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EVALUATION OF ANTIDEPRESSANT ACTIVITY OF LEAF EXTRACT OF TERMINELIA CATAPPA IN EXPERIMENTAL ANIMALS

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ABSTRACT
Objective: *Terminalia catappa* (combretaceae) is a traditional medicinal plant known as *almond tree.* This plant has been used for the treatment of a variety of diseases. The leaves of *Terminalia catappa* showed anti microbial, anti sickiling, anti ulcer activities. **Methods**: This study was undertaken to evaluate the possible antidepressant effect of *Terminalia catappa* leaf extract (AETC) using Tail suspension test(TST) & Forced swim test (FST). 24 albino mice of either sex weighing between 18-25gm were randomly selected and divided into 4 equal groups. Group-I (control) received 1%CMC (10ml/1000gm), Group-II, standard(25mg/kg fluoxetine) III & IV received AETC in doses of 250,500 mg/kg orally (P.O.) respectively. Drug treatment was given before 30 minutes. 30 minutes after last dose of drug or standard the immobility period was recorded. **Results**: AETC produced significant antidepressant like effect at dose of 500 mg/kg as indicated by reduction in immobility times of mice in TST & FST. The efficacy of AETC at 500mg/kg was found to be comparable to that of Fluoxetine at doses of 25mg/kg. **Conclusion:** The results of the present study indicate that AETC possesses significant antidepressant activity compared to that of Fluoxetine.

KEYWORDS: Terminalia catappa, Forced swim test, Tail suspension test, Antidepressants, Immobolity time.

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.

Symptoms of depression include agitation, restlessness, and irritability, dramatic change in appetite, often with weight gain or loss, extreme difficulty concentrating, fatigue and lack of energy, feelings of hopelessness and helplessness, feelings of worthlessness, self-hate, inappropriate guilt, inactivity, withdrawal from usual activities, a loss of interest or pleasure in activities that were once enjoyed (such as sex),thoughts of death or suicide, trouble sleeping or excessive sleeping.

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 the present review is focused on the medicinal plants and plant-based formulations having antidepressant activity in animal studies and in humans.[2]

Terminalia catappa belongs to the family of Combretaceae. The primary chemical constituents of Terminalia catappa include tannins, flavanoids (isovitexin, vixten, rutin) triterpinoids. The plant is used for anticarcinogenic, anti-HIV and hepatoprotective properties.[3]

MATERIALS AND METHODS
Plant material collection and authentication
The plant material of Terminalia catappa leaves used for the investigation were collected from A M Reddy memorial college of pharmacy premises, narasaraopet, Guntur dist. The plant was **identified** and authenticated by **Dr. S.M. Khasim**, department of botany from Acharya Nagarjuna University, nagarjuna nagar 522510. Guntur district, Andhra Pradesh.

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.[4-6]

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.

PHARMACOLOGICAL STUDY

A. Acute Oral Toxicity study
B. Models for antidepressant activity
C. Acute Oral Toxicity study (dose fixation)[7]

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[8-11]

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.

2. TAIL SUSPENSION TEST[12][13]

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 using stopwatch. 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

STATISTICAL ANALYSIS

Results were plotted by graphical representation.

RESULTS

Preliminary Phytochemical screening

The aqueous extract of Terminalia catappa was subjected to Preliminary Phytochemical tests and the results were tabulated in table no 01. The results showed the presence of, alkaloids, flavanoids, glycosides, saponins, tannins.

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.

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.

LIST OF ABBREVIATIONS

ANOVA	**Analysis of Variance**
ATPase	Adenosine tri Analysis of Variance
AC	Adenyl cyclise
cAMP	cyclic Adenyl Mono Phosphate
Ca	Calcium
CMC	Carboxy Methyl Cellulose
CPCSEA	Committee for the Purpose of Control & Supervision of Experiments on Animals
COMT	Catechol Ortho Methyl Transferase
Ctl	Control

DAG	Diacyl glycerol
DA	Dopamine
Fig	Figure
FOB	Functional Observational Battery
5-HT	Serotonin
Kg	Kilogram
MDD	Major Depressive Disorder
Mg	Milligram
MAOI	Monoamine Oxidase inhibitor
Min	Minute
AETC	Aqueous extract of Terminalia catappa
MTD	Maximum Tolerance Dose
No.	Number
NE	Nor-epinephrine
OECD	Organisation for Economic Co-Operation and Development
PIP_2	Phosphatidyl Ionositol Diphosphate
PLC	Phospholipase C
p.o	Per oral
RIMA	Reversible inhibitor of MAO-A
s.c	Sub cutaneous
SSRI	Selective Serotonin reuptake inhibitor
Std	Standard
Tab	Table
Temp	Temperature
WHO	World Health Organization
+ve	Positive
-ve	-ve
°C	Degree Centigrade

TABLES

Table No.01: Preliminary Phytochemical tests

S.No.	Phytochemical Tests	Inference
1	Test for Alkaloids	+ve
2	Test for flavanoids	+ve
3	Test for Glycosides	+ve
4	Test for Saponins	+ve
5	Test for tannins	+ve

Table No: 02 Effect of AETC on immobility time in Forced swim test in mice

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

Table No: 03 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

FIGURES

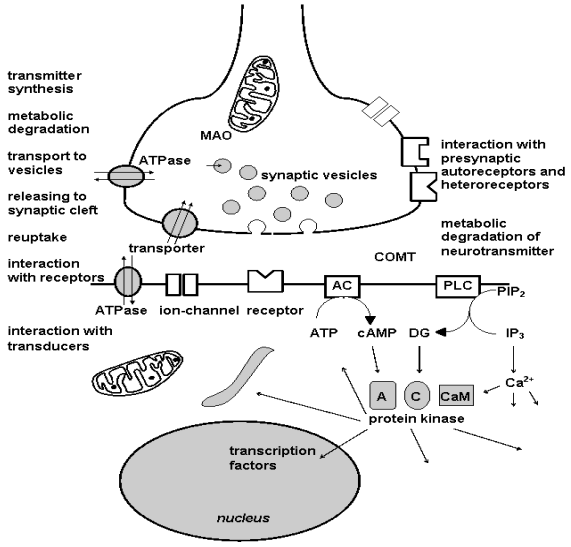

Fig No. 1: Potential mechanisms of antidepressants

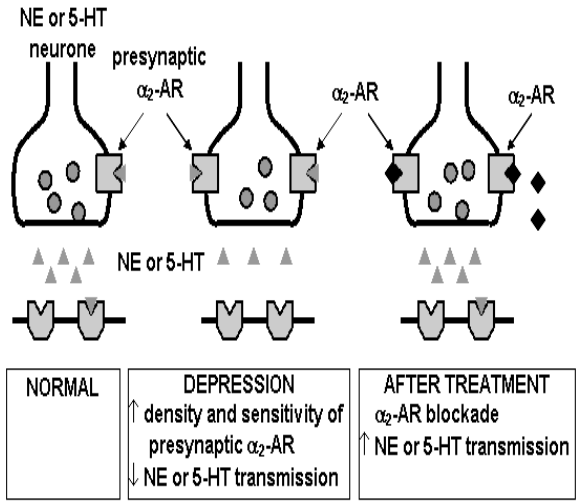

Fig No. 2: Mechanism of action of a2-adrenoceptor blockers

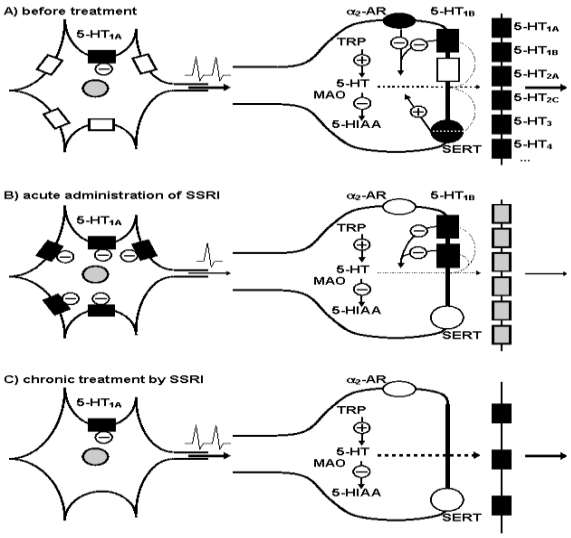

Fig No. 3: Mechanism of actionj of selective serotonin reuptake inhibitors (SSRI)

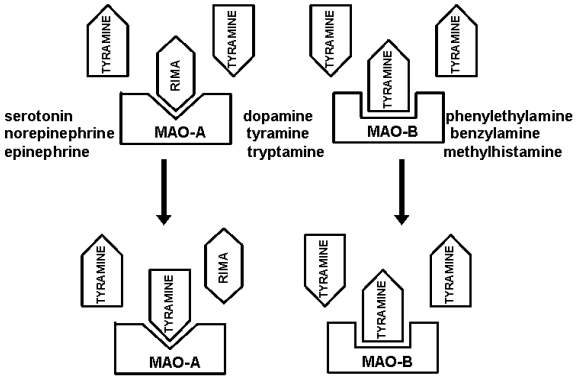

Fig No. 4: Mechanism of action of reversible inhibitors of MAO-A (RIMA)

DISCUSSION

Modern day lifestyle leads to numerous stress conditions, among which depression is a widely prevalent senile neurological disorder. It is mainly caused by decreased brain levels of monoamines like Noradrenaline, Dopamine and Serotonin. Depression is a mental disorder associated with lot of morbidity due to its high incidence in the community. Hence it is necessary to look for Anti depressants with proven advantage and favorable benefit-to-risk ratio. 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. Therefore, there is an immense requirement for alternative remedies for depression.

The present work was subjected to investigation for the evaluation of the Anti depressant activity of aqueous extract of Terminalia catappa leaves in animal models.

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 Forced swim test and Tail suspension test were used. These tests were quite sensitive and relatively specific to all major classes of Anti depressants. The immobility displayed by rodents when subjected to unavoidable stress such as FST & TST are thought to reflect a state of despair or lowered mood, which are thought to reflect depressive disorders. In addition, immobility time has been shown to be reduced by treatment with Anti depressant drugs.

Results showed that the administration of the AETC produced a diminution of duration of immobility time of mice exposed to the both FST & TST. And in the present study, the AETC (500mg/kg, po) administered to mice produced significant 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.[14]

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 the future.

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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