

# Antidepressant-Like Activity of Methanolic Extract of the Seeds of *Trachysperum ammi* in Swiss Albino Mice

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## Abstract

*Trachysperum ammi* has been traditionally used for the treatment of neurological disorders such as depression and anxiety. To date, *T. ammi* has reported for its chemical constituents in different diseases condition. The traditional evidence convinced us to perform the antidepressant-like activity of methanolic extract of *Trachysperum ammi* (META). The antidepressant activity of META assessed by using forced swimming test (FST), tail suspension test (TST), and locomotor activity test. The seed parts of META at doses level of 50, 100 and 200 mg/kg body weight administered orally to examine the CNS stimulants activity test in mice behavioral models. Here, we reported that META significantly reduced immobility time in the FST after repeated administration of 50, 100 and 200 mg/kg to mice for 14 days. The intensity of immobility significantly reduced at all of the doses ( $p < 0.05$ ) whereas, we were found the strongest effect observed at 200 mg/kg. The antidepressant-like effect of META caused the reduction ( $p < 0.05$ ) in the immobility in TST of mice when orally administered with 50, 100 and 200 mg/kg for 14 days, respectively. Additionally, we were executed locomotor activity test to check the motor stimulating activity. META has employed at a dosage of 50, 100 and 200 mg/kg for 14 days, the results have found that 50 mg/kg produced the locomotion effects as similar to the control group. Interestingly, the locomotion, rearing, and defecation significantly ( $p < 0.05$ ) increased at the dosage of 100 and 200 mg/kg of META. Our present findings suggest that the seed parts of *Trachysperum ammi* may possess antidepressant-like activity which may use as a supportive treatment to management of neurological disorders.

## Keywords

*Trachyspermum ammi*, Antidepressant, CNS Stimulants, Forced Swimming Test, Tail Suspension Test, Traditional Medicine

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## 1. Introduction

Mental depression is a chronic mental disorder that distresses a person's mood, thoughts, physical health, and behavior. Combinations of biological and emotional components associated with depression. Retardation of thought, action, and appetite are biological symptoms & emotional indicators include mystery, apathy and pessimism, low self-esteem consisting of feeling of guilt, inadequacy, and ugliness, indecisiveness, and loss of motivation [1]. World Health Report showed evidence that about 450 million people all over the world suffer from mental or behavioral syndrome [2]. It indicates about 12.3% of the worldwide burden of disease, and it may rise at 15% percent rate in 2020 [3]. Patients with major depressive disorder have symptoms that reflect changes in brain, monoamine neurotransmitters, specifically norepinephrine, serotonin, dopamine [4]. It anticipated that in 2020, after cardiovascular disease, depression may place at the second greatest increase rate of morbidity as a socioeconomic burden [5]. The number of drugs is available for treatment against depression, however, those drugs possess some serious side effects such as dry mouth, fatigue, gastrointestinal and respiratory problems, anxiety, agitation, drowsiness as well as cardiac arrhythmias [6]. Medicinal plants create an opportunity for alternative treatment for depression [7]. Drugs of natural origin are considered as safer and less complicated than synthetic drugs [8]. The aim of this study was to find out a new antidepressant drug from the natural origin.

*Trachyspermum ammi* is grown in the natural of Egypt and cultivated in Iraq, Iran, Afghanistan, Pakistan, and India. *T. ammi* L. belongs to family Apiaceae which is a highly valued medicinally important seed spice. The seed contains 2% - 4.4% brown colored oil known as ajwain oil. The main component of this oil is thymol. The oil exhibits fungicidal [9], antimicrobial [10], and anti-inflammatory effects on humans. It plays an important role as remedial agent for flatulence, atonic dyspepsia, and diarrhea [11]. It also cures abdominal tumors, abdominal pains, and piles. *T. ammi* has been shown to possess hypolipidemic [12], digestive stimulant [13], antihypertensive, hepatoprotective, antispasmodic, bronchodilator [14], anti-lithiasis, diuretic [15], abortifacient [16], galactogogic [17], antiplatelet-aggregator, antitussive [18], anti-filarial [19], gastroprotective [20], nematocidal [21], anthelmintic [22], detoxification of aflatoxins [23], and ameliorative effects [24]. Thymol also used in toothpaste and perfumery [9]. Seeds of *T. ammi* are used traditionally in Lebanon as anti-rheumatic. Fixed oil from the seed contains resin acids, palmitic acid, petroselinic acid, oleic acid and linoleic acid [25].

## 2. Materials and Methods

### 2.1. Plant Material Collection and Extraction

The seed of *Trachysperum ammi* was collected from the local market of Jessore, Bangladesh. A herbarium sheet was prepared of that sample and sent for identification and authentication which was done by a Senior Scientific Officer at Bangladesh National Herbarium, Dhaka, Bangladesh. About 500 g of seeds powdered by using mortar-pestle and was dissolved in 750 mL of methanol. The powdered material was dissolved in methanol for 72 h in a beaker and mixture was stirred every 18 h using a sterile glass rod. Room temperature also carefully maintained at  $25^{\circ}\text{C} \pm 2^{\circ}\text{C}$ . The desired filtrate obtained after 3 times repetition by using the Whatman No. 1 filter paper and sterilized cotton filter. Filtrated solvent evaporates by the rotary evaporator; the percentage of yield of extract was 4.80%.

### 2.2. Experimental Animals

Swiss Albino mice of both sex (20 - 25 g) collected from the Animal Husbandry of Jahangirnagar University, Dhaka, Bangladesh. Animals were maintained under standard environmental conditions (temperature:  $25^{\circ}\text{C} \pm 2^{\circ}\text{C}$ , relative humidity: 55% - 65% and 12 h light/dark cycle). During acclimatization period, food pellets provided to the mice with fresh water and *libitum*. The animals allowed acclimatizing to the laboratory condition for 14 days before experimental treatment. All the experimental animals treated following the Ethical Principles and Guidelines for Scientific Experiments on Animals (1995) formulated by the Swiss Academy of Medical Sciences and the Swiss Academy of Sciences. All the experimental animals were treated following the Ethical Principles and Guidelines for Scientific Experiments on Animals formulated by Ethical Review Committee, Faculty of Biological Sciences & Technology, Jessore University of Science & Technology (Ref: ERC/FBS/JUST/2017-02).

### 2.3. Drugs and Treatments

Imipramine hydrochloride (Sandoz, Novartis Bangladesh Ltd) used as the reference drug or positive control in antidepressant-like activity tests. All animals housed in a controlled room (temperature,  $25^{\circ}\text{C} \pm 1^{\circ}\text{C}$ ; humidity, 45% - 50%; light-dark cycle, 12 h each). Mice were divided randomly into control, positive control, and three experimental groups. Each group contained 5 mice and treated Deionized water 0.1 ml/mice, Imipramine HCl (30 mg/kg), META (50 mg/kg), META (100 mg/kg), and META (200 mg/kg) respectively. Test solutions were administered orally using oral gavage once daily between 1-3 p.m. over a period of 14 days. All the experiments of these investigations were carried out at the Pharmacology Laboratory of the Department of Pharmacy, Jessore University of Science & Technology, Bangladesh.

## 2.4. Experimental Methods

### 2.4.1. Forced Swimming Test (FST)

FST performed according to the method which described by Porsolt *et al.*, (1977) with some modifications [26] [27]. Animals exposed to a situation of forced swimming that based on behavioral despair, in which their movements reduced after a period of vigorous activity (struggling). However, the movements of swimming required to keep their heads above the water. Experimental mice placed in an acrylic cylinder (45 cm height = 20 cm diameter) filled with water at  $25^{\circ}\text{C} \pm 1^{\circ}\text{C}$  to a depth of 17 cm. According to above-mentioned apparatus, a trial session carried out (14-day treatment) which allowed the mice to swim for 15 minutes. Mouse considered immobile if it remained floating in the water, except for small movements to keep its head above the water. The FST performed between 1-3 p.m. and recorded using a video camera. The tapes evaluated by observers not informed about the kind of treatment each animal had received [28].

### 2.4.2. Tail Suspension Test (TST)

This test was performed according to the method described by Steru *et al.*, (1985) [29] with slight modifications. TST is simple, reliable, and widely accepted behavioral despair model as well as screening antidepressant effect. TST involves suspending the tail of the mice upside down which shows the state of agitation and immobility as well this reflects a state of depression. TST apparatus contains two stands, each with a clamp located 22 cm from the floor, were placed at intervals of 23 cm. Each mouse was hung 5 cm from the end of its tail on a stand and recorded with a video camera for 6 min. The TST performed between 1-3 p.m. Immobility time was evaluated by observers.

### 2.4.3. Measurement of Locomotor Activity Test (MLAT)

The locomotor activity test performed according to the method of Carlini *et al.*, (1986) [30] with some modifications. A mouse placed in an open field apparatus composed of an arena 40 cm in diameter divided into 64 approximately equal areas. During open field observations, each mouse individually placed in the center of the arena 15 h after the last treatment. Following behavioral parameters observed: locomotion (number of line crossings), rearing frequencies (number of times seen standing on hind legs), and number of defecations within 5 min. Open field observations performed between 8-10 a.m.

## 2.5. Statistical Analysis

Statistical analysis of the experimental data performed 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 presented as mean value  $\pm$  SEM ( $n = 5$ ). The difference between the group was considered significant at a level of  $p^* < 0.05$ . The statistically significant results marked with a star (\*) sign in the table as well as in the graph.

### 3. Results

#### 3.1. Forced Swimming Test (FST)

The META at doses level of 50, 100 and 200 mg/kg body weight on forced swimming test in mice observed (**Table 1**). The extracts of *T. ammi* significantly reduced the immobility time in FST. Interestingly, *T. ammi* reduced the immobility time notable at 200 mg/kg when compared with the control group (**Figure 1**). Imipramine HCl also showed the same antidepressant manner.

#### 3.2. Tail Suspension Test (TST)

The META at doses level of 50, 100 and 200 mg/kg body weight on tail suspension in mice showed the positive result (**Table 2**). The immobility time in the TST using mice markedly reduced after acute 14 days treatment with Imipramine HCl (30 mg/kg). Administration of extracts of *T. ammi* at dosages of 50, 100, and 200 mg/kg significantly reduced the immobility time (**Figure 2**).

#### 3.3. Measurement of Locomotor Activity Test (MLAT)

The META at doses level of 50, 100 and 200 mg/kg body weight on the measurement of locomotor activity test in mice observed. The extracts of *T. ammi* (50 mg/kg) shown that the same locomotion effect of the control group (**Table 3**). However, 100 mg/Kg and 200 mg/kg doses of *T. ammi* shown the significant increase of locomotion, rearing, and defecation. All the test animals compared with positive control (**Figures 3(a)-3(c)**).

**Table 1.** Effect of META in forced swimming test on mice.

Treatment	Doses	Immobility time
Deionized water	0.1 ml/mice	106.20 ± 17.890
Imipramine Hydrochloride	30 mg/kg	18.50 ± 3.403*
META	50 mg/kg	46.25 ± 5.250*
META	100 mg/kg	41.0 ± 2.121*
META	200 mg/kg	31.80 ± 7.479*

Values are presented as mean ± SEM, where n = 5. Control = Distilled water, 0.1 ml/mice, Imipramine HCl = 30 mg/kg, Group META = 50, 100 and 200 mg/kg body weight. \*p < 0.05 compared with the control group (Dunnett's test).

**Table 2.** Effect of META in tail suspension test on mice.

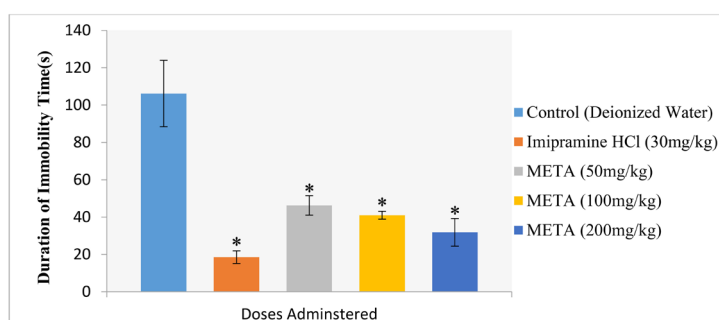
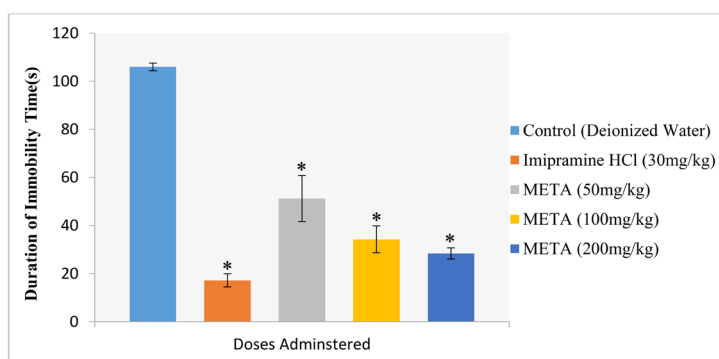
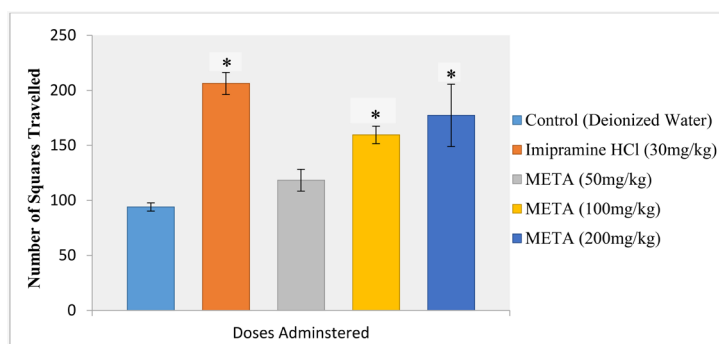
Treatment	Doses	Immobility time
Deionized water	0.1 ml/mice	105.87 ± 1.612
Imipramine Hydrochloride	30 mg/kg	17.25 ± 2.750*
META	50 mg/kg	51.25 ± 9.690*
META	100 mg/kg	34.25 ± 5.677*
META	200 mg/kg	28.4 ± 2.293*

Values are presented as mean ± SEM, where n = 5. Control = Distilled water, 0.1 ml/mice, Imipramine HCl = 30 mg/kg, Group META = 50, 100 and 200 mg/kg body weight. \*p < 0.05 compared with the control group (Dunnett's test).

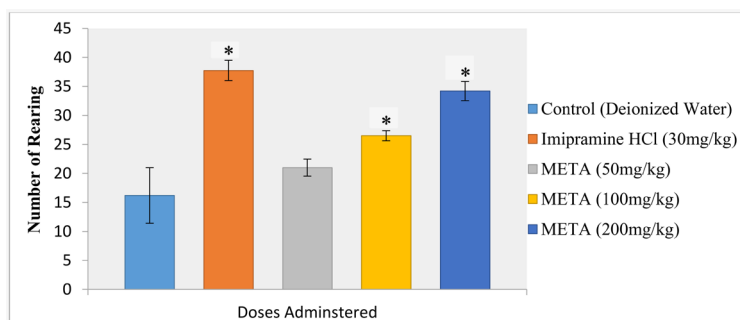
**Table 3.** Effect of META in locomotor activity test on mice.

Treatment	Doses	Locomotion	Rearing	Defecation
Deionized water	0.1 ml/mice	94.0 ± 3.768	16.2 ± 4.841	0.80 ± 0.583
Imipramine Hydrochloride	30 mg/kg	206.25 ± 10.0*	37.75 ± 1.75*	3.25 ± 0.25*
META	50 mg/kg	118.2 ± 9.903	21 ± 1.472	2.00 ± 0.408
META	100 mg/kg	159.5 ± 7.963*	26.5 ± 0.866*	2.25 ± 0.25*
META	200 mg/kg	177.2 ± 28.34*	34.2 ± 1.655*	3.00 ± 0.316*

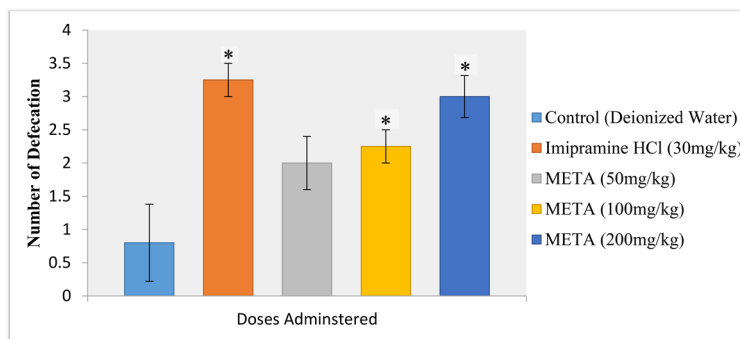
Values are presented as mean ± SEM, where n = 5. Control = Distilled water, 0.1 ml/mice, Imipramine HCl = 30 mg/kg, Group META = 50, 100 and 200 mg/kg body weight. \*p < 0.05 compared with the control group (Dunnett's test).

**Figure 1.** Graphical representation of effect of META in forced swimming test on immobility time in mice. \*p < 0.05 compared with the control group (Dunnett's test).**Figure 2.** Graphical representation of effect of META on tail suspension test on immobility time in mice. \*p < 0.05 compared with the control group (Dunnett's test).

(a)



(b)



(c)

**Figure 3.** (a) Graphical representation of effect of META on measurement of locomotor activity test of locomotion in mice. \* $p < 0.05$  compared with the control group (Dunnett's test). (b) Graphical representation of effect of META on measurement of locomotor activity test of rearing in mice. \* $p < 0.05$  compared with the control group (Dunnett's test). (c) Graphical representation of effect of META on measurement of locomotor activity test of defecation on mice. \* $p < 0.05$  compared with the control group (Dunnett's test).

#### 4. Discussion

Many of the plants used as crude extracts and purified natural products [31] [32] which have potential medicinal properties [33]. The aimed of our present study to evaluate the antidepressant-like effects of methanolic extract of the seeds of *T. ammi* using behavioral animal models. Our present study indicates that the antidepressant-like effect of META found to compare with the standard drug Imipramine hydrochloride (30 mg/kg). Imipramine hydrochloride acts by inhibiting norepinephrine reuptake and has used as a standard drug in majority studies. Rodents displayed immobility when unavoidable stress subjected such as forced swimming is thought to reflect a state of despair or lowered mood. This condition reflects depressive disorders in humans. Additionally, the antidepressant drugs treatment reduced the immobility time. Moreover, a significant correlation found between the clinical efficacy of antidepressant drugs and their potency in this model. In the present study, META significantly reduced immobility time in the FST after repeated administration of 50, 100 and 200 mg/kg to mice for 14 d. The intensity of immobility reduction was statistically significant at all doses ( $p^* < 0.05$ ) but strongest at a dosage of 200 mg/kg.

META exhibited a reduction in the time of immobility at the dose of 50 and 100 mg/kg. Interestingly, 200 mg/kg was produced the higher reduction of immobility compared with the control group. The efficacy of immobility decreased in the FST & TST which may occur with psycho-stimulants, exert an indiscriminate motor stimulating activity [34]. The motor stimulating activity of META was performed with the open field test to exclude the confusion. The administration of META at a dosage of 50, 100 and 200 mg/kg for 14 d exerts statistically significant ( $p^* < 0.05$ ) at the doses of 100 and 200 mg/kg as well as also indicates that the reduction of immobility time after 14 d administration of META attributed to an inherent antidepressant effect. Thus, the effective dosage of META in the FST seems to be around 200 mg/kg body weight.

The beneficial effect of Imipramine hydrochloride in TST model seems to be due to increased availability of these neurotransmitters (NE) and serotonin (5HT) at the postsynaptic site following reuptake inhibition [35]. Some researchers already have shown the adaptogenic effect of the plant extract via normalization of the various stress parameters and monoaminergic levels [36]. Those studies may provide a hint about extract which involved in possible antidepressant-like effect through the restoration of normal monoaminergic NE [37]. The action of the triterpenoid and saponins resulted in the enhancement of the nerve impulse transmission. Neurochemical assays suggested that treatment by triterpenoid and saponins improved brain antioxidant activity to varying degrees after the behavioral despair test [38]. The pattern of CNS effects observed through this experiment suggests us the involvement of norepinephrine NE system on its antidepressant-like effect.

## 5. Conclusion

The findings obtained from forced swimming test (FST), tail suspension test (TST), and measurement of locomotor activity test (MLAT) clearly indicate that the methanolic extract of the seeds of *Trachysperum ammi* possesses a significant antidepressant-like activity. The outcome also indicates that the antidepressant-like activity observed without the involvement of non-specific motor stimulation. However, different research approach must be needed to elucidate the mechanism of action of *Trachysperum ammi*. The experimental findings suggest the antidepressant-like effects that may involve in norepinephrine neurotransmitters system.

## Ethical Approval

All procedures performed in this study involving animals were approved in accordance with the ethical standards of the Ethical Review Committee, Faculty of Biological Sciences and Technology, Jessore University of Science and Technology, Jessore, Bangladesh (Ref: ERC/FBS/JUST/2017-02).

## Consent for Publication

Not applicable.



## Availability of Data and Material

Not applicable.

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## Authors' Contributions

Md. Rashidur Rahman designed, and supervised the experimental work. Mohammad Ali, Mostakim Sharif, and Sadiur Rahman Sajon coordinated forced swimming test, tail suspension test, and locomotor activity test and interpreted the results. Md. Abdul Mannan has done statistical analysis and drawn the graphs. Md. Shahed-Al-Mahmud drafted the manuscript. All authors read and approved the manuscript.

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## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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## Abbreviations

META: Methanolic Extract of the seeds of *Trachysperum ammi*

FST: Forced Swimming Test

TST: Tail Suspension Test

NE: Neurotransmitters

Min: minutes