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Evaluation of Antidepressant Activity of Aqueous Extract of Withania Somnifera [Aswagandha] Roots in Albino Mice

Dr.P.Bharathi[1], Dr. V.Seshayamma[2], Dr. G. Hari Jagannadharao[3], Dr.N.Sivakumar[4]

[1](Post graduate student, Department of Pharmacology, ASRAMS, India)
[2](Professor& HOD, Department of Pharmacology, ASRAMS, India),
[2](Professor, Department of Pharmacology, ASRAMS, India)
[2](Associate Professor, Department of Pharmacology, ASRAMS, India)

Abstract: *Anti-depressants play a major role in today's life style. There are evidences of the ayurvedic formulation withania somnifera (roots) being effective in various neuro- psychiatric conditions. The anti-depressant activities of aqueous extract* ***Withania somnifera*** *roots (AEWS) were studied using - Forced swim test (FST). Effect of different doses of AEWS (30,40,50 mg/kg), Imipramine (15mg/kg)were studied on behavioural despair tests induced immobility time . WS produced dose dependent decrease in immobility time in FST, maximum effect being observed with WS 50 mg/kg. The findings support the use of WS as potential adjuvant in depressive disorders.*

Keywords: *Withania somnifera, anti depressant activity, forced swim test.*

I. Introduction

Depression is a heterogeneous disorder that affects a person's mood, physical health and behavior. It is caused not only by changing lifestyle as perceived by the general public but also by some of the allopathic drugs for example, anti hypertensive drug, reserpine that depletes neuronal storage granules of nor epinephrine, serotonin and dopamine, causes clinically significant depression in more than 15% of patients. Patients with major depression have symptoms that reflect changes in brain monoamine neurotransmitters, specifically norepinephrine, serotonin and dopamine. The prevalence of depression in the general population worldwide is estimated to be about 5%. Among patients, it ranges from 9% in ambulatory medical patients to 30% in hospitalized patients. According to a World Health report about 450 million people suffer from a mental or behavioral disorder, yet only a small proportion of them receive even the basic treatment.

Depression accounts for about 12% of the global burden of disease which is expected to rise to 15% by 2020. The major problems of existing allopathic antidepressant drugs include delayed clinical benefit, serious side-effects, and a response rate of less than 50 percent. Commonly used drugs for depression are monoamine oxidase inhibitors and tricyclic antidepressants (TCAs). They increase the synaptic concentration of at least two of three neurotransmitters, namely 5-HT, NE and dopamine (DA). The combined effect of serotonin selective reuptake inhibitor (SSRI) and serotonin reuptake transporter (SERT) inhibitor increases synaptic concentration of 5-HT and its duration of action. Therefore, identification and validation of plant derived substances for the treatment of various depressive disorders attracts the attention of researchers.

II. Materials And Methods

2.1 Test Drug: Withania somnifera roots aqueous extract was obtained from Laila neutraceuticals, Vijayawada.
2.2 Test dose: A pilot study was conducted with different doses (5 mg/kg, 10 mg/kg, 20 mg/kg, 30mg/kg , 40 mg/kg and 50 mg/kg) to assess the appropriate dose for the study. The antidepressant activity were observed at the dose of 40 and 50 mg/kg of body weight and hence the same doses were used in the study.
2.3 Chemicals: Imipramine, Normal saline and other chemicals were of analytical grade.
2.4 Instruments: Glass cylinder (25 × 12 × 25 cm3), Stop watch.
2.5 Animals: Swiss albino mice weighing around 25 g – 30 g of either sex were obtained from Central animal house, Alluri sita rama raju academy of medical sciences, Eluru. Animals were maintained under standard laboratory conditions at an ambient temperature of 25°C. Animals had free access to food and water with a natural light and dark cycle. Animals were acclimatized for at least 5 days before behavioral experiments. The study protocol was approved by Institutional Animal Ethics Committee (IAEC) of the college and the experiments were carried out as per CPCSEA guidelines.

III. Experimental Design

3.1 Groups: Group I – Control (Normal saline 1 ml/kg),
Group II – Standard (Imipramine 15 mg/kg),
Group III – AEWS 30mg/kg ,
Group IV – AEWS 40 mg/kg,
Group V – AEWS 50 mg/kg.

3.2 Forced-swim test: Forced swim test was proposed as a model to test antidepressant activity. The Mice were forced to swim individually in glass jar (25 x 12 x 25 cm^3) containing fresh water up to 15 cm height and maintained at 25 0C. After an initial period of vigorous activity for two minutes, each animal assumed a typical immobile posture. A mouse was considered to be immobile when it remained floating in the water without struggling and making only minimum movements of its limbs necessary to keep its head above the water. The total duration of immobility was recorded during the next 4 min of the total test duration of 6 minutes after administering the drugs to the respective groups of animals.

IV. Statistical Analysis

The data obtained in present investigation was subjected to statistical analysis. All results are expressed as Mean ± SEM (standard error of mean); Six animals in each group. Statistical analysis was carried out by using student's t test. P values < 0.05 were considered significant.

V. Results

5.1 Effect of AEWS on immobility periods in behavioral despair tests:

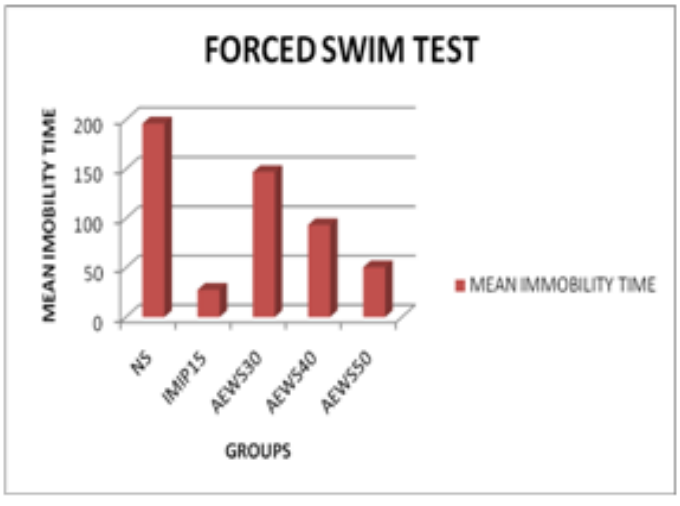
The anti-depressant effect of Withania somnifera (WS), imipramine was studied by looking at the changes in the duration of immobility in animal model namely Forced swim test (FST) .

The anti-depressant effect: FST Model suggested statistically significant antidepressant effect of imipramine and different doses of WS. The inhibition of FST induced immobility time was highest (80%) for the standard, followed by 74 % for AEWS 50 mg/kg, 52 % for AEWS 40mg/kg and 11% for AEWS 30 mg/kg in FST model. There were significant differences between the standard and different dosage forms of AEWS indicating that test drug has some effect. The higher dose of test drug 50mg/kg showed a greater inhibition comparable with standard; however the difference was not statistically significant.

5.2 Mean and its standard error (SEM) of duration of immobility (in seconds) induced by forced swim test (FST)

Groups(n=6 each)	Doses	FST
1.Control NS	1mg/kg	196.16±3.03
2.Imipramine	15mg/kg	27.66±2.01
3.T1:AEWS	30mg/kg	147±2.46
4.T2:AEWS	40mg/kg	93.3±2.82
5.T3:AEWS	50mg/kg	50.5±2.47

5.3 Bar Diagram



VI. Discussion

The introduction of drugs like amitriptyline,fluvoxamine, imipramine, citalopram, venlafaxine and others have revolutionized the treatment of depression. The amazing efficacy of imipramine and fluoxetine in these depressive disorders has paved the way for the introduction and use of newer anti-depressant agents. However, the safety factor in respect of both the imipramine and fluoxetine anti-depressant drugs has been rather intriguing and hence a definite need is visualized for the introduction of safer antidepressant drugs having no troublesome adverse effects. The present study was selected to evaluate anti depressant activity of AEWS. The major biochemical constituents of Ashwaganda root are steroidal alkaloids and steroidal lactones in a class of constituents called withanolides. About 12 alkaloids, 35 withanolides, and several sitoindosides from this plant have been isolated and studied. A sitoindoside is a withanolide containing a glucose molecule at carbon 27. Much of Ashwaganda's pharmacological activity has been attributed to two main withanolides, withaferin A and withanolide D. FST widely used to screen newer antidepressant drugs .

This test is quite sensitive and relatively specific to all major classes of antidepressant drugs including tricyclics, selective serotonin reuptake inhibitors, monoamine oxidase (MAO) inhibitors and atypicals. Imipramine is a pre-synaptic uptake inhibitor of both nor-adrenaline as well as serotonin. Since catecholamines and 5-HT have been implicated in the aetiology of depression, the positive effect of these drugs in FST seems to be due to increased availability of these neurotransmitters at the postsynaptic receptor sites following their reuptake inhibition. In FST, mice were forced to swim in a restricted space, which induced a characteristic behavior of immobility. This immobility reflects a state of despair in animals and is claimed to reproduce a condition similar to depression in humans. Animals after anti-depressant treatment struggle more even in desperate situation, and they spend less time with immobility. In the present study, AEWS in the dose of 40 and 50 mg/kg produced significant dose-dependent antidepressant-like effect in behaviour despair test (FST), as they reduced the immobility time. Also, the decrease in produced by WS 50mg/kg mainly was comparable to that produced by the standard imipramine (15 mg/kg).

VII. Conclusion

A number of studies on WS, or its major active principles, have shown an antioxidant, adaptogen, anxiolytic, antidepressant, memory enhancing, anti-inflammatory, anti-ulcerogenic, anti-parkinsonian and anti-carcinogenic properties. In the present study aqueous extract of Withania somnifera roots has shown promising results in experimental depression**.** These studies are valuable for identifying lead compounds for anti-depressant drugs, keeping in mind the side effects of presently used antidepressants.The standardization of the extracts, identification and isolation of active principles along with pharmacological studies of these principles may be considered for further detail studies. Still further human studies are needed to prove the safety and efficacy of long term administration of aqueous extract of Withania somnifera root. In the light of observations made it may be envisaged that Withania somnifera can be used as a potential adjuvant in the treatment of depressive disorders.

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