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EVALUATION OF CELASTRUS PANICULATUS IN LEARNING AND MEMORY OF RATS BY T- MAZE TEST

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ABSTRACT

Present research work was performed to evaluate the effect of *Celastrus paniculatus* against scopolamine induced dementia in rats. Learning and memory enhancing potentials of the *Celastrus paniculatus* were compared with donepezil. Memory performance was studied in rats by using T-Maze apparatus. Rats of either sex were divided into six group each group contain six animals. On day 1st, 8th and 15th each animal was tested for learning and memory by using T-Maze. Scopolamine group show decline in memory performance while the donepezil group show significant decrease in time which leads to effective learning and memory as compared to other groups. Celastrus paniculatus extract show increase in memory performance as compared to other groups. This shows the memory enhancing activity of aqueous extract of *Celastrus paniculatus*.

KEYWORD: Celastrus paniculatus, T-Maze, Donepezil, Scopolamine.

INTRODUCTION

Learning is an indispensable step in memory retention however, it is a process affected by individual basal states, such as emotion, attention, motivation and perception. In fact, emotional states, such as fear and aversion, can modulate, by enhancing or impairing, memory formation.[1] Because the available animal models of learning and memory have a limited ability to detect the effects of drugs on learning and memory. Therefore, the proposed T-Maze task is an attempt to assess the effects of drugs on learning and memory concomitantly in rats. The T-Maze is an apparatus derived from the elevated plus-maze which is widely used to evaluate an ethological view of rodents.[2] The T-Maze consists of two side (goal) arms can contain discriminative stimuli (cues) such as patterns or objects that the animal must respond to, generally to obtained a reward. With dimensions stem (50 x 10

cm) start arm (50 x 10 cm) walls (30 cm).

Treatment of memory impairment associated with cognitive disorders such as Alzheimer's disease (AD) is still inadequate and requires development of new drugs. Nootropic agents like cholinesterase inhibitors are most commonly used drugs for treatment of AD. Currently Acetylcholinesterase inhibitors (AchE) have been approved for use in the treatment of AD like tacrine, donepezil, rivastigmine and galantamine. However, the resulting adverse effects associated with these agents like nausea, diarrhea, vomiting and hepatotoxicity have limited their use.[3] *Celastrus paniculatus* a plant known for centuries as "Elixir of life" belongs to family Celastraceae is a large woody, climbing shrub, height up to 10-18m tall and common to all over the hilly parts of the India. *Celastrus paniculatus* is an Indian plant having remarkable reputation. The plant present varying degree of therapeutic value some of which useful in the treatment of cognitive dysfunction, epilepsy, insomnia, rheumatism, gout and dyspepsia.[4] *Celastrus paniculatus* is well known for its capability to improve memory. According to ayurvedic science, *Celastrus paniculatus* may be used as a stimulant nervine tonic, rejuvenant, sedative and diuretic.[5] Plant has important role in enhancing cognitive function and the natural luminosity. It is a warming herb used internally in the treatment of inflammation of muscles and joint.[6] The seed are used to heal indolent ulcers and sores as well as infectious skin condition such as scabies in the form of poultice.[7] Recently aqueous seed extract of *Celastrus paniculatus* show antioxidant properties by decreasing the lipid peroxidation and augmenting endogenous antioxidant enzymes in brains. So the aqueous extract of *Celastrus paniculatus* was investigated for its cognitive enhancing and oxidant property.

PREPARATION OF AQUEOUS EXTRACT OF *CELASTRUS PANICULATUS*

Seeds were collected during October. The seeds were dried and coarsely grounded. The coarse powder about 200gm of seed was extracted with 6 parts boiling water for 5 hours and filtered to yield the extract. The extracts were then concentrated in magnetic stirrer at the temperature up to 40^0C. The extract was stored in air tight container and then kept in a refrigerator.

MATERIAL AND METHOD

ANIMALS

All experiments were carried out using healthy Wistar albino rats of either sex (150- 200gm) obtained from the animal house of the department of pharmacy, M.J.P. Rohilkhand

University, Bareilly, 243001 Uttar Pradesh and animal were housed in a well ventilated polypropylene cage at 12:12 hour light/dark schedule controlled temperature (25±2^{O}C), humidity (50-55%) with food and water. Animal were housed in group for at least one week before using them for experiment.

DRUGS AND CHEMICALS

Donepezil (Alkem laboratory) as standard drug, scopolamine (Buscopan from German remedies) and distilled water, will be taken from the stores of department of pharmacy, M.J.P. Rohilkhand University, Bareilly.

EXPERIMENTAL PROTOCOL

Six groups and each group consisted of six rats of either sex were employed in this present study.

Treatment

Group 1, n = 6: Control group.

Animal treated with distilled water 5ml/kg orally for 15 days.

Group 2, n =6: standard drug (donepezil).

Animal treated with standard drug donepezil 3mg/kg, orogastric feeding, two hours prior to experiment for 15 days.

Group 3, n =6: scopolamine.

Animal treated with drug scopolamine 1mg/kg, intra peritoneal injection, thirty minutes prior to experiment for 15 days.

Group 4, n=6: extract (*Celastrus paniculatus*).

Animal treated with extract 200mg/kg, per oral, one hour prior to experiment for 15 days.

Group 5, n=6: extract + scopolamine.

Animal treated with extract (200 mg/kg p.o.) + scopolamine (1mg/kg, i.p.) for 15 days.

Group 6, n=6: donepezil + scopolamine.

Animal treated with donepezil (3 mg/kg p.o.) + scopolamine (1mg/kg, i.p.) for 15 days.

Table 4.1 Experimental animal divided in to six groups.

GROUPS	TREATMENT
Group 1	Control group (5ml/kg, p.o.)
Group 2	Scopolamine (1mg/kg, i.p.)
Group 3	*Celastrus paniculatus* (200mg/kg, p.o.)
Group 4	Scopolamine (1mg/kg, i.p.) + *Celastrus paniculatus* (200 mg/kg)
Group 5	Donepezil (3mg/kg orogastric)
Group 6	Donepezil (3mg/kg orogastric) + scopolamine (1mg/kg, i.p.).

Method of testing

After 2 days of dieting, animals are subjected to three 10 minute adaptation session (one session per day for three consecutive days). During which they are allowed to freely explore the Maze with all doors open and both arms bait with food. On 4th day and for five consecutive days (one session consisting of 11 trials per day cut off time 10 min). The rat are forced (by blocking the previous visit arm) to visit one arm at the time eat the food reward and return to the starting compartment. Rats are confined to the starting compartment for 5 second between trials. Divided animal in six groups each consisting of six animals. After treatment the T-Maze test was carried out on the 1st, 8th, and 15th day of treatment. Scopolamine was administered to the rats as intraperitoneal injection at a dose of 1mg/kg body weight for 15 days 30 minute prior to memory experiments. Donepezil was administered to rat through orogastric feeding at a dose 3mg/kg body weight for 15 days 2 hour prior to memory experiment. *Celastrus paniculatus* was administered to the rat as orally at a dose of 200 mg/kg body weight 1 hour prior to memory experiment for 15 days. The animal was left at the tail end the presentation of the food in one of the arm is in such a way that it is concealed from the sight of the rat. The animal has to move forward and turn left or right of the T-Maze. The move was considered to be a positive response if the rat reaches near the sealed food and return to the starting arm. Trials were taken for 15 days and timing was note down.

RESULTS

Following groups are evaluated by using T-Maze model, each group consist of six rats. Distilled water (5ml/kg), donepezil (3ml/kg) was administered two hour prior to memory experiment, scopolamine(1mg/kg) was administered thirty minute prior to experiment and *Celastrus paniculatus* extract was administered one hour prior the memory experiment for 15 days. Note down the response as rat reaches near the sealed food and return to the starting arm. Trials were taken for 15 days and timing was note down. According to these parameters

graph are plotted and their learning and memory activity is evaluated. Each value is mean value obtained from the T-Maze test and expressed as mean ± SEM.

Treatment	Day 1	Day 8	Day 15
Control group	6.47 ± 0.13	5.33 ± 0.14	4.46 ± 0.18
Scopolamine	14.49 ± 0.19	15.02 ± 0.17	15.40 ± 0.18
Donapezil	4.86 ± 0.73	4.45 ± 0.74	3.8 ± 0.42
Celastrus paniculatus extract	4.71 ± 0.37	4.06 ± 0.28	3.40 ± 0.32
Donepezil + Scopolamine	7.44 ± 0.81	6.07 ± 0.35	5.24 ± 0.41
Extract + Scopolamine	6.16 ±0.77	5.50 ± 0.41	4.41 ± 0.48

Effect of control (distilled water) and scopolamine on learning and memory

Control (distilled water) (5 ml/kg) administered group was found significant decrease ($P<0.0001$) in time taken to reach the sealed food and return to start arm as compare to scopolamine (1 mg/kg) treated group, during T-Maze test conducted on day 1^{st}, 8^{th} and 15^{th} (Fig 1).

Effect of scopolamine, *Celastrus paniculatus* extract and donepezil on learning and memory

Celastrus paniculatus extract (200 mg/kg) and donepezil (3 mg/kg) administered groups were found significant difference ($P<0.0029$)) in time taken to reach the sealed food and return to start arm as compare to scopolamine (1 mg/kg) treated group, during T-Maze test conducted on day 1^{st}, 8^{th} and 15^{th} (Fig. 2).

Effect of distilled water, donepezil, donepezil + scopolamine on learning and memory

Donapezil (3 mg/kg) administered group was found no significant change but donepezil (3 mg/kg) + Scopolamine (1 mg/kg) administered group was found significant difference ($P<0.0112$) in time taken to reach the sealed food and return to start arm as compare to control group, during T-Maze test conducted on day 1^{st}, 8^{th} and 15^{th} (Fig. 3).

Effect of scopolamine, donepezil, donepezil + scopolamine on learning and memory

Donepezil (3 mg/kg) and donepezil (3 mg/kg) + scopolamine (1 mg/kg) administered groups were found significant difference ($P<0.0107$) in time taken to reach the sealed food and return to start arm as compare to scopolamine (1 mg/kg) treated group, during T-Maze test conducted on day 1^{st}, 8^{th} and 15^{th} (Fig. 4).

Effect of distilled water, *Celastrus paniculatus* and donepezil on learning and memory

Celastrus paniculatus extract (200 mg/kg) administered group was found significant difference (P<0.0346) but donepezil (3 mg/kg) was found no significant change in time taken to reach the sealed food and return to start arm as compare to control group, during T-Maze test conducted on day 1st, 8th and 15th (Fig. 5).

Effect of distilled water, extract + scopolamine and donepezil + scopolamine on learning and memory

Celastrus paniculatus extract (200 mg/kg) + scopolamine (1 mg/kg) administered group was found no significant change but donepezil (3 mg/kg) + scopolamine (1 mg/kg) administered group was found significant difference (P<0.0112) in time taken to reach the sealed food and return to start arm as compare to control (5 ml/kg) treated group, during T-Maze test conducted on day 1st, 8th and 15th (Fig. 6).

Effect of scopolamine, *Celastrus paniculatus* + scopolamine and donepezil + scopolamine on learning and memory

Celastrus paniculatus extract (200 mg/kg) + scopolamine (1 mg/kg) and donepezil (3 mg/kg) + scopolamine (1 mg/kg) administered groups were found significant difference (P<0.0071) in time taken to reach the sealed food and return to start arm as compare to scopolamine (1 mg/kg) treated group, during T-Maze test conducted on day 1st, 8th and 15th (Fig. 7).

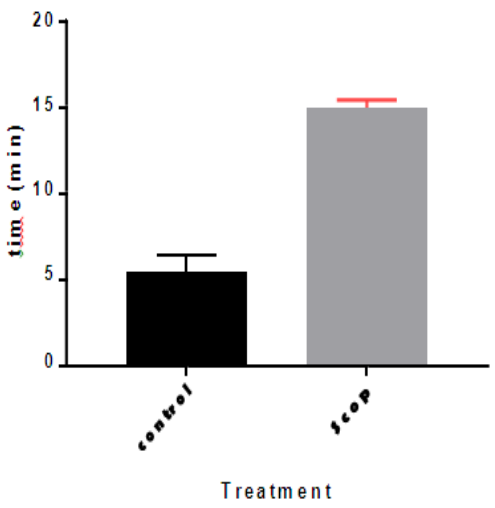


Fig. 1

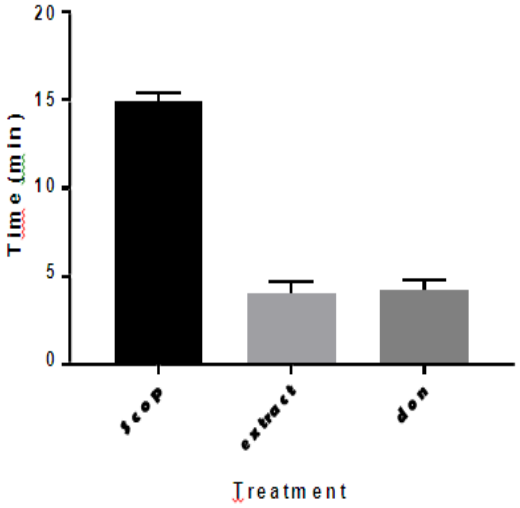


Fig. 2

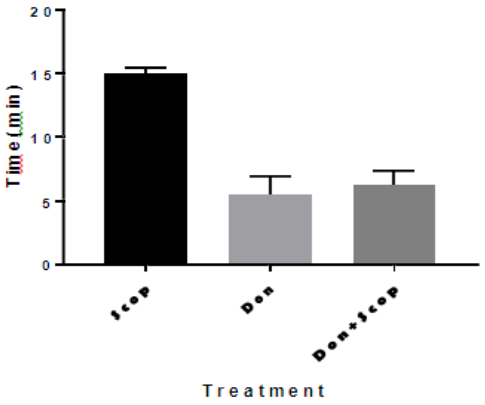
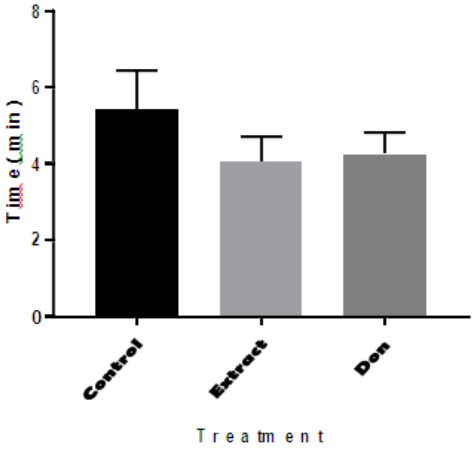


Fig. 3



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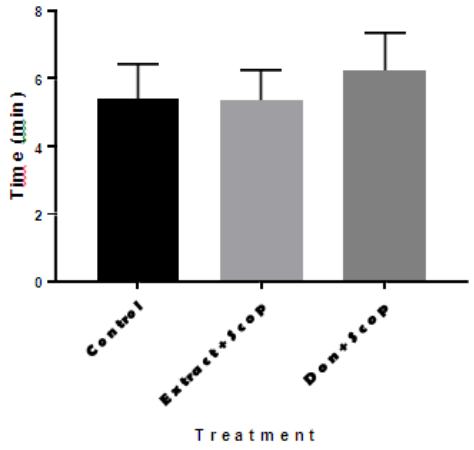

Fig. 5

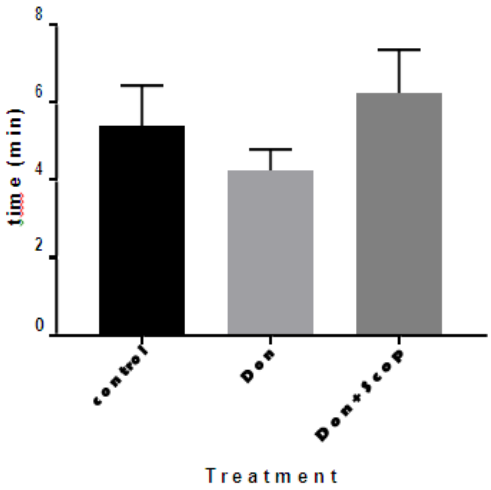

Fig. 6

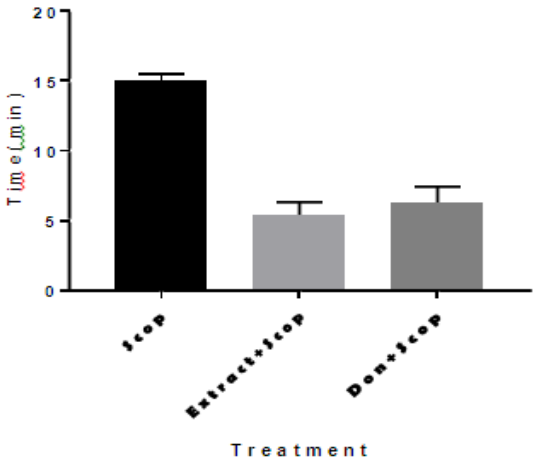

Fig. 7

DISCUSSION

In present study, *Celastrus paniculatus* is investigated for its activity on learning and memory. To evaluate learning and memory activity T-Maze was selected as it is simple, less time consuming, quick and having good results. The animal was left at the tail end the presentation of the food in one of the arm is in such a way that it is concealed from the sight of the rat. The animal has to move forward and turn left or right of the T-maze. The move was considered to be a positive response if the rat reaches near the sealed food and return to start arm. Trials were taken for 15 days and timing was note down. On the basis of evaluation methods following result are obtained from various groups of rats by T-maze apparatus.

Control group was treated with distilled water and scopolamine group was treated with scopolamine (1mg/ kg, i.p.) 30 minute prior the memory experiment. Control group take less time to reaches near the sealed food and return to the starting arm. While the scopolamine group takes more time as compared to the control group which showed a decline in memory performance in rats as scopolamine causes amnesia by interfering with acetylcholine transmission in the central nervous system. This study is supported by earlier studies on scopolamine.[8]

Control group when compared with donepezil group and donepezil + scopolamine group. Donepezil group take less time as compared to other groups as donepezil improved learning and memory.[9]

Scopolamine group, donepezil group, donepezil + scopolamine group when compared with each other. Donepezil group takes less time to return to the starting arm which show increase in learning and memory while the scopolamine group show decline in memory performance as it blocks the cholinergic neurotransmission, leading to memory impairment in rats.

Control group, *Celastrus paniculatus* group and donepezil group when compared. *Celastrus paniculatus* group take less time to reaches to the sealed food and return to the starting arm. This showed increase in memory performance. As *Celastrus paniculatus* enhances cognition due to increase acetylcholine level in rat brain.[10]

Scopolamine group, *Celastrus paniculatus* extract and donepezil when compared. *Celastrus paniculatus* extract group take less time to reach to the sealed food and return to the starting compartment as compared to scopolamine group. It was reported that aqueous seed extract

show antioxidant activity by decreasing the lipid peroxidation and augmenting endogenous antioxidant enzyme in brain. The aqueous extract of *Celastrus paniculatus* was investigated for its cognitive enhancing in rats.

Control group, *Celastrus paniculatus* extract + scopolamine and donepezil + scopolamine when compared. *Celastrus paniculatus* extract + scopolamine show maximal drug response and enhancement in learning and memory.

Scopolamine, *Celastrus paniculatus* extract + scopolamine, donepezil + scopolamine when compared. *Celastrus paniculatus* extract + scopolamine show maximum effect. The result showed that *Celastrus paniculatus* extract is having activity for learning and memory in rats and the result are equivalent to donepezil group (standard drug).

SUMMERY AND CONCLUSION

The following observation can be summarized on the basis of the results obtained in the present study on T-Maze.

- Scopolamine (1mg/kg) group show decline in memory performance in comparison to other

  groups. As it blocks the cholinergic neurotransmission, leading to memory impairment in rats. Scopolamine is a muscarinic cholinergic receptor antagonist, which cause cholinergic dysfunction, impaired cognition and oxidative stress in rats.
- Donepezil (3mg/kg) group show significant decrease in time which leads to effective learning and memory as compare to other groups. Donepezil is widely accepted as a modern drug for dementia. At present study it is used as standard drug.
- *Celastrus paniculatus* extract (200mg/kg) group show increase in memory performance as compared to other groups and show significance decrease in time. As *Celastrus paniculatus* enhances cognition due to increase acetylcholine level in rat brain. It was reported that aqueous seed extract show antioxidant activity by decreasing the lipid peroxidation and augmenting endogenous antioxidant enzyme in brain. The aqueous extract of *Celastrus paniculatus* was investigated for its cognitive enhancing property in rats.

From the above data it can be concluded that aqueous extract of *Celastrus paniculatus* show enhance activity in learning and memory when compared with other groups in T-maze model. It may be uses as natural ayurvedic remedy for treatment of learning and memory.

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