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Anti-Depressant Activity of Ethanolic Extract of Ghompherna Globosa in Swiss Albino Mice

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Abstract: ***The antidepressant activity of Ethanolic extract of Gomphrena globosa (EEGG) in Swiss albino mice. Ethanolic extract of Gomphrena globosa (EEGG) Leaves was prepared by a continuous method using Soxhelt apparatures. The phytochemical screening followed by acute oral toxicity studies in mice. EEGG in doses of 100 and250 mg/kg body weight was administered to test groups 1 and 2 respectively. Imipramine hydrochloride 10 mg /kg body weight was administered to Standard group by oral route. The group second group received 100mg/kg, (p.o) of EEGG + 10 mg/kg (p.o) of Imipramine. Control group received normal saline 10mg/kg body weight. Anti depressant activity was identified by using modified forced swimming test (FSH) and Tail suspension test (TST). Period of immobility was observed in both the models which was indicative of anti depressant activity. Standard statistical methods were used to evaluate the results. The results showed significant dose dependent antidepressant effect of EEGG in swiss albino mice for both the models in all the test groups (Test group I, II, III, & IV). EEGG possess significant antidepressant activity. However, further investigations are required to determine its active constituents and molecular level of target mechanism of the extract for further use in humans.***

Keywords: Antidepressant, imipramine, Gomphrenaglobose, Forced swimming test, Tail suspension test

1. Introduction

Depression is a type of serious neurological disorder, characterized by disturbances in sleep and appetite as well as deficit in cognition and energy. It is mental illness that significantly affects a person's thought, hopelessness, increased irritability, anger, feeling guilt, sadness & worthlessness. Depression afflicts about 10 - 25 % of women and 5 - 12 % of men and considered as the most common mood disorder that manifests as a single or recurrent episode and is always associated with significant socioeconomic problems, morbidity and mortality. [1]

Various treatment options for depression are available including Psychotherapies, Electroconvulsive Therapy (ECT), Light Therapy, monoamine oxidase inhibitors, selective serotonin reuptake inhibitors. More over these drugs have unusual side effects like - MAOIs - Insomnia, hypotension, weight gain, hypertensive crisis. TCAs -anti-cholingeric side effects (dry mouth, tachycardiac, constipation, urinary retention and blurred vision), tremor, SSRIs-headache, nausea, other gastro Intestinal effects, sexual dysfunction.[2]

Gomphrena globose, commonly known as globe amaranth, Makhmali, and Vadamali, is an edible plant from the family Amaranthaceae. The round -shaped flower inflorescences are a visually dominant feature and cultivars have been propagated to exhibit shades of magenta, purple, red, orange, pink, and lilac within the flowerheads, the true flower are small and inconspicuous. The plant fixes C_4 pathway. At, maturity, the flower heads are approximately 4 cm long and the plant grow up to 24 inches in height.[3]

It consist of kaempferol 3-O—rutinoside based on chromatographic and mass spectrometry techniques. Other flavonoids include quercetin, kaempferol, and isorhamnetin derivatives. Which is consisting of pharmacological activities like Antibacterial, anti fungal, anti-oxidant, detoxifying and used in treatment of high blood pressure& diabetes. Therefore, the present investigations was carried out to evaluate the anti- depressant activity of ethanolic extract of leaves of Gomphrena globose by stress induced depression by forced Swim test model and tail suspension test model in Swiss albino mice.[4]

2. Materials & Methods

Animals: Swiss albino mice (20-25 g) of either sex were used in this study. They were produced from Mahaveer Enterprise, Hyderabad. The animals were acclimatized for one week under laboratory conditions. They were housed in polypropylene cages and maintained constant temperature at 27+-2 ^{0}C under 12 hrs. dark /light cycle.They were fed with standard rat pellet feed and water and libitum. The husk in the cages was renewed every day to ensure hygeinity and maximum comfort for animals.[5]

Grouping:
Animals were randomly divided into 4 groups of 6 each and received drugs as follow:

Group I: Control group is treated with drug normal saline (10ml/kg)
Group II: Standard group treated with drug impramine (20mg/kg)
Group III: Test group-I-EEGG (100mg/kg p.o)
Group IV: Test group-2-EEGG (250 mg/kg p.o)

Chemicals: Ethanol, Normal saline, imipramine (sun pharmaceuticals) [6]

Plant Materials and Preparation of Drug Solution

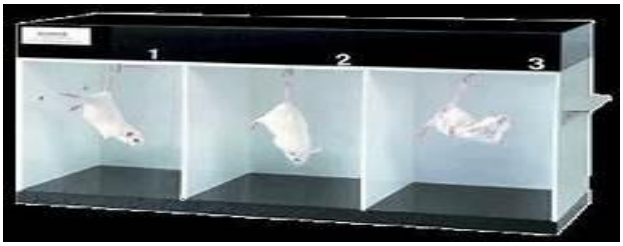
Gomphrena globosa flowers (1.5 kg) were prepared locally from a botanist in Tirupati and Authenticated by Dr. K. Madhava Chetty Msc, M.Ed., M.Phill., ph.D, PG DPD Plant Taxonomist (IAAT : 357) Assistant Professor in the department of botany Sri Venkateswara University with the accession no.1723 and the specimen was deposited in the Herbarium, Dept. of Botany, Sri Venkateswara University. The Gomphrena globose flowers are shade dried and powered.The dried powder material (100 mg/kg) of the Gomphrena globose flowers was powdered and passed through sieve no.16. This powder material was extract with ethanol and by using soxhalate apparatus for 48 hrs. The extract was collected and subjected to distillation to remove alcohol. [7] The extract was heated up to 45C in hot air oven till it become solid or semisolid, now collect the extract and store it in a air tight container. The concentrated ethanolic extract of Gomphrena globosa flowers (EEGGF) was used to evaluate the antidepressant activity. Stock solution was prepared by using solvent as Normal saline before dosing from which the different doses were administered by selecting the appropriate concentration. Before starting the actual experiment phytochemicals screening of the ethanolic extract and acute oral toxicity study was carried out.[8]

Forced Swimming Test

The mice of 20-25gm were used. They were individually forced to swim in an open cylindrical container (diameter 11cm, height 15cm), containing 6cm of water at 27+2 ^{0}C.All the mice were divided into different groups. The first group (depressed animals) Assigned as control received only vehicle (0.9 % Normal saline -10 ml/kg, i.p).The second group received standard drug imipramine (10 mg / kg, p.o), the other two group received acute dose of the test drugs (EEGG-100 and 250mg/kg). The total duration of immobile was recorded during the last 4 min of the 6 min period. Each mice was judged to be immobile when it ceased struggling and remained floating motionless in the water, making only those movements necessary to keep its head above water. A decrease in the duration of immobility is indicative off an antidepressant effect.[9]

Tail Suspension Test

Mice weighing 20-25 g were used. Animals were transported from the housing room to the testing area in their own cages and allowed to adapt to the new environment for 1 h before testing. All the mice divided into different groups, each group consisting of 6 animals. The first group received only vehicle (control), the second group received standard drug imipramine (20mg/kg, p.o) and other two group received test drug (EEGG-100 and 250 mg/kg) before 30 min prior to testing. For the test the mice were suspended on the tip of the tail. The duration of immobility was recorded for periods of 5 min. Mice were considered immobile when they hang passively and completely motionless for a at least 1 min.[10]



Learned Helplessness Test

Learned helplessness was produced in mice (25g) by exposure to electric shock (0.The plat.7mA) for 1 h on a schedule of 10s of shock/min. The apparatus is a 30*45*30 cm box with a grid floor. At a height of 20 cm above the floor, a platform (7.5 * 7.5 cm) cm can be inserted through one side wall to allow a jump -up-escape response. The platform is not available during training. After the appropriate treatment, the animals were tested for acquisition of a jump up escape in the same apparatus. [11] At the beginning of a trial, the platform is pushed into box and a 0.4 mA shock initiated. Shock is terminated in 10 s if the animals have not escaped onto the platform by this time. If an escape response occurred, the animal was allowed to remain on the platform for the duration of 10 s, and then returned to the grid floor. Ten such trails with an intertribal interval of 20 s are given. In a naive control group of rates, this training resulted in 80 % acquiring learned helplessness behavior.[12]

3. Results

Preliminary Phytochemical Studies

The preliminary phytochemical of ethanolic extract of flowers of Gomphrena globose revealed the presence of Proteins, Tannins, Phenols, Alkaloids, Steroids, Saponins as represented in table.[13] Table no: 1:1 -The phytochemical profile of the flower extract

Phytochemicals	*Presence/Absence*
Proteins	+
Tannins	+
Phenols	+
Flavanoid	-
Alkaloids	+
Steroids	+
Saponins	+
Quinones	-
Terpenoid	-
Cardiac glycosides	-

Present: (+), Absent : (-) Absent, Flower: Gomphrena globosa

Table 1.2: Acute Toxicity Studies

Group (no =10)	Treatment (mg/kg)	No of animals dead	No of animals alive	Behavioral changes with in 48 h
1	100	0	10	None
2	300	0	10	None
3	500	0	10	None
4	1000	0	10	None
5	1500	0	10	Observed
6	2000	2	8	Observed

Phytochemical screening tests for the detection of various active constituents. The extract showed the presence of alkaloids, tannins, steroids, phenolics and flavonoids, carbohydrates and glycosides in crude extract of Gomphrena globosa flowers as depicted in table no 1.1[14]

Acute Oral Toxicity Study

The procedure was followed as per OECD 423 guidelines. Different doses of EEGG were orally administered (100 - 2000 mg/kg), while the control group received only the vehicle.The groups were observed for 48 hrs and at the end of the period mortality was recorded for each group. The EEGG up to 2000mg/kg and 1500mg/kg body weight, there were signs of toxicity like abdominal contractions observed. So, the doses selected for the antidepressant activity were 100 and 250 mg/kg.[15]

Table 1.3: Effect of EEGG on FST induced duration of immobility in rats

Groups	Treatment	Duration of immobility (sec) MEAN + SEM
G-1-Control	Normal saline (10mg/kg, i.p)	200.5+4.79
G-II-Std	Imipramine 10 mg/kg (p.o)	122.0+4.31
G-III-I stdose	EEGG 100mg/kg (p.o)	134.7+5.23
G-IV-IInddose	EEGG 250mg/kg (p.o)	102.67+4.96

Valves are expressed as mean + S.E.M for n=6 animals in each group. Data analysis was performed using one way ANOVA followed by Tukey"s Multiple Comparison Test.P<0.001 vs control (Depressed animals).[16]

The administered with imipramine -10mg/kg showed the decreased duration of immobility. Thus showing the significant (p<0.001) difference as compared to control. There was a significant (p<0.001) dose dependent decrease in duration of immobility in animals treated with 100 and 250 mg/kg doses of EEGG. [17]

Table 1.4: Effect of EEGG on TST induced duration of immobility in Mice

Group	*Treatment*	*Immobility*
G-1-Control	Normal saline (10mg/kg, i.p)	171+5.65
G-II-Std	Imipramine 10 mg/kg (p.o)	106+3.60
G-III-I stdose	EEGG 100mg/kg (p.o)	124+4.37
G-IV-IInddose	EEGG 250mg/kg (p.o)	80.8+5.32

Valves are expressed as mean +S.E.M for n=6 mice in each group. Data analysis was performed using one way ANOVA followed by Tukeys Multiple comparison test. A significant (***p<0.001vs control) decrease in the duration of immobility was seen with the standard drug imipramine and EEGG in all tested doses as compared to the control (group - 1).[18]

Table 1.5: Effect of EEGG on Learned helplessness model induced duration of immobility in Mice

Group	Treatment	Escape failure(N)during 10 trails (MEAN +SEM)	Avg.time to climb the pole (10 sec) MEAN +SEM
G-1-Control	Normal saline (10mg/kg, i.p)	9.66+0.21	9.33+0.33
G-II-Std	Imipramine 10 mg/kg (p.o)	6.66+0.42***	6.0+0.51***
G-III-I stdose	EEGG 100mg/kg (p.o)	7.33+0.55**	6.66+0.33***
G-IV-IInddose	EEGG 250mg/kg (p.o)	5.20+0.30***	5.0+0.22***

Data indicated as mean +SEM valves, n=6. Data were analyzed by the one way ANOVA followed by Tukey, doses Multiple comparison test. P<0.01, ***p<0.001-campared with control.[19]

A significantly decreased escape failure after pretreatment with EEGG (100 and 250 mg/kg) and also decreased time to climb the pole during 10 sec. in contrast to control rats with prior experiences of inescapable shocks, which exhibited marked increase in escape failure. Imipramine also showed a similar activity.[20]

4. Conclusion

The present study has proved that the ethanolic extract of Gomphrena globose possess significant antidepressant activity due to its reduction in the immobility period in FST, TST, reduces the number of escape failure in learned helplessness. Among the (100 and 250 mg/kg) doses of EEGG, the doses 250 mg/kg of body weight. It was concluded that the 100mg/kg body weight. It was concluded that the that presence might be the reason for its more antidepressant activity.[21]

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