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Evaluation of Antidepressant Activity of *Eclipta Alba* In Animal Models

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Abstract: *In the present study, EALE (200 mg/kg) produced significant antidepressant effect in FST & TST. These models of depression are widely used to screen new antidepressant drugs. The tests are quite sensitive and relatively specific to all major classes of antidepressant drugs including TCAs, SSRIs, MAOI, Atypical antidepressants. The forced swimming test is the most widely used tool for assessing antidepressant activity pre-clinically. The widespread use of this simple model is mainly due to its ability to detect a broad spectrum of antidepressant agents. It has been argued that TST (Tail Suspension Test) is less stressful than FST (Forced swim test) and has greater pharmacological sensitivity. The results obtained from TST are in concordance with the validated FST. Environmental factors and hereditary factors play a major role in producing deficient monoaminergic transmission in central nervous system thereby producing symptoms of depression. Ecliptin alkaloid & Culumbin, a flavonoid present in EALE may be facilitating monoaminergic transmission there by producing antidepressant effects.*

Keywords*- Ecliptin, Culumbin, antidepressant, monoaminergic, FST, MAOI.*

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I. Introduction

Depression is a heterogeneous disorder that affects person's mood, physical health and behaviour. According to the World Health Report approximately 450 million people suffer from a mental or behavioral disorder, yet only a small minority of them receives even the most basic treatment, accounting for 12.3% of the global burden of the disease. It is expected to rise to 15% by 2020. In the search for new therapeutic products for the treatment of neurological disorders, medicinal plant research, worldwide, has progressed constantly, demonstrating the pharmacological effectiveness of different plant species in a variety of animal models. Patients with major depression have symptoms that reflect changes in their brain neurotransmitters, specifically nor epinephrine, serotonin and dopamine. A muscle relaxant is a drug which effects skeletal muscle function and decreases the muscle tone. The sedative action of a drug along with antidepressant action is useful in the treatment of depression associated with anxiety. Since all the synthetic drugs available for the treatment of depression have various adverse effects associated with problematic interactions, our aim was to explore the potential of plants in the management of depression [1,2].

Depressive disorders are mood disorders that come in different forms, just as do other illnesses, such as heart disease and diabetes. Three of the most common types of depressive disorders are discussed below. However, remember that within each of these types, there are variations in the number, timing, severity, and persistence of symptoms. There are sometimes also differences in how individuals express and/or experience depression based on age, gender, and culture [3].

Major depression is characterized by a combination of symptoms that last for at least two weeks in a row, including sad and/or irritable mood (see symptom list), that interfere with the ability to work, sleep, eat, and enjoy once-pleasurable activities. Difficulties in sleeping or eating can take the form of excessive or insufficient of either behaviour. Disabling episodes of depression can occur once, twice, or several times in a lifetime [4,5].

The first step to obtaining appropriate treatment is accurate diagnosis, which requires a complete physical and psychological evaluation to determine whether the person may have a depressive illness, and if so, what type. As previously mentioned, the side effects of certain medications, as well as some medical conditions, can include symptoms of depression. Therefore, the examining physician should rule out (exclude) these possibilities through an interview, physical examination, and laboratory tests. Many primary care doctors use screening tools, symptoms tests, for depression, which are usually questionnaires that help identify people who have symptoms of depression and may need to receive a full mental health evaluation [6].

A diagnostic evaluation also includes a mental-status examination to determine if the patient's speech, thought pattern, or memory has been affected, as often happens in the case of a depressive or manic-depressive illness. As of today, there is no laboratory test, blood test, or X-ray that can diagnose a mental disorder. Even the powerful CT, MRI, SPECT, and PET scans, which can help diagnose other neurological disorders such as stroke or brain tumors, cannot detect the subtle and complex brain changes in psychiatric illness. However, these techniques are currently useful in research on mental health and perhaps in the future they will be useful for diagnosis as well [7].

II. Experimental

2.1: Preparation of *Eclipta Alba* Leaf Extract (EALE).

Leaves were collected and shade dried. They were crushed into coarse powder and extracted with 90% ethanol using soxhlet apparatus for 24 hrs. The extract was concentrated under pressure and then dried in air. The concentrated ethanolic extract was suspended in poly ethylene glycol. Freshly prepared solution was used for each experiment.

2.2: Animals used for the study.

About 36 albino rats of either sex weighing between 200-250 gms procured from disease free animal house of Sainath Agencies, Uppal, Hyderabad were used for the present study. Animals had free access to food and water and maintained under standard laboratory conditions with a natural light and dark cycle. The animals were acclimatized for at least five days before behavioral experiments. Experiments were carried out between 9.00 and 15.00 hrs. Experimental protocol was approved by the institutional animals' ethics committee before the start of the study.

2.3: Study Design.

The animals were selected randomly for each experiment and divided into 6 equal groups. Drugs (PEG, EALE, Fluoxetine, Imipramine) administered orally (P.O.) for 7 and 14 successive days. Sixty minutes after last dose, immobility period was recorded in two different animal models of depression like, Forced Swim Test (FST) and Tail suspension test (TST).

2.4: Laboratory Models for Testing Antidepressant Activity.

2.4.1: Forced Swim Test (FST): Forced Swim Test or behaviour despair was proposed as a model to test for antidepressant activity.

Depression was produced by forcing the animal to swim individually in a glass jar containing fresh water of 15cm height and maintained at 25 ^{0}C. This constituted pre-test session. Twenty-four hour later each animal was again forced to swim. After an initial 2 min period of vigorous activity, each animal assumed a typical immobile posture. The total duration of immobility was recorded in next 4 min of a total 6 min test. The change in the immobility period was calculated after administering drugs to the groups as mentioned in the above table.

2.4.2: Tail Suspension Test (TST): The total duration of immobility induced by tail suspension was measured. Depression was produced by suspending the animal from the edge of a table 50 cm above the floor by an adhesive tape placed approx. 1cm. from the tip of the tail. Immobility time was recorded during a 6 min period. Changes in the immobility duration were studied after administering drugs in separate groups of animals. The antidepressant activity was expressed as reduction in the immobility duration between the control, standard and animals treated with test drug.

III. Results And Discussions

The observation of acute toxicity study indicated that there was no death in 2000mg/kg dose after 72 hrs. EALE at the dose of 100 mg/kg had no beneficial effect on immobility period of rats in both the models of depression i.e. FST & TST. The decrease in immobility period in both the models was observed starting from 200 mg/kg. But the increase in dose from 200 to 400 mg/kg did not produce any further reduction in immobility period, suggesting the ceiling effect at 200 mg/kg. At the dose 200 mg/kg, EALE showed antidepressant effect which is comparable to that of Imipramine and Fluoxetine at the dose of 15 & 20 mg/kg respectively (Table 1). The comparable anti depressant effect of EALE with that of TCA (imipramine) and SSRI (fluoxetine) suggest possible involvement of either nor-adrenergic or serotonergic system.

Table 1
Effect of EALE on Immobility Period (sec) of rats using Forced Swim Test

Group	Drug	Dose	Immobility period		
			Pre treatment	Post treatment (7 days)	Post treatment (14 days)
1	PEG	1ml/100gm	193.12±3.02	192.5±2.38	192.54±2.38
2	EALE	100mg/kg	196±2.06	194.56±1.78*	193.92±2.01*
3	EALE	200mg/kg	195.07±2.04	145.65±1.62$^{b**\alpha\delta}$	145.33±1.55$^{b**\alpha\delta}$
4	EALE	400mg/kg	195.2±1.82	162.25±1.32$^{b*\alpha\delta}$	161.07±1.85$^{b*\alpha\delta}$

5	Fluoxetine	20mg/kg	194.48±1.82	115.65±0.66[b]	109.78±0.72[b]
6	Imipramine	15mg/kg	192.35±1.18	136.91±1.18[b]	132.6±1.06[b]

*Values as Mean ± SEM ,n=6, 1. a = p < 0.05, b = p < 0.001 as compared to pre treatment value, 2. * = p < 0.001, ** = p < 0.05 when compared to standard (Both Fluoxetine & Imipramine), 3.α = p < 0.001when compared to control, 4. δ = p < 0.001 when EALE (100) is compared to EALE (200) and EALE (400).*

Table 2
Effect of EALE on immobility period (sec) of rats using Tail Suspension Test

Group	Drug	Dose	Pretreatment	Post treatment after		
				4 days	7 days	14 days
1	PEG	1ml/100gm	192.59±2.20	192.56±1.92	191.02±2.95	190.06±2.80
2	EALE	100mg/kg	191.10±2.35	190.45±2.25	191.04±2.40	190.02±2.28
3	EALE	200mg/kg	189.00±1.35	190.05±1.25	153.25±1.92[*αβ]	155.18±1.88[*αβ]
4	EALE	400mg/kg	190.45±2.25	190.07±2.15	166.09±.75[* αβ]	164.20±2.44[*αβ]
5	Fluoxetine	20mg/kg	189.42±1.75	185.56±1.57	103.52±0.92[*c]	104.62±1.02[*c]
6	Imipramine	15mg/kg	190.5±2.23	188.35±2.01	126.75±2.22[*c]	124.57±2.13[*c]

Values as Mean ± SEM , Student's t test n = 6, 1. P<0.001 when compared to pre treatment , 2.a=P<0.05, b=P<0.01, c=P< 0.001 when compared to control, 3.α =P<0.05, β=p<0.001 When compared to standard.*

In the present study, EALE (200 mg/kg) produced significant antidepressant effect in FST & TST. These models of depression are widely used to screen new antidepressant drugs. The tests are quite sensitive and relatively specific to all major classes of antidepressant drugs including TCAs, SSRIs, MAOI, Atypical antidepressants. The forced swimming test is the most widely used tool for assessing antidepressant activity pre-clinically. The widespread use of this simple model is mainly due to its ability to detect a broad spectrum of antidepressant agents. It has been argued that TST (Tail Suspension Test) is less stressful than FST (Forced swim test) and has greater pharmacological sensitivity. The results obtained from TST are in concordance with the validated FST. Environmental factors and hereditary factors play a major role in producing deficient monoaminergic transmission in central nervous system thereby producing symptoms of depression. Ecliptin alkaloid & Culumbin, a flavonoid present in EALE may be facilitating monoaminergic transmission there by producing antidepressant effects.

IV. Conclusion

Hence *Eclipta alba* leaf extract possesses antidepressant effect in animal models of depression which was comparable to that of Imipramine and Fluoxetine as demonstrated in this study. The phytochemical analysis, separation of active ingredients and further investigation in this line is essential to establish its therapeutic benefits.

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