Original Article

Amelioration Of Atlantia Monophylla In Chronic Unpredictable Stress Induced Depression Like Behaviour In Wistar Rats

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Abstract

Introduction**:** Depression is a debilitating and pervasive illness that may influence the person in many ways andit is distinguished by some of the indications like changes in behavioral, psychological and physiological levels in brain. Hippocampus is implicated in the pathophysiology and treatment of various mood disorders.

Methods: The chronic unpredictable mild stress (CUMS) model has been used as one of the animal models for depression. Aqueous extract of Atlantia monophylla (AEAM) was selected and screened for its anti-depressant activity in CUS model using Fluoxetine, a selective serotonin reuptake inhibitor (SSRI) as standard. Animals (Wistar albino rats) were selected to CUS procedure for 28 days and all the days (Day 1 – Day 28) AEAM was administered at doses of 250mg/kg and 500mg/kg body weight and behavioral, biochemical parameters were analyzed at the end of treatment.

Results: CUSexposure produced a depression like behavior corroborated by the lengthened immobility time in forced swim test apparatus. In Actophotometer decreased locomotor activity and in the hole board test, decline in the number of head dips and line crossings. Biochemical findings revealed that reduction in the levelsof oxidative parameters like superoxide dismutase, catalase. AEAM at the doses of 250mg/kg and 500mg/kg body weight produced significant effectson behavioral and biochemical tests when compared to CUS group.

Conclusion: In conclusion, the present study advocate that the repeated administration of AEAM notably reversed CUS induced depressive like behavior and oxidative damage in dose dependent manner.

Keywords: Aqueous extract of Atlantia Monophylla, Antidepressant, Chronic unpredictable stress model.

INTRODUCTION

Depression is a chronic malady that affects all age groups. Although several effective antidepressants available today, the ongoing armamentarium of therapy is somewhat sparse, with unsatisfactory results over one in three of all subjects treated [1]. Depression is indicated by disturbances in appetite and sleep, shortfall in cognition and energy. Thoughts of guilt, worthlessness, and suicide are common. Stroke and Coronary artery diseases are more customary in patients having depression, and depression may deliberately aggravate the prediction for patients with a diversity of concomitant Aesculapian health [2]. Recent investigations have divulged that development of advanced neurons in the hippocampus after antidepressant administration diminished behavioral changes in the continuous stress-induced rats. Even though a maximum number of antidepressants available, 30% to 40% of patients having depression disappoint to acknowledge the first-line antidepressant treatment [4]. Present day, natural medicines, with their high safety margins, had demonstrated to be productive pharmacotherapy in treating the depression. Till now, no scientific study was reported on *Atlantia monophylla* against depression. We investigate the antidepressant activity of *Atlantia monophylla* against chronic unpredictable stress induced depression model in rats.

MATERIALS AND METHODS:

Collection of plant material, authentication and extraction of Plant material:

Aerial parts of Atlantia monophylla collected in the region of Tirupathi, Andhrapradesh andauthenticated by Dr. Madhava Chetty, Taxonomist, SVU, Tirupathi. 500 gm of the powdered aerial parts Atlantia monophylla extracted by maceration method using water as solvent (AEAM).The maceration was continued for 7 days after which, the contents were filtered and

concentratedby rota evaporator. A brownish and resinous greenish extract respectively was obtained which wascalculated for the yield (20grams) and stored in desiccator till further study.

Animals:

Female Wistar Rats weighing (200-220 g) were received from the veterinary college, Bangalore, acclimatized for two weeks before experimentation. Animals are placed 12 hour light/ dark cycleunder constant temperature (22 $\pm 2^0$ C) and humidity (50± 10%) and animals were under normal pellet diet and water *ad libitum*. Here all the experiments were performed between Mornings 10:00to Evening 04:00. The experimental procedures on animals were in consent with the Committee for the Purpose of Control and Supervision of Experiments on Animals, CPCSEA (Approval Number (IAEC/XV/09/RIPER/2020).

Drug treatment:

Fluoxetine, a selective serotonin reuptake inhibitor, used as positive control for antidepressant action. Five groups of six animals in each were assigned randomly: Vehicle control, CUMS plus Vehicle, CUMS + AEAM (250 mg/kg), CUMS + AEAM (500 mg/kg) and CUMS plus Fluoxetine (20 mg/kg). AEAM and Fluoxetine aread ministered orally between 9:30 Am and 10:30 Am once per day for four weeks.

Chronic Unpredictable Stress model:

Rats were divided into five groups. (1) Non-Stressed, Control group (2) Stressed, CUS group (3) CUS with Low dose of Test (4) CUS with High dose of Test and (5) CUS with Standard treatment,positive control (Fluoxetine 10 mg/ kg). Each group consisting of six animals (n=6) and every group is placed in individual cages. Control group rats were kept undisturbed in their home cages,whereas rats in the CUS group were subjected to various stressors for 28 days (four weeks). The stressors include food deprivation, Water deprivation, overnight illumination, Slant cage, cold water immersion, foot shock and forced swimming. To avoid predictability, rats were exposed to these stressors at different times on each day. Behavioral tests were started at day 29 after 24 hoursof last foot shock.

Statistical Analysis: All values are expressed as mean±sem. Data was analyzed by One way ANOVA followed by Dunnett's multiple comparison test. $P<0.05$ is considered to be significant.

RESULTS:

Despair Swim Test:

Table 1: Effect of AEAM on Duration of Immobility.

S. NO	GROUPS	DURATION OF IMMOBILITY (Sec)
1	NORMAL CONTROL	129.3± 5.011
2	CUS GROUP	187.3± 5.408^{****}
3	CUS+ AEAM (250 mg/kg)	139.8± $2.892^{\#\#\#\#}$
4	CUS+ AEAM (500 mg/kg)	170± $2.852^{@@@@}$
5	CUS+ Fluoxetine (10 mg/kg)	158± 3.933^{**}

The values expressed are mean ± SEM, one way ANOVA followed by Dunnett's test ****P < 0.0001 as compared with the control, $^{\#\#\#\#}$ P < 0.0001 as compa1ed with the CUS group, $^{@@@@}$ P <0.0001 as compared with the CUS group and **P < 0.05 as compared with the CUS group.

Table 2: Effect of AEAM on hole board test.

S.NO	GROUPS	NO. OF HEAD DIPS (Sec)
1	NORMAL CONTROL	27 ± 1.653
2	CUS GROUP	7.5 ± 0.8851^{****}
3	CUS+ AEAM (250 mg/kg)	14 ± $0.7303^{\#\#\#\#}$
4	CUS+ AEAM (500mg/kg)	17.33 ± $0.6146^{@@@@}$
5	CUS+ Fluoxetine (10 mg/kg)	23.5 ± 0.9574^{**}

The values expressed are mean ± SEM, one way ANOVA followed by Dunnett's test. ****P <0.01 as compared with the control, $^{\#\#\#\#}$ P < 0.0001 as compared with the CUS group, $^{@@@@}$ P <0.0001 as compared with the CUS group and **P < 0.05 as compared to CUS group

Table 3: Effect of AEAM on Superoxide Dismutase.

S.NO	GROUPS	SOD (U/mg Protein)	% Of Control
1	NORMAL CONTROL	1.71 ± 0.017	100
2	CUS GROUP	0.54 ± 0.093^{****}	29.38
3	CUS+ AEAM (250 mg/kg)	1.16 ± $0.049^{\#\#\#\#}$	69.61
4	CUS+ AEAM (500mg/kg)	1.33 ± 0.046^{***}	79
5	CUS+ Fluoxetine (10 mg/kg)	1.66± 0.036^{*}	86.18

The values expressed are mean ± SEM, one way ANOVA followed by Dunnett's test ****P < 0.01as compared with the control, #### P < 0.0001 as compared with the CUS group, ***P < 0.05 as compared with the CUS group and *P < 0.05 as compared with the CUS group.

Table 4: Effect of AEAM on catalase.

S.NO	GROUPS	Catalase (U/ mg Protein)	% Of control
1	NORMAL CONTROL	233.1 ± 16.64	100
2	CUS GROUP	97.2 ± 7.546****	44.09
3	CUS+ AEAM (250 mg/kg)	149.5 ± 10.07***	65.61
4	CUS+ AEAM (500 mg/kg)	199.4 ± 19.48ns	82.43
5	CUS+ Fluoxetine (10 mg/kg)	212.1 ± 8.252ns	88.89

The values expressed are mean ± SEM, one way ANOVA followed by Dunnett's test.
****P < 0.0001 as compared to control, *** P < 0.001 as compared to CUS group and ns P < 0.05as compared to CUS group.

DISCUSSION:

It is generally believed that chronic stress plays an important role in onset and relapse of depression[3]. In this regard, an animal model of CUS induced depression has been developed to stimulate the pathogenesis of depression in humans. Several studies suggest that CUS can induce long-termbehavioral disturbances resembling symptoms of clinical depression and that CUS induceddepression model can be used for evaluating the efficacy of antidepressant candidates through behavioral tests like sucrose preference and forced swim tests. Sucrose preference test is an indicator of Anhedonia like behavioral change. Human major depression was model by inducing a decrease in responsiveness to rewards reflected by a reduced consumption and/ or preference ofsweetened solutions. The results of present study showed that rats subjected to CUS procedure consumed less sucrose solution when compared to normal rats. Chronic stress has been shown to dramatically increase the immobility time of rat in forced swim test, a manifestation of "behavioraldespair" [4]. Consistently, CUS, as observed in the present study, resulted in an increased immobility time in forced swim test in rats indicates, aqueous extract of *Atlantia Monophylla* produced antidepressant like action in CUS exposed rats. Further studies are warranted to explore the mechanism of action of *Atlantia monophylla* in the treatment of Depression.

CONCLUSION:

In conclusion, long-term *Atlantia Monophylla* treatment during the course of CUMS was foundto alleviate CUS induced depression. Whether there is a central action of *Atlantia Monophylla* that it is critically important for its anti-depressive effect will be further investigated.

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