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EVALUATION OF ANTI-DEPRESSANT ACTIVITY OF LEAF EXTRACT OF TERMINALIA CATAPPA IN EXPERIMENTAL ANIMALS

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ABSTRACT

Aim: The main aim of the study is to evaluate the antidepressant activity of Terminalia catappa using different animal models in mice. **Methods**: The leaves of Terminalia catappa were collected and shade dried at room temperature and grinded coarsely before extraction. The leaves were extracted by hot maceration by using distil water. The resulting extract was collected in to air tight container. Thus, the prepared extract was used for further pharmacological evaluation. All the animals were fed with pellets standard diet and water was supplied ad libitum under strict hygienic conditions. All the experimental protocols were approved by Institutional Animal Ethical Committee (IAEC).All the animal studies were performed as per rules and regulations in accordance to guideline of CPCSEA registration. All the animals were fasted 3hrs & 1 hr according to experiment done prior to oral administration of vehicle/standard/test compounds. All experiments were carried out during the light period (9:00 to 17:00 h) to avoid circadian rhythm. **Results**: Results indicated that the organization of the AETC delivered a decrease of term of idleness time of mice presented to the both FST and TST. What's more, in the present investigation, the AETC (500mg/kg, po) directed to mice delivered note worthy. Anti depressant effect in both FST & TST and their efficacies were found to be comparable to Fluoxetine (25mg/kg, po). **Conclusion:** Anti depressant activity of aqueous extract of Terminalia catappa was found to be significant at high dose (500mg/kg, po). The flavanoids and tannins present in AETC may be facilitating monoaminergic transmission there by producing antidepressant effects.

KEYWORDS: Antidepressant effects; Depression; Terminalia catappa; Phytochemical analysis.

INTRODUCTION

Depression is a mental disorder characterized by a pessimistic sense of inadequacy and a despondent lack of activity with sad feelings of gloom, inadequacy and is present with depressive mood, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, low energy, and poor concentration.[1] It is mainly caused by decreased brain levels of monoamines like nor adrenaline, dopamine and serotonin. Depression affects about up to 20% of the population across the globe. At present 121 million people are estimated to suffer from depression. It is about twice as common in women as in men. An estimated 5.8% of men and 9.5% of women experience a depressive episode in their lifetime.[2]

Although a number of synthetic drugs are being used as standard treatment for clinically depressed patients, they have adverse effects that can compromise the therapeutic treatment. Thus, it is worthwhile to look for antidepressants from plants with proven advantage and favorable benefit-to- risk ratio. A number of medicinal plants and medicines derived from these plants have shown antidepressant properties by virtue of their medicinal constituents. The present study is focused on the medicinal plants and plant-based formulations having antidepressant activity in animal studies and in humans.[3]

The plant Terminalia catappa belongs to the family Combretaceae. The tree grows to 35 m (115 ft) tall, with an upright, symmetrical crown and horizontal branches. Terminalia catappa has corky, light fruit that are dispersed by water. The seed within the fruit is edible when fully ripe, tasting almost like almond. As the tree gets older, its crown becomes more flattened to form a spreading, vase shape. Its branches are distinctively arranged in tiers. The leaves are large, 15–25 cm (5.9–

9.8 in) long and 10– 14 cm (3.9–5.5 in) broad, ovoid, glossy dark green and leathery. They are dry- season deciduous; before falling, they turn pinkish-reddish or yellow-brown, due to pigments such as violaxanthin, lutein, andzeaxanthin. The trees are monoecious, with distinct male and female flowers on the same tree. Both are 1 cm (0.39 in) in diameter, white to greenish, inconspicuous with no petals; they are produced on axillary or terminal spikes. The fruit is a drupe 5–7 cm (2.0–2.8 in) long and 3–5.5 cm (1.2–2.2 in) broad, green at first, then yellow and finally red when ripe, containing a single seed. There are no significant work has been carried out on the antidepressant effect of this plant extract. Hence, the present study is designed to evaluate the antidepressant activity of Terminalia catappa using different animal models in mice.

MATERIAL AND METHODS

The leaves of Terminalia catappa were collected and shade dried at room temperature and grinded coarsely before extraction. The leaves were extracted by hot maceration by using distil water. The resulting extract was collected in to air tight container. Thus, the prepared extract was used for further pharmacological evaluation.

Materials

- Aqueous extract of the Terminalia catappa leaves
- Fluoxetine (Fludac, Cadila)

Preliminary Phytochemical analysis

Aqueous extract of Terminalia catappa leaves was subjected to preliminary phytochemical analysis to test for presence of various Phytoconstituents by the following methods.[50-52]

1) Test for Alkaloids

To the extract dilute hydrochloric acid was added and filtered. The filtrate was treated with various reagents.

a) Mayer's test

The filtrate was treated with Mayer's reagent. Appearance of cream color indicates the presence of alkaloids.

b) Dragendorff's-test

The filtrate was treated with Dragendorff's reagent. Appearance of reddish brown precipitate indicates the presence of alkaloid.

c) Hager's-test

The filtrate when treated with Hager's reagent, appearance of yellow color precipitate indicates the presence of alkaloid.

2) Test for Carbohydrate and Reducing sugar

Small quantity of the filtrate was dissolved in 4ml of distilled water and filtered. The filtrate was subjected to the following test.

a) Molisch's-test

A small portion of the filtrate was treated with Molisch's reagent and Sulphuric acid. Formation of a violet ring indicates the presence of carbohydrate.

b) Fehling's-test

The extract was treated with Fehling's reagent A and B. The appearance of reddish brown precipitate indicates the presence of reducing sugar.

c) Benedict's-test

The extract was treated with Benedict's reagent. The appearance of reddish orange precipitate indicates the presence of reducing sugar.

d) Barfoed's-test

The extracts was treated with Barfoed's reagent and heated. The appearance of reddish orange precipitate indicates the presence of non-reducing sugar.

3) Test for Steroids

a) Libermann burchard test

The extract was treated with 3ml of acetic anhydride, few drops of Glacial acetic acid followed by a drop of conc. Sulphuric acid. Appearance of bluish green color indicates the presence of steroids.

4) Test for Proteins

a) Biuret'stest

The extract was treated with copper sulphate solution, followed by addition of Sodium hydroxide solution. Appearance of violet color indicates the presence of proteins.

b) Millon's test

The extract was treated with Millon's reagent. Appearance of pink color indicates the presence of proteins.

5) Test for Tannins

The extract was treated with 10% Lead acetate solution; appearance of white precipitate indicates the presence of Tannins.

6) Test for Flavonoids

a) 5ml of extract was hydrolyzed with 10% sulphuric acid and cooled. Then, it was extracted with diethyl ether and divided into three portions in three separate test tubes. 1ml of diluted sodium carbonate, 1ml of 0.1N sodium hydroxide, and 1ml of strong ammonia solution was added to the first, second and third test tubes respectively. In each test tube, development of yellow color demonstrated the presence of flavonoids.

b) Shinoda's test

The extract was dissolved in alcohol, to which few magnesium turnings was added followed by conc. HCl drop wise and heated, the appearance of presence of flavonoids.

7) Test for flavanone

To the extract 10% sodium hydroxide was added; appearance of yellow color shows the presence of flavanone.

8) Test for glycosides

The extract was treated with glacial acetic acid and few drops of ferric chloride solution. Followed by the addition of conc. Sulphuric acid, formation of ring at the junction of two liquids indicates the presence of glycosides.

9) Test for saponins

Foam test: - About 1ml of the extract was diluted to 20ml of distilled water and shaken well in a test tube. There is no reaction seen this indicates the absence of Saponins.

10) Test for Test for Triterpenoids

The substance was warmed with Thionyl chloride. Pink color indicates the presence of Triterpenoids.

Animals

Albino mice of either sex weighing between 18-25 gm were used in this study. All the animals were procured from Sainath Agency, bapuji nagar musheerabad hyd-48 for experimental purpose. After procuring, the animals were acclimatized for 7 days in quarantine room and housed in groups of six under standard husbandry conditions like room temperature (23±2°C), relative humidity (30- 70%) and 12/12 h light/dark cycle. All the animals were fed with pellets standard diet and water was supplied ad libitum under strict hygienic conditions. All the experimental protocols were approved by Institutional Animal Ethical Committee (IAEC). All the animal studies were performed as per rules and regulations in accordance to guideline of CPCSEA registration.

All the animals were fasted 3hrs & 1 hr according to experiment done prior to oral administration of vehicle/standard/test compounds. All experiments were carried out during the light period (9:00 to 17:00 h) to avoid circadian rhythm.

Pharmacological study

A. Acute Oral Toxicity study
B. Models for antidepressant activity

A. Acute Oral Toxicity study (dose fixation)

Dose fixation was done by referring previous paper of terminalia catappa article on anti ulcer activity of ethonolic extract of terminalia catappa leaves against gastric ulcers by pyloric ligation induced model in rats.

Invivo Pharmacological Models in Mice

a) Behavioral tests

1. Forced Swim Test[4-7]

Animals were divided into 4 groups of 6 animals in each, weighing between 18-25gms

Group I – Control (1% CMC 10ml/kg, p.o) Group II – Standard (Fluoxetine 25mg/kg p.o) Group III –Low dose (AETC 250 mg/kg, p.o) Group IV – High dose (AETC 500 mg/kg, p.o)

Experiment was carried out in narrow glass cylinder (13 cm in diameter × 24 cm high) containing water (25°C) to a depth of 10 cm, from which they cannot escape. All the animals were fasted for 3hrs prior to the oral administration of vehicle/standard/test compounds. Thirty minutes later, the animals were subjected to swim for 6 minutes; the first two minutes the animal is allowed to adjust to the new conditions; the next four minutes the immobility time was measured with a stopwatch at 30, 60,120 and 240 minutes after oral administration. Immobility time was the time during which the animals will be necessary to keep afloat.

Figure 1: Forced Swim Test Apparatus.

2. Tail Suspension Test[8-9]

Animals were divided into 4 groups of 6 animals in each weighing between 18-25gms.

Group I – Control (1% CMC 10ml/kg, p.o) Group II – Standard (Fluoxetine 25mg/kg p.o) Group III – Low dose (AETC 250 mg/kg, p.o) Group IV – High dose (AETC 500 mg/kg, p.o)

The control, test and standard compounds were administered p.o., 60 minutes prior to testing. The mice were suspended on the edge of a shelf 58cm above the table top by adhesive tape placed approx. 1cm from the tip of tail. The duration of immobility was recorded for the period of 6minutes by usingstopwatch. After the initial period of vigorous motor activity, the mice became still. Mice were considered immobile when they hanged passively and completely motionless. The duration of immobility time was recorded before the treatment and 60 minutes after the treatment.

Figure 2: Tail Suspension Test Apparatus.

RESULTS

Acute Oral Toxicity study

Dose fixation was done by referring previous paper of terminalia catappa article on anti ulcer activity of ethonolic extract of terminalia catappa leaves against gastric ulcers by pyloric ligation induced model in rats.

Forced Swim Test

The result of the effect of aqueous extract of Terminalia catappa on the duration of immobility is shown in table 02 & fig no. 12. The animals treated with 500mg/kg, p.o of AETC and Fluoxetine 25mg/kg, p.o showed significant decrease in immobility time but not 250mg/kg, p.o of AETC when compared with control.

Table 1: Effect of AETC on immobility time in Forced swim test in mice.

S.NO	TREATMEN T	30MIN	60MIN	120MIN
1.	CONTROL	216	192	189
2.	FLUOXETIN E (25mg/kg)	83	68	64
3.	AETC (250mg/kg)	210	190	205
4.	AETC (500mg/kg)	125	96	110

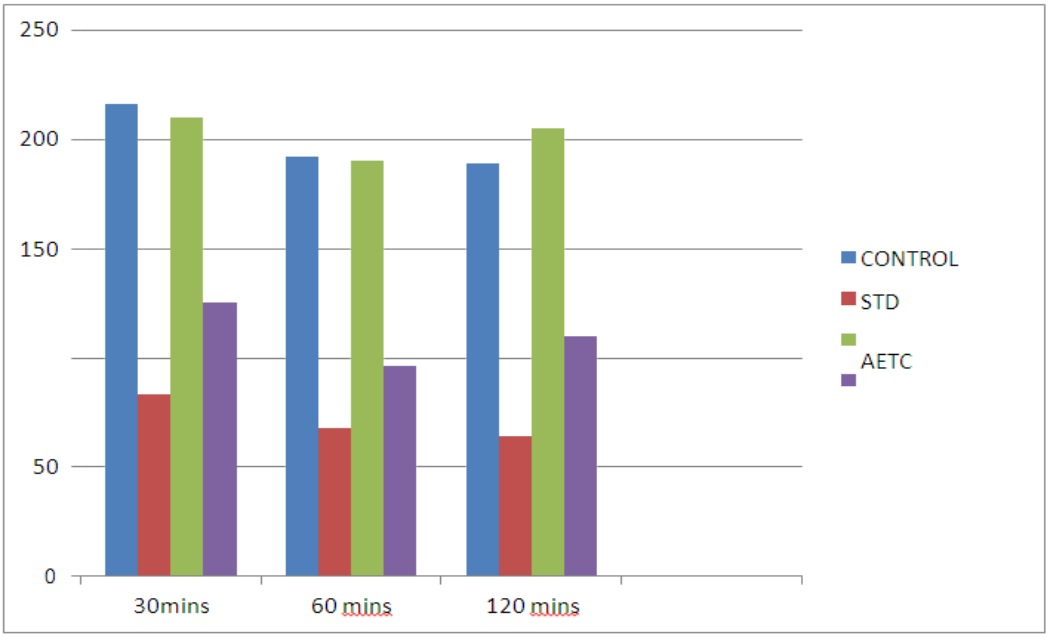

Figure 3: Histograms of AETC on immobility time in Forced swim test in mice.

Tail suspension test

The results were presented in table 03 & fig no 13, revealed that the immobility time was significantly decreased in animals treated with 500 mg/kg, p.o of AETC and Fluoxetine 25mg/kg, p.o but not 250 mg/kg, p.o of AETC when compared with control.

Table 2: Effect of AETC on immobility time in Tail suspension test in mice.

S.NO	TREATMENT GROUPS	POST TREATMENT MEAN±SEM
1	CONTROL	265
2	FLUOXETINE(25mg/kg)	152
3	AETC(250mg/kg)	257
4	AETC (500mg/kg)	180

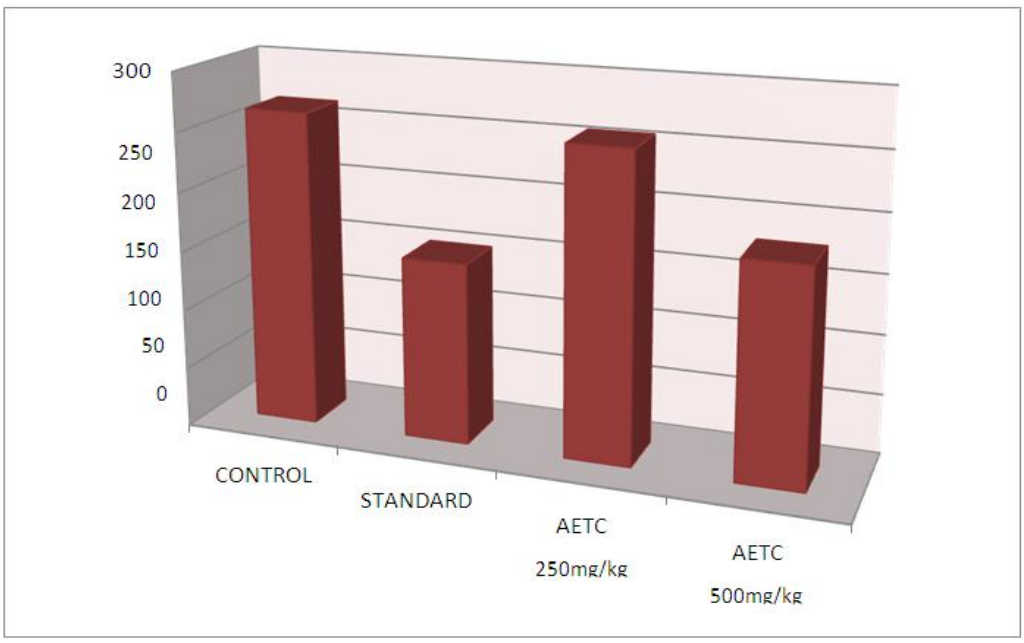

Figure 4: Histograms of duration of immobility in Tail suspension test.

DISCUSSION

Cutting edge way of life prompts various stress conditions, among which sadness is a generally predominant decrepit neurological scatter. It is fundamentally brought about by diminished mind levels of monoamines like Noradrenaline, Dopamine and

Serotonin. Sorrow is a psychological issue related with parcel of dismalness because of its high rate in the network. Thus it is important to search for Antidepressants with demonstrated preferred position and great advantage to- chance proportion. Albeit various manufactured medications are being utilized as standard treatment for clinically discouraged patients, they have unfriendly impacts that can bargain the remedial treatment. Hence, there is a huge prerequisite for elective solutions for discouragement. The present work was exposed to examination for the assessment of the Energizer movement of watery concentrate of Terminalia catappa leaves in animal models.[10]

Dose fixation was done by referring previous paper of terminalia catappa article on anti ulcer activity of ethonolic extract of terminalia catappa leaves against gastric ulcers by pyloric ligation induced model in rats. For the purpose of investigation of Anti depressant activity, two animal models viz., the Constrained swim test and Tail suspension test were utilized. These tests were very touchy and moderately explicit to every single significant class of Antidepressants. The idleness showed by rodents when exposed to unavoidable pressure, for example, FST and TST are thought to mirror a condition of misery or brought down temperament, which are thought to reflect burdensome issue. Likewise, fixed status time has been demonstrated to be diminished by treatment with Stimulant medications.[11,12]

Results indicated that the organization of the AETC delivered a decrease of term of idleness time of mice presented to the both FST and TST. What's more, in the present investigation, the AETC (500mg/kg, po) directed to mice deliverednoteworthy Anti depressant effect in both FST & TST and their efficacies were found to be comparable to Fluoxetine (25mg/kg, po). From all the above, the Anti depressant activity of aqueous extract of Terminalia catappa was found to be significant at high dose (500mg/kg, po). The flavanoids and tannins present in AETC may be facilitating monoaminergic transmission there by producing antidepressant effects.[13] However, further research is required to establish the exact underlying mechanism and also to assess potential of developing AETC as an antidepressant drug in clinical practice for thefuture.

CONCLUSION

The AETC contained alkaloids, flavanoids, glycosides, saponins, tannins. The findings of the present investigation suggests that the Anti depressant activity of AETC was significant at high dose (500mg/kg, p.o) in Forced swim test, Tail suspension test is may be showing the Anti depressant activity by acting through Adrenergic system. However, more extensive Pharmacological studies of this plant are required for complete understanding of the Anti depressant activity of aqueous extract of Terminalia catappa.

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