

Antidepressant activity of *Trigonella foenum* leaves in Wistar albino rats

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ABSTRACT

Background: To evaluate antidepressant activity of ethanolic extract of *Trigonella foenum* in animal models.

Methods: A total of 60 healthy male Wistar albino rats weighing 220-250 grams were used and they were divided into 10 groups of 6 rats in each. First five groups (1st -5th) were evaluated by Forced Swim Test (FST) and remaining by Tail Suspension Test (TST). 1st group (control) received normal saline 10 mg/kg, 2nd group (standard) Imipramine 10 mg/kg and 3rd, 4th and 5th groups (test) respectively received *Trigonella foenum* leaf ethanolic extract [TFEE] in different doses 100 mg, 200 mg, and 400 mg/kg per orally for 14 days. They were evaluated for antidepressant activity using FST after 60 minutes of drug administration on 14th day. Similarly, remaining five groups (6th to 10th) received the same drugs and evaluated using TST after 60 minutes of drug administration. Duration of immobility was noted for six minutes for each rat.

Results: One way ANOVA and Tukey Kramer test were used for statistical analysis. The immobility periods were expressed in mean±SD. The immobility period in FST were 207.16±28.7, 50.08±2.9, 46.14±1.2, 40.5±3.4 and 40.0±3.6 seconds respectively for control, standard and three test groups of TFEE (100/200/400 mg/kg). Similarly, immobility periods of 163.11±31.9, 125.03±11.2, 138.81±16.44, 138.16±12.65, 127.58±4.3 seconds were noted for TST for remaining six groups. It was found that TFEE possess statistically significant (p<0.05) antidepressant activity, as evidenced by decrease in the immobility time in both the tests when compared to control group.

Conclusions: Present study results demonstrated that TFEE possess antidepressant property in experimental models of depression.

Keywords: Anti depressant activity, Forced swim Test, Suspension test, *Trigonella foenum*, Tail

INTRODUCTION

The central nervous system (CNS) associated diseases are appearing as a major threat because of increasing mental stress, workload and strain which have become inherent to the present day competitive world. Anxiety and Depression are the major two contributors for worldwide burden of diseases. These two disorders share many common features and are under diagnosed and under treated, which worsens other co-morbid conditions or lead to secondary social or disease burden.¹

Depression is a most common diverse mood disorder. It is a chronic disorder that upsets a person's mood, thoughts, physical health and performance. Symptoms of this mind disorder are biological elements like impedance of thought, sleep disorder, loss of appetite and libido. The symptoms of emotional factors in depression are sadness, apathy, pessimism, low self-respect, feeling of guilt, loss of zeal and indecisiveness.^{2,3}

Though several drugs are available, all are having limitations and there is an urgent need for alternative

medications for these disorders.¹⁻³ Traditional medicine offers several treatment options for mood disorders, most of them based on plant products which are empirically tested and proved to be safe in the past for human consumption. Medicinal herbs are still the preferred remedy for nearly 80% of people around the world, mainly in the developing countries to cure and improve the general health. This is primarily due to the common belief that plant derived drugs are without any adverse effects along with being economical and locally accessible.⁴ India is well-known for the culinary uses of spices since ages, and these spices are known to be pharmacologically active and proven to be safe. Most of the spices affect the digestion, metabolism and CNS directly or indirectly through their effects on neuro-endocrine system. *Trigonella foenum* or Fenugreek is the most commonly used spices and is known to possess several pharmacological actions like hypoglycemic, hypolipidemic, antimicrobial effects etc.⁵⁻⁹

As per WHO and ICMR there is an emphasis on the need for screening the traditional medicinal preparations for their efficacy and safety.¹⁰ This study is designed to meet such a need of scientific validation of *Trigonella foenum* leaf for antidepressant property, upon completion the findings of the study may also help in developing new therapeutic agents and strategies.

Wistar albino rats were used for this study in terms of their better predictive power of pharmacological actions in humans, availability of animals and testing devices in our institution and also due to many other advantages like ease of handling, and housing etc. They also possess good resistance to infections.¹¹⁻¹³

METHODS

Experimental animals

A total of 60 (n=60) healthy adult male Wistar albino rats, weighing 220-250 g, were selected for the study after obtaining approval from Institutional Animal Ethics Committee. Animals were handled with care throughout the experimental procedures as per CPCSEA guidelines. Clean polypropylene cages were provided to house the animals, under standard housing conditions in the animal house. The room temperature in the animal house was maintained at 24±2°C with equal light and dark cycle (12:12). The rats were given a standard diet consisting of pellets and water.

Plant material

Leaves of *Trigonella foenum* graecum L (2000 g) were procured from the local market of Mangalore, Karnataka, India and were authenticated by plant Taxonomist from the Department of Applied Botany, Mangalore University.

Preparation of ethanolic extract of *Trigonella foenum* leaves (TFEE).

Fresh leaves were purchased and cleaned with running tap water to remove extraneous particles. They were shade dried, powdered and extracted using 90% ethanol in soxhlet apparatus for 72 hours. This extract was then filtered, concentrated using reduced pressure and dried with a rotary evaporator for 4 hours. The total yield was 5%.

For studying the effect of TFEE on depression, the animals were divided into 10 groups of six rats in each group. First five groups (1st -5th) were evaluated by Forced Swim Test (FST) and remaining by Tail Suspension Test (TST). First group of rats (control) received normal saline 10mg/kg, second group (standard) Imipramine 10 mg/kg and third, fourth and fifth groups (test) respectively received *Trigonella foenum* leaf ethanolic extract [TFEE] in different doses 100 mg/kg, 200 mg/kg and 400 mg/kg per orally for 14 days. They were evaluated for antidepressant activity using FST after 60 minutes of drug administration on 14th day. Duration of immobility was noted for six minutes for each rat in all groups. Similarly, remaining five groups (6th to 10th) received the same drugs and evaluated for antidepressant activity using TST after 60 minutes of drug administration.

The levels of depression were assessed using the following standard tests.

Force swim test (FST)

The FST is the most commonly used pharmacological model for evaluating antidepressant activity. The rodents develop immobility after they are placed in an inescapable cylinder of water and this shows that there is cessation of persistent escape-directed behavior. The apparatus comprises a clear plexiglass cylinder (46 cm high X 21 cm diameter) filled to 30 cm depth with water. This depth was adequate to prevent adult rats from supporting themselves by using their paws or tails and balancing on the base of the cylinder. Water was changed between each swim session to prevent possible effects from an alarm substance released by rats during the swim session. During the period of the test, the time of immobility was recorded for five minutes, during which the rats made no further attempts to escape, and only moved to keep the head above the water.^{14,15}

Tail suspension test

This test is a simplistic means of gauging potential antidepressants. The immobility shown by rodents when exposed to an inevitable and inescapable stress has been assumed to reflect behavioral despondency which in turn may reflect depressive disorders in humans.

Clinically effective antidepressants lessen the immobility period that rats show after active and futile attempts to flee when suspended by the tail. The tail suspension test has been seen to be an easy way to test potential antidepressant compounds.^{14,15}

Statistical analysis

Results are expressed as mean±SD. One-way analysis of variance (ANOVA) was carried out and the statistical comparisons among the groups were performed with Tukey Kramer test using Prism statistical package program. P <0.05 was considered significant.

RESULTS

It was observed that (Table 1), there was a significant decrease (p <0.001) in immobility time for the animals which was treated with TFEE [group III, IV, V] on comparing with the normal rats which received only normal saline [group I]. The immobility time for the animals which was treated with TFEE 200 and 400 mg/kg body weight [group IV, V] was significantly decreased (p <0.01) on comparing with the rats which received the standard drug Imipramine [group II].

Table 1: Effect of ethanolic extract of *Trigonella foenum* leaves on immobility period in forced swim test.

Group		Duration of immobility in seconds
I	Control (NS)	207.166±28.736
II	Imipramine	50.083±2.937 ^a
III	TFEE 1	46.143±1.20 ^a
IV	TFEE 2	40.5±3.425 ^{a,b}
V	TFEE 3	40.0±3.693 ^{a,b}

One way ANOVA followed by Tukey Kramer test. N=06
 Imipramine: 10 mg/kg body weight orally for 14 days
 TFEE₁: 100 mg/kg body weight orally for 14 days
 TFEE₂: 200 mg/kg body weight orally for 14 days
 TFEE₃: 400 mg/kg body weight orally for 14 days
 a : p<0.001, considered very high significant on comparing with control group; b: p<0.01, considered significant on comparing plant extract treated groups with standard drug, Imipramine

Table 2: Effect of ethanolic extract of *Trigonella foenum* leaves on immobility period in forced swim test.

Group		Duration of immobility in seconds
VI	VI Control (NS)	163.11±31.950
VII	Imipramine	125.03±11.20 ^a
VIII	TFEE 1	138.81±16.44 ^a
IX	TFEE 2	138.16±12.65 ^a
X	TFEE 3	127.583±4.33 ^a

One way ANOVA followed by Tukey Kramer test. N=06
 Imipramine: 10 mg/kg body weight orally for 14 days
 TFEE₁: 100 mg/kg body weight orally for 14 days
 TFEE₂: 200 mg/kg body weight orally for 14 days
 TFEE₃: 400 mg/kg body weight orally for 14 days
 a: p<0.001, considered very high significant on comparing with normal group.

It was observed that (Table 2), there was a significant decrease (p <0.001) in immobility time for the animals

which was treated with TFEE [group VIII, IX, X] on comparing with the normal rats which received only normal saline [group VI]. There was no significant difference in the immobility time between the test groups [group VIII, IX, X] and the standard drug group [group VII].

DISCUSSION

On the basis of the clinical association of depressive episodes and stressful life events, many of the animal models for the evaluation of antidepressant drug activity assess stress precipitated behaviors. The Force Swim Test and Tail Suspension Test are the most commonly used animal models for anti depressant activity.^{14,15}

These tests are quite sensitive and relatively specific to all major classes of antidepressants. The rodents develop immobility after they are placed in an inescapable cylinder of water and this shows that there is cessation of persistent escape-directed behavior. This state of behavioral dependency in animals is claimed to produce a condition akin to human depression.^{14,15}

It has been proven that the shortening of immobility time depends mainly on the enhancement of central 5-HT and catecholamine neurotransmission.^{15,16} In this study, *Trigonella foenum* ethanolic extract showed significant antidepressant activity as evidenced by decrease in immobility time of force swim test and tail suspension test.

The antidepressant activity of this plant extract can be attributed to the various phytochemicals present in its ethanolic extract. There are abundant studies showing that phytochemicals like phytosterols, phenolic compounds, flavanoids and glycosides show antidepressant activity.¹⁷

Studies have shown that, one of the active components of *Trigonella foenum* is 4-Hydroxy isoleucine. This alkaloid compound has the ability to increase the levels of dopamine. It is a known fact that depletion of dopamine levels can lead to depression.¹⁸

Apart from its action on dopamine levels, TFEE has shown the antidepressant property, by virtue of its antioxidant activity as free radical induced oxidative stress is important in the pathogenesis of major depression.^{19,20}

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Animal Ethics Committee

REFERENCES

1. Paulson GW. Environmental effects on the central nervous system. *Environment Health Perspectives*. 1977 Oct;20:75-96.
2. Dhingra D, Sharma A. A review on antidepressant plants. *Natural Product Radiance*. 2006;5(2):144-52.

3. Suttajit S. The roles of neurotransmitters, hormones and brain-derived neurotrophic factors in the pathogenesis of depression. *Chiang Mai Medi J.* 2009;48(1):35-41.
4. Gupta LM, Raina R. Side effects of some medicinal plants. *Curr Sci.* 1998;75(9):897-900.
5. Sowmya P, Rajyalakshmi P. Hypocholesterolemic effect of germinated fenugreek seeds in human subjects. *Plant Foods Human Nutr.* 1999;53(4):359-65.
6. Pandian RS, Anuradha CV, Viswanathan P. Gastroprotective effect of fenugreek seeds (*Trigonella foenum graecum*) on experimental gastric ulcer in rats. *J Ethnopharmacol.* 2002;81(3):393-7.
7. Sharififar F, Khazaeli P, Alli N. In vivo evaluation of anti-inflammatory activity of topical preparations from Fenugreek (*Trigonella foenum-graecum* L.) seeds in a cream base. *Iranian J Pharmaceut Sci.* 2009;5(3):157-62.
8. Sharma RD, Raghuram TC, Rao NS. Effect of fenugreek seeds on blood glucose and serum lipids in type I diabetes. *Eur J Clin Nutr.* 1990;44(4):301-6.
9. Dhananjaya DR, Vijay KS, Chandrashekar GP, Makhija IK, Shivakumara S. Anxiolytic activity of ethanolic extract of *Trigonella foenumgraecum* seeds. *Arch App Sci Res.* 2011;3(1):91-5.
10. Badyal DK, Desai C. Animal use in pharmacology education and research: The changing scenario. *Indian J Pharmacol.* 2014;46(3):257.
11. Ghosh MN. Toxicity studies. *Fundamentals of experimental pharmacology.* 1984;2:4-6.
12. Rodgers RJ, Cao BJ, Dalvi A, Holmes A. Animal models of anxiety: an ethological perspective. *Braz J Med Biol Res.* 1997;30:289-304.
13. Otobone FJ, Martins JV, Trombelli MA, Andreatini R, Audi EA. Anxiolytic and sedative effects of a combined extract of *Passiflora alata* Dryander and *Valeriana officinalis* L. in rats. *Acta Sci Health Sci.* 2005 Dec;27(2).
14. El Refaey H, Amri HS. Effects of antidepressants on behavioral assessment in adolescent rats. *Bahrain Med Bull.* 2011;33(2):83-9.
15. Santosh P, Venugopl R, Nilakash AS, Kunjbihari S, Mangala L. Antidepressant activity of methanolic extract of *Passiflora foetida* leaves in mice. *Int J Pharm Pharm Sci.* 2011;3(1):112-5.
16. Landén M, Thase ME. A model to explain the therapeutic effects of serotonin reuptake inhibitors: the role of 5-HT₂ receptors. *Psychopharmacol Bull.* 2006;39(1):147.
17. Pharmacopoeial and related drugs of biological origin. *Trans and Evans Pharmacognosy*, 15th ed. 2002:171-420.
18. Sridevi P, Verma HV, Rangarao P. Synthesis of derivatives of 4-hydroxy isoleucine from fenugreek and evaluation of their anti diabetic activity. *Int J f Phytopharmacy.* 2014;4(1):06-10.
19. Santoshi R, Ghodake et al. A study of oxidative stress and influence of antioxidant vitamins supplementation in patients with major depression. *Curr Neurobiol.* 2012;3(2):107-11.
20. Behr GA, Moreira JC, Frey BN. Preclinical and clinical evidence of antioxidant effects of antidepressant agents: implications for the pathophysiology of major depressive disorder. *Oxidative Med Cellular Longevity.* 2012 27;2012.

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