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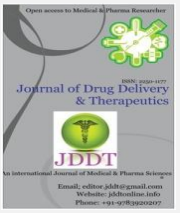

Open Access Research Article

MEMORY ENHANCING ACTIVITY OF HYDROALCOHOLIC EXTRACT OF *TERMINALIA CATAPPA* LEAVES

Ankur Joshi[1], Neelesh Malviya[2]

[1]Modern Institute of Pharmaceutical Sciences, Indore, M.P., India

[2]Smriti College of Pharmaceutical Education, Indore, M.P., India

E-mail address: ankurpharmacology@gmail.com

ABSTRACT

The present study was to evaluate the effect of *Terminalia catappa* on cognitive functions and cholinesterase (ChE) activity in scopolamine-induced amnesia in rats. The extract of *Terminalia catappa* was administered orally at three doses (100, 200 and 300 mg/kg) for 7 and 14 consecutive days to the respective groups of rats. Piracetam (120 mg/kg) was used as a standard nootropic agent. Learning and memory parameters were evaluated using elevated plus maze (EPM) and passive avoidance. Brain cholinesterase activity was evaluated. It was observed that *Terminalia catappa* at the above- mentioned doses after 7 and 14 days of administration in the respective groups significantly reversed scopolamine (1 mg/kg i.p.)- induced amnesia, as evidenced by a decrease in the transfer latency in the EPM task and step-down latency in the passive avoidance task. *Terminalia catappa* reduced the brain ChE activity in rats.

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INTRODUCTION:

Alzheimer's disease (AD) is a progressive neurodegenerative disorder that's slow in onset but, ultimately, results in dementia, uncommon behavior, personality change and, ultimately, death. Formation of memory is the most complex process and involves multiple neural pathways and neurotransmitters. It is documented that the cholinergic neural system plays a crucial role in learning and memory in humans and animals. Despite the great strides that have been made in the understanding and management of Alzheimer's disease (AD) and other neurodegenerative diseases, and disease related complications are increasing unabated. A variety of synthetic drug therapies are available for the treatment of Alzheimer but they associated with severe side effects and expensive. Therefore, there's an urgent need of exploring all the available options to address the menace of this disease. Plant medication and herbal formulations are frequently thought of to be less toxic and free from side effects than synthetic one. In spite of the presence of known synthetic medicines in the pharmaceutical market, remedies from medicinal plants are used with success to treat this disease[1,2].

MATERIAL AND METHODS:

Experimental design

The experimental design was planned such that the effect of *Terminalia catappa* at doses of 100, 200 and 300 mg/kg could be evaluated after 7 and 14 days against scopolamine-induced amnesia. For this purpose, the rats were divided into two sets of eight groups each (16 groups). The treatment period for animals of set I and set II was 7 and 14 days, respectively. At the end of the treatment period, all the animals were subjected to scopolamine (1 mg/kg i.p.) 60 min. The cognitive paradigms were evaluated 45 min after the scopolamine administration using the elevated plus maze (EPM) and passive avoidance models. Further, the animals were euthanized by cervical decapitation, and the brains were isolated to evaluate the anticholinesterase (ChE) activity of *Terminalia catappa*.

Exteroceptive behavioral models [3-5]

EPM

The EPM served as the exteroceptive behavioral model (wherein the stimulus existed outside the body) to evaluate learning and memory in rats. The plus maze apparatus consisted of two open (50 cm × 10 cm × 40 cm) and two enclosed arms (50 cm × 10 cm × 40 cm), with an open roof, arranged such that the two open arms were opposite each other. The maze was elevated to a height of 50 cm from the ground to measure the anxiety index in rats.

Passive shock avoidance paradigm

Passive avoidance, based on negative reinforcement, was recorded to examine the long-term memory. The apparatus consisted of a box (27 cm × 27 cm × 27 cm) having three walls of wood and one wall of Plexiglas, featuring a grid floor (made up of 3 mm stainless-steel rods set 8 mm apart), with a wooden platform (10 cm × 7 cm × 1.7 cm) in the center of the grid floor. The box was illuminated with a 15 W bulb during the experimental period. Electric shock was delivered to the grid floor. The rats were initially trained and the step-down latency (SDL) was recorded. SDL is defined as the time taken by the rat to step down and place all four paws on the grid floor. Rats showing SDL in the range of 2-15 s during the training session were taken for the acquisition and the retention tasks. The acquisition task was carried out 90 min after the training session.

Biochemical Estimations

Estimation of ACh Levels in the Brain by Quantifying ChE Inhibition

After assessing the learning and memory paradigms in scopolamine- induced amnesia, rats from each group were euthanized by cervical decapitation. The whole brain was immediately removed and chilled in ice-cold phosphate buffer. After washing in ice-cold phosphate buffer, the brains were homogenized in 5 ml of phosphate buffer in a glass TEFLON homogenizer. The brain homogenate was then evaluated for enzyme activity using Augustinsson's method of analysis.

RESULTS AND DISCUSSION:

Exteroceptive behavioral models: EPM: The effect of the vehicle, scopolamine control, *Terminalia catappa* (100, 200 and 300 mg/kg) and piracetam (120 mg/kg) were evaluated at the end of days 7 and 14. The scopolamine (1 mg/kg) control group showed a significant ($P < 0.01$) increase in TL values on the acquisition as well as on the retention days as compared with vehicle control rats, indicating impairment in learning and memory. In the AT on day 7 for set I and on day 14 for set II, the *Terminalia catappa* at dose levels 100, 200 and 300 mg/kg demonstrated decrease in the TL as compared to the scopolamine control group. The results obtained were found to be statistically significant ($P < 0.01$). In the RT on day 8 for set I and day 15 for set II, the *Terminalia catappa* at the dose levels 100, 200 and 300 mg/kg demonstrated a significant ($P < 0.01$) decrease in the TL as compared to the scopolamine control group. Piracetam (120 mg/kg p.o.) exhibited marked decrease ($P < 0.01$) in TL in comparison with the scopolamine control group. However, *Terminalia catappa* at the dose levels 200 and 300 mg/kg showed a decrease in the TL, which is comparable to that shown by piracetam ($P < 0.01$) [Table 1].

Table 1: Effect of the extract of *Terminalia catappa* on transfer latency (elevated plus maze paradigm) in scopolamine-induced amnesia in rats

Treatment Groups	TL on acquisition day (sec)		TL on retention day(sec)	
	7 day	14 day	7 day	14 day
Vehicle control	95.17±14.92	39.83±5.89	55.33±8.77	23.83±4.13
Scopolamine hydrobromide	143.67±17.2	118.8±11.03	128.33±19.53	118.83±26.13
Terminalia catappa (100)+ Scopolamine (1)	65.17±7.98	32.17±7.71	40.16±8.16	12.67±2.5
Terminalia catappa (200)+ Scopolamine (1)	55.5±4.75	17.33±4.73	23.83±3.69	10.17±2.33
Terminalia catappa (300)+ Scopolamine (1)	30.5±6.67	15.33±3.05	16.83±1.74	3.5±0.34
Piracetam(120)+ Scopolamine (1)	52.17±9.85	26.67±3.60	34.17±5.21	7.33±2.13

Values are expressed as mean ± SEM at n=6; one way ANOVA followed by Dunnett's Test

Passive shock avoidance paradigm: Scopolamine hydrobromide (1 mg/kg i.p.) decreased SDL on the AT and RT training, indicating impairment of memory. There is a slight increase in SDL after the administration of *Terminalia catappa* (100, 200 and 300 mg/kg p.o.) for 7 days as compared with the scopolamine control group on the AT and RT, indicating improvement in learning and memory of rats. However, in the AT, *Terminalia catappa* at the dose levels 100 and 200 mg/kg p.o. increased SLD, which is comparable to standard piracetam, but failed to exhibit a significant change when compared with the scopolamine control after 14 days of administration. However, *Terminalia catappa* (100, 200 and 300 mg/kg) was found to significantly ($P < 0.05$) decrease the SDL on RT when compared with the scopolamine control after 14 days of administration [Table 2]. *Terminalia catappa* 100, 200 and 300 mg/kg) after 14 days of administration showed a slight decrease in the SDL on acquisition day as compared to the groups that received the day 7 administration. However, on the retention day, *Terminalia catappa* (100, 200 and 300 mg/kg) after 14 days of administration showed a marked increase in the SDL as compared to the day 7 administration groups [Table 2].

Table 2: Effect of the extract of *Terminalia catappa* on step-down latency (passive avoidance paradigm) in scopolamine-induced amnesia in rats

Treatment Groups	SDL on acquisition day (sec)		SDL on retention day(sec)	
	7 day	14 day	7 day	14 day
Vehicle control	2.67±0.67	1.83±0.47	3.16±0.79	2.16±0.60
Scopolamine hydrobromide	2.83±0.47	1.17±0.17	1.67±0.49	1.83±0.30
Terminalia catappa (100)+ Scopolamine (1)	3.67±1.41	3.00±0.58	4.00±0.85	6.00±1.51
Terminalia catappa (200)+ Scopolamine (1)	2.00±0.51	3.16±0.87	4.17±1.35	6.67±2.35
Terminalia catappa (300)+ Scopolamine (1)	2.00±0.76	3..33±0.72	5.00±1.49	5.67±1.89
Piracetam(120)+ Scopolamine (1)	2.5±0.76	3.5±0.72	5.83±1.25	7.00±2.13

Values are expressed as mean ± SEM at n=6; one way ANOVA followed by Dunnett's Test

Table 3: Effect of the extract of *Terminalia catappa* on AChE Inhibition Activity

Treatments (mg/kg)	AChE concentrated (μMol/minute/g of tissue)	Inhibition of AChE activity (%)
Control	6.742±0.18	
Scopolamine hydrobromide	10.39±0.35	35.11
Terminalia catappa (100)+Scopolamine (1)	5.683±0.28	45.30
Terminalia catappa (200)+Scopolamine (1)	4.907±0.31	50.12
Terminalia catappa (300)+Scopolamine (1)	4.967±0.31	52.19
Piracetam(120)+ Scopolamine hydrobromide(1)	3.968±0.19	61.8

Values are expressed as mean ± SEM at n=6; one way ANOVA followed by Dunnett's Test

Estimation of AChE activity in the brain:

In the standard group, the animals treated with piracetam (120 mg/kg p.o.) produced a significant reduction of AChE enzyme activity. In the treatment group, the animals treated with *Terminalia catappa* at 100, 200 and 300 mg/kg produced a significant reduction of AChE enzyme activity and as compared to positive control. Percentage inhibition of AChE activity of treatment group has shown a significant increase when compared to positive control [Table 3].

RESULTS AND DISCUSSION:

The present study suggests that *Terminalia catappa* possesses memory enhancing activity in view of its facilitatory effect on the retention of spatial memory in scopolamine-induced amnesia. There is a decrease in the TL, i.e. rats were able to locate the dark zone immediately after exposure to the open arm in the EPM paradigm, which is an indicator of cognition improvement. In case of the passive avoidance paradigm, the SDL is increased on administration of *Terminalia catappa*. This suggests that the animal has the retention of memory of the shock once entered in the shock-free zone. The long-term administration of the *Terminalia catappa* extract (14-day administration) exhibited pronounced effect in the reversal of the scopolamine-induced amnesia in case of the passive avoidance paradigm as compared to the 7-days administration.

It is well known that cholinergic neuronal systems play an important role in the cognitive deficits associated with AD, ageing and neurodegenerative diseases.(24) In our study, Piracetam (120 mg/kg p.o.) and *Terminalia catappa* (100, 200 and 300 mg/kg p.o.) significantly lowered this activity. Hence, the memory- enhancing effect of the Terminalia catappa can be attributed to its anti-ChE activity. Therefore, the memory-improving activity of *Terminalia catappa* may be attributed to the anti- AChE, procholinergic, neuroprotective and nutritive properties of the *Terminalia catappa*. Hence, *Terminalia catappa* may be used in delaying the onset and reducing the severity of Alzheimer's disease. However, further investigations are warranted to explore the possible involvement of other neurotransmitters such as glutamate, Gamma aminobutyric acid (GABA) and catecholamines, responsible for the memory-improving property of *Terminalia catappa*.

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