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RESEARCH ARTICLE

The antipsychotic activity of alcoholic extract of *Withania coagulans* fruits in Swiss albino mice in haloperidol-induced catalepsy

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ABSTRACT

Background: Psychosis is considered as the diminished relationship with reality. In this serious mental disorder, people suffering have hallucinations or delusions as prominent symptoms. The hallucinations are sensory involvements that arise in the absence of an actual stimulus, whereas the delusions are the thoughts that are contrary to actual evidence. The numerous neuroleptic medications used today are not devoid of the adverse drug reactions. The *Withania coagulans* (WC) - A susceptible species, is not explored much for its central nervous system effects except in late seventies. Therefore, it was thought worthwhile to investigate this plant further for its antipsychotic activity. **Aims and Objectives:** This study aims to investigate the antipsychotic activity of alcoholic extract of WC fruits in Swiss albino mice (SAM) in haloperidol-induced catalepsy. **Materials and Methods:** Haloperidol-induced catalepsy was the test used for assessing the antipsychotic activity of alcoholic extract at the doses of 200 mg/kg, 500 mg/kg, and 1000 mg/kg of WC fruits in SAM. **Results:** There was statistically ($P > 0.05$) no significant association between alcoholic extract of WC fruits at the doses of 200 mg/kg, 500 mg/kg, and 1000 mg/kg with antipsychotic activity in SAM in haloperidol-induced catalepsy. **Conclusion**: Alcoholic extract of WC fruits did not demonstrate antipsychotic activity in haloperidol-induced catalepsy in SAM.

KEY WORDS: Antipsychotic; Swiss Albino Mice; Alcoholic Extract; *Withania coagulans*; Catalepsy

INTRODUCTION

Psychosis is considered as the diminished relationship with reality.[1] People suffering from psychosis have hallucinations or delusions as prominent symptoms.[2,3] The hallucinations are sensory involvements that arise in the absence of an actual stimulus.[4] The delusions are the thoughts that are contrary to actual evidence.[5] Some people with psychosis may also experience loss of motivation and social withdrawal.[6]

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There are numerous antipsychotic remedies available for the cure of schizophrenia. Yet these medications cause parkinsonism like adverse drug reactions in human. The cataleptic signs in rodents can be matched to the Parkinson-like extrapyramidal adverse effects in human seen clinically with administration of antipsychotic medicines.[7] Catalepsy is defined as a nervous condition having persistent rigidity of the limbs, mutism, complete inactivity, fixed posture, and decreased sensitivity to pain regardless of outside stimuli.[8] Mechanism of catalepsy is to obstruct dopamine D2 receptors and to deliver a state of catalepsy in animals by decreasing dopaminergic transmission in basal ganglion. Thus, the phenomenon of catalepsy can be used for assessing the effectiveness and the possible adverse effects of neuroleptics.

Withania coagulans (WC) is rarely found and so it is considered as *"Vulnerable* species."[9] Consequently, not

considerable work is executed on this plant to see the influence on the brain. In 1977, Budhiraja *et al*. reported central nervous system (CNS) depressant activity of this plant.[10] Afterward, this plant was not at all explored for the CNS activity, though plenty of work was completed on diabetes and other diseases. Therefore, it was thought valuable to scrutinize cataleptic antipsychotic activities of WC.

MATERIALS AND METHODS

Haloperidol-Induced Catalepsy

Catalepsy was produced by injection haloperidol 1 mg/kg intraperitoneally half an hour after the pretreatment with test drug or half an hour after pretreatment with vehicle (distilled water) for control. Both the front limbs of the mice were placed over 4.5 cm high wooden block and the time for which animal maintained the cataleptic posture was measured. The end point of catalepsy was considered when both front paws were removed from the bar or if the animal moved its head in an exploratory manner. First, the time period for which mouse maintained the cataleptic posture was recorded. Later, this period was converted into cataleptic scores by modified method of Costall and Naylor as follows: [11]

Time	Score
0–10 s	0
11–30 s	1
31–60 s	2
1–2 min	3
>2 min	4.

Control, Standard, and Test Drugs

Distilled water was given as vehicle for control. The animals were treated (30 min before haloperidol administration) with the test drugs (WC fruits alcoholic extract (WCFAlcE) 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. Recordings were done on day 1, day 15, and day 30 for all the groups. The recordings were taken at 1/2 h, 1 h, 2 h, and 4 h after haloperidol 1 mg/kg administration to the respective groups.

Drugs were given in the following manner:
Control: Vehicle (distilled water) 2 mL/kg p. o. once a day for 30 days

ALC-200: WCFAlcE 200 mg/kg p. o. once a day for 30 days

ALC-500: WCFAlcE 500 mg/kg p. o. once a day for 30 days

ALC-1000: WCFAlcE 1000 mg/kg p. o. once a day for 30 days

Where, WCFAlcE = WC fruits alcoholic extract.

Ethical approval

A study was approved by the Institutional Ethics Committee of Mahatma Gandhi Institute of Medical Sciences, Sevagram (MGIMS)

RESULTS

As the haloperidol was used to induce the catalepsy, therefore, there was no standard to compare with the test drugs. Therefore, the test drugs of ALC-200, ALC-500, and ALC-1000 were compared with the control only. As shown in Table 1, on day 1, there was no statistically significant effect on haloperidol-induced catalepsy. Although ALC-200 and ALC-500 showed the increasing trend of catalepsy scores on ½ h to 4 h, it was statistically not different. In contrast, for the ALC-1000 starting from the ½ h to 2 h, it showed increasing trend on day 1, but up till 4 h, the trend decreased and it was no different statistically from that of control.

As shown in Table 1, on day 15, there was no statistically significant effect on haloperidol-induced catalepsy. Although ALC-200 and ALC-500 showed the increasing then decreasing trend of catalepsy scores on ½ h to 4 h, it was statistically not

Table 1: Effect of oral administration of WCFAlcE on catalepsy scores

Treatment	Control	ALC-200	ALC-500	ALC-1000
Day 1				
½ h	1.33±0.51	2.00±1.41	2.50±1.04	1.66±0.81
1 h	3.00±0.63	2.33±1.21	2.50±1.04	2.50±0.54
2 h	2.50±1.04	2.50±1.04	2.83±1.16	3.50±0.54
4 h	3.33±1.21	2.66±1.03	2.83±1.16	3.00±0.3
Day 15				
½ h	1.00±0.89	2.50±1.64	2.33±1.86	2.33±1.62
1 h	3.16±0.75	3.16±0.75	3.00±1.09	3.33±1.21
2 h	2.16±0.98	1.83±0.75	2.16±1.16	3.33±0.81
4 h	2.50±1.37	2.66±0.81	2.50±1.04	3.16±0.75
Day 30				
½ h	2.00±1.09	2.16±1.47	2.66±1.50	2.00±1.09
1 h	3.33±1.21	2.66±1.21	2.83±1.16	3±1.09
2 h	2.83±1.16	2.83±1.16	2.83±1.16	3.33±0.81
4 h	3.00±1.26	3.00±1.26	2.66±1.21	3.33±1.21

*P<0.05, **P<0.01, and ***P<0.001 when compared to control group, WCFAlcE: WC fruits alcoholic extract, Control: Vehicle (distilled water) 2 ml/kg p. o. once a day for 30 days, ALC-200: WCFAlcE 200 mg/kg body weight p. o. once a day for 30 days, ALC-500: WCFAlcE 500 mg/kg body weight p. o. once a day for 30 days, ALC-1000: WCFAlcE 1000 mg/kg body weight p. o. once a day for 30 days

different ($P > 0.05$). Similarly, for the ALC-1000 starting from the ½ h to 1 h, it showed increasing trend, thereafter it remained stationary from 1 h to 2 h, after that until 4 h, the trend decreased and there was no difference statistically from that of control.

As shown in Table 1, on day 30, there was no statistically significant effect on haloperidol-induced catalepsy as well. For the dose of ALC-200, though there was increasing trend of catalepsy scores on ½–4 h, it was statistically not significant. For the dose of ALC-500, catalepsy score increased from 2.66 at ½ h to 2.83 at 1 h remained stationary at 2 h but came back to 2.66 at 4 h. It was statistically insignificant ($P > 0.05$). For the dose of ALC-1000, it showed increased trend up to 2 h but was stationary by 4 h. This was not different than that of controls too.

DISCUSSION

As observed in Table 1, there was statistically no significant difference in the catalepsy scores on ½ h, 1 h, 2 h, and 4 h with all the three doses of 200 mg/kg, 500 mg/kg, and 1000 mg/kg of WCFAlcE compared to control on day 1, day 15, and day 30.

There are no previous articles reported which studied the WC effect on the haloperidol-induced catalepsy in rodents. However, Kumar and Kulkarni showed that the polyherbal formulation of *Withania somnifera* (WS) (similar species as that of WC) significantly ($P < 0.05$) blocked the haloperidol-induced catalepsy in mice.[12] As very few scientific studies have been reported on the effect of WC on CNS, so we had to rely on data available on WS which belongs to the same genus. We have got no actions for antipsychotic activity which is difficult to explain based on the current studies including ours. As WC contains some withanolides like coagulin, coagulanolides, withacoagulin, coagulins B-S which are not present in WS can explain difference of action between two species of same genus.[13]

The antipsychotic agents which increase the dopamine transmission will inhibit the haloperidol-induced catalepsy.[14] In contrast, the agent which has antidopaminergic activity will potentiate the haloperidol-induced catalepsy.[15,16] Our test drug neither increased nor decreased the neuroleptic-induced catalepsy. However, further studies are warranted based on the mechanism of action on dopamine receptors to understand this limitation. More detailed studies involving individual withanolides and also specifically targeted neurotransmitters responsible for individual actions can through light on the neuropharmacological profile of the plant under consideration. Thus, we can conclude that our test drug does not have any activity on the dopamine receptors.

CONCLUSION

Alcoholic extract of WC fruits did not demonstrate antipsychotic activity in haloperidol-induced catalepsy in Swiss albino mice.

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