

RESEARCH ARTICLE

The antidepressant activity of the alcoholic extract of *Withania coagulans* fruits in Swiss albino mice by forced swimming testAmit S Kamdi¹, Pankaj N Bohra², Suvarna M Kalambe³, Ajay R Chandrakapure¹¹Department of Pharmacology, Government Medical College, Chandrapur, Maharashtra, India, ²Department of Pediatrics, SNEH Foundation, Pune, Maharashtra, India, ³Department of Research and Development, Sanjeevani Multipurpose Society, Chandrapur, Maharashtra, India

Correspondence to: Amit S Kamdi, E-mail: dramit99@gmail.com

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ABSTRACT

Background: Depression is one of the most upsetting mood disorders. The various antidepressant medications used today are having the adverse drug effects. *Withania coagulans* – a vulnerable species, is not explored much for its effects on mood except in the late 70s. Therefore, it was thought worthy to explore anti-depressive activities of the alcoholic extract of *W. coagulans* fruits in Swiss albino mice using forced swimming test. **Aims and Objectives:** This study aims to study the antidepressant activities of the alcoholic extract of *W. coagulans* fruits in Swiss albino mice using forced swimming test. **Materials and Methods:** Forced swimming test was used for assessing the anti-depressive activity of *W. coagulans* fruits alcoholic extract. If the extract had antidepressant activity, then it was expected that the period of mobility would increase and immobility would decrease. This decrease in immobility, if found statistically significant, was considered for antidepressant activity. **Results:** There was statistically highly significant ($P < 0.001$) association observed between alcoholic extract of *W. coagulans* fruits with depressive effect on mood in Swiss albino mice. **Conclusion:** The alcoholic extract of *W. coagulans* fruits did not demonstrate antidepressant activity in Swiss albino mice. In contrast, it revealed depressive effect on the mood in the forced swimming test.

KEY WORDS: Antidepressant; Swiss Albino Mice; Alcoholic Extract; *Withania coagulans*; Forced Swimming Test


INTRODUCTION

The prevalence of all depressive disorders taken together is more than 20% of world population. However, in India, this prevalence is about 16% which is comparable to western countries.^[1] The depression was found to be 21–84% of the cases reported in primary health-care centers in India.^[2,3] According to the World Health Organization, depression is defined as a “common mental disorder, characterized by

sadness, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, feelings of tiredness, and poor concentration.”^[4] The main neurotransmitters involved in major depressive disorder are norepinephrine, dopamine, and serotonin (5-HT).

There are various drugs available for the treatment of depression. However, these drugs cause numerous side effects in human. Immobility time in rodents can be compared to the depressive symptoms in human; in contrast, increase in mobility time is seen clinically with administration of anti-depressive drugs.^[5] Therefore, the phenomenon of forced swimming test can be used for measuring the efficacy of anti-depressive drugs.

Withania coagulans is categorized as “vulnerable species.”^[6] As a result, not much work is done on this plant to see the effect on mood. In 1977, Budhiraja *et al.* reported central nervous system (CNS)-depressant activity of this plant.^[7]

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Thereafter, this plant was not much explored for the CNS activity, though lot of work was done on diabetes and other diseases. Therefore, it was thought worthwhile to investigate anti-depressive activities of the alcoholic extract of *W. coagulans*.

MATERIALS AND METHODS

Control, Standard, and Test Drugs

Distilled water was given as vehicle for control. Imipramine was used as the standard drug. The animals were treated 30 min before the experiment with the test drugs (WCFAIcE of 200 mg/kg, 500 mg/kg, and 1000 mg/kg doses p. o.). However, the test drug was given every day for 30 days throughout the period of experiment. The mice were observed for 5 min. Recordings were done on day 1, day 8, day 15, day 23, and day 30 for all the groups. The recordings were taken half an hour after drug administration to the respective group.

Drugs were given in the following manner in both the models of antidepressant activity:

- Control: Vehicle (distilled water) 2 ml/kg p. o. once a day for 30 days.
- Standard: Standard drug (imipramine) 15 mg/kg i. p. once half an hour before test.
- ALC-200: WCFAIcE 200 mg/kg p. o. once a day for 30 days.
- ALC-500: WCFAIcE 500 mg/kg p. o. once a day for 30 days.
- ALC-1000: WCFAIcE 1000 mg/kg p. o. once a day for 30 days.
- Where WCFAIcE = *W. coagulans* fruits alcoholic extract.

Forced Swim Test (FST)

The mice were placed individually in the glass cylinder (40 cm in height, 25 cm in diameter) tank. The water level

(temp. 25°C) was 15 cm from the bottom and was marked on the tank to ensure that the volume of water was consistent across mice. The dimensions of the tank were selected in a way that the mice were not able to touch the bottom of the tank, either with their feet or their tails, during the swim test. The height of the tank was high enough to prevent the mice from escaping from the tank. After 5 min, the animals were removed from water, dried, and returned to their home cages. They were again placed in cylinder 24 h later. The mice were observed for the 6 min. However, the first 1 min was discarded as this was the period required for the acclimatization. Therefore, the activity was observed for 5 min only. The total duration of immobility was measured for 5 min. The mice were considered immobile when they were motionless. The index of depression in this experimental model was considered as the immobility duration over a specified period. If any antidepressant drug was given, then it was expected that the period of mobility would increase and immobility would decrease.

Ethical Approval

The study was approved by the Institutional as well as the Animal Ethics Committee of MGIMS, Sevagram.

RESULTS

As shown in Table 1, on day 1 and day 8, there were no statistically significant differences in both the parameters such as the average time spent by mice in active swimming (mobility) and average time spent by mice by staying motionless or stopping swimming (immobility) for all the three doses of 200 mg/kg, 500 mg/kg, and 1000 mg/kg of WCFAIcE compared to control. However, on day 15, day 23, and day 30, there were statistically highly significant differences observed in both the parameters of mobility and immobility for all the three doses of 200 mg/kg, 500 mg/kg, and 1000 mg/kg of WCFAIcE compared to control.

Table 1: Effect of oral administration of WCFAIcE on time spent in seconds (Mean±SD) in mobility and immobility positions in the forced swim test ($n=6$ in each group)

Day	Variables	Control	Standard	ALC-200	ALC-500	ALC-1000
1	Mobility	110.16±6.85	116.50±20.89	111.50±11.39	116±14.14	126±24.45
	Immobility	189.83±6.85	183.50±20.89	188.50±11.39	184±14.14	174±24.45
8	Mobility	121.66±7.68	182±18.33***	109.16±12.63	112±12.42	118.50±14.06
	Immobility	178.33±7.68	118±18.83***	190.83±12.63	188±12.42	181.50±14.06
15	Mobility	124.50±5.24	198.50±14.08***	104.83±6.36***	102.33±9.15***	98.66±9.24***
	Immobility	175.50±5.24	101.50±14.08***	195.16±6.36***	197.66±9.15***	201.30±9.24***
23	Mobility	117±8.02	210.16±11.19***	96.33±10.07**	86.33±7.50***	68.50±15.35***
	Immobility	183±8.02	89.83±11.19***	203.66±10.07**	213.66±7.50***	231.50±15.35***
30	Mobility	119.50±8.31	225±13.19***	93.66±12.61**	80.50±13.54***	55±11.18***
	Immobility	180.50±8.31	75±13.19***	206.33±12.61**	219.50±13.54***	245±11.18***

* $P<0.05$, ** $P<0.01$, and *** $P<0.001$ when compared to control group. WCFAIcE: *Withania coagulans* fruits alcoholic extract, mobility: Time spent by mice when actively swimming, immobility: Time spent by mice when stopped swimming, control: Vehicle (distilled water) 2 ml/kg p. o. once a day for 30 days, standard: Standard drug (imipramine) 15 mg/kg i. p. once half an hour before test, ALC-200: WCFAIcE 200 mg/kg body weight p. o. once a day for 30 days, ALC-500: WCFAIcE 500 mg/kg body weight p. o. once a day for 30 days, ALC-1000: WCFAIcE 1000 mg/kg body weight p. o. once a day for 30 days

Mobility

As clarified from Table 1, the average mobility period by the mice in the FST decreased highly significantly ($P < 0.001$) on days 15, 23, and 30 for all the three doses of 200 mg/kg, 500 mg/kg, and 1000 mg/kg of WCFAlcE compared to control. Furthermore, the dose–response relationship was noted in this decrease. In contrast, for the standard highly significant increase was observed for the same.

Immobility

As clarified from Table 1, the average immobility period by the mice in the FST increased highly significantly ($P < 0.001$) on days 15, 23, and 30 for all the three doses of 200 mg/kg, 500 mg/kg, and 1000 mg/kg of WCFAlcE compared to control. Furthermore, the dose–response relationship was noted in this increase. In contrast, for the standard highly significant decrease was observed for the same.

DISCUSSION

As observed in Table 1, the average mobility period by the mice in the FST decreased highly significantly ($P < 0.001$) on days 15, 23, and 30 for all the three doses of 200 mg/kg, 500 mg/kg, and 1000 mg/kg of WCFAlcE compared to control. Furthermore, the dose–response relationship was observed for this decrease. In contrast, from Table 1, immobility period increased highly significantly ($P < 0.001$) for above doses on those days.

There are no former studies reported which studied *W. coagulans* effect on the FST in mice. However, Bhattacharya *et al.* demonstrated that *Withania somnifera* glycowithanolide (similar species as that of *W. coagulans*) decreased the forced swimming-induced immobility time in rodents.^[8] Furthermore, Kamdi *et al.* studied the antipsychotic activity of the alcoholic extract of *W. coagulans* fruits in Swiss albino mice in haloperidol-induced catalepsy.^[9]

FST is considered as the most reliable model of antidepressant screening.^[10] It is proposed that antidepressant drugs decrease the period of immobility.^[5] However, we used both the mobility and immobility time for the evaluation of our results. We have avoided the influence of depth and temperature of water which are the strength of our study. Depth of water had profound impact on the immobility period of mice; therefore, in our experiment, we used the water level of 15 cm so that mouse could touch the bottom neither with tail nor with legs.^[11] At higher temperature of 35°C immobility time of mice decreased, to avoid the impact of temperature, we kept the temperature of water at 25°C.^[12]

CONCLUSION

Although we have taken all the necessary precautions, we got the opposite effect of that of the antidepressant drugs.

It is possible that our test drug has a depressant effect on mood. Further, evaluation is required in the animal models of depression as the FST tests the antidepressant activity in the compound.

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