Advanced Herbal Medicine, 2016; 2(4): 22-28.

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# Antidepressant activity of ethanol extract of *Zea mays* husk

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Received: 26/Nov/2016 Accepted: 11/Dec/2016

## ABSTRACT

**Background and aims:** *Zea mays* L. (Poaceae) husk extract is used traditionally in Ibibio traditional medicine for the treatment of various diseases such as malaria, pains, inflammatory diseases and central nervous system disorders.
**Methods:** The husk extract (187-748 mg/kg) was evaluated for antidepressant activity in mice using open field, force swimming and tail suspension tests. Determination of median lethal dose ($LD_{50}$) and phytochemical screening of the husk extract were also carried out using standard methods.
**Results:** The husk extract increased significantly the line crossing, walling and rearing activities of mice in open field test ($P<0.05$-$0.001$) and reduced significantly the immobility time in force swimming test ($P<0.05$-$0.001$). However, the immobility time in tail suspension tests was significantly increased by the extract ($P<0.05$-$0.001$).
**Conclusion:** The husk extract of *Z. mays* has prominent antidepressant activity which is due to the activities of its phytochemical constituents such as phenolic compounds.

**Keywords:** Antidepressant, *Zea mays*, CNS stimulant.

Original article

## INTRODUCTION

*Zea mays* L. (Poaceae) known as maize or corn, is an annual grass plant cultivated for human consumption and rearing of animals. It was introduced to Nigeria in the 16th century.[1] It is tall with strong erect stalks and a fibrous root system. The plant has long narrow leaves that are spaced alternately on opposite side of the stem and bears ears that are enclosed in modified leaves known as husks.[2] Besides its nutritive values, maize grains, leaves, cornsilks, and stalk, inflorescence are also used in ethnomedicine for the treatment of several ailments. The corn silk is used as an antidiabetic and diuretic, while decoction of the silk is consumed for the treatment of urinary troubles and gallstones.[3-5] The ash of the cob is used for the treatment of cough[4] as well as inflammatory diseases and depression. The husks are used in the treatment of pains and arthritis.[6] Warm tea of the husks is used for the treatment of malaria and diabetes in Ibibio traditional medicine. Analgesic, anti-inflammatory, and antioxidant activities have been reported on the husk extract.[6,7] Arabinoxylan, which has immunological effects, has been isolated from the husk extract,[8] while eight phenolic compounds (gallic acid, protocatechuic acid, chlorogenic acid, cafeic acid, femlic acid,

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rutin, resveratrol, and kaempferol) have also been detected in ethanol husk extract of *Zea mays*.[7] Information on the biological activities of the husk extract is scarce. The aim of this study was to investigate the antidepressant activity of the husk extract to confirm its use in traditional medicine to treat depression.

## METHODS

The fresh husk of *Zea mays* were collected in August, 2015 from Farmland in Amassoma in Southren Ijaw LGA, Bayelsa State, Nigeria. The husks were identified and authenticated as *Zea mays* by Dr. Margaret Bassey, a taxonomist in the Department of Botany and Ecological studies, University of Uyo, Uyo, Nigeria. Herbarium specimen (FPH 614) was deposited at the Faculty of Pharmacy Herbarium, University of Uyo, Uyo.

The plant parts (husks) were washed, chopped into smaller pieces and dried on laboratory table for 2 weeks. The dried husks were pulverized using electric grinder. The powdered husk was macerated in 50% ethanol for 72 h. The liquid ethanol extract obtained by filtration was evaporated to dry in a rotary evaporator 40 °C. The extract (yield 2.83%) stored in a refrigerator at -4°C until they were used for the experiments reported in this study.

Phytochemical screening of the crude husk extract was carried out employing standard procedures and tests, to reveal the presence of chemical constituents such as alkaloids, flavonoids, tannins, terpenes, saponins, anthraquinones, reducing sugars, and cardiac glycosides.[9,10]

In this experiment, Swiss albino mice (18-25 g) of either sex were used for these experiments. The animals were housed in standard cages and 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.

The median lethal dose ($LD_{50}$) of the crude husk extract was determined by estimating acute toxicity of the extract in Swiss albino mice model using the method of Lorke.[11] This involved intraperitoneal administration of different doses of the extract (1000-5000 mg/kg) to groups of 3 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 h was recorded.

For the evaluation of antidepressant activity 3 models were used. In the open field test model, 25 rats were randomly divided into groups of 5 rats each and treated as follows for 5 days before open field test. Animals in control group received normal saline, 2 ml/kg *p.o.* Imipramine (5.0 mg/kg, *p.o.*) was given to the positive control group and ethanol husk extract of *Zea mays* (187, 374 and 748 mg/kg, *p.o.*) were respectively given to 3 different groups according to the doses. 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.[12] 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 was also used to evaluate antidepressant activity and another set of 25 mice was 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 husk extract of *Zea mays* (187, 374 and 748 mg/kg, *p.o.*). For assessing antidepressant activities, it was employed the method described by Porsolt

et al.[13] 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) was further employed in the evaluation of antidepressant activity of the husk extract. In this test, 25 mice of either sex were randomly divided into groups of 5 mice each and treated as follows for 5 days before the test; control (normal saline, 2 ml/kg *p.o.*), imipramine (5.0 mg/kg, *p.o.*) and ethanol husk extract of *Zea mays* (187, 374 and 748 mg/kg, *p.o.*). The total duration of immobility induced by tail suspension was measured according to the methods described by Steru et al.[14] 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.

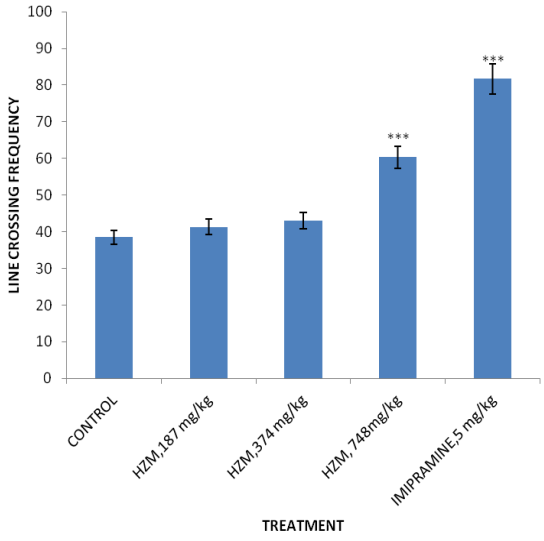
GraphPad Instat 3 (San Diego, USA) was used to analyze data obtained from this work statistically and by using one way ANOVA followed by a post test (Turkey-Kramer multiple comparison test). Differences between means was considered significant at 1% and 5% level of significance, that is P≤0.01and 0.05.

## RESULTS

Results of phytochemical screening of the crude ethanol husk extract revealed the presence of chemical constituents such as alkaloids, flavonoids, tannins, terpenes, saponins, cardiac glycosides and sugars.

The median lethal dose ($LD_{50}$) of the crude husk extract was calculated to be 1874.83 mg/kg. The physical signs of toxicity observed included excitation, paw licking, increased respiratory rate, decreased motor activity, gasping and coma which was followed by death.

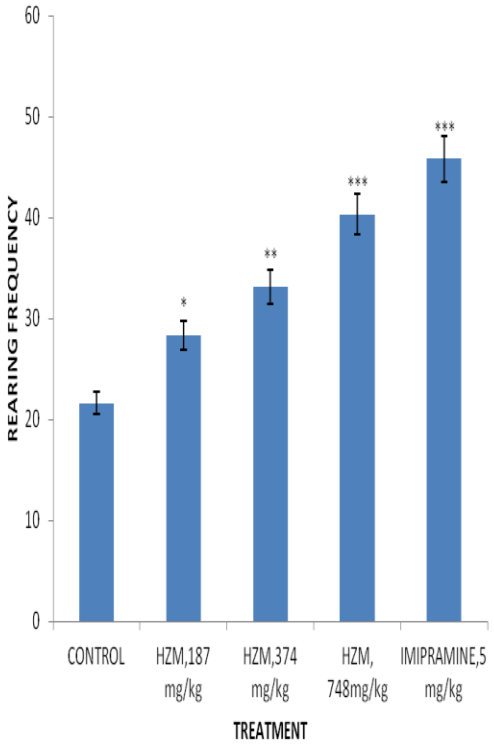
In the open field test, administration of husk extract of *Z. mays* (187-748 mg/kg) for 5 days caused significant (P<0.05-0.01) increased the frequency of line crossing in a dose-dependent fashion which was significant (P<0.01) at the highest dose of the extract (748 mg/kg) when compared to control. The standard drugs, imipramine (5 mg/kg), similarly caused a significant increase in the locomotor activity of the rats as evident in the frequency of the line crossing (Graph 1).




**Graph 1:** Bar diagram shows the effect of *Zea mays* husk extract on line crossing frequency of rat

*Results are represented as mean ± SEM with n=6 in each group; ***: P<0.001 when compared with control group.*

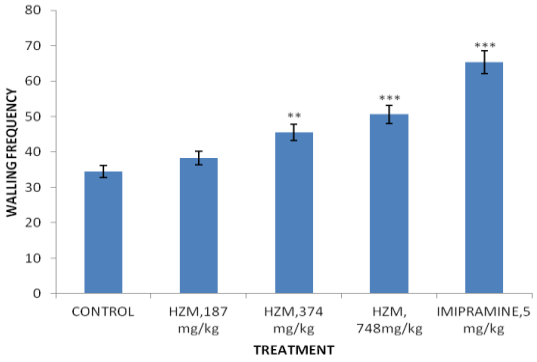
The husk extract of *Z. mays* (187-748 mg/kg) further caused significant increase (P<0.01-0.001) in walling frequency of the rats at high doses (374 and 748 mg/kg) when compared to control. The low dose (187 mg/kg) had no effect on the locomotor activity of the rats. The standard drug, imipramine (5 mg/kg), produced a significant increase in the walling frequency of the animals.(Graph 2).




**Graph 2:** Bar diagram shows the effect of *Zea mays* husk extract on rearing frequency of rat

*Results are represented as mean ± SEM with n=6 in each group; *: P<0.05, P<0.01; ***: P<0.001 when compared with control group.*

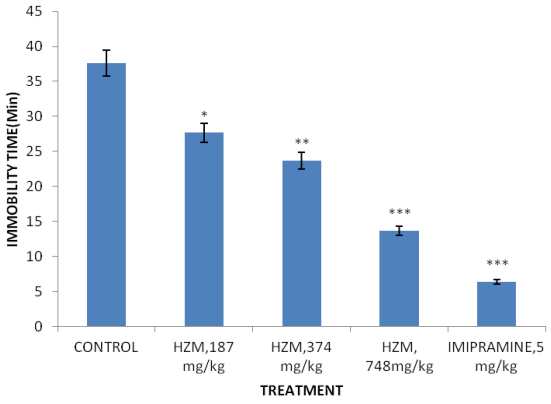
Similarly, the husk extract of the *Zea mays* (187-748 mg/kg) caused significant (P<0.001) dose-dependent increase of the rearing frequency of rats administered with the extract for 5 days. However, the standard, imipramine (5 mg/kg), exerted a significant increase in the rearing frequency when compared to control (P<0.001) (Graph 3).




**Graph 3:** Bar diagram showing the effect of *Zea mays* husk extract on walling frequency of rat

*Results are represented as mean ± SEM with n=6 in each group; *: P<0.05, P<0.01; ***: P<0.001 when compared with control group.*

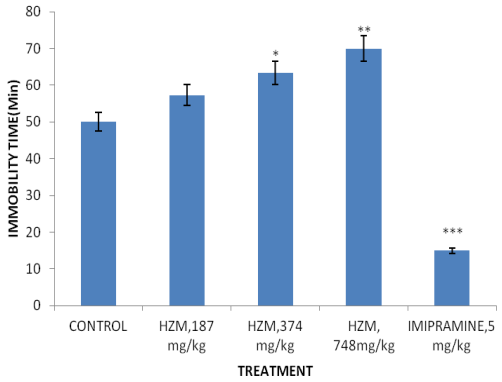
On force swimming test, administration of the ethanol husk extract of *Z. mays* (187-748 mg/kg) to rats for 5 days significantly (P<0.05-0.001) and dose dependently reduced immobility time of the rats during force swimming test when compared to control. However, standard drug, imipramine (5 mg/kg) also produced a significant reduction in the immobility time of the rats when compared to control(P<0.001) (Graph 4).




**Graph 4:** Bar diagram shows the effect of *Zea mays* husk extract on the immobility duration (in min) of mice in force swimming test.

*Results are represented as mean ± SEM with n= 6 in each group; *: P<0.05, P<0.01; ***: P<0.001 when compared with control group.*

The activities of rats pretreated for 5 days with husk extract of *Zea mays* (187-748 mg/kg) increased significantly (0.05-0.01) the immobility time of rats during tail suspension test when compared to control. The standard drug, imipramine (5 mg/kg), exerted a significant reduction of the immobility time of the rats when compared to control (P<0.001) (Graph 5).




**Graph 5:** Bar diagram shows the effect of *Zea mays* husk extract on the immobility duration (in min) of mice in Tail suspension test

*Results are represented as mean ± SEM with n=6 in each group; *:P<0.05, P<0.01; ***P < 0.001 when compared with control group.*

## DISCUSSION

In this study, evaluation of the effect of ethanol husk extract of *Zea mays* on central nervous system was carried out in rats using different models: Open field test, tail suspension test and force swimming test. The husk extract (187-748 mg/kg) was found to cause significant dose-dependent increases in the frequencies of line crossing, walling and rearing activities of the pretreated rats. The extract also reduced significantly the immobility time of the rats in force swimming test, while that of rats in tail suspension tests were increased especially at all doses.

Monitoring of locomotor activity of animals has been used in assessing effect of drug on the CNS. An increased movement is a measure of the level of excitability of the CNS15 and its decrease may be intimately related to sedation resulting from depression of the CNS.[16] Central nervous system stimulants are known to increase locomotor activity, while agents with depressant activity cause reduction in movements.[17] The husk extract was found to increase significantly line crossing, rearing and walling activities during open field test suggesting stimulatory effect on the CNS. However, it is noteworthy that several established antidepressants decrease locomotor activity.[18]

The husk extract was found to have reduced immobility time of rats during force swimming while that in tail suspension tests was increased. Psycho stimulants may also reduce immobility in FST and TST models, but in contrast to antidepressants, these cause marked motor stimulation in locomotor activity test.

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.[19] 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.[13,14] These tests are quite sensitive to major antidepressant drugs including tricyclics, serotonin-specific

reuptake inhibitors, MAO inhibitors, and atypical antidepressant.[13,14,20]

Forced swimming and tail suspension tests which represent the behavioural despair model, claimed to reproduce a condition similar to human depression.[13,14,21] 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.[19] 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.[13] This was observed in this study. The extract was also found to similarly reduced immobility time of rats during forced swimming suggesting that the extract may be acting in a mode similar to that of imipramine, a tricyclic antidepressant (TCA) which blocks the reuptake of both serotonin and norepinephrine.

However, the results of this study suggest that the husk extract exhibited antidepressant activity with a strong psychomotor stimulation but with a little depressant action as demonstrated in tail suspension test. Phytochemical constituents such as flavonoids have been implicated in antidepressant action on the CNS, while polyphenols especially flavonoids like quercetin and rutin have also been reported to exhibit antidepressant effect.[22,23] The husk extract of *Z. mays* has been reported to contain phenolic compounds such as gallic acid, protocatechuic acid, chlorogenic acid, cafeic acid, femlic acid, rutin, resveratrol, and kaempfero.[17] These phytochemical constituents may be responsible for the observed activity of the husk extract in this study.

## CONCLUSION

From the results of this study, the husk extract possess significant antidepressant activity which is due to its rich phenolic content. It will be interesting to isolate and characterize the active ingredient in this extract.

## CONFLICT OF INTEREST

There is no conflict of interest.

## ACKNOWLEDGEMENT

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

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**How to cite the article:** Okokon J, Nelson E, Sunday M. Antidepressant activity of ethanol extract of *Zea mays* husk. Adv Herb Med. 2016; 2(4): 22-28.