Section: Pharmacology

Original Research Article

EVALUATION OF ANTIDEPRESSANT ACTIVITY OF AQUEOUS EXTRACT OF TURNERA DIFFUSA IN ALBINO MICE

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ABSTRACT

Background: According to the WHO, 1 in 20 adults are affected by depression and mental health issues requiring treatment in nearly 15% of the adult population. Regular use of antidepressants may cause physical dependence, tolerance, deterioration of cognitive function. In the view of adverse effects of synthetic drugs, investigating plants, based on their use in traditional systems of medicine, is a sound, and cost-effective strategy to develop new drugs. The objective of study is to evaluate antidepressant activity of Turnera diffusa in albino mice and to compare its effect with the standard drug Amytriptiline. **Materials and Methods:** 60 albino mice (n=60) of either sex weighing 20-30g were divided into 10 groups of 6 mice each. Five groups each for forced swimming test and tail suspension test model. In forced swimming test model, the mice will be dropped individually in the glass cylinder for about 6 minutes. The last 4 minutes of the testing period is considered for taking the parameters, as the first 2 minutes are for habituation. The floating or immobility time is noted down i.e., floating in upright position except for the small movements to keep their heads above water.Each mouse was pretreated with drugs 30 minutes before in both models. Groups 1 to 5 were administered normal saline (control), Amitriptyline (20 mg/kg), Turnera diffusa (50mg/kg), Turnera diffusa (75mg/kg), Turnera diffusa (125mg/kg) respectively. In the Tail Suspension Test (TST) mice are suspended from a metal rod mounted 50cm above the surface by fastening the tail to the rod with the adhesive tape for 6minutes.The immobility time is noted down in the last 4 minutes. Groups 5 to 10 were administered normal saline (control), Amitriptyline (20 mg/kg),Turnera diffusa (50mg/kg), Turnera diffusa (75mg/kg), Turnera diffusa(125mg/kg) respectively. **Result:** The data were analysed separately using one way analysis of variance (ANOVA), using statistical software Graph Pad In Stat version 3.06. P values of < 0.05 were considered as statistically significant. Turnera diffusa exhibited significant antidepressant activity. At a dose of 50mg/kg, 75mg/kg antidepressant activity was significant and comparable with the standard Amitriptyline 20mg/kg ($p<0.01$). At a dose of 125mg/kg antidepressant activity was highly significant when compared to standard ($p<0.001$) **Conclusion:** The present study demonstrated antidepressant effect of Turnera diffusa. Further detailed studies are required to confirm its use in clinics.

INTRODUCTION

Depression is a leading cause of years lived with disability (YLDs) worldwide, contributing substantially to global burden of disease. Major depressive disorder (MDD) affects hundreds of millions of people at any given time. Global Burden of Disease (GBD) studies consistently rank depression among the top contributors to non-fatal disease burden across regions and ages. Incidence and Prevalence vary by region, age, gender and socioeconomic status.

Women have higher lifetime risk of depression than men, riskier in low- and middle-income countries (LMICs) where mental health care access is limited. [1,2]

A substantial treatment gap exists, many individuals with depression do not receive adequate care, due to stigma, lack of access, cost, and workforce shortages Depression is associated with increased risk of comorbidities (cardiovascular disease, diabetes), suicide, reduced work productivity, and higher healthcare utilization.[1]

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Depression & anxiety are "modernization borne diseases". pharmacotherapeutic approaches for management of these include TCAs, norepinephrine & SSRI, MAOIs, Atypical antidepressants.[2] Regular use of which may cause physical dependence, tolerance, deterioration of cognitive function.[3] In the view of adverse effects of synthetic drugs, investigating plants, based on their use in traditional systems of medicine, is a sound, and cost-effective strategy to develop new drugs.

"Food is Medicine" is one of the basic concepts of traditional Siddha Indian Medicine. Many Ayurvedic plants are known to have antidepressant and antianxiety properties. One of them is Turnera diffusa, commonly known as Damiana. It is a small shrub that grows 1-2 meters high and have nice aroma and serrated leaves. Yellow coloured small flowers bloom in summer. The medicinal part of the plant is its leaves, which are harvested during the flowering season. Turnera diffusa has a long history of traditional use as herbal medicine throughout the world. Its medicinal properties are: aphrodisiac, antidepressant, antianxiety, diuretic, analgesic, cough-suppressant and mild laxative. [4-6] The exact mechanism of action is not known.

Hence the present study was under taken to evaluate the antidepressant property of aqueous extract of Turnera diffusa which if proved, could be used in case of depression associated with anxiety.

Objectives

1. To evaluate antidepressant activity of Turnera diffusa in albino mice.
2. To compare its effect with the standard drug Amytriptiline.

MATERIALS AND METHODS

Materials Used

1. 10 groups of 6 mice in each group, weighing 20-30gm each.
2. Aqueous extract of Turnera diffusa in doses of 50 mg/kg, 75mg/kg, 125mg/kg.
3. Amitriptyline20mg/Kg body weight
4. Normal saline as control.
5. Animals: Albino mice of either sex weighing between 20-30gm were obtained from

Central Animal House, SSIMS & RC, Davangere, Karnataka. The animals were housed under standard conditions with free access to food and water and ab libitum. The study was approved from the Institutional Animal Ethics Committee, SSIMS & RC, Davangere.

Inclusion Criteria

Albino mice of either sex weighing between 20-30gm.

Healthy animals with normal activity.

Exclusion Criteria

Albino mice<20 gm or >30 gm.

Pregnant mice.

Animals previously used in other experiments.

Turnera diffusa was tested for antidepressant property in two in vivo models of experimentally induced depression using.

1. The Forced Swimming Test (FST), developed by Roger Porsolt (Porsolt et al, 1977) [8, 9, and 11]. is used. End point: The immobility time in the last 4 minutes
2. The Tail Suspension Test (TST) developed by Steru (Steru et al 1980) [8, 10, and 11]is used. End point: The immobility time in the last 4 minutes

A total of 60(n=60) animals will be divided into 10 groups of 6 each. Among which, 5 groups will be subjected to forced swimming test and 5 groups to tail suspension test.

Forced swimming test:

Group 1(Control): Normal saline 1ml

Group 2(Standard): Amitriptyline20mg/Kg body weight

Group 3: Turnera diffusa 50mg /Kg body weight

Group 4: Turnera diffusa 75 mg /Kg body weight

Group 5: Turnera diffusa 125 mg/Kg body weight

The mice were marked for identification as per groups and were placed in separate labelled cages accordingly. One day prior to test, mice will be dropped into glass cylinder (height 25cm, diameter 10cm, containing water level of 10cm, maintained at 23- 25 degree Celsius) for about 15 minutes and then taken out for towel drying. This is done for adaptation of animals.

On the next day, the mice will be dropped individually in the glass cylinder for about 6 minutes. The last 4 minutes of the testing period is considered for taking the parameters, as the first 2 minutes are for habituation. The animals receive the test drug/standard drug/control per orally 30 min before the test. The floating or immobility time is noted down i.e., floating in upright position except for the small movements to keep their heads above water.

Tail Suspension Test (TST)

Group 1(control): Normal saline 1ml.

Group 2(standard): Amitriptyline20mg/Kg body weight.

Group 3: Turnera diffusa (50mg/kg).

Group 4: Turnera diffusa (75mg/kg).

Group 5: Turnera diffusa (125mg/kg).

After 30 minutes of per oral administration of test drug/standard drug/control, mice are suspended from a metal rod mounted 50cm above the surface by fastening the tail to the rod with the adhesive tape for 6minutes.

The measuring principle is based on the energy developed by a mouse trying to escape from its suspension. The immobility time is noted down in the last 4 minutes. Immobility here refers to the absence of any body or limb movements except for those caused by respiration

Parameters noted:

a) **Forced Swimming Test:** The duration of active behavior (climbing and swimming) and the period of immobility are noted. Decrease in the period of immobility after the drug administration

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is taken as the evidence of its antidepressant activity

b) **Tail Suspension Test:** The duration of immobility is noted. Decrease in the period of immobility after the drug administration is taken as the evidence of its antidepressant activity.

Statistical Analysis: Descriptive data that include mean, standard deviation and range value were found for each group and used for analysis. One way analysis of variance (ANOVA) was used for simultaneous multiple group comparison followed by statistical software Graph Pad In Stat version 3.06. Significance is established for a probability value (p value) of less than 0.05 and is considered highly significant when $p < 0.001$.

RESULTS

Immobility time in forced swim test [Table 1 and Figure 1]

The immobility time is decreased in the standard group (amytriptilline) when compared to control group and is statistically significant (p value < 0.01). At a dose of 50mg/kg, 75mg/kg antidepressant activity was significant and comparable with the standard Amitriptyline 20mg/kg. ($p<0.01$). At a dose of 125mg/kg antidepressant activity was highly significant when compared to standard. ($p<0.001$)

Immobility time in tail suspension time [Table 2, Figure 5]

There is a decrease in mean duration of immobility in standard group (amytriptyline), Test 1 (Turnera diffusa 50 mg/kg), Test 2 (Turnera diffusa 75mg/kg), Test 3(Turnera diffusa 125 mg/kg) in comparison to that of control group and is statistically highly significant $p<0.001$).

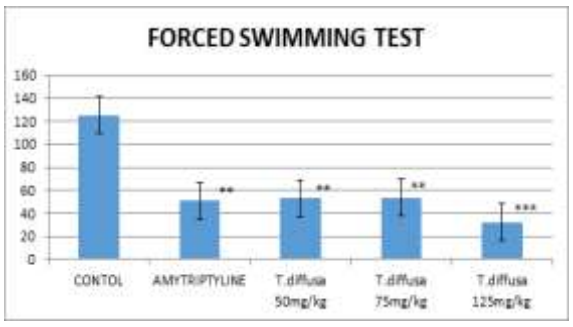

Figure 1: Mean immobility time in forced swim test.

Figure 2: mouse swimming in glass cylinder

Figure 3: towel drying

Figure 4: warming

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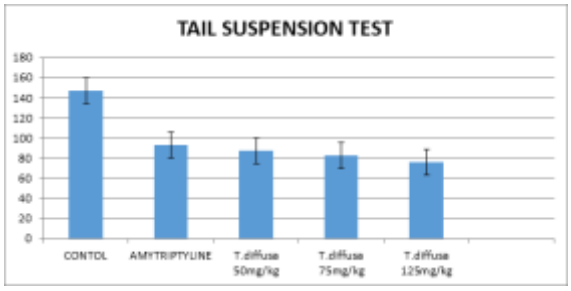

Figure 5: Comparison of mean Immobility time in tail suspension time.

Figure 6: tail suspension test.

Table 1: comparison of immobility time in forced swim test

FST	Control	Amytript-Yline	T. diffusa (50mg/kg)	T. diffusa (75mg/kg)	T. diffusa (125mg/kg)
MEAN	125.3	50.6	53.16	53.8	32.16
SD	33.1	41.0	33.0	36.6	19.96
SEM	13.5	16.7	13.5	14.9	8.1
pVALUE		<0.01(**)	<0.01(**)	<0.01(**)	<0.001(***)

Table 2: Comparison of immobility time in tail suspension time

TST	CONTROL	AMYTRIPT-YLINE	T. diffusa (50mg/kg)	T. diffusa (75mg/kg)	T. diffusa (125mg/kg)
MEAN	146.6667	93.33333	87.5	82.5	76
SD	16.66933	24.25421	21.10579	25.24876	9.703951
SEM	6.8	9.9	7.3	10.3	3.96
pVALUE		<0.001(***)	<0.001(***)	<0.001(***)	<0.001(***)

DISCUSSION

Turnera diffusa's chemical composition is complex. The main constituents include aluminoids, alpha-copaene, alpha-pinene, arbutin, barterin, beta-sitoserol, cymene, cymol, luteolin, tannins, thymol, triacontane, trimethoxyflavones, tetraphyllin B (cyanoglycoside), gonzalitosin I (flavonoid), damianin, tricosan-2-one, hexacosanol (hydrocarbons) a volatile oil containing α-pinene, β-pinene, p-cymene and 1,8-cineole and β-sitosterol (phytosterol).[4,7]

Damiana is known to produce central nervous system depressant activity. [5,6]

Despite their being a number of models that could potentially be used to screen for antidepressant activity, the conventional methods namely the FST and TST models remain the mainstay of antidepressant drug screening protocol.[8] FST model is the most validated experimental method for evaluation of antidepressant drug. Aqueous extract of Turnera difussa at the dose of 50, 75, 125mg/kg showed significant antidepressant effect in both FST and TST induced depression and the results were comparable with and even better than (at dose 125mg/kg in FST) the standard drug Amytriptiline.[9,10]

The exact mechanism of its CNS depressant action is not known. Many chemical constituents may be attributed for its antidepressant and others actions on CNS. However, our results are preliminary and further extensive studies of each chemical constituent are warranted to extrapolate animal data to human use.[11-13]

CONCLUSION

Aqueous extract of Turnera difussa has shown in vivo antidepressant activity in both FST and TST models and may be useful in the treatment of depression. At a dose of 50mg/kg, 75mg/kg antidepressant activity was significant and comparable with the standard Amitriptyline 20mg/kg. ($p<0.01$). At a dose of 125mg/kg antidepressant activity was highly significant when compared to standard. ($p<0.001$).

The present study showed that Turnera diffusa has significant antidepressant activity. It may be used as an alternative or add on therapy for depression. Further detailed studies with larger sample size and clinical trials are required to establish the therapeutic potential.

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