EVALUATION OF ANTIDEPRESSANT LIKE ACTIVITY OF *TRIGONELLA FOENUM GRAECUM* LINN. SEEDS IN MICE.

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Summary

The methanolic extract of *Trigonella foenum graecum* Linn. Seeds (METFGS) was investigated for its antidepressant activity in mice. Tail suspension test (TST) and forced swim test (FST) were used for the study. The results showed that METFGS (250 and 500 mg/kg, i.p.), daily for 7 days significantly reduced the immobility during FST and TST in a dose dependant manner. The efficacy of the extracts were found to be comparable with the standard tricyclic antidepressant agent - imipramine. Saponin glycosides and flavonoids present in seeds of fenugreek may be responsible for significant antidepressant like activity probably through interaction with adrenergic, dopaminergic, serotonergic and GABAergic system.

Key Words: METFGS, depression, Forced swim test, Tail suspension test.

Introduction

Depression is one of the most frequently occurring disorders, affecting about 10-15% of the population each year. Depression refers to a wide range of mental health problems characterized by the absence of positive effect (loss of interest and enjoyment in ordinary things and experiences), low mood and a range of associated emotional, cognitive, physical and behavioral symptoms. Since all the synthetic drugs available for the treatment of depression have various adverse effects and problematic interactions. Several herbal drugs have been introduced during the recent past for decreasing depression in many emotional and physical disorders. Although depression is one of the major neuropsychiatric disorders, the success rate of medication for any drug is about 60%, which means that approximately.

Trigonella foenum graecum (TFG) has been used since ancient times in Indian folklore medicine for its many medicinal properties[1]. TFG is reported to possess anxiolytic[2], nootropic[3], immunomodulatory[4] and hypoglycemic[5] properties. In the present study, antidepressant activity is investigated in view of its reported anxiolytic and nootropic activity.

The major aim of this is to provide a possible explanation for the relative inefficacy of currently used antidepressants and to propose a novel mechanism of action, which might improve the success rate of clinical treatment.

In view of this, the present study was undertaken to investigate antidepressant like effect of *Fenugreek* seeds.

Methods

Plant material

The Seeds of *Trigonella foenum graecum* Linn. were collected from the local market of Harapanahalli in the month of May 2006 and authentication was done by Mr. K. Prabhu, Professor of Pharmacognosy, S.C.S. College of Pharmacy, Harapanahalli. A voucher specimen has been deposited at the museum of college.

Preparation of extract

The dried seeds were coarse powdered and defatted with petroleum ether (60 – 80^{0}C) using Soxhlet extractor. The marc obtained was then subjected to extraction with methanol (64 – 65.5^{0}C). The extract was concentrated using rotary flash evaporator. The dried extract was stored in airtight container in refrigerator below 10^{0}C. Percentage yield of extract was 14.39%.

Experimental animals

The albino mice of wistar strain 20 – 30 g were used throughout the experimentation. The animals were procured from Nijalingappa Medical College, Bagalkot, Karnataka. After randomization into various groups, animals were acclimatized for period of 10 days under standard husbandory condition as follows Room temperature : 27 ± 3^{0}C, Relative humidity : 65 ± 10%, 12 hrs. light/dark cycle. All the animals were fed with rodent pellet diet (Gold mohr, Lipton India Ltd.,) and water was allowed ad-libitum under strict hygenic condition. Ethical clearance for performing experiments on animals was obtained from Institutional Animal Ethics Committee (IAEC).

Acute toxicity study (LD_{50})

An acute toxicity of METFGS was carried out in female albino mice (20 – 30 g), those maintained under standard conditions. The animals were fasted over night prior to the experiment. Fixed dose (OECD Guideline No. 420) method of CPCSEA was adopted for toxicity studies[6].

The methanolic extract of TFG seeds was subjected to the antidepressant activity.

Evaluation of antidepressant activity

Albino mice of either sex weighing 20 – 30 g were selected and divided into four groups of six each separately for both the experimental models. All the animal of different groups were treated as follow.

Group I – Control (Received only vehicle i.p.)

Group II – Standard (*Imipramine* 5 mg/kg i. p.)

Group III – METFGS (250 mg/kg i.p.)

Group IV – METFGS (500 mg/kgi. p.)

Tail suspension test (TST):

The animals of all groups were treated for 7 days as mentioned above. The total duration of immobility induced by tail suspension was measured according to the method of Steru et al. On prescribed day one hour after treatment all mice were suspended individually 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 test for animals of all groups.[7]

Forced swim test (FST):

All the animals of different groups were treated for 7 days. Forced swim test was proposed as a model to test antidepressant activity by Porsolt et al. The mice were forced to swim individually in a circular tank (46 cm tall X 20 cm in diameter) filled with tap (22 ^{o}C) to a depth of 20 cm and left for 6 min. During this period the behavior of the animals were recorded by an observer. Mice were considered to be immobile when it remained floating in the water without struggling and making only minimum movements of its limbs necessary to keep its head above water. The total duration of immobility was recorded during the next 4 min of total 6 min test. The changes in immobility duration were studied after administrating drugs in separate groups of animals. Each animal was used once.[8]

Results

Acute toxicity study

The METFGS was studied for acute toxicity at dose of 2000 mg/kg i.p. in female albino mice. The extract was found devoid of mortality of animals. Hence 2500 mg/kg was considered as LD_{50} cut off value. So dodes selected for extract as per the OECD guidelines No.420 (Annexure -2d) fixed dose method are mentioned below.

1. 250 mg/kg (1/10th of 2500 mg/kg)

2. 500 mg/kg (1/5th of 2500 mg/kg.)

Antidepressant activity

Tail suspension test

In the present study, the immobility showed by the mice in TST in a duration of 6 min. considered as study parameter. METFGS 250 as well as METFGS 500 mg/kg elicted the effect by reducing the immobility time. The obtained results were found significant and in dose dependent fashion.

The results are tabulated in Table no.1 .

Table no.1

Effect of METFGS on Tail suspension test in mice

Groups	**Mean immobility (sec)**	**% reduction in immobility**
Control (Received only vehicle i.p.)	160.33 ±10.243	_
Standard. (Imipramine 5mg/kg i.p)	75.83±14.834***	52.70%
METFGS 250 mg/kg i.p	98.33±9.110**	38.67%
METFGS 500 mg/kg i.p.	77.50±5.793***	51.66%

Values are mean ± SEM (n = 6).
** p < 0.01, *** p < 0.001 as compared to control.

Forced swim test

METFGS 250and 500 mg/kg, i.p. reduced the immobility time in the forced swim test. Imipramine was used as reference drug for these studies.as expected imipramine (5mg/kg, i.p.) reduced the immobility time during forced swimming in mice.

Table no.2

Effect of METFGS on Forced swim test in mice

Groups	Immobility Time (mean ± SEM)	% reduction in immobility
Control (Received only vehicle i.p.)	139.16±8.910	_
Standard. (Imipramine 5mg/kg i.p)	62.50±10.970***	55.08%
METFGS 250 mg/kg i.p	76.66±12.170**	44.91%
METFGS 500 mg/kg i.p.	69.33±7.460***	50.17%

Values are mean ± SEM (n = 6).
** $p < 0.01$, *** $p < 0.001$ as compared to control.

Discussion

Depression is a common, debilitating, life-threatening illness with a significant incidence in the population. Numerous antidepressant compounds are now available, presumably acting via different mechanisms including serotonergic, noradrenergic and/or dopaminergic systems. Heterogeneity of the clinical responses to antidepressant and mood- stabilizing drugs and susceptibility to adverse effects are the major clinical problems[9]. Over 20 animal models of depression have been developed [10].

Both FST and TST are widely used to screen new antidepressant drugs.[7,11,,12,13] These tests are quite sensitive and relatively specific to all major classes of antidepressant including tricyclics 5-HT reuptake inhibitors, MAO inhibitors[11,7,13]. The TST and FST induces a state of despair in animals. The immobility referred to as behavioral despair in animals is claimed to produce a condition similar to human depression[7].

In the present study methanolic extract of TFGS in two different doses administered for 7 successive days, produced significant antidepressant like effect in mice challenged to TST and FST. The efficacies of the extract were found to be comparable with a standard TCA-imipramine. An interesting finding of the present study is that, the antiimmobility effect of METFGS in TST and FST exhibited a significant and dose dependent effect. The flavonoid apigenin[15], which selectively binds with high affinity to the central benzodiazepine receptor, possesses important anxiolytic[16,17] and antidepressant activities [18].

Literature survey indicates that Shatavari possess the saponins like Shatavarine I-V, responsible to exert the antidepressant like activity[19]. Saponin glycosides are the main chemical constituents present in the seeds of fenugreek [1] and in the present investigation also preliminary tests for flavonoids and tannins, which may be responsible for significant antidepressant property of test extracts. Hence, the METFGS showed antidepressant like activity probably through interaction with adrenergic, dopaminergic, serotonergic, and GABAergic systems.

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