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MEMORY ENHANCING ACTIVITY OF *BARRINGTONIA ACUTANGULA (L.)* 0N CORTICOSTERONE INDUCED DEMENTIA IN MICE

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ABSTRACT

The present study was undertaken to investigate the effects of *Barringtonia acutangula (L.)* on learning and memory in mice. Morris water maze and passive avoidance paradigm were employed to test learning and memory. Two doses (100 and 200mg/kg, p.o.) of methanolic extract were administered for 21 successive days in separate group of animals. The dose of 200 & 400-mg/kg p.o. of EEBA significantly improved learning and memory of mice in dose dependent manner. Furthermore, this dose significantly reversed the amnesia induced by Corticosterone (5 mg/kg, s.c) induced amnesia. Hence *Barringtonia acutangula (L.)* appears to be a promising candidate for improving memory and it would be worthwhile to explore the potential of this plant in the management of dementia and Alzheimer's disease. However, further studies are necessitated to identify the exact mechanism of action.

Keywords: *Barringtonia acutangula (L.),* Alzheimer's disease.

INTRODUCTION

Alzheimer's disease is a progressive neurodegenerative brain disorder that is slow in onset but leads to dementia, unusual behavior, personality changes and ultimately death. Alzheimer's disease is characterized by acetylcholine depletion, amyloid β protein aggregation, and neurofibrillary tangle. The neurotransmitter acetylcholine has important recognition functions such as memory, and it is synthesized in certain neurons by the enzyme choline acetyltransferase from choline and acetyl-CoA. Acetylcholinesterase (AChE) is an enzyme that hydrolyses acetylcholine into choline and acetate. Therefore, it promotes dementia by loss of neurotransmitter in the brain. A decrease in acetyl choline in the brain of patients with Alzheimer's disease appears to be a critical element in producing dementia.

The cause of Alzheimer's disease is not known clearly. Recently, the mainstay treatments for the Alzheimer's disease are acetylcholinesterase inhibitor which increases the availability of acetylcholine at cholinergic synapses. AChE inhibitors from general chemical classes such as physostigmine, tacrine, galantamine and heptylphysostigmine have been tested for the symptomatic treatment of Alzheimer's disease. However, non-selectivity of these drugs, their limited efficacy, and poor bioavailability, adverse cholinergic side effects in the periphery, narrow therapeutic ranges and hepatotoxicity are among the severe limitations to their therapeutic success. Therefore it is worthwhile to explore the utility of traditional medicines for the treatment of various cognitive disorders [1-10].

Barringtonia acutangula (L.) Gaertn. (*Family*: Lecythidaceae) an evergreen tree of moderate size is called as Hijja or Hijjala in Sanskrit. The fruit is spoken of as samudra-phala and various part of this plant used as a folklore medicine for curing various ailments like

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hemiplegia, pain in joints, eye diseases, stomach disorders, anthelmintic, diarrhoea, cough, dyspnoea, leprosy, intermittent fever, and spleenic disorders. An aqueous extract of the bark is found hypoglycemic and is reported to be used in pneumonia, diarrhea, asthma and leaf juice is given for diarrhea. Fruit is bitter, acrid, anthelmintic, emetic, expectorant and vulnerary. It is prescribed in gingivitis, as an astringent and tonic. Whole plant was reported to possess flavonols, phenolic acids, triterpenoids, tannins and steroidal compounds such as barringtogenic acid, tangulic acid and acutangulic acids. The fruit possessed saponins based on barringtogenol B, C and D. The therapeutic potential of this plant were reported to be antitumor, antibiotic, inhibit growth of Helicobacter pylori and antifungal activities [11-17].

Therefore, the present study was performed to verify the memory enhancing effect of *Barringtonia acutangula (L.)* on mice.

MATERIALS AND METHODS

Plant material

The leaves of *Barringtonia acutangula* was collected from Tirumala hills, Tirupati, Andhra Pradesh. India. The plant was identified and authenticated by Dr.K.Madhava Chetty, Department of botany, S.V.University, Tirupati. The voucher specimen of the plant was deposited at the college for further reference. The leaves were dried under shade, powdered and stored in an air tight container.

Preparation of extract

The collected leaves were dried at room temperature, pulverized by a mechanical grinder, sieved through 40mesh. About 120g of powdered materials were extracted with ethanol (90%) using soxhlet apparatus. The extraction was carried out until the extractive becomes colourless. The extracts is then concentrated and dried under reduced pressure. The solvent free semisolid mass thus obtained is dissolved in normal saline and used for the experiment. The percentage yield of prepared extract was around 10.5%w/w.

Phytochemical analysis

The ethanol extract of *Barringtonia acutangula* was subjected to qualitative analysis for the various phyto-constituents. Standard methods were used for preliminary qualitative phytochemical analysis of extract [18].

Animals used

Male albino mice (30-40g) were obtained from the animal house in A.M.Reddy Memorial College of Pharmacy, Narasaraopet, Guntur, Andhra Pradesh. The animals were maintained in a well-ventilated room with 12:12 hour light/dark cycle in polypropylene cages. The animals were fed with standard pellet fed (Hindustan Level Limited, Bangalore) and water was given *ad libitum*. Ethical committee clearance was obtained from IAE (Institutional Animal Ethics Committee) of CPCSEA.

Treatments

Animals were divided into four groups, each consisting of six male albino mice. The methanol extract of *Barringtonia acutangula (L.)* was blackish oily extract divided into two doses EEBA-200mg/kg, EEBA-400mg/kg given orally daily for 21 days, 30 min before Corticosterone injection. Corticosterone (VHB lifesciences, 5mg/kg) was dissolved in absolute ethanol and subsequently diluted in water to the final concentration of 10% ethanol and injected subcutaneously in a volume 1ml/kg [19-21].

Group – I: Normal control mice administered normal saline (0.9% w/v),

Group – II: Disease control administered Corticosterone inj subcutaneously (5mg/kg).

Group – III: Corticosterone + EEBA 200mg/kg,

Group – IV: Corticosterone + EEBA 400mg/kg given orally for 21 days, 30min before Corticosterone administration.

Morris Water Maze Test

The modified procedure from morris (Morris, 1989). The Morris water maze is a circular pool (90cm in diameter and 45cm in height) with featureless inner surface. The circular pool was filled to a height of 30cm with water (18 ± 1°C), in which 500ml of milk was mixed. A white platform (6cm in diameter and 29cm I height) was centered in one of four quadrants of the pool (Southest area) and submerged 1cm below the water surface so that it was invisible at water level. In the water maze experiments the first week of the experiment was dedicated to swimming training for 60s. All animals were four groups we investigated the 3 weeks for treatment.

In these days the mice were given one session of two trails each day for 21 days. During each trial, the mouse's escape latency, measured with a stop watch, were recorded. The parameter was averaged for each session of trials and for each mouse. One the mouse located the platform, it was permitted to remain on it for 10s. If the mouse did not locate the platform within 120s, it was placed on the platform for 10s. During this period, the platform was located in a fixed position.

In the last day of training, mice were given a probe trial which considered of removing the plat form from the pool and allowing the mice to swim for 60's in search of it. A record was kept of the swimming time in the pool quadrant where the platform had previously been placed. Solutions of EEBA were given orally 30min prior to the consective training [22].

Passive Shock Avoidance Paradigm

Passive Avoidance behavior based on negative reinforcement was used to examine the long term memory.

The apparatus consisted of a box (27x27x27cm) having three walls of wood and one wall of plexi glass featuring a grid floor (3mm stainless steel rods set 8mm apart), with a wooden platform (10x7x1.7cm) in the center of a grid floor. The box was illuminated with a 15W bulb during the experimental period; electric shock (20VAC) was delivered to the grid floor. Training was carried out in two similar sessions. Each mouse was gently placed in the wooden platform set in the center of the grid floor. When the mouse stepped down and placed on the wooden platform set in the center of the grid floor.

When the mouse stepped down and placed all its paws on the grid floor, shocks were delivered for 15 sec and the step down latency (SDL) was recorded. SDL was define as the time taken by the mouse to step down from wooden platform to grid floor with its entire paw on the grid floor, animals showing SDL in the range (2-15 sec) during the first test were used for the second session and the retention test. The second-session was carried out 90min after the first test. When the animals stepped down before 60sec, electric shocks were delivered for 15sec. During the second test, animals were removed from the shock free zone if they did not step down for a period of 60sec. Retention was tested after 24h in similar manner, except that the electric shocks were not applied to the grid floor. Each mouse was again placed on the platform, and the SDL was recorded, with an upper cut-off time of 300sec.

In this passive avoidance shock test we devided four groups of animals. Group-I: Normal control group for mice (n=6), normal saline (0.9% w/v) was administered P.O. for 8 days. After 90 min of administration on 8th day, SDL was recorded retention was examined after 24h, Group-II and Group-III (n=6 each); EEBA (200 and 400mg/kg) respectively orally for 8 days. SDL was recorded after 90 min of administration on 8th day and after 24h. In this 30 min before corticosterone inj administration subcutaneously. Group-IV: Corticosterone (5mg/kg) was administered subcutaneously in the negative control mice for upto 8 days continuously and 8th day SDL was recorded, retention was examined after 24h [23,34].

Statistical analysis

The statistical significance of the results of Morris water maze as well as passive shock avoidance tasks were analysed using ANOVA, followed by Tukey-Krammer multiple comparison test, the P values <0.05 were considered as significance.

RESULTS

Morris water maze test

The methanol extract of *Barringtonia acutangula (L.)* (EEBA) showed the significant activity in 21 days study. Saline treated control mice rapidly learned the location of the submerged platform at 21st day compared 0thday, Corticosterone inj (5mg/kg) group memory impairment was rapidly increased significantly (P<0.001) from 0 to 21st day compare to saline treated control. EEBA treated mice (200 and 400mg/kg) found the platform significantly (P<0.001) earlier than Corticosterone injected mice and also significantly (P<0.001) than saline treated control from 6th day to 21st day (Table 1).

Passive Shock Avoidance Paradigm

In this passive Avoidance model the higher dose of EEBA-400mg/kg pretreatment for 8 days successively protected mice (P<0.001) against Corticosterone induced memory impairment. The step down latency (SDL) of Corticosterone injected mice was significantly (P<0.001) poor when compared to that of saline treated mice (Table 2). EEBA (400mg/kg P.O) profoundly increased step-down latency (SDL) significantly (P<0.001) compared to saline treated mice, indicating improvement in memory. EEBA (200mg/kg P.O) increased SDL significantly (P<0.001) compared to saline treated mice and lesser than EEBA (400mg/kg P.O) treated group.

Table 1. Effect of *Barringtonia acutangula (L.)* transfer latencies of mice on morris water maze test

Groups	Treatment	Transfer Latency							
		0	3	6	9	12	15	18	21
I	Normal control	13.14± 0.12	11.05± 0.21	11.05± 0.13***	9.28± 0.10***	7.12± 0.16***	7.44± 0.21***	8.56± 1.22***	9.18± 0.32***
II	EEBA 200mg/kg	7.33± 0.24	8.17± 0.74	10.51± 1.3***	13.57± 0.14***	11.22± 1.14***	9.34± 1.12***	7.34± 0.24***	7.14± 0.22***
III	EEBA 400mg/kg	6.52± 0.32	9.45± 0.24	11.31± 0.21***	11.15± 0.21***	9.51± 0.22***	8.24± 0.27***	7.62± 0.24***	7.42± 0.21***
IV	Corticosterone	7.19± 0.33	12.17± 0.12	23.5± 1.17	34.24± 1.24	47.13± 1.15	56.21± 1.12	65.21± 1.26	68.23± 1.12

Values are expressed as mean±SEM, ANOVA followed by Tukey-Krammer multiple comparision test, 6 male albino mice in each group. *** P<0.001, as compared to corticosterone injected group.

Table 2. Effect of *Barringtonia acutangula (L.)* on step down latency (SDL) using passive avoidance apparatus.

Group	Treatment	Dose (mg/kg)	SDL after 24h (score/sec±SEM)
I	Normal saline	---	110.54±4.28
II	EEBA	200	192.33±4.23***
III	EEBA	400	253.46±4.52***
IV	Corticosterone	5	22.19±2.18***

Values are expressed as Mean ± SEM, ANOVA followed by Tukey-Krammer multiple, 6 male albino mice is comparison test each group.***P<0.001, as compared to control.

DISCUSSION AND CONCLUSION

In this study, memory was assessed using Morris water maze and the Step-down Avoidance test. The effect of *Barringtonia acutangula (L.)* on memory impairment induced by Corticosterone in male albino mice was performed by using methanol extract; Corticosterone significantly impaired other forms of hippocampus-dependent memory such as object recognition and retrieval of the passive avoidance behavior. Corticosterone, the predominant glucocorticoid in rodents, chronic administration of Corticosterone it damages hippocampal subregion CA_3 that leads to impair spatial memory. Also chronically elevated levels of Corticosterone inj administration is mice for 21 days can produce neuronal atrophy and cell death in the hippocampus while leaving other brain regions, the elevated levels of Corticosterone changes in various neurotransmitters such as catecholamines, serotonin and γ-amino butyric acid (GABA) in several brain structures. In the hippocampus Corticosterone impairs GABA-mediated inhibitory neurotransmission and causes neurodegeneration via diminished expression of $GABA_A$ receptors. High amounts of corticosterone enhance action of norepinephrine (NE) via β-adreno receptors and increased dopamine (DA) turnover in prefrontal cortex is accompanied by the decreased spatial memory performance [20-22].

In this study we investigated the two memory assessment behavioral model, Morris water maze test and passive avoidance paradigm in both models the methanol extract of *Barringtonia acutangula (L.)* showed significant activity on memory impairment induced by chronic administration of Corticosterone 5mg/kg subcutaneously into the male albino mice. In this morris maze test chronically elevated levels of Corticosterone administered for 21 days that leads to memory impairment occurs in the hippocampal subregion. This can be overcome by the EEBA treated (200 and 400mg/kg) two groups showed significant action compared to saline treated mice and only Corticosterone treated mice, Corticosterone treated mice showed increasing latency period due to memory impairment. In the treatment 0^{th} day to 1^{st} day there is no action on the mice.

In the passive avoidance paradigm Corticosterone injected mice showed decreased step down latency compared to saline treated mice after 24 hours later. In this continuously 8 days cortecosterone occurs. The EEBA treated (200 and 400mg/kg) showed significant activity and increasing the SDL after 24 hours compared to normal as well as Corticosterone treated mice the higher dose of EEBA (400mg/kg P.O) pretreatment for 8 days successively protected mice against Corticosterone induced memory impairment. The higher dose of EEBA (400mg/kg P.O) increased the SDL after 24 hours then the EEBA treated (200mg/kg P.O) group [21-25].

The plant *Barringtonia acutangula (L.)* contain rich flavonoids can effects the neurotransmitters and acetylcholinesterase activity in the brains of rodents treated with scopolamine inducing dementia. Oxygen-free radicals and other products of oxidative metabolism have been shown to be neurotoxic. The protective effect of *Barringtonia acutangula (L.)* extract may be attributed to antioxidant property due to rich in flavonoids by virtue of which susceptible brain cells get exposed to less oxidative stress resulting in reduced brain damage and improved neuronal function there by enhancing the memory. There conditions were showed the neuroprotective role of methanol extract of *Barringtonia acutangula (L.)* Corticosterone induced memory deficits.

It is concluded from the current study, that the methanol extract of *Barringtonia acutangula (L.)* possess significant Memory enhancing activity and may prove to be effective for the treatment of dementia and other cognitive disorders. However further studies required to elucidate the exact mechanism of action for develop its as potent memory enhancing drug. These natural memory enhancing drugs will help to develop new drug candidates for dementia therapy.

REFERENCES

1. Yalla Reddy K, Mohana Lakshmi S, Saravana Kumar A. Review On Effect Of Natural Memory Enhancing Drugs On Dementia. *International Journal of Phytopharmacology*, 1(1), 2010, 1-7.
2. Amzad Hossaina M, Raj Nagoorub M, Abdullah Bin Gansau J. New flavone from the Leaves of local medicinal plant *Corydyline terminalis* kunth. *International Journal of Biological & Pharmaceutical Research*, 3(2), 2012, 223-226.

3. Uma S, Kavimani S, Raman KV. Effect of Saraswatarishta on learning and memory. *International Journal of Phytopharmacology*, 1(1), 2010, 15-19.
4. Yalla Reddy K, Saravana Kumar A, Mohana Lakshmi S, Surendar Angothu. Antioxidant properties of methanolic extract of *oxalis Corniculata. International Journal of Phytopharmacology*, 1(1), 2010, 43-46.
5. Prakash Yoganandam G, Ilango, Diptanu Biswas K. Herbal medicine–an overview of adverse reactions and Interaction with food and drugs. *International Journal of Phytopharmacology*, 1(2), 2010, 53-56.
6. Amritpal Singh, Sanjiv Duggal, Asish Suttee, Aswinder Singh, Shankar Katekhaye. *Eclpita alba* linn. - ancient remedy with therapeutic Potential. *International Journal of Phytopharmacology*, 1(2), 2010, 57-63.
7. Parija SC, Behera, Bisoi PC. HPTLC Detection of polyphenols and flavonoids of *Careya arborea* leaves and study of antimicrobial effect. *International Journal of Phytopharmacology*. 3(1), 2012, 36-41.
8. Ambawade SD, Kasture VS, Kasture SB, Anxiolytic activity of Glycyrrhiza glabra linn. *Journal of natural remedies*, 2, 2009, 130-134.
9. Amritpal Singh. Review of ethnomedicinal uses and pharmacology of *Evolvulus Alsinoides Linn*. *ethnobotenical leaflets*, 12, 2008, 734-40.
10. Anna Walesiuk, Jan J. Braszko. Preventive action of Ginkgo biloba in stress and corticosterone induced impairment of spatial memory in rats. *Phytomedicine*, 16, 2009, 40-46.
11. Jain SK. Dictionary of Indian folkmedicine and ethanobotany, National Botanical Research Institute, Lucknow, India, 1991, 33.
12. Sahoo TA. Antibacterial activity of Barringtonia acutangula Linn. against selected urinary tract pathogens. *Ind J Pharm Sci*, 70(5), 2008, 677-680.
13. Anonymous, The Wealth of India, Raw. First supplement serious, Volume I, II, CSIR, Delhi, 2000.
14. Rahman MM, Polfreman D, Mac Geachan J, Gray AI. Antimalarial activities of Barringtonia acutangula. *Phyto Res*, 19(6), 2005, 543-5.
15. Bhamarapravati S, Pendland SL, Mahady GB. Extracts of spice and food plants from Thai traditional medicine inhibit the growth of the human carcinogen Helicobactor pylori. *In vivo*, 17(6), 2003, 541-544.
16. VijayaBharathi R, Jerad Suresh A, Thiruma M, Sriram L, Geetha Lakshmi S, Kumudhaveni B. Antibacterial and antifungal screening on various leaf extracts of Barringtonia acutangula. *Int J Research in Pharm Sci*, 1(4), 2010, 407-410.
17. Sahoo S, Panda PK, Behera PS, Mishra SR, Ellaiah P. Antifungal activity of Barringtonia acutangula against selected human pathogenic fungi. *Indian Drugs*, 45(1), 2008, 26-30.
18. Harbone JP. Phytochemical methods, a guide to modern technique of plant analysis *(Chapmann and Hall, London)*, 1973, 1-271.
19. Juan Wang, Hai-Yan Zhang, Xi-can Tang. Cholinergic deficiency involved in vascular dementia, possible mechanism and strategy of treatment. *Acta pharmacologica sinica*, 2009, 1671-4083.
20. Julio Rubio, Haixia Dang, Mengjuan Gong, Xinmin Liv, Shi-lin Chen, Gustavo F. Gonzales. Aqueous and hydroalcohdic extracts of black maca (lepidium meyenij) improve scopolamine-induced memory impairment in mice. *Food and chemical toxicology*, 45, 2007, 1882-1890.
21. Kanowski S, Herrmann W.M, Stephan K, Wierich W, Horr R. Proof of efficacy of the *Ginkgo Biloba* special extract EGB 761 in outpatient suffering from mild to moderate primary degenerative dementia of Alzheiner type of multi-infarct dementia. *Pharmcophychology*, 29, 1996, 47-56.
22. Permender Rathee, Hema Chaudhary, Sushila Rathee, Dharmender Rathee. *Natural memory boosters phcog Rev*, 2(4), 2008, 249-56.
23. Perry N, Court G, Bidet N, Court J, Perry E. European herbs with cholinergic activities, Potential in dementia therapy. *Int Journal Geriatr Psychiatry*, 1996, 1063-1069.
24. Pomilio AB, Traj Temberg S, Vitale AA. High performance capillary electrophoresis analysis of mate infusions from stems and leaves of ilex paraguariensis using automated micellar electro kinetic capillary chromatography. *phytochemical analysis*, 13, 2002, 235-241.
25. Pulok Kumar Mukherjee, Venkatesan Kumar Mainak, Peter J, Houghton. Acorus calamus scientific validation of ayurvedic tradition from natural resources. *Pharmaceutical Biology*, 45,2007, 651-666.