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Neuroprotective effect of barringtonia Racemosa on haloperidol induced catalepsy in experimental animal model

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***Abstract*---**Barringtonia racemosa L. (Lecythidaceae) is an ancient and mangrove associate plant. It possesses antidepressant activity, antioxidant activity, anti-inflammatory activity, antidiabetic activity and antifungal activity. In the present study, we investigated the anticataleptic activity of extract of Barringtonia racemosa fruit on haloperidol induced catalepsy in rats. Chloroform extract of Barringtonia racemosa fruit was prepared and evaluated for anti-cataleptic property. The rats were divided into 4 groups (n=6). Group I is served as control. Group II [(haloperidol 1.0 mg/kg body weight, i. p. in Haloperidol induced catalepsy (HIC)]. Group III (CEBR, 200 mg/kg body weight, p. o.). Group IV (CEBR, 400 mg/kg body weight respectively p. o.). The anti-cataleptic effect of Barringtonia racemosa, was evaluated by locomotor activity and rota rod test using rat models. Barringtonia racemosa extract (200 and 400 mg/kg body weight, p. o.) was found to decrease the duration of catalepsy significantly ($P < 0.01$) in standard bar test as compared to haloperidol group. Comparatively, CEBR (400 mg/kg body weight, p. o.) was more potent anti-cataleptic activity than CEBR (200 mg/kg body weight, p. o.).

***Keywords*---**anticataleptic activity, haloperidol, powderpuff, barringtonia racemosa.

Introduction

Neurodegenerative diseases are appearing as a major threat in the future because of increasing mental stress, work load and strain which seem to be absolutely necessary in day today life. A neurodegenerative disease is caused by the

progressive loss of structure or function of neurons. Some factors like atmospheric pollutants, toxins also cause neurodegenerative diseases like Parkinson's disease and Alzheimer's disease.[1] These diseases are recognized by symptoms like tremor, slowed movement, rigid muscles, impaired posture and balance, loss of automatic movements.[2] Catalepsy is a condition in which the animal maintains imposed posture for long time before regaining the normal posture. Catalepsy is a sign of extrapyramidal effect of drugs that inhibit dopaminergic transmission or increase histamine release in brain.[3] Neuroleptic induced catalepsy has long been used as a model for the Parkinson. In counteracting the catalepsy induced by haloperidol Anticholinergic drugs are most effective in experimental animals. But these anti-cholinergic drugs produce various side effects like dryness of mouth, constipation and urinary retention. Hence an alternate for newer drugs with fewer side effects is on-going. Many medicinal plants have been associated with the prevention of neurodegenerative diseases.[4] *Barringtonia* racemosa L. (Lecythidaceae) is an ancient and mangrove associate plant. It is widely distributed in Eastern Africa and Asia. *Barringtonia racemosa* has been used in traditional Asian medicine. It is commonly known as Powderpuff Mangrove.[5] The *Barringtonia racemosa* fruit has traditionally been used for the treatment of cough, asthma and diarrhoea. An active components of *Barringtonia racemosa* fruit have been identified and isolated such as Bartogenic acid.[6] It possesses antidepressant activity, antioxidant activity, anti-inflammatory activity, antidiabetic activity and antifungal activity. Keeping in view of the antidepressant activity and antioxidant activity of the *Barringtonia racemosa* fruit, the present has been designed in order to investigate the anti-cataleptic effect of the herbal drug using animal models.

Materials and Methodology

Materials

The *Barringtonia racemosa* fruit were collected from Konkan costal region. This material was identified and authenticated by Dr. H. M. Pandit, Formerly Head and Associate Professor of Botany; Andheri (west), Mumbai, India and a specimen no. is bak p 11193354. The fruit of *Barringtonia racemosa* was reduced to coarse powder manually, powder pretreated with hexane and extracted by Soxhlet extraction method to obtain chloroform extract of *Barringtonia racemosa* (CEBR). Haloperidol was procured from RPG Life Sciences Ltd. The other chemicals and solvents used in the extraction were of analytical grade. Albino wistar male rats (120-150 gm) were used for the Pharmacological activities. The animals were given standard diet. A study was approved by the Institutional Ethics Committee of TVES HLMC College of Pharmacy, Faizpur.

Methodology

Haloperidol is used as inducing agent. Haloperidol (1.0 mg/kg, i.p) was administered daily to the rats for a period of 15 days to induce catalepsy. Plant extract was administered orally 30 min before to haloperidol treatment. Albino wistar male rats weighing 120-150 gm was divided into four groups of six animals each (n=6) as

- Group I: The animals served as control.
- Group II: The animals served as negative control (haloperidol 1.0 mg/kg, i.p)
- Group III: The animals served as low dose of CEBR (haloperidol 1.0 mg/kg, i.p and treated with
- CEBR 200 mg/kg, p.o)
- Group IV: The animals served as high dose of CEBR (haloperidol 1.0 mg/kg, i.p and treated with
- CEBR 400 mg/kg, p.o)

Behavioural parameter

Evaluation for behavioural parameters such as locomotor activity (Actophotometer) and motor coordination (Rotarod test) has conducted. [7,8,9] The actophotometer is used for measuring locomotor activity. An actophotometer consists of a cage with six lights and six photocells positioned in the outer bottom periphery so that only one beam is blocked at a time by single rat. When the light rays fall on the photocells, photocells get activated. The light beam is interrupted when the animal crosses the light beam; the number of cut-off interruptions has been recorded for 10 minute. The effect on locomotor activity was measured for 10 min at every 30 min upto 2 hours using actophotometer. Using a Rotarod apparatus, a motor coordination test was performed. [10,11,12] The rotarod apparatus consists of a motor rod with a drum of 7.0 cm diameter. During the test session, it was adjusted to a speed of 20 rpm. The latency to fall in a test session of 180 s was taken as a measure of motor coordination. All the animals were previously trained to remain on the rod rotating at the speed of 20 rpm for a period of 5 min. On the next day all the groups were treated with respective doses & groups were challenged with haloperidol as per the treatment protocol except the normal group & the time required to fall off the rotating rod was noted for each animal. Recording was taken on day 2, day 8 and day 15 for all groups.

Cataleptic Behavior

Catalepsy was measured by means of a standard bar test, as the time during which the animal maintained an imposed position with both front limbs raised and resting on wooden bar (diameter 1 cm), suspended 4 cm above the table top. The end point of catalepsy was considered to occur when both front paws were removed from the bar or if the animal moved its head in an exploratory manner. The intensity of catalepsy was assessed by counting time in seconds until the mouse brought both forepaws down to the table top, with a maximum cut-off time of 180 s. Animals would be judged to be cataleptic if they maintained this position for 30 s or more. [13,14] Catalepsy score was measured for each hour upto 4 hours for all groups.

Result

In the Actophotometer, the animals treated with haloperidol (1.0 mg/kg, i.p) alone for 15 days showed a significant ($P < 0.001$) increase in locomotor activity on 15 day when tested at different time intervals. CEBR was evaluated for effect on locomotor activity in rat using bar test on the 15 days. It was observed that there was a significant reduction ($p < 0.01$) in the cataleptic behaviour between 60 and

120 min with the low dose of test extract (200 mg/kg body weight) as compared to the positive control. CEBR at high dose (400 mg/kg body weight *p.o.*) showed a significant reduction in the locomotor activity between 30 to 120 min when results were compared to control ($p < 0.01$) and disease control ($p < 0.01$). The values were shown in the table no 1.

Table 1
Effect of CEBR on locomotor activity

Groups	Number of movements per 10 min.			
	30 min	60 min	90 min	120 min
I	316.17 ± 1.49	322.17 ± 0.70	330.17 ± 0.31	334.67 ± 0.33
II	265.67 ± 0.84	260.33 ± 0.42	249.17 ± 0.48	232.67 ± 0.84
III	286.33 ± 0.49	296.83 ± 0.60**	306.67 ± 0.49**	317.67 ± 0.84**
IV	296.67 ± 0.49**	308.33 ± 0.42**	315.83 ± 0.40**	327.67 ± 0.56**

Values are expressed as Mean ± SEM, (n=6). Statistical analysis was performed by using ANOVA followed by Dunnett's test. Results were compared with control group (** $p < 0.001$), disease control (** $p < 0.001$).

In the rotarod apparatus, the animals treated with haloperidol (1 mg/kg, i.p) for 1, 8 and 15 day showed a significant ($P < 0.001$) decrease in fall off time on 15 day when tested. It was observed that there was a significant raise ($p < 0.01$) in fall off time with the low and high dose of test extract (200 and 400 mg/kg body weight) as compared to the positive control. The values were shown in the table no 2.

Table 2
Effect of CEBR on muscle rigidity (Rota rod test)

Groups	Fall off time in secs			
	0 Day	2 Day	8 Day	15 Day
I	125.83 ± 0.60	125.67 ± 0.33	125.33 ± 0.33	125.67 ± 0.31
II	126.17 ± 0.17	118.17 ± 0.48	62.83 ± 0.79	56.83 ± 0.40
III	126.33 ± 0.21	124.67 ± 0.71	101.67 ± 1.12	88.33 ± 0.33**
IV	125.83 ± 0.31	124.83 ± 0.67	114.67 ± 0.61	94.83 ± 0.48**

Values are expressed as Mean ± SEM, (n=6). Statistical analysis was performed by using ANOVA followed by Dunnett's test. Results were compared with control group (** $p < 0.001$), disease control (** $p < 0.001$).

In the standard bar test, the animals treated with haloperidol (1 mg/kg, i.p) for 15 days showed a significant ($P < 0.001$) increase on 15 days when tested at different time intervals. CEBR was evaluated for catalytic behavior in rat using bar test on the 15 days. It was observed that there was a significant reduction ($p < 0.01$) in the cataleptic behavior between 60 and 180 min with the low dose of test CEBR (200 mg/kg body weight) as compared to the positive control. CEBR at high dose (400 mg/kg body weight *p.o*) showed a significant reduction in the cataleptic behaviour between 60 to 240 mins when results were compared to standard ($p <$

0.01) and disease control (p <0.01). The values were depicted shown in the table no 3.

Table 3
Effect of CEBR on catalepsy (Standard bar test)

Groups	Cataleptic Score (in secs)			
	60 min	120 min	180 min	240 min
I	15.67 ± 0.21	15.17 ± 0.31	15. ± 0.26	14.83 ± 0.33
II	166.33 ± 1.48	173.17 ± 0.91	176.17 ± 0.40	183.67 ± 1.23
III	147.83 ± 0.31**	143.33 ± 0.49**	135.83 ± 0.31**	125.33 ± 0.49
IV	157.67 ± 0.42**	161.17 ± 0.31**	168.33 ± 0.33**	175.83 ± 0.40**

Values are expressed as Mean ± SEM, (n=6). Statistical analysis was performed by using ANOVA followed by Dunnett's test. Results were compared with control group (** p < 0.001), disease control (** p < 0.001)

Discussion

Neurodegenerative disorder are characterized by degeneration of dopamine producing neurons in the substantia nigra leading to resting tremor, bradykinesia, shuffling gait, flexed posture and rigidity. Still, the cause of the degeneration is not well defined. The models of Parkinson's disease are characterized by measures of akinesia, such as in bar test for immobility. Neuroleptics such as haloperidol can produce a sustained but reversible akinesia, due to blockade of dopamine D2 receptors. Neuroleptics like haloperidol induced catalepsy in rats were used to evaluate the drugs for their anti-cataleptic activity. In the present study, the CEBR was screened for its effect in haloperidol induced catalepsy in rat. In the present study behavioural parameters were evaluated using actophotometer, rota rod test and standard bar test apparatus to assess the haloperidol induced catalepsy in rat. The animals which were treated for 15 days with haloperidol showed severe cataleptic responses along with alleviated locomotor and motor coordination. The group treated with CEBR at a dose 400 mg/kg showed normal locomotor activity and motor coordination without any cataleptic behavior when compared with the haloperidol-treated group. The group treated with 200 mg/kg of CEBR showed some cataleptic behavior when compared to CEBR at a dose of 400 mg/kg treated group. Anti-cataleptic activity of CEBR might be due to the action on dopaminergic transmission, and on D2 receptors and therefore increases the dopamine levels.

Conclusion

It can be concluded that the *Barringtonia racemosa* extract was found to be effective in reducing cataleptic scores in rat model of haloperidol induced catalepsy. This study suggests that the test drug can be used as an alternative agent in preventing the haloperidol/neuroleptics induced extrapyramidal symptoms in parkinsonian patients. Hence concluded that the extracts of *Barringtonia racemosa* exert good neurodegenerative activity. Further studies are to be designed to explore and understand the bio-actives present in respective

extracts. Also, activity guided fractionation can be performed to identify the potential bioactive from the plant.

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