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Evaluation of Anti-Depressant Activity of Ethanolic Extract of Carissa Macrocarpa by Using Albino Mice

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ABSTRACT

Depressive disorder is a prevalent psychiatric disorder, which affects 21% of the world population. The presently using drugs can impose a variety of side effects including cardiac toxicity, hypopiesia, sexual dysfunction, body weight gain, and sleep disorders. Carissa macrocarpa was investigation for antidepressant activity. Antidepressant activity of ethanolic extract of Carissa macrocarpa was investigated by using Tail suspension test, Forced swim test and locomotor activity models. Fluoxetine and Imipramine were used as reference standards.

Keywords: Cardiac toxicity, Hypopiesia, Carissa macrocarpa.

INTRODUCTION

Depression is one of the most common psychiatric disorders with high mortality, morbidity and economic burden worldwide. Depression is consideredas syndrome referring to a constellation ofdepressive symptoms and nosological category is a combination of misery and lethargy. Depression is heterogeneous disorder that affects one's mood, physical health and behaviour. Patients with major depression have symptoms that reflect changes in brain monoamine neuroendocrine response to pharmacological challenge, neuroreceptor and transporter binding revealed that depressive patients show abnormalities in serotonergic, noradrenergic and dopaminergic system. Emotional, cognitive, immune, autonomic and endocrine system shares of misery and lethargy. Depression is heterogeneous disorder that affects one's mood, physical health and behaviour. Patients with major depression have symptoms that reflect changes in brain monoamine neurotransmitters, specifically norepinephrine, serotonin and dopamine. According to International Classification of Diseases-10 and Diagnostic and Statistical Manual-IV depression episodes are recognized as individual suffering from depressed or sad mood, showing loss of energy and diminished activity. Theoretical explanation of depression includes loss of interest, virtually in all activities, a significant reduction in productivity and negative impact on health. Major depressive disorders have been traditionally considered as a neurochemical disorder etiologically. For decades depression has been linked particularly to disturbance in serotonergic and noradrenergic neurotransmitters. Major depression involves disturbance in emotional, cognitive, immune, autonomic and endocrine functions. Assessment of cerebrospinal fluid (CSF) chemistry, neurotransmitters, peptides, hormones and cytokines as well as their receptor as a common language to communicate with eachother. This interplay is important during stress response. Stressful events are the precipitating factors for the onset ofdepression Dysfunction in the neurotransmitter levels result in the systemic effect with hyper activation of hypothalamic pituitary adrenal axis (HPA) besides psychological and behavioural consequences which result in hypercortisolaemia causing a wide array of organ and immune changes. One among the affected part is hippocampus which expresses

high number of steroid receptors, has key role in declarative memory tasks and many other cognitive functions.

AIM OF STUDY

The aim of the present study is to investigate the antidepressant activity of Carissa Macrocarpa leaf's in male albino Swiss micewith the ethanolic extract of leaf's.

OBJECTIVES OF STUDY: The objectives of the study is

- To assess the antidepressant activity of Carissa macrocarpa leaf's in mice by following in vivo models:

1. Tail suspension test
2. Forced swim test
3. Locomotor activity

MATERIALS AND METHODS

Tail suspension test (TST): Tail suspension test commonly employed behavioural model for screening antidepressant- like activity in mice, was first given by Steru et.al. Animals were moved from their housing colony to laboratory in their own cages and allowed to adapt to the laboratory conditions for 1- 2 hr. Each mouse was individually to the edge of a table, 50 cm above the floor, by adhesive tape animals during the test6. The total period of immobility was recorded manually for placed approximately 1 cm from the tip of the tail. Each animal under test was both acoustically and visually isolated from other 6 min. Animal was under study movement, hung and compile considered to be immobile when it didn't show any body tely motionless. The test was conducted in a dim lighted room and each mouse was used only once in the test. The observer, recording the immobility of animals.

Forced swim test (FST):

Forced swim test, the mostfrequently used behavioural model for screening antidepressant (Figure 1).

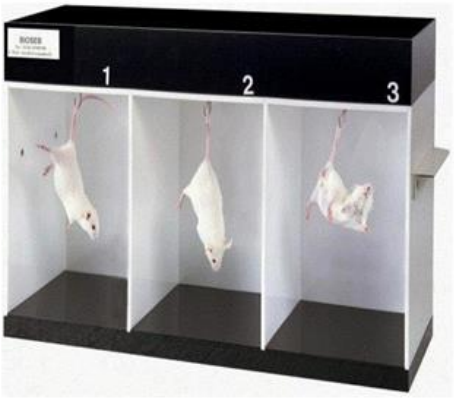

Figure 1: Vigorous movement during initial 2min period of the test.

passively - like activity in rodents, was first proposed by Porsolt 1977. The procedure was same as followed previously. Mice were individually forced to swim in open glasschamber (25 ×15 × 25cm) containing fresh water to a height of 15 cm and maintained at 26°±1°C. At this height of water, animals were not able to support themselves by touching the bottom or the side walls of the chamber with their hind- paws or tail. Water in the chamber was changed after subjecting each animal to FST because "used water"has been shown to alter the behaviour. Each animal showed. Vigorous movement during initial 2min period of the test. The durationof immobility was manually recorded during the next 4 min of the total 6 min testing period. Mice were considered to be immobile when they ceased struggling and remained floating motionless in water, making only those movements necessary to keep their head above water. Following swimming session, mice were towel dried and returned to their housing conditions (Figure 2).

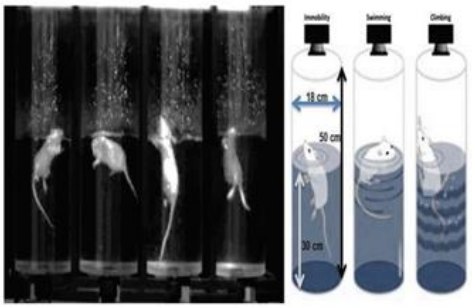

Figure 2: Water in the chamber was changed after subjecting each animal to FST because "used water"has been shown to alter the behaviour.

Locomotor activity:

- Weigh the animals and number them.
- Turn on the equipment (check and make sure that all the photocells are working for recording).
- Place individually each mice in theactivity cage for 10 minutes note the basal activity score of all the animals.
- Inject fluoxetine and after 30 minutes retest each mouse for activityscores for 10 minutes. Note thedifference in the activity scores before and after fluoxetine (Figure 3).

Figure 3: Inject fluoxetine and after 30 minutes retest each mouse for activityscores for 10 minutes. Note thedifference in the activity scores before and after fluoxetine.

RESULTS

Preparation of ethanolic extract

S. No.	Extract	Percentage yield
1.	Carissa macrocarpa leaves(ethanolic)	33.33%

Table 1: Percentage yield of plant Extract.

Preliminary Phytochemical Screening

The qualitative phytochemical analysis of Carissa macrocarpa leaves extract showed the presence of reducing sugars, saponins, glycosides, flavonoids, steroids, terpenoids and amino acids. The plant extract showed negative result against alkaloids (Tables 2-3) and (Figures 4-5).

Phytochemical constituents	**Carissa macrocarpa Leaves (Ethanol)**
Alkaloids	--
Steroids	--
Terpenoids	+
Flavonoids	+
Anthraquinones	+
Tannins	+
Saponins	--
Phenol	+
Carbohydrates	+
No. of chemical compounds In Extract	6

Table 2: Preliminary phytochemical screening of *Carissa macrocarpa*.

Animalgroups	**TST Time in sec**					**Average time in sec**
Control(saline water)	160	171	183	200	228	188.4 ± 5
Standard (Imipramine)	120	134	139	165	178	147.2 ±4
Test (EECM)100mg/kg	103	126	133	146	152	132 ±6
Test (EECM)200mg/kg	106	123	118	145	147	127.8 ±3
Test (EECM)300mg/kg	101	109	105	124	119	111.6 ±9

Table 3: Effects of EECM and fluoxetine on duration of immobility in the TST.

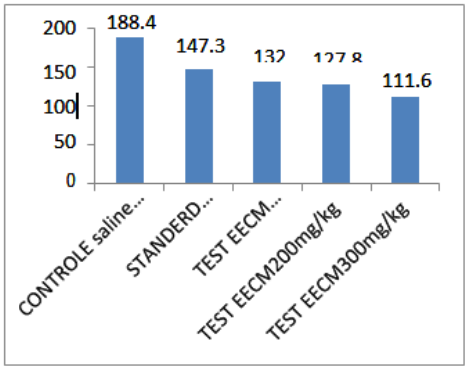

Figure 4: Tail suspension test (TST) commonly employedbehavioural model for screening antidepressant- like activity in mice.

Forced swim test:

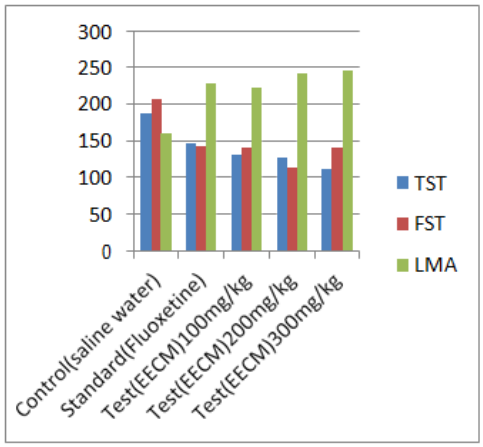

Figure 5: Furthermore,depletion studies carried out in treated and untreated patients indicated a role of serotonin and nor adrenaline in depression.

CONCLUSION

Data in the literature demonstrated that drugs that alter general motor activity may give positive results in the forced swimming test. The effects produced by EECM and fluoxetine(20mg/kg) upon the locomotor activity demonstrated that these products do not modify the spontaneous locomotor activity of mice, which indicates that the plant extract antidepressant effects without modifying significantly this parameter. Therefore, it is probable that these effects arenot related to the stimulation of general motor activity. It has been established that the shortening of immobility time in the forced swimming and the tail suspension tests depends mainly on the enhancement of central 5- HT and catecholamineneurotransmission. Early evidence of a role for noradrenaline in depression came from the discovery those drugs, either causing or alleviating depression, acted to alter the noradrenaline metabolism. Furthermore, depletion studies carried out in treated and untreated patients indicated a role of serotonin and nor adrenaline in depression.

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