disorders.

Keywords: *Panicum maximum*, antidepressant, CNS stimulant

Received: January, 2018

Published: March, 2018

1. Introduction

Panicum maximum Jacq (Poaceae) is a perennial, tuft grass with a short, creeping rhizome regarded as the most valuable fodder plant and extensively used to make hay. The stem of this robust grass can reach a height of up to 2m, the leaf sheath are found at the bases of the stems and are covered in fine hairs. It is a tropical grass and widely distributed in Africa and other tropical regions of the world (Van Oudtshoorn, 1999).

Phytochemical components such as phytol, pentadecanoic acid, Hexadecanoic acid, dodecanoic acid, 8,11,14-eicosatrienoic acid (Z,Z,Z), mono and sesquiterpenes such as terpinen-4-ol, borneol and germanicol have been reported on the leaf extract (Okokon et al, 2014).

The Ibibios of Akwa Ibom State, Nigeria use the leaves ethnomedically in the treatment of various ailments such as malaria, microbial infections, rheumatism pain, inflammation, diabetes and central nervous system disorders.

Antidiabetic (Antia et al, 2010), antimalarial and analgesic (Okokon et al, 2012), antibacterial (Gothandam et al, 2010; Doss et al, 2011a; Doss et al, 2011b), anti-inflammatory and antipyretic (Okokon et al, 2011), antifungal (Kanife, 2012), anticancer, antioxidative, and antileishmanial (Okokon et al, 2014) activities of the leaf extract have been reported.

In this study, we investigated the *in vivo* antidepressant activity of ethanol leaf extract of *Panicum maximum*.

2. Methods

2.1 Plants collection

The fresh leaves of *Panicum maximum* were collected in August, 2017 at Farmland in Uyo, Uyo LGA, Akwa Ibom State, Nigeria. The leaves were identified and authenticated as *Panicum maximum* a taxonomist in the Department of Botany and Ecological studies, University of Uyo, Uyo, Nigeria. Herbarium specimen was deposited at the Faculty of Pharmacy Herbarium (FPH 76c), University of Uyo, Nigeria.

2.2 Extraction

The plant parts (leaves) were washed and air-dried on laboratory table for 2 weeks. The dried leaves were pulverized using a pestle and mortar. The powdered leaf was macerated in 95% ethanol for 72 hours. The liquid ethanol extract obtained by filtration was evaporated to dryness in a water bath at 60°C. The yield of the extract was stored in a refrigerator at -4°C until it was used for the experiment reported in this study.

2.3 Animals

The animals (Swiss albino mice) of either sex were used for these experiments. The animals were housed in standard cages and were maintained on a standard pelleted feed (Guinea feed) and water *ad libitum*. Permission and approval for animal studies were obtained from the College of Health Sciences Animal Ethics Committee, University of Uyo.

2.4 Evaluation of antidepressant activity

Open field test

Rats 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 *Panicum maximum* (48,96, and 144 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) and to monitor locomotor activity of animals which indicate effect of drug on the CNS. The observed parameters were the number of squares crossed (with the four paws) and number of walling and rearing activities, recorded for 5 min testing period. Increases in these activities indicate antidepressant activity and vice versa.

Forced swimming test

Mice 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 ethanol leaf extract of *Panicum maximum* (48, 96, and 144 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. The CNS stimulatory or antidepressant effect of the leaf extract was indicated by its potential to reduce immobility time of mice during force swimming test.

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 *Panicum maximum* (48,96, and 144 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. The CNS stimulatory or antidepressant effect of the leaf extract was indicated by its potential to reduce immobility time of mice during tail suspension test

2.5 Statistical analysis and data evaluation

Data obtained from this work were analyzed statistically using ANOVA (One-way) followed by a post test (Tukey-Kramer multiple comparison test). Differences between means were considered significant at 5% level of significance ($P \leq 0.05$).

3. Results

Open field test

Administration of leaf extract of *P. maximum* (48-144 mg/kg) for 5 days caused significant ($p < 0.05 - 0.01$) dose-dependent increase in the frequencies of line crossing (**Figure 1**), rearing (**Figure 2**) and walling (**Figure 3**) activities when compared to control. The observed increased activities of the extract-pretreated mice indicated CNS stimulatory effect and thus, antidepressant activity. 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 which also are indication for antidepressant activity.

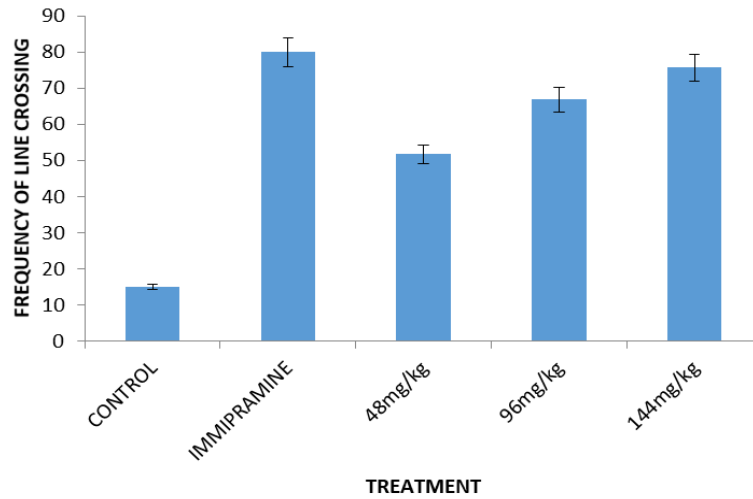


Figure 1: Effect of ethanol leaf extract of *Panicum maximum* on frequency of line crossing of rats.

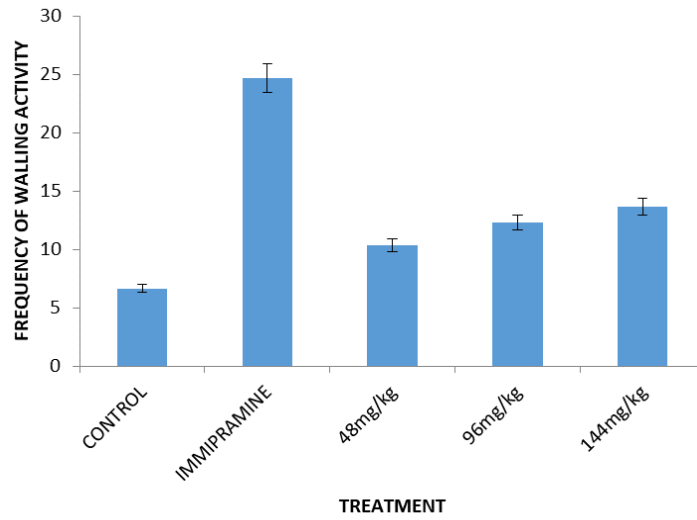


Figure 2: Effect of ethanol leaf extract of *Panicum maximum* on frequency of Walling activity of rats.

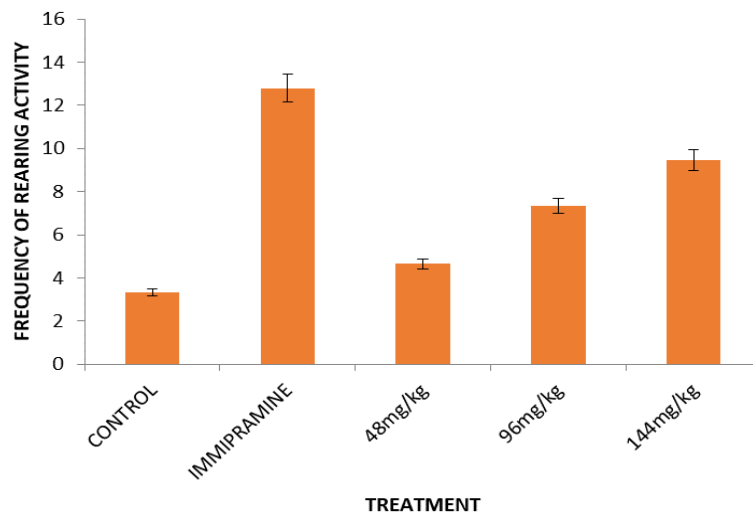


Figure 3: Effect of ethanol leaf extract of *Panicum maximum* on frequency of rearing activity of rats.

Effect on Force Swimming Test

Administration of the ethanol leaf extract of *P. maximum* (48-144 mg/kg) to mice for five days significantly ($p < 0.001$) reduced immobility duration though in dose-dependent fashion in mice during force swimming test when compared to control. The standard drug, imipramine (5 mg/kg) similarly produced a significant ($p < 0.001$) reduction in the immobility time of the mice when compared to control. (Figure 4). The reduced observed immobility time by the extract and imipramine-pretreated mice are demonstration of their antidepressant activities. The effect of the extract (48 -144 mg/kg) was higher than that of the standard drug, imipramine portraying a superior antidepressant action.

Effect on Tail Suspension Test

Administration of the ethanol leaf extract of *P. maximum* (48-144 mg/kg) to mice for five days significantly ($p < 0.001$) reduced immobility duration in a non-dose-dependent fashion during tail suspension test when it was compared to control. The extract (48- 144 mg/kg) exerted prominent reductions in the immobility time which were higher than that of the standard drug. The standard drug, imipramine (5 mg/kg), exerted a significant ($p < 0.001$) reduction of the immobility time of the mice when compared to control (Figure 5). These reductions in observed immobility time by the extract and imipramine-pretreated mice are clear demonstration of antidepressant activities of the extract and drug.

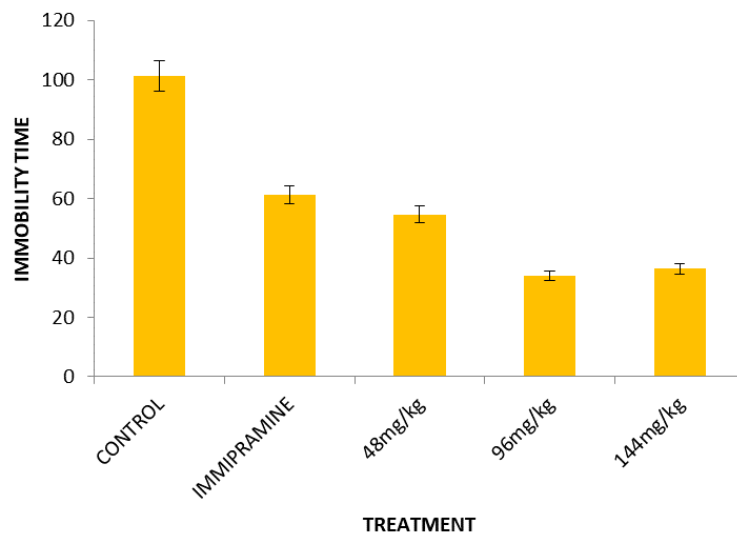


Figure 4: Effect of ethanol leaf extract of *Panicum maximum* on behavior of mice during forced swimming test

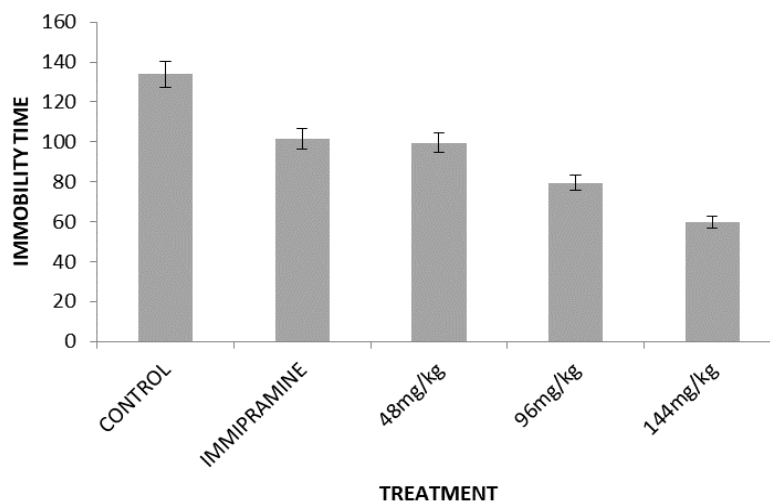


Figure 5: Effect of ethanol leaf extract of *Panicum maximum* on behavior of mice during Tail climbing test

4.0 Discussion

In this study, evaluation of the effect of ethanol leaf extract of *Panicum maximum* 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 (48 - 144 mg/kg) was found to cause significant dose-dependent increases in the frequency of line crossing, walling and rearing activities of the pretreated mice. It also reduced significantly the immobility time of the mice in force swimming and tail suspension tests.

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 CNS stimulatory effect of the leaf extract was further supported by its potential to reduce 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 which represent the behavioural despair model, 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 was reported to contain chemical constituents such as alkaloids, flavonoids, tannins, terpenes, saponins, anthraquinones, reducing sugars, and cardiac glycosides (Okokon 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). The leaf extract of *P. maximum* has also been reported to contain phytol,

pentadecanoic acid, Hexadecanoic acid, dodecanoic acid, 8,11,14-eicosatrienoic acid (Z,Z,Z), mono and sesquiterpenes such as terpinen-4-ol, borneol and germanicol among others (Okokon et al, 2014). These polyunsaturated fatty acids are known to possess antidepressant activity (Naveen et al, 2013; Su et al, 2015). Omega-3 PUFAs have been suggested to provide a range of neurobiological activities through modulation of neurotransmitters, anti-inflammation, anti-oxidation and neuroplasticity thereby exerting antidepressant action (Su, 2008; Lu et al, 2010; Su, 2012; Su et al, 2015). These phytochemical constituents may be responsible for the observed activity of the leaf extract in this study.

The results of this study show that ethanol leaf extract of *Panicum maximum* possess antidepressant activity which supports its use in ethnomedicine for the treatment of central nervous system disorders.

Conflict of Interest declaration

The authors declare no conflict of interest.

Acknowledgments

The authors are grateful to Mr. Cosmas Obi of Department of Pharmacology and Toxicology, Niger Delta University for his technical assistance.

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