

**EVALUATION OF ANTIDEPRESSANT ACTIVITY OF *MEDHOVIKAS*: A  
POLYHERBAL FORMULATION**

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**Summary**

To date, the search for novel pharmacotherapy from medicinal plants for psychiatric illnesses has significantly progressed. The aim of the present study was to evaluate the antidepressant effect of *Medhovikas* by using forced swim test (FST) and tail suspension test (TST). In this study *Medhovikas*, a polyherbal formulation at two dose (200 and 400 mg/kg) levels, standard polyherbal formulation, Mentat (200 and 400 mg/kg) and standard imipramine (15 mg/kg) were administered on test day to separate group of young swiss albino mice. From these two animal models it was found that, *Medhovikas* showed significant reduction in the duration of immobility in FST and TST at both dose levels in dose dependent manner and the effect of high dose i.e., 400 mg/kg was comparable with standard drug, imipramine. *Medhovikas* also showed better antidepressant effect than standard polyherbal formulation, Mentat. Our result confirmed that *Medhovikas* possess significant antidepressant activity.

*Keywords:* *Medhovikas*, antidepressant effect, forced swimming test, tail suspension test

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**Introduction**

Depression is a common, debilitating, life-threatening illness with an increasing morbidity and mortality. Furthermore, the World Health Organization revealed that depression is the fourth leading cause of disability worldwide, exceeded by lower respiratory infections, perinatal conditions and HIV/AIDS [1]. A number of the population suffers with this condition at some time during their life. To date, the efficacy of the drugs for this condition are very limited so the need for newer, better-tolerated and more efficacious treatments is remaining high. Therefore, herbal therapies should be considered as alternative/complementary medicines. Recently, the search for novel pharmacotherapy from medicinal plants for psychiatric illnesses has progressed significantly [2]. In this regard, Suveda herbals, Tirupati, Andhra Pradesh has developed a herbal formulation “*Medhovikas*” with few ingredients (Each 100g contains *Bacopa monniera*-10g, *Centilla asiatica*-30g, Cows ghee- 10g, Sugar- 25g, Honey-25g) to combat depression.

But there is lack of scientific data regarding the antidepressant effect of 'Medhovikas'. Hence the present study was undertaken to evaluate antidepressant activity of 'Medhovikas' by employing forced swim test (FST) and tail suspension test (TST). Standard antidepressant drug imipramine, a tricyclic antidepressant and a standard polyherbal formulation, Mentat (Himalaya drug co., Bangalore) were employed to standardize the animal models of depression and to compare the antidepressant efficacy of Medhovikas.

### **Materials and Methods**

#### ***Experimental Animals***

Albino Swiss mice of either sex (20-30 g) were obtained from Institutional Animal Breeding House, Vels University, Pallavaram, Chennai-117. Animals were housed in plastic cages at an ambient temperature ( $25\pm 2^{\circ}\text{C}$ ) and relative humidity of 45-55%. A 12:12 hr light- dark cycle was maintained during the experiments. They were fed with balanced rodent pellet diet from Poultry Research Station, Nandanam, Chennai- 35 and water *ad libitum* throughout the experimental period. Animals were acclimatized to their environment for at least one week before experimentation. The animals were randomly divided into different groups. Each animal was housed separately after recording its body weight.

#### ***Drugs and Chemicals***

Medhovikas (Suveda Herbals, Tirupati)

Mentat<sup>R</sup> (Himalaya Drug Co., Bangalore)

Imipramine hydrochloride (Sigma-Aldrich, St. Louis, USA)

### ***EVALUATION OF ANTIDEPRESSANT ACTIVITY***

#### ***Forced swim test (FST) [3, 4]***

Behaviour despair was proposed as a model to test for antidepressant activity. Animals were divided into six groups of six animals each. Normal control group, receiving a single dose of 0.5 mL/100g of the vehicle. Group 2 reference drug group, being treated with imipramine (15 mg/kg). Groups 3 and 4 being treated with standard polyherbal formulation, Mentat at two dose levels (200 and 400 mg/kg) and group 5 and 6 being treated with test formulation Medhovikas with doses of 200 and 400 mg/kg respectively. The animals were forced to swim individually, for 15 min, on first day. This constituted the 'pretest' session. Twenty four hours later, 30 min after treatment of with vehicle/standard/ test sample as mentioned above, each mouse was gently dropped and were forced to swim individually in a glass jar (25 x 12 x 25 cm<sup>3</sup>sub) containing fresh water of 15 cm height and maintained at  $25^{\circ}\text{C}$  ( $\pm 3^{\circ}\text{C}$ ) and was left for 6 minutes. After an initial 2 min period of vigorous activity, each animal assumed a typical immobile posture. A mouse was considered to be immobile when it remained floating in the water without struggling, making only minimum movements of its limbs necessary to keep its head above water. The total duration of immobility was recorded during the next 4 min of a total 6 min test. The changes in immobility duration were studied after administering drugs in separate groups of animals. Each animal was used only once.

#### ***Tail suspension test (TST) [5, 6, 7]***

The tail-suspension test was the second method for assessing the antidepressant effect of the formulation. Thirty minutes after the treatment with vehicle/standard/test sample injection

similar to that of FST model, mice were subjected to the test. Mice were suspended on the edge of a table 50 cm above the floor by the adhesive tape placed approximately 1 cm from the tip of the tail. After the initial period of vigorous motor activity, the mice became still and the immobility time was measured with a stopwatch, for a total duration of 6 minutes. Mice were considered immobile when they hung passively and completely motionless. The total duration of immobility induced by tail suspension was measured as a facile means of evaluating potential antidepressants.

### Statistical analysis

Values were expressed as mean  $\pm$  SEM from 6 animals. Statistical difference in mean was analyzed using one way ANOVA (analysis of variance) followed by Dunnet's tests. A p-values  $<0.05$  were considered significant.

### Results

Medhovikas showed significant reduction in the duration of immobility time in both forced swim test (FST) and tail suspension test (TST) compared to control at both dose levels in dose dependent manner. Immobility was reduced 38.7% with 200 mg/kg dose and 52.7% with 400 mg/kg in FST similarly in TST, 33.9% with 200 mg/kg and 49.6% with 400 mg/kg compared to control group. Where as the standard polyherbal formulation, Mentat (200 and 400 mg/kg) and standard imipramine also showed significant reduction in immobility time. Medhovikas showed better antidepressant activity compared to standard polyherbal formulation (Mentat) and antidepressant effect of medhovikas at high dose (400 mg/kg) was comparable with that of standard drug i.e., imipramine (15 mg/kg) in both the test models.

#### Effect of Medhovikas on immobility in forced swim test and tail suspension test

Treatment	<i>Forced Swim Test (FST)</i>		<i>Tail Suspension Test (TST)</i>	
	Immobility time (sec)	Change %	Immobility time (sec)	Change %
Control	146 $\pm$ 3.93	---	111.2	---
Imipramine (15 mg/kg)	73 $\pm$ 1.5**	-50	57.1**	-48.6
Mentat (200 mg/kg)	126.2 $\pm$ 1.9**	-13.6	92.7**	-16.6
Mentat (400 mg/kg)	99.7 $\pm$ 2.9 **	-31.7	78**	-29.8
Medhovikas (200 mg/kg)	89.5 $\pm$ 2.8 **	-38.7	73.5**	-33.9
Medhovikas (400 mg/kg)	69.0 $\pm$ 1.0**	-52.7	56 **	-49.6

Values are expressed as mean  $\pm$  S.E.M. (n=6), \*p<0.05, \*\*P< 0.01 compared to control.

### Discussion and Conclusion

Depression and mental health problems in general and senile neurological disorders in particular, are widely prevalent in modern fast-paced life with a multitude of stressful conditions. Animal models like mother-infant separation in monkeys, amine depletion by reserpine, learned helplessness etc. are available for creating depression and testing substances for antidepressant action. Even though none of the animal models corresponds to inherited condition clinical depression in man, the animal models were used for screening substances for antidepressant activity as some of the underlying biochemical mechanisms were common to clinical depression and experimentally produced depression in animals [8]. Rodents forced to swim in small enclosures (cylinders) from which there is no escape rapidly become immobile after an initial period of vigorous activity [9]. Initially, immobility was interpreted as evidence they had learned that escape was impossible and had given up hope. Immobility was therefore given the name "behavioral despair." It has subsequently been shown in numerous laboratories that immobility is reduced by a wide range of clinically active antidepressant drugs [10]. As a consequence, forced swim test and tail suspension tests were now widely used to screen novel substances for potential antidepressant activity. The immobility displayed in rodents subjected to an unavoidable and inescapable stress has been hypothesized to reflect behavioural despair, which in turn may reflect depressive disorders in humans. In fact, there is a significant correlation between the potency of antidepressants in both forced-swimming and tail-suspension tests and clinical potency of the drugs [11]. Hence Forced Swim Test (FST) and Tail Suspension Test (TST) are best viewed as simple tests for antidepressants. From our present study, the results obtained after a single administration of *Medhovikas* at two dose levels 200 and 400 mg/kg showed significant reduction in the immobility time of animals in dose-dependent manner, namely, the animals were more active in both employed models, and standard poly polyherbal formulation Mentat used in our study also showed significant reduction in immobility time which was qualitatively comparable with standard imipramine but less effective than *Medhovikas*, which means that the antidepressant effect of *Medhovikas* was stronger. From these investigations, it can be concluded that *Medhovikas* possess significant antidepressant activity and at high dose (400 mg/kg), antidepressant effect of *Medhovikas* was comparable with standard imipramine (15mg/kg). However detailed experimental studies should be performed to elucidate the mechanism of action and to support this suggestion.

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