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Antidepressant Activity of *Foeniculum Vulgare* in Forced Swimming and Tail Suspension Test.

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ABSTRACT

Mental depression is a major disorder of mood prevalent in a large percentage of the population and it disrupt the normal social life. The need of effective and well tolerated antidepressants has prompted to examine herbal plants that have been traditionally used for depression. *Foeniculum vulgare* is the common source of the well-known oil; particularly used in aromatherapy and regarded as a tonic to the nervous system. So our aim is to compare the effects of the antidepressant drug fluoxetine and *Foeniculum vulgare* on depressive behavior in albino rats. Both Forced swimming test (FST) and Tail suspension test (TST) were used for screening antidepressant effect. The ethanolic extract of *Foeniculum vulgare* at two different doses (100,200mg/kg,i.p.), fluoxetine(10mg/kg) and saline were administered 30mts prior to the tests and the immobility period was recorded for 6mts. The antidepressant effect of *Foeniculum vulgare* was compared to that of fluoxetine. Both fluoxetine (10mg/kg) and *Foeniculum vulgare* (200mg/kg) produced significant antidepressant effect by reduction in immobility period as compared to control. However findings suggested that fluoxetine (10mg/kg) is more effective than *Foeniculum* alone. The results of the present study indicated the antidepressant activity of *Foeniculum vulgare* and potential for use of an adjuvant in depression.

Keywords: Antidepressant, Forced swimming test, Tail suspension test, *Foeniculum vulgare*

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INTRODUCTION

Depression is an extremely common psychiatric condition about which a variety of neurochemical theories exist. World wide it is a major cause of disability and premature death [1]. Pharmacological manipulation of monoamine transmission remains the most successful therapeutic approach still now. Drugs that increase the nor adrenaline and 5-hydroxy tryptamine level show significant antidepressant activity. Current drugs like SSRI and atypical antidepressants have side effects like Insomnia, nausea, Increased anxiety and sexual dysfunction [2]. Currently research is going on herbal therapies which could be an effective alternative Studies proved that herbal plants like Hibiscus sabdariffa, Piper tuberculatum, Gastrodia elata, Valeriana officinalis, Rosmarinus officinalis possess significant antidepressant activity [3-7]. Herbal drugs like st. John's wort is used for mild to moderate depression with minimal side effects [8]. Fennel (*Foeniculum vulgare*), is a plant species in the genus *Foeniculum* It is a member of the family Apiaceae It is a hardy, perennial, umbelliferous herb, with yellow flowers and feathery leaves. It is a highly aromatic and flavorful herb with culinary and medicinal uses, and is one of the primary ingredients of absinthe. Fennel has a long history of herbal use and is a commonly used household remedy, being useful in the treatment of a variety of complaints, especially those of the digestive system. The seeds, leaves and roots can be used, but the seeds are most active medicinally and are the part normally used. Florence fennel seed and its essential oil are used as stimulant, aromatic, diuretic and purgative and it is proved that it has the antidiabetic, antioxidant, hepatoprotective, antifungal, antispasmodic, antiosteoporotic and antithrombotic effect [9-10]. Fennel essential oil aromatherapy is a well known one to relieve depression and lift up mood [11]. So the aim of our study is to prove the antidepressant effect of *Foeniculum vulgare* in animal models.

MATERIALS AND METHODS

Collection of the plant extract

Foeniculum vulgare seeds were purchased from local market and were identified by the Director, National institute of Herbal science –West Tambaram, Chennai.

Preparation of the plant extract

The *Foeniculum vulgare* seeds were dried in shade, powdered and passed through a 40 mesh sieve. Dried powder (200 gms) was taken and soaked in 1000 ml of ethanol for 72 hours after which the filtrate is obtained concentrated to dryness at room temperature. The extract is stored at 4°C for future use.

Phytochemical Screening

Freshly prepared *Foeniculum vulgare* extract were subjected to standard phytochemical screening tests for various constituents by standard methods. It showed the presence of various phytoconstituents like alkaloids, flavonoids, tannins, phenols, terpenoids and saponins.

Acute toxicity studies

Acute toxicity study was performed according to organization for Economic co-operation and development (OECD) guideline test ANNEX-423 [12] Ethanolic extract of *Foeniculum vulgare* seeds was administered orally in doses at 5,50,300 and 2000 mg/kg b.w to the groups of rats(no-3) and the percentage mortality was recorded for a period of 24 hours, During the first hour after the drug administration, the rat were observed for any gross behavioral change and the parameter observed were hyperactivity,grooming,convulsion,sedation and loss of righting reflex. Respiration, salivation, urination and defecation were also noted. Based on the above toxicity study, direct limit test was done. After 48 hrs the same dose was administered to 2 more female rats and the observation was done same as for the previous rat. The rats were observed for 14 days and no adverse observation was found morphologically. The weight of the animal was recorded on 7th and 14th day.

Experimental Design

The Wister albino rats, weighing between 150-200g of either sex were selected for the experiment. Prior to experiment the rats were divided randomly in to four groups (no-4). First group treated as control (Normal saline) and second and third groups were treated with the ethanolic extract of *Foeniculum vulgare* (100 mg/kg, 200 mg/kg). Fourth group was treated with Fluoxetine (10mg/kg -Lilly co). All injections were given intraperitoneally at 30mts before the FST and TST. The study was approved by Institutional Animals Ethics committee (IAEC.No.01/05/2011).

Methods

The Wister albino rats were housed in groups of four polycarbonate cages. They were maintained on a 12-h light-dark cycle in a temperature-controlled (22°C) colony room and had free access to food and water. The experiments were performed according to the Guide for the care and use of laboratory animals, and the Ethics Committee for Experiments on Animals

Forced swimming test in rat

The procedure used has been previously described by Porsolt et al [13]. The animals were forced to swim inside a cylinder filled with water, without the possibility of escaping, the resulting anxiety produces vigorous swimming activity and attempts at escaping by diving or climbing the walls of the cylinder. When the animals ceased all movements except those necessary for survival .(An animal is judged to be immobile whenever it remains floating passively in the water in a slight hunched but upright position, its nose just above the surface). This was classified as induced depression. Wister rats of both sex weighing between 150-200g were used. They were separated one day before the experiment with free access to food and water. Rats were individually forced to swim inside a vertical Plexiglas cylinder (height: 40cm; diameter:18cm,containing 15cm of water maintained at 25 C) On the first day rats placed in the cylinders for the first time are initially hyperactive, vigorously swimming in circles, trying to climb the wall or diving to the bottom. After 2-3

min activity begins to subside and to be interspersed with phases of immobility or floating of increased length. After 5-6 min immobility reaches a plateau where the rats remain immobile for approximately 80% of the time. After 15 mins in the water the rats were removed and allowed to dry in a heated enclosure (32C) before being returned to their home cages. They are again placed in the cylinder 24h later and the total duration of immobility was recorded during the next 4 min of a total 6min test. They received their respective drugs 30mts prior to test session.

Tail suspension test

The method described by Steru, et.al [14]. was used. The animals were hung by the tail on a plastic string 58cm above the surface with the help of an adhesive tape. The duration of immobility was observed for a period of 8mts. They received their respective drugs 30mts prior to test session .The duration of immobility was recorded during the last 6 minutes of the observation period. Rats were to be immobile only when they hung passively and were completely motionless.

Statistical Analysis

The mean \pm S.E.M. values were calculated to each group. The data were analyzed using one-way Anova followed by Tukey multiple comparison test. P < 0.05 was considered to be statistically significant.

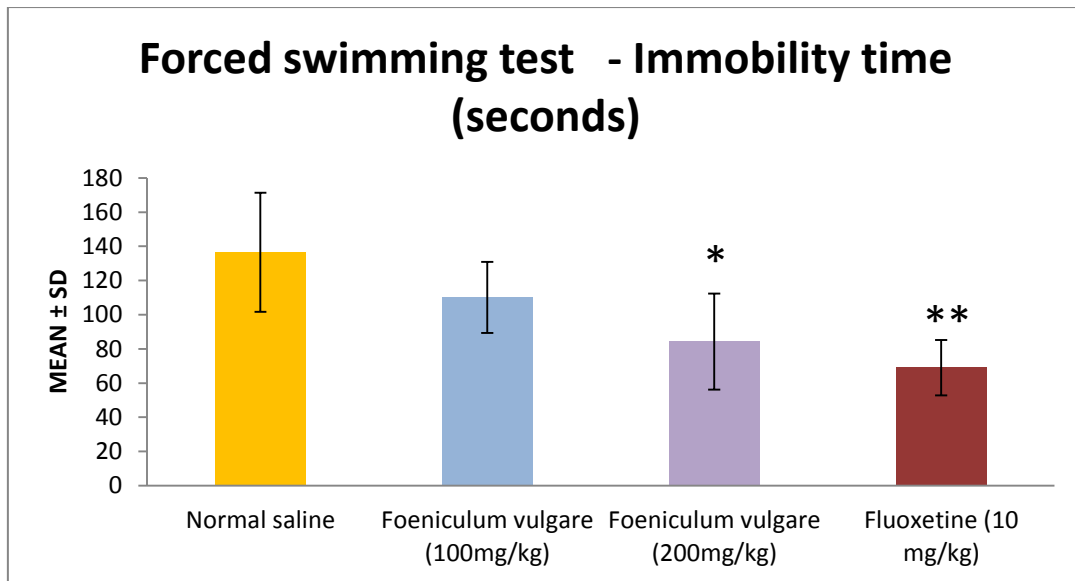
RESULTS

Forced swimming test

It was observed that there was significant reduction in immobility time in *Foeniculum vulgare* group (200mg/kg) ($p < 0.05$) when compared to control group. Similarly Fluoxetine group (10mg/kg) showed significant reduction in immobility time ($p < 0.01$).

Table 1: Effect of *Foeniculum vulgare* on immobility time using Forced swimming test

Groups	Immobility time(sec)
Control	136.50 \pm 34.789
<i>Foeniculum vulgare</i> (100mg/kg)	110.17 \pm 20.808
<i>Foeniculum vulgare</i> (200mg/kg)	84.33 \pm 28.099*
Fluoxetine (10mg/kg)	69.00 \pm 16.29**
Values are expected as mean \pm SEM (no=6) ** $p < 0.01$ statistically significant as compared to control group. * $p < 0.05$ statistically significant as compared to control group	



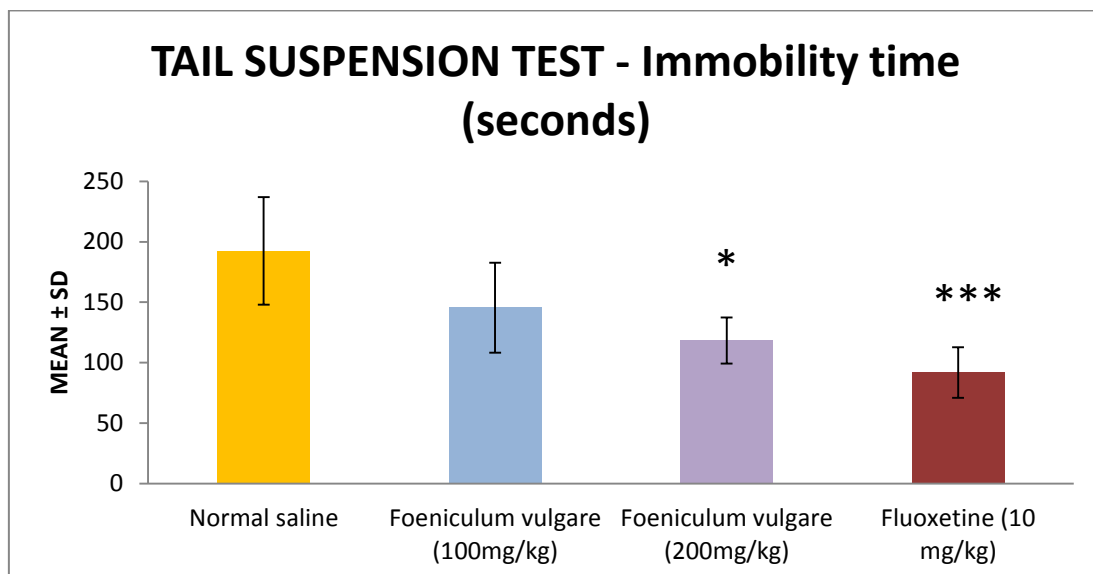
Tail suspension test

There was significant reduction in immobility time in *Foeniculum vulgare* group (200mg/kg) ($p < 0.05$) and Fluoxetine group (10mg/kg) ($p < 0.001$) when compared to control group.

Table 2: Effect of *Foeniculum vulgare* on immobility time using Tail suspension test

Groups	Immobility time(sec)
Control	192.50±44.581
<i>Foeniculum vulgare</i> (100mg/kg)	145.50±37.206
<i>Foeniculum vulgare</i> (200mg/kg)	118.33±18.949*
Fluoxetine (10mg/kg)	91.83 ±20.923 ***

Values are expressed as mean ± SEM (no=6) *** $p < 0.001$ statistically significant as compared to control group ** $p < 0.01$ statistically significant as compared to control group. * $p < 0.05$ statistically significant as compared to control group



DISCUSSION

In the present study antidepressant activity of *Foeniculum vulgare* has been studied. The ethanolic extract of *Foeniculum vulgare* (200mg/kg) shows significant antidepressant activity in both FST and TST. Both Forced swimming and Tail suspension test represents the behavioral despair model and they reproduce a state similar to human depression. These tests are quite sensitive and specific and the state of despair is reduced by several agents like tricyclics, 5HT-reuptake inhibitors, MAO inhibitors and atypical [15]. In the present study, *Foeniculum vulgare* (200mg/kg) produced significant antidepressant-like effect in rats in both FST and TST as compared to the control group, and finding indicated that fluoxetine possess stronger antidepressant activity than *Foeniculum vulgare* (200mg/kg). Recently, oxidative stress was linked with the pathophysiology of major depression, with significant correlations being found between the severity of depression and erythrocyte superoxide dismutase/lipoperoxidation levels [16-18]. Meanwhile, treatment with antidepressants reduces the oxidative stress related to depressive disorder. Additionally, some species such as *Bacopa monniera*, *Hibiscus tiliaceus*, and *Asparagus racemosus*, all of which are reported to have antidepressant properties, also possess antioxidant activity [19-22]. Several studies suggested that flavonoids exhibit antioxidant property which is evidenced experimentally by the increase of the plasma antioxidant status [23]. Natural products like St. John's wort and *Ginkgo biloba* contains Flavonoids and terpenoids which is responsible for its antidepressant action [24-25]. This evidence supports the antidepressant activity of *Foeniculum vulgare*. Fennel is a source of phytoestrogens. The estrogenic activity of *Foeniculum vulgare* which promote growth of breast tissue and reproductive organs in women and premature thelarche in girls [26]. The main constituent of the essential oils of fennel and anise, anethole, has been considered to be the active estrogenic agent [27]. Studies have proved that estrogens produce antidepressant-like actions by themselves and importantly facilitate the action of clinically used antidepressants [28-29]. According to the monoamine theory, monoamine oxidase inhibitors increase the nor adrenaline and 5-hydroxy tryptamine levels and used in depression. Herbal plants like *Rhodiola rosea* L increase the monoamine level by its monoamine oxidase –A inhibiting action found to be effective in depression [30]. Fennel contains psoralen which is a monoamine oxidase A inhibitor and it increase the monoamine level. So the antioxidant, monoamine oxidase inhibiting and estrogenic effect of the fennel seed may be responsible for its antidepressant effect.

CONCLUSION

So the study has proved that the ethanolic extract of *Foeniculum vulgare* has significant antidepressant like activity in albino rats. However further study is needed to find out the active principle which is responsible for its antidepressant like activity.

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