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ORIGINAL ARTICLE

Effect of *Musa sapientum* Stem Extract on Animal Models of Depression

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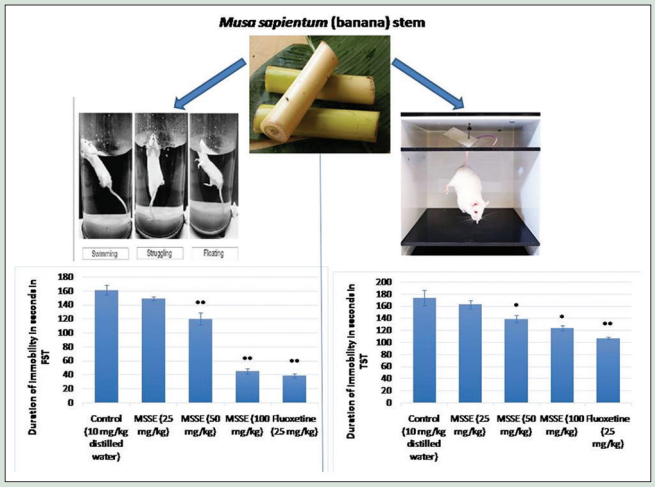
ABSTRACT

Background: *Musa sapientum*, the banana plant, has shown to possess antioxidant activity in previous studies. Oxidative stress has been linked to the pathogenesis of major depressive disorder (MDD) with evidence of increased serum levels of oxidative stress biomarkers in MDD patients. **Objective:** The present study aimed to evaluate the antidepressant activity of *M. sapientum* stem extract (MSSE) in experimental models in mice. **Materials and Methods:** Forced swim test (FST) and tail suspension test (TST) were carried out in five different groups (n = 6/group) of mice. The vehicle, standard drug, and the three test groups were orally administered distilled water (10 mL/kg), fluoxetine (25 mg/kg), and incremental doses of 25, 50, and 100 mg of MSSE, respectively, 45 min prior to the experiment. **Results:** On FST, the duration of immobility in control group, which was 161.5 ± 6.78 (in seconds, mean ± standard error of mean [SEM]), decreased to 149.33 ± 2.70 (25 mg/kg MSSE), 120.17 ± 8.35 (50 mg/kg MSSE), and 45.17 ± 4.11 (100 mg/kg MSSE) in the treated groups. On TST, the duration of immobility in control group, which was 173.83 ± 12.65 (mean ± SEM), decreased to 163.17 ± 6.91 (25 mg/kg MSSE), 139.0 ± 5.9 (50 mg/kg MSSE), and 124.0 ± 4.42 (100 mg/kg MSSE) in the treated groups. The difference in the duration of immobility was statistically significant at middle and higher doses, i.e. 50 and 100 mg/kg MSSE (P < 0.05) respectively, when compared with the control group in both the tests. **Conclusion:** A significant antidepressant-like activity was found in MSSE, which could be a potential natural compound for use in depression.

Key words: Depression, *Musa sapientum*, oxidative stress

SUMMARY

- The five groups - vehicle, standard drug, and the three test groups were administered distilled water (10 mL/kg), fluoxetine (25 mg/kg), and incremental doses of 25, 50, and 100 mg of *Musa sapientum* stem extract (MSSE), respectively
- The duration of immobility decreased in the treated groups as compared to the control group on both, forced swim and tail suspension, tests
- The difference in the duration of immobility was statistically significant at middle and higher doses, i.e., 50 and 100 mg/kg MSSE (P < 0.05), when compared with the control group in both the tests.



Abbreviations Used: MDD: Major depressive disorder; MSSE: *Musa sapientum* stem extract; FST: Forced swim test; TST: Tail suspension test; GSH: Glutathione, MDA: Malondialdehyde; SOD: Superoxide dismutase

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INTRODUCTION

Depression is a common disorder with a lifetime prevalence of 8–12% in the general population.[1] More than 350 million people worldwide are estimated to be suffering from this disorder which often becomes a chronic and recurrent problem resulting in substantial morbidity and health burden. It is recognized as the fourth leading cause of disability worldwide by the World Health Organization and it is predicted to become the largest contributor to disease burden by 2030.[2] Pharmacotherapy of depression is often unsatisfactory with more than one-third of the depressed patients not responding properly to the currently available drugs.[3] Even in the responders, the cost and the associated adverse effects of prolonged therapy with antidepressant medications have been important limiting factors in proper and satisfactory management of the disease. This has led to an increased research for developing effective and cheaper alternatives to the already marketed antidepressant drugs. Exploring the antidepressant potential in plant-derived compounds has been of particular interest in this context, as there is a need for less costly and safer drugs for the patients of depression, especially from the poor socioeconomic background.

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Musa sapientum, commonly known as banana, is an herbaceous plant of *Musaceae* family. Different parts of the banana plant contain carotenoids, phenolic compounds, and biogenic amines such as dopamine, serotonin, noradrenaline, tryptophan, and tyrosine, which are relevant to the pathophysiology of mental disorders.[4] The parts of the plant have been used traditionally for their medicinal value in many ailments such as peptic ulcers, hypertension, diarrhea, dysentery, and diabetes. Studies on experimental animal models have confirmed the therapeutic potential of the extracts from different parts of this plant.

Oxidative stress has been linked to the pathogenesis of major depressive disorder (MDD), and studies have found significantly increased serum levels of oxidative stress biomarkers in MDD patients in the acute phase as compared to those of healthy controls.[5] The plant extract has been shown to possess antioxidant activity in previous studies.[6,7]

The evidence of antioxidant activity in *M. sapientum* in earlier studies prompted us to assess it for the antidepressant activity, which to the best of our knowledge has not been done in any earlier study. Hence, the present study was undertaken to evaluate the antidepressant activity of *M. sapientum* stem extract (MSSE) in experimental models in mice.

MATERIALS AND METHODS

Animals

Swiss albino mice of either sex weighing between 25 and 30 g were used for the study. The mice were procured from the Lala Lajpat Rai University of Veterinary and Animal Sciences, Hisar, Haryana, and were housed in the Central Animal House under the standard laboratory conditions at an ambient temperature of 22°C ± 2°C and on natural light-dark cycle in groups of 6 in polypropylene cages. Pellet diet was given to the animals and water was available *ad libitum*. The animals were acclimatized to laboratory conditions prior to experimentation and were given only water on the night before the day of experiment to avoid the influence of food on drug absorption. Proper care of animals was taken as per the guidelines of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) for laboratory animal facilities, and permission from the Institutional Animal Ethics Committee (Regn No. 1173/ac/po/08/CPCSEA) was obtained.

Plant material and preparation of aqueous extract

Fresh Banana stems were collected in the autumn season, and the stem sample was authenticated by the National Institute of Science Communication and Information Resources (Ref. No. NISCAIR/RHMD/Consult/2014/2414-194). The upright concentric layers of leaf sheaths forming the pseudo stem were peeled off to reveal the central pale white stem. This central pale white stem was cut into small pieces. One hundred gram stem was crushed with 20 mL distilled water in a mixer followed by filtration through a sterile muslin cloth to get aqueous extract. The whole process was carried out at room temperature. The extract was lyophilized and stored in a refrigerator at 4°C to be used in the experiments.

Animal models for depression

Forced swim test

Each mouse was placed inside a vertical Plexi glass cylinder (40 cm in height and 18 cm in diameter), containing water up to a height of 15 cm maintained at 24–25°C.[8] After the initial 2–3 min of vigorous struggling activity, the animal usually assumes a typical immobile posture. A mouse was considered to be immobile when it remained floating in the water without trying to struggle, making only minimum movements of its limbs, necessary to keep its head above water. During the test, each animal was placed in the water for 6 min. The duration of immobility was recorded during the last 4 min of the forced swim test (FST). An antidepressant effect is indicated when there is a decrease in the duration of immobility. The mouse was then taken out of the water and placed back in the cage after it had become dry. Each mouse was used only once, and fresh water was used for every subsequent new animal studied.

The tail suspension test

In this test, each mouse was suspended from the edge of a 58 cm high table top with the help of an adhesive tape placed approximately 1 cm from the tip of the tail.[9] The duration of immobility was recorded for 5 min. Mice were considered immobile when they hung passively and remained completely motionless, except respiratory movements, for at least 1 min. The duration of immobility in the different groups was compared. A decreased duration is indicative of antidepressant effect.

Both the above-mentioned tests for depression were carried out in five different groups (n = 6/group) of mice. The vehicle, standard drug, and the three test groups were orally administered distilled water (10 mL/kg), fluoxetine (25 mg/kg, Fludac, manufacturer: Cadila Pharmaceuticals), and incremental doses of 25, 50, and 100 mg of MSSE, respectively, 45 min prior to the experiment.

Statistical analysis

Data were analyzed by one-way ANOVA followed by *post hoc* Tukey's test. $P < 0.05$ was considered significant in all the experiments.

RESULTS

Effect of *Musa sapientum* stem extract on the duration of immobility in forced swim test in mice

MSSE produced a decrease in the duration of immobility in the animals in a dose-dependent manner. The results are shown in Table 1. The duration of immobility in control group was 161.5 ± 6.78 (in seconds, mean ± standard error of mean [SEM]) which decreased to 149.33 ± 2.70 (25 mg/kg MSSE), 120.17 ± 8.35 (50 mg/kg MSSE), and 45.17 ± 4.11 (100 mg/kg MSSE) in the treated groups. The difference in the duration of immobility was statistically significant ($P < 0.01$) with middle and higher doses, i.e., 50 and 100 mg/kg MSSE, when compared to the control group.

Fluoxetine (25 mg/kg) showed a decrease in the duration of immobility to 38.5 ± 3.28 which was highly significant ($P < 0.01$) when compared to the control group. Although fluoxetine produced more decrease in the duration of immobility as compared to the higher dose of MSSE (100 mg/kg), the difference was not statistically significant.

Effect of *Musa sapientum* stem extract on the duration of immobility in tail suspension test in mice

MSSE produced a decrease in the duration of immobility in the animals in a dose-dependent manner. The results are shown in Table 2. The duration of immobility in control group was 173.83 ± 12.65 (mean ± SEM) which decreased to 163.17 ± 6.91 (25 mg/kg MSSE), 139.0 ± 5.9 (50 mg/kg MSSE), and 124.0 ± 4.42 (100 mg/kg MSSE) in the treated groups. The difference in the duration of immobility was statistically significant with middle and higher doses, i.e., 50 and 100 mg/kg MSSE ($P < 0.05$), when compared with the control group.

Fluoxetine (25 mg/kg) showed a decrease in the duration of immobility to 107.17 ± 1.96 which is highly significant ($P < 0.01$) when compared to control group. Although fluoxetine produced more decrease in the duration of immobility as compared to the higher dose of MSSE (100 mg/kg), the difference was not statistically significant.

Table 1: Effect of *Musa sapientum* stem extract on the duration of immobility on forced swim test

Group	Treatment	Duration of immobility (s), mean±SEM
Control (distilled water)	10 mL/kg, p.o.	161.5±6.78
MSSE	25 mg/kg, p.o.	149.33±2.70
MSSE	50 mg/kg, p.o.	120.17±8.35**
MSSE	100 mg/kg, p.o.	45.17±4.11**
Fluoxetine	25 mg/kg, p.o.	38.5±3.28**

***P*<0.001 as compared to control group. SEM: Standard error of mean; MSSE: *Musa sapientum* stem extract

Table 2: Effect of *Musa sapientum* stem extract on the duration of immobility on tail suspension test

Group	Treatment	Duration of immobility (s), mean±SEM
Control (distilled water)	10 mL/kg, p.o.	173.83±12.65
MSSE	25 mg/kg, p.o.	163.17±6.91
MSSE	50 mg/kg, p.o.	139±5.90*
MSSE	100 mg/kg, p.o.	124±4.42*
Fluoxetine	25 mg/kg, p.o.	107.17±1.96**

**P*<0.05 as compared to control group; ***P*<0.001 as compared to control group. SEM: Standard error of mean; MSSE: *Musa sapientum* stem extract

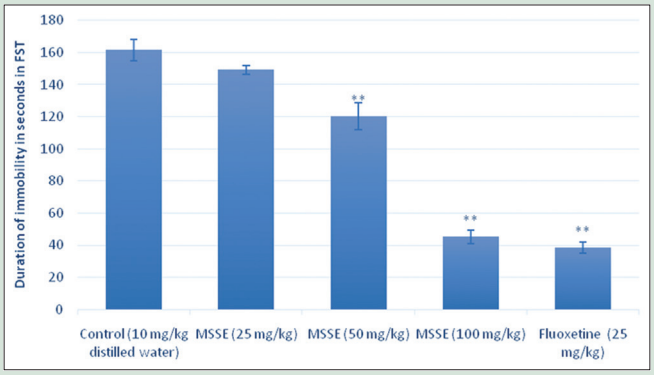

Figure 1: Effect of *Musa sapientum* stem extract on the duration of immobility on forced swim test. ***P* < 0.001 as compared to control group

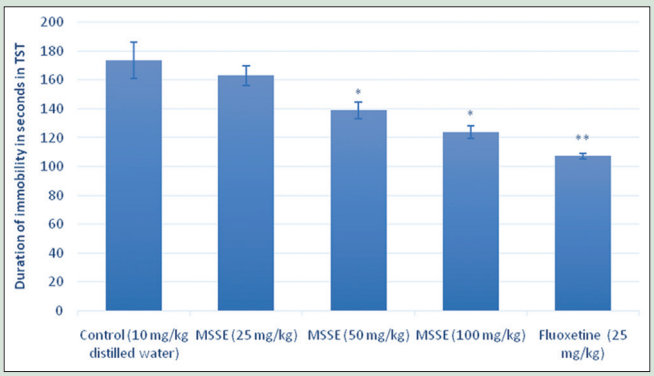

Figure 2: Effect of *Musa sapientum* stem extract on the duration of immobility on tail suspension test. ***P* < 0.001 as compared to control group; **P* < 0.05 as compared to control group

DISCUSSION

Drugs currently in use to treat depressive disorder have the limitations of high cost and numerous adverse effects. This has triggered research in the area of herbal psychopharmacology. Earlier studies have shown that phytochemicals such as fatty acids, phenols, alkaloids, flavonoids, saponins, and terpenes from medicinal plants facilitate the maintenance of normal physiological function of the major inhibitory neurotransmitters.[10] Polyphenolic compounds have been shown to be involved in the modulation of mental health including brain plasticity, behavior, mood, depression, and cognition.[11] In traditional medicine, several plants have been tried and have been reported to be helpful in the management of depressive disorders. Phytochemicals appear as a potential and promising class of therapeutic leads for the treatment of depressive disorders, and these compounds need to be explored for their potential efficacy.

M. sapientum is a widely available plant in South East Asia which has been evaluated for its antioxidant properties in a few previous studies. One of these studies attributed the hepatoprotective quality of the plant extract to its antioxidative property. The study showed that the plant extract prevented rise in malondialdehyde and increased glutathione and superoxide dismutase (SOD) levels in treated group.[12] Another study found decreased serum lipid peroxidation and increased serum SOD in diabetic rats treated with the plant extract.[6] One more study found the antiulcerogenic activity of the plant extract to be related to its antioxidant activity.[13]

Oxidative stress can be an important factor in the genesis of mood disorders such as anxiety and depression. Patients with depression have decreased antioxidant defenses and more oxidative DNA damage as compared to nondepressed individuals, and studies have found significantly increased serum levels of oxidative stress biomarkers in depressed patients in the acute phase as compared to those of healthy controls.[14]

Previous studies have shown the pathophysiological relationships between oxidative stress and depression. A meta-analysis of 115 studies, from 1990 to 2015, comparing the oxidative stress markers between depressed patients and healthy controls found lower total antioxidant levels and higher oxidative damage in depressed patients than controls. It was further seen that there was an increase in the antioxidant levels and decrease in the oxidative damage product levels after antidepressant medication.[15] In the light of the evidence of antioxidant activity in *M. sapientum* extract from the earlier studies, assessment of its potential as an antidepressant compound was done, as this aspect has not been explored earlier.

Under stress, there are normally counter-regulatory responses such as adaptive neuroplasticity and neurogenesis. Severe stress produces depression-like pictures associated with disruption of this counter-regulatory stress system.[16] The antidepressant-like property of MSSE was evaluated by applying FST and tail suspension test (TST), the commonly used models for behavioral despair in the experimental models.

FST is the most commonly used animal model for assessing antidepressant-like behavior. The swim test involves the scoring of active or passive behavior when the animals are forced to swim in a cylinder which allows no escape way.[8] This behavioral test for antidepressant drugs meets the predictive validity criteria for the different groups of antidepressants. Reduction in the passive behavior is interpreted as an antidepressant-like effect in the FST. TST is another model commonly used to evaluate the potential antidepressants. The unavoidable stress with no escape in the animals results in immobility

reflecting, despair, and hopelessness, which may be akin to the human depressive disorders.[9] Established antidepressants have been seen to reduce the immobility, normally displayed by the animals after an initial struggle.

MSSE produced a significant decrease in the duration of immobility in the animals in both the tests as compared to the vehicle control group in a dose-dependent manner, with more profound effect at the middle and higher doses. Fluoxetine, a commonly used and established antidepressant, showed the expected effect of a significant decrease in the duration of immobility; the effect being comparable to that of 100 mg/kg MSSE, however without any statistically significant difference [Figures 1 and 2].

We carried out the experiments to evaluate the antidepressant-like potential of MSSE presumably based on the premise of prior studies showing its antioxidant properties. Although the results were significant for the antidepressant-like effects, we can only assume that antioxidant activity may have played a role in the mechanisms behind these effects. There could be other mechanisms operating, including the modulation of neurotransmitters; as the results were comparable to fluoxetine, a selective serotonin reuptake inhibitor. Our study was of an early exploratory nature, and these mechanisms need to be explored and elucidated in future studies.

CONCLUSION

Significant antidepressant-like activity of MSSE is suggested by the results from this experimental study. There was a dose-dependent antidepressant-like activity in the animals subjected to FST and TST. Therefore, MSSE could be a potential natural compound for use in depression. However, further biochemical, molecular, and clinical studies are required to identify the active constituents of the extract and ascertain its effectiveness and mechanism of action in depression.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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