

ORIGINAL CONTRIBUTION

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Evaluation of the antidepressant-like activity of the methanolic extract of the seeds of *Sesamum indicum*

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Abstract

Background: The search for novel pharmacotherapy from medicinal plants for central nervous system (CNS) disorders has become of importance since new agents with improved efficacy for more effective therapy are required. *Sesamum indicum* has been extensively used in Bangladesh and other Indian Subcontinent as medication for various diseases including CNS disorders. It was found to have antioxidant, antitumor, antihypertensive, neuroprotective, hypoglycemic, antimicrobial, anticonvulsant and wound healing activity.

Results: The result showed robust and dose-dependent antidepressant-like activity. There are statistically significant ($p^* < 0.05$) reductions in the duration of immobility time both in forced swimming and tail suspension test. In open field test, measurement of locomotion, defecation and rearing are evaluated. There is statistically significant ($p^* < 0.05$) increase in locomotion, rearing and defecation of mice compared to control group.

Conclusions: These results clearly demonstrates that methanolic extract of the seeds of *Sesamum indicum* has potential antidepressant activity and further studies should be conducted to identify, isolate and evaluate its potential active compound responsible for such effect.

Keywords: Antidepressant, Depression, Sesame, TST, FST, OFT

Background

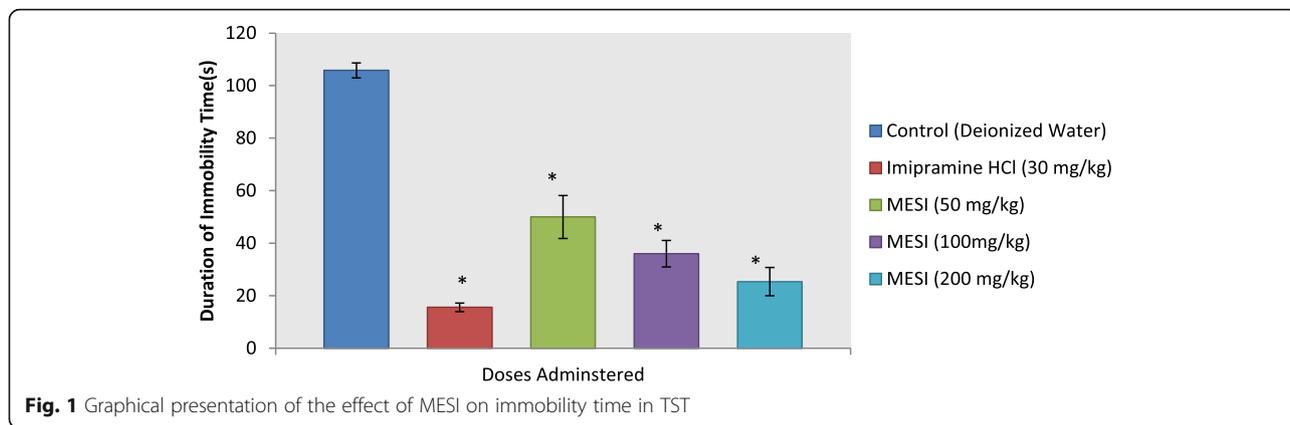
Depression is becoming a rising concern in the current world as almost 450 million people around the world suffer from it according to WHO. Depression along with anxiety is now the most prevalent mental disorders all over the world; together they are responsible for 50% of psychiatric and substance use disorders [1]. According to some epidemiological studies, more than 20% of the general populations have at least one of these disorders during their lifetime [2]. Nearly one in four women and one in six men experience depression in their life [3], and up to 65% of individuals have recurrent episodes of the disorder [4–6]. Now, Depression has been found to be the fourth leading cause of overall disease burden and the leading cause of nonfatal disease burden worldwide [7]. Drugs such as Tricyclic antidepressants, Monoamine Oxidase Inhibitors, Selective Serotonin

Reuptake Inhibitors currently is used for the treatment of depression which possess some serious drawbacks like insomnia, weight gain, sedation, anxiety etc. As it is well known that natural source have less side effects and complications [8], our goal was to find a new antidepressant drug of natural origin.

Sesamum indicum Linn. (Pedaliaceae) is an annual shrub with white bell-shaped flowers with a hint of blue, red or yellow with branches or without branches. It is grown for the production of seeds which is rich in oil content. It comes in a variety of colors, cream-white to charcoal-black. Sesame is found in tropical, subtropical, and southern temperate areas of the world, particularly in India, China, South America and Africa. It was found to have antioxidant [9], antitumor [10], antihypertensive [11], neuroprotective [12], hypoglycemic [13], antimicrobial [14], anticonvulsant [15] and wound healing activity [16]. It was also found to prevent high fat diet induced obesity [17].

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Materials & methods

Collection & Preparation of extract

Seeds of *Sesamum indicum* were collected from the local market of Jessore and evaluated for identity and authenticated by the Senior Scientific Officer, Bangladesh National Herbarium, Dhaka, Bangladesh. The Seeds were washed with tap water and then dried under the shade. The seeds then powdered by using mortar and pestle. The powdered seeds then dipped into absolute methanol for 7 days. The extract was filtered and solvent was evaporated using rotary evaporator and crude extract with oily and paste like consistency was obtained.

Experimental animal

The animals used for this study were male Albino Swiss mice (6–8 weeks and 20–30 g). A total of 75 animals were used for this study (25 for each test). The animals used for this study were purchased from Jahangirnagar University, Dhaka. The animals were housed in groups of 5 and were allowed to acclimatize to laboratory conditions for a minimum of 5 days before the time of experimentation. All animals had free access to standard animal feed and clean water and were maintained on a 12/12 h of light/dark cycle. The ambient temperature was 22 ± 3 °C. All animals used in the study were cared for and treated humanely throughout the study period following international guidelines.

Table 1 Effect of MESI in TST

| Treatment | Doses | Immobility time |
|--------------------------|------------|-----------------|
| Deionized water | 01 ml/mice | 105.8 ± 2.853 |
| Imipramine Hydrochloride | 30 mg/kg | 15.6 ± 1.631* |
| MESI | 50 mg/kg | 50.0 ± 8.156* |
| MESI | 100 mg/kg | 36.0 ± 5.05* |
| MESI | 200 mg/kg | 25.4 ± 7.718* |

Values are presented as mean ± SEM (n = 5)
 P* < 0.05 compared with the control group (Dunnett’s test)

Grouping & Dosing

There were five groups of animals for each model. All animals were randomly assigned to different groups. Group I received the vehicle (2% Tween 80 in deionized water) and served as control. Group II received the standard drug imipramine hydrochloride (30 mg/kg) and served as positive control. The test groups were divided into three groups, III-V, which received increasing doses of the extract at 50 mg/kg, 100 mg/kg, and 200 mg/kg, respectively. The different doses of the extract were dissolved in 2% Tween 80 solution and were administered for 14 days at a fixed time.

Experimental Methods & Procedures

All tests were performed in the Pharmacology Laboratory of Department of Pharmacy, Jessore University of Science & Technology.

Tail suspension test (TST)

This method was developed by Steru (1985) and is used with slight modifications [18]. This method was employed on the observation that a mouse suspended by the tail shows alternate agitation and immobility which indicates a state of depression. TST induced immobility is reduced by a large number of clinically active and atypical anti-depressant effect. A total of 25 mice were treated with control, extract or Imipramine hydrochloride and were placed in the middle of the stand. Two stands, each with a

Table 2 Effect of MESI in FST

| Treatment | Doses | Immobility time |
|--------------------------|------------|-----------------|
| Deionized water | 01 ml/mice | 106 ± 3.007 |
| Imipramine Hydrochloride | 30 mg/kg | 20.8 ± 1.985* |
| MESI | 50 mg/kg | 56.75 ± 4.56* |
| MESI | 100 mg/kg | 36.8 ± 3.153* |
| MESI | 200 mg/kg | 27.8 ± 2.131* |

Values are presented as mean ± SEM (n = 5)
 P* < 0.05 compared with the control group (Dunnett’s test)

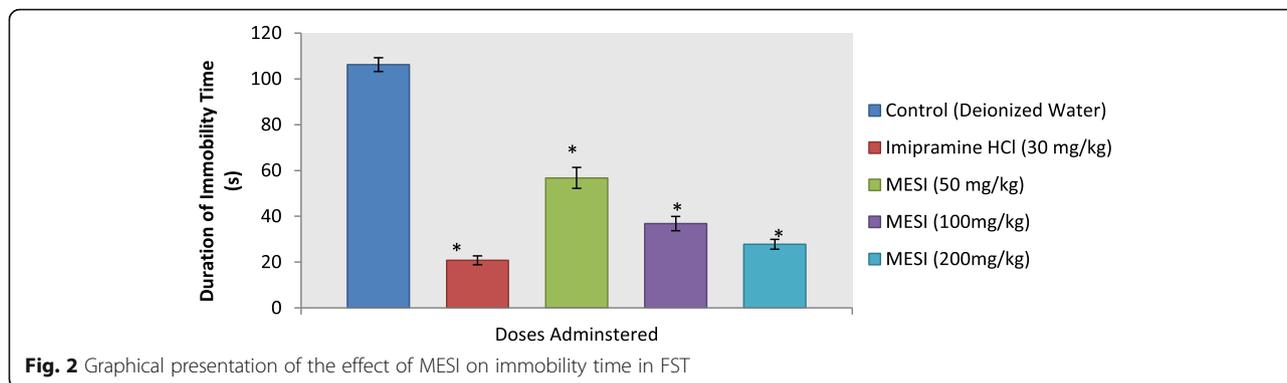


Fig. 2 Graphical presentation of the effect of MESI on immobility time in FST

clamp located 22 cm from the floor, were placed at intervals of 23 cm. A mouse was hung 5 cm from the end of its tail on a stand, and observed for 6 min. Immobility time was evaluated by observers.

Forced swimming test (FST)

This method was developed by Porsolt (1977) and is employed with some modifications [19]. The male mice were forced to swim individually in a transparent glass container (20 cm in diameter and height of 40 cm) containing fresh water of 19 cm height which was maintained at 25 °C (± 3 °C) and allowed to swim for 5 min. The mice were judged to be immobile when they remained floating without struggling, and making movements necessary only to keep their heads above the water. The total duration of immobility was recorded using a stop watch.

Open field test (OFT)

The OFT was carried out in order to rule out any non-specific locomotor effect the extract might possess. The locomotor activity test was performed according to the method of Carlini (1986) with slight modifications [20]. Mice were placed in an open field apparatus composed of an arena divided into 64 approximately equal areas. For open field observations, each mouse was individually placed in the center of the arena 15 h after the last treatment. The locomotion (number of line crossings), rearing frequencies (number of times seen standing on hind legs), and number of defecations within 5 min was observed and calculated.

Statistical analysis

The results obtained from these tests were statistically evaluated using SPSS 23.0 version software. The statistical analysis was done by one-way analysis of variance (ANOVA) followed by Dunnett’s post hoc test. The results were presented as mean value ± SEM (n = 5). The difference between group was considered significant at a level of p* < 0.05. The statistically significant results are marked with a star (*) sign in the table as well as in the graph.

Results

Effect of MESI in TST

The extract reduced the duration of immobility time in the tail suspension test (Table 1 and Fig. 1). Dunnett’s Post hoc analysis confirmed that the extract significantly decreased the immobility time in comparison to the control group (p* < 0.05).

Effect of MESI in FST

The extract significantly reduced the duration of immobility time in the forced swimming test (Table 2 and Fig. 2). Dunnett’s post hoc analysis demonstrated that the test treatments significantly decreased the immobility time in comparison to the control group (p* < 0.05).

Effect of MESI in OFT

The effect of treatment with absolute methanol seed extract of *Sesamum indicum* on the locomotor behavior of mice in the OFT is presented in Table 3. The outcome of the test revealed that the doses of the extract that were able to display antidepressant-like response. The total square crossing, rearing and defecation are recorded. The defecation, locomotion, and rearing increased with increasing dose compared to control group as shown in Figs. 3, 4 and 5.

Discussion

Behavioral despair based tests

The duration of immobility has been shown to be reduced by treatment with antidepressant drugs and a statistically

Table 3 Effect of MESI in OFT

| Treatment | Doses | Locomotion | Rearing | Defecation |
|--------------------------|------------|----------------|---------------|--------------|
| Deionized water | 01 ml/mice | 98.4 ± 7.07 | 25.4 ± 1.435 | 1.2 ± 0.2 |
| Imipramine Hydrochloride | 30 mg/kg | 208.6 ± 13.58* | 35.8 ± 1.428* | 3.4 ± 0.4* |
| MESI | 50 mg/kg | 129.75 ± 5.12* | 27.75 ± 0.854 | 1.75 ± 0.25 |
| MESI | 100 mg/kg | 137.2 ± 9.015* | 30.8 ± 1.356* | 2.8 ± 0.49* |
| MESI | 200 mg/kg | 167.4 ± 5.38* | 34.2 ± 1.281* | 3.4 ± 0.245* |

Values are presented as mean ± SEM (n = 5)
P* < 0.05 compared with the control group (Dunnett’s test)

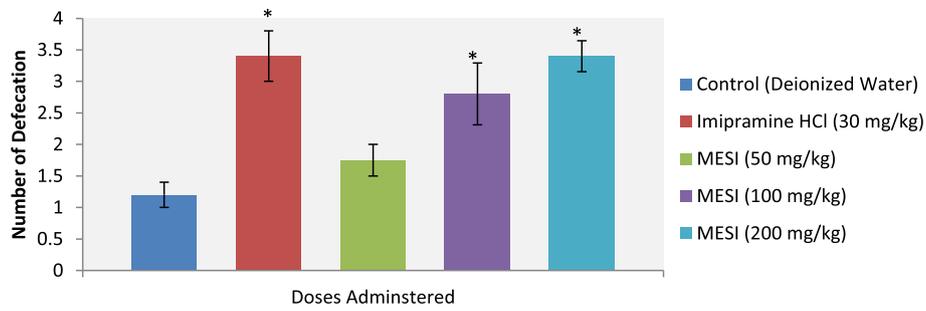


Fig. 3 Graphical presentation of the effect of MESI on Defecation

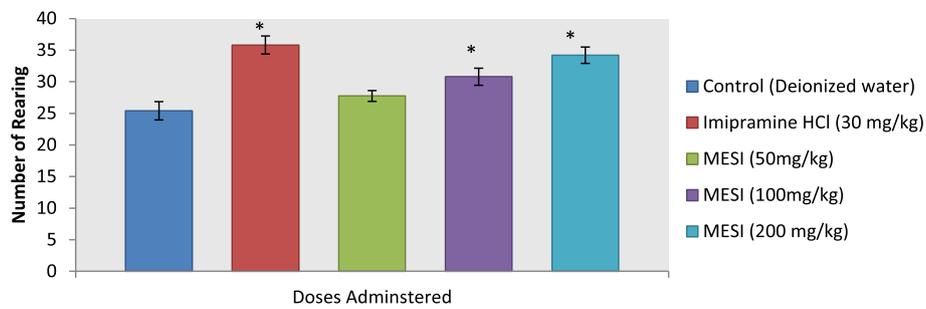


Fig. 4 Graphical presentation of the effect of MESI on Rearing

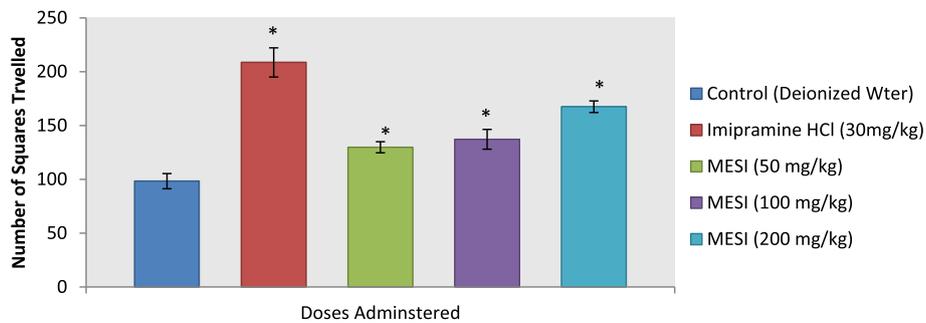


Fig. 5 Graphical presentation of the effect of MESI on Locomotion

significant correlation was found between the clinical efficacy of antidepressant drugs and their potency in both models ($p^* < 0.05$).

After administering the test dose of 50, 100 and 200 mg/kg of seed extract show a statistically significant antidepressant-like activity in the TST ($p^* < 0.05$). The MESI exhibited a reduction in the time of immobility at the dose of 50 and 100 mg/kg. Finally, 200 mg/kg was found best compared to controlled group. In FST; the seed extract displayed a notable reduction in the duration of immobility in comparison to the control animals, which is suggestive of a considerable antidepressant-like activity. The statistically significant reduction in immobility was seen at all doses. This indicates an increase in the concentration of the active principles or in the ability to neutralize the effect of inhibitors with increasing dose of the extract.

The variability in the response of different antidepressants in these models, however, indicates potentially different substrates and neurochemical pathways mediating performance in these tests. The highest percent reduction in time of immobility was seen in the TST than FST, possibly due to the fact that any possible confounds induced by stressful hypothermic exposure in the FST are not present in TST.

Effect on locomotor activity in the OFT

In this study, it was demonstrated that the crude extract of *Sesamum indicum* seeds significantly alter the spontaneous locomotor activity of mice during the OFT evaluated by statistical analysis ($p^* < 0.05$). It is indicative that increase in dose of extract increases the number of squares travelled or passively locomotion. Although compared to imipramine hydrochloride increase in locomotion is not significant but compared to controlled group increase in locomotion is significant and this implies that the extract have active ingredient that is responsible for antidepressant-like activity.

Conclusion

Based on the findings obtained from this study, it is safe to infer that the methanolic extract of the seeds of *Sesamum indicum* possesses a significant antidepressant-like activity. This is indicated by the decrease in the duration of immobility in established behavioral despair based models of depression. The antidepressant-like effect of the methanol fractions of the extract as observed in the TST and FST were found statistically significant. The outcome of OFT indicates that effect on locomotor activity at all extract doses, the antidepressant-like activity observed is not caused by a non-specific motor stimulation. Hence, further studies on this plant should be pursued in order to reap the best possible therapeutic benefits.

Abbreviations

FST: Forced Swimming Test; MESI: Methanolic Extract of the Seeds of *Sesamum indicum*; OFT: Open Field Test; TST: Tail Suspension Test

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Availability of data and materials

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

MRR designed, coordinated and analyzed all the experiments. MS, MA and SSR have done all the experiments. MS have done the statistical analysis and wrote the manuscript. All authors read and approved the manuscript.

Ethics approval and consent to participate

All Experimental rules were approved by the Ethical Review Committee, Faculty of Biological Sciences, Jessore University of Science & Technology, Jessore-7408, Bangladesh.

Competing interests

The authors declare no conflict of interest. Authors are solely responsible for the writing and content of this article.

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