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Original Article

Evaluation of Nootropic Potential of the Fruits of *Artocarpus altilis* by *in vivo* and *in vitro* Studies

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ABSTRACT

Background: *Artocarpus altilis* is an evergreen plant having a variety of medicinal values due to the presence of compounds like cyclopropane sterols, quercetin, camphorol, artocarpine, and many more. The fruits typically contain cycloprane sterols. **Objectives:** The present study was carried out to evaluate the nootropic potential of the ethanolic extract of the fruits of *Artocarpus altilis* (EFAA). **Materials and Methods:** The nootropic activity was evaluated using various models. The animals were divided into eight groups (*n*=6) consisting of normal control, amnesic control (scopolamine: 1mg/kg), standard drug (piracetam, 200mg/kg), extract, piracetam with scopolamine and three test groups (200, 400 and 800mg/kg, orally). Various *in vivo* models like Elevated Plus maze, Hebb-William's Maze, and Y-maze were used to evaluate the nootropic potential of EFAA. The brain was isolated, homogenized, and used for biochemical analysis like percentage inhibition of brain Acetylcholinesterase enzyme using Ellman's method and microplate array method. **Results:** The study revealed that EFAA has significant dose-dependent nootropic activity. A significant decrease in Initial transfer latency, retention transfer latency, the total number of arm entries and AChE enzyme activity, and an increase in percentage alteration. **Conclusion:** The findings from the present study suggest that EFAA demonstrated a nootropic effect.

Keywords: Acetyl-cholinesterase, Amnesia, *Artocarpus altilis*, Cognitive functions, Scopolamine.

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INTRODUCTION

Nootropic drugs are also called smart drugs or memory enhancers, which improve the characteristic of cerebral function associated with intellectual performance. They are psychotropic agents that enhance the cognitive function of the CNS by improvising its integrative utility.[1] Various phytoconstituents like flavonoids, alkaloids, phenol, steroids, triterpenes are present in different parts of *Artocarpus altilis* responsible for its reported activities.[2,3]

Studies have been already carried out on *Artocarpus altilis* for activities against hyperglycemia, hyper-cholesterol, microorganism, hypertension, gastrointestinal nematode, mosquito, etc.[4] Based on the claims made by traditional / folklore medicines and practitioners, an attempt was made to scientifically validate the efficacy of the extract of *Artocarpus altilis* as fruits as a nootropic agent. Studies have established a correlation between neurotransmitter acetylcholine and memory functions. Cholinergic dysfunction is observed in Alzheimer's disease. Inhibitors of acetylcholinesterase have been tried in the management of Alzheimer's disease. The estimation of cholinesterase inhibition and assessing the acetylcholine level is the basis for the possible nootropic effect of new drugs. The literature survey revealed that there is a paucity of published data available on the nootropic activity of plant extract of *Artocarpus altilis*. Hence the present study was undertaken.

MATERIALS AND METHODS

Collection and Identification of the Plant Materials

The fruits of *Artocarpus altilis* were collected from in and around Mangalore, Karnataka, India, in November and were authenticated.

Preparation of Extract

The plant materials were cleaned and dried under shade. The dried fruits were crushed into a coarse powder. The coarse powder was extracted by Soxhlet extractor with ethanol and was concentrated using a rotary flash evaporator at 40°C. The extract obtained was stored in desiccators and made free from moisture and humidity.

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Animals

Healthy adult male albino Wistar rats weighing 150-200g were used for the study. The animals were obtained from the in house animal house facility (1781/PO/EReBi/S/2014/CPCSEA), Deralakatte, Mangalore. The rats were housed in polypropylene cages and maintained under standard conditions (12 hr light/12 hr dark cycle; 25± 3°C; 35–60% humidity). Food and drinking water was provided.

Acute Oral Toxicity Study

A preliminary study was conducted to assess the acute pharmacological effects and safety of the drug. The acute toxicity studies were performed as per OECD 425 guidelines using female albino Wistar rats.[5] Limit test was performed by single oral administration of the test drug to one animal at the dose of 2000 mg/kg body weight. The animal was observed continuously once in half an hr for the next 4 hr for general behavioral, neurological, and autonomic profile and finally for death after 24 hr. The animals were observed for CNS toxicity symptoms for 24 hr.[6] As no mortality was observed, the same dose was administered sequentially to four more animals and the results were recorded.

Selection of Dose

Three dose levels were selected, namely 200 mg/kg, 400mg/kg and 800mg/kg body weight on the basis of the result of acute oral toxicity study.

Nootropic Activity

The animals were randomly divided into eight groups heaving six animals in each group (n=6), and the following treatment schedule was followed.

Group I (Normal control)

Animals received a daily single oral dose of saline from day 1 to day 8 (10ml/kg body weight, orally).

Group II (Scopolamine)

Animals received a daily single oral dose of saline from day 1 to day 8 (10ml/kg body weight, orally) followed by a single dose of scopolamine (1mg/kg) on 8th day. (Validation of amnesia induction by scopolamine).

Group III (Piracetam)

Animals received a daily single oral dose of piracetam from day 1 to day 8 (200 mg/kg body weight, orally). (Assessment of inherent nootropic potential of piracetam for comparison with test extracts).

Group IV (EFAA)

Animals received a daily single oral dose of EFAA from day 1 to day 8 (800mg/kg body weight, orally). (Assessment of inherent nootropic potential of EFAA).

Group V (Piracetam + Scopolamine)

Animals received a daily single oral dose of piracetam from day 1 to day 8 (200 mg/kg body weight, orally) followed by a single dose of scopolamine (1mg/kg) on the 8thday. (Assessment of nootropic activity of piracetam in amnesic animals).

Group VI, VII and VIII

Animals received a daily single oral dose of the plant extract (EFAA) in three different doses (200, 400 and 800 mg/kg) followed by a single dose of scopolamine (1mg/kg) on the 8th day. After 45 min of administration of scopolamine, the nootropic activity was assessed by using three maze-models (i) Elevated plus Maze, (ii) Y-maze and (iii) Hebb-Williams maze. The trials were again carried on the Next Day (9th day) and the retention index was recorded, which served as the scale for determining the nootropic potential of the drug.

Elevated Plus Maze (EPM) Test

EPM test has been used to assess the learning and memory in rodents. Transfer latency has been used as a parameter for the assessment of memory and learning.[7-9] The animal is placed in one of the open arms of the maze facing away from the central platform. The time taken by the animal to move from the open arm to the closed arm is recorded as ITL (Initial Transfer Latency). For all the trials, the cut-off time is 90 sec. The ITL is recorded as 90 sec if the animal fails to finish the task in the given time. Once the animal entirely enters the closed arm of the maze, then the time is noted. After this, the animals are returned to their home cages. The RTL (Retention Transfer Latency) is recorded after 24 hrs in the same manner as to how the ITL was recorded.

The transfer latency measured on the first and second-day trials will serve as an acquisition (learning) and retention (memory), respectively. From these, inflexion ration (IR) was calculated using the formula,

$$IR = L_0 - L_1 / L_1$$

IR = Inflexion ratio

L_0 = Initial transfer latency in seconds

L_1 = Retention transfer latency in seconds

A fall in transfer latency on subsequent maze exposures was taken as an index of successful retention.[10,11]

Y-Maze Test

The Y-maze test is used to measure spatial working memory and short-term memory through spontaneous alteration in behavior in rats. Using food as a reward to reach the goal, animals are required either to execute a specific search sequence or minimize errors in the quest for food. Hence, temporal measurement and error scoring is the key parameters recorded for the evaluation of drug effects administered after training.[12] The three identical arms are randomly designed: start arm, in which the animal starts to explore (A), reward arm, with food stimuli (B), and another arm (C). Each rat is initially placed at the end of arms A, allowed to move freely, and the sequence and number of arm entries were recorded over 8 min period. Rats tend to explore the maze systematically, entering each arm in turn. The ability to alternate requires that the rats know which arm they had already visited. The percentage of triads in which the animals enter all three arms sequentially without returning to the arm which it has left was recorded as an 'alternation' to estimate short-term memory. Arms were cleaned with water spray between tests to remove odors and residues. The % alternation score for each animal is defined as the ratio of the actual number of alternations to the possible number (defined as the total number of arm entries minus two) multiplied by 100 as shown by the following equation:

$$\% \text{ Alternation} = [(\text{Number of alternations}) / (\text{Total arm entries} - 2)] \text{ X } 100$$

Hebb-William's Maze

The Hebb-Williams Maze is an incentive-based exteroceptive behavioral model useful for measuring the spatial and working memory of rats. It mainly consists of three components viz. animal chamber (start box), which is attached to the middle chamber (exploratory area) and a reward chamber at the other end of the maze in which the reward (food) is kept. The box is partitioned with wooden slats into blind passages leaving just one twisting corridor leading from the entry to the reward chamber. The learning and memory assessment for control and treated rats were conducted at the end of treatment under zero watts red colored bulb to minimize the nocturnal cycle disturbances. During the study, the animals were exposed to food and water *ad libitum* only for one hour after the maze exposure for the day is completed to ensure motivation towards the reward chamber.[13] On the first day (i.e., the eighth day of drug treatment), each rat was placed in the animal chamber, and the door was opened to facilitate the entry of the animal into the next chamber. The doors of the start box were closed immediately after the animal moved into the exploratory area to prevent its back entry. Time taken (in seconds) by the animals to reach the reward chamber from the start box (initial transfer latency, ITL) were noted for each animal. After the experiment, the animals were returned to their home cages, and transfer latency was recorded again after 24 hr of the first exposure (retention transfer latency, RTL). Fall in transfer latency on subsequent maze exposures were taken as an index of successful retention.[14]

Biochemical Analysis

Just after the experiment, the animals were anesthetized and were sacrificed by cervical dislocation. The skull was cut open, and the whole brain was removed carefully, which was then weighed, kept on an ice bath, washed with cold saline, and homogenized. For homogenizing, approximately 20 mg of tissue/ml of phosphate buffer (pH 8.0 0.1M) was used, which was then placed in a Potter-Elvehjem homogenizer. The homogenate was centrifuged at 3000 rpm for 10 min, and the final cloudy supernatant liquid was used for the estimation of acetylcholine esterase activity.[1]

Estimation of Acetylcholinesterase Activity by Ellman's Method

0.4ml of an aliquot of rat brain homogenate was added to a cuvette containing 2.6 ml phosphate buffer (0.1M, pH 8.0) and 100 µl of DTNB was added. The content of the cuvette was mixed thoroughly by bubbling air, and absorbance was measured at 412 nm. About 20 µl of the substrate, i.e., acetylthiocholine iodide, was added and change in absorbance per min was observed. The rate of the reaction was calculated by the following formula.[15]

$$R=5.74\times10^{-4}\times \Delta A/C_0$$

Estimation of Acetylcholinesterase by Microplate Assay

Acetylcholinesterase activity was measured using 96- well microplate reader based on Ellman's method. In the 96- well plates, 25 µl of 15mm. ACTI in water, 125 µl of samples OF 3mm. DTNB in buffer C (50mm Tris-HCl, pH 8, containing 0.1 M NaCl and 0.02 M $MgCl_2$, 50 µl of buffer B (50mm Tris-HCl, pH 8, containing 0.1% bovine serum Albumin), 25 µl of samples (10mg/ml, in MeOH, diluted ten times with buffer A (50 mm Tris-HCl, pH 8), to give a concentration of 1 mg/ml), were added and the absorbance was measured at 405 nm every 13 sec for five times. The rates of reactions were calculated by Microplate Manager Software version 4.0.[15,16]

Statistical Analysis

All the data were represented as Mean ± SEM. The data obtained were subjected to a one-way Analysis of Variance (ANOVA) test, followed by *Post hoc* Scheffe's test using SPSS computer software version 10. A *p*-value of less than 0.05 was considered statistically significant.

RESULTS

Elevated Plus-maze

Both Initial transfer latency (learning) and retention transfer latency (memory) increased significantly in the scopolamine challenged group. Interestingly, piracetam decreased ITL and

Table 1: Effect of *Artocarpus altilis* extract on Transfer Latency and Inflexion Ratio using Elevated plus maze.

Treatment	ITL	RTL	Inflexion Ratio
Normal (Vehicle)	49.33±9.01	44.50±9.81	0.13±0.02
Scopolamine (1mg/kg)	57.00±7.06	54.00±6.20	0.04±0.00
Piracetam (200mg/kg)	21.66±1.2[a,b]	17.50±2.04[a,b]	0.18±0.02
Extract (800mg/kg)	23.67±1.21[a,b]	20.34±1.05[b]	0.16±0.02
Piracetam (200mg/kg) + Scopolamine (1mg/kg)	24.33±0.91[a,b]	22.50±1.08[b]	0.19±0.01
Extrct (200mg/kg) + Scopolamine (1mg/kg)	43.34±2.62	39.67±2.17	0.08±0.01
Extract (400mg/kg) + Scopolamine (1mg/kg)	39.67±2.64	35.66±1.70	0.12±0.08
Extract (800mg/kg) + Scopolamine (1mg/kg)	25.00±0.68[a,b]	23.34±0.98[b]	0.08±0.01

The values are expressed as- Mean ± SEM (n=6). a = p<0.05 when compared to Vehicle (Normal) group, b = p<0.05 when compared to disease control (Scopolamine treated) group. ITL: Initial transfer latency, RTL: Retention transfer latency, IR: Inflexion ratio

Table 2: Effect of *Artocarpus altilis* extract on Transfer Latency using Hebb-William's maze.

Treatment	ITL	RTL
Normal (Vehicle)	110.8±7.98	101.3±6.93
Scopolamine (1mg/kg)	149.6±10.6	132.8±9.05
Piracetam (200mg/kg)	47.50±2.67[a,b]	36.16±3.74[a,b]
Extract (800mg/kg)	53.83±3.34[a,b]	44.50±3.41[a,b]
Piracetam (200mg/kg) + Scopolamine (1mg/kg)	49.83±1.95[a,b]	40.00±1.69[a,b]
Extract (200mg/kg) + Scopolamine (1mg/kg)	103.6±10.42	96.67±9.83
Extract (400mg/kg) + Scopolamine (1mg/kg)	67.00±3.49[a]	61.16±3.67
Extract (800mg/kg) + Scopolamine (1mg/kg)	55.67±4.94[a,b]	46.00±4.26[a,b]

The values are expressed as- Mean ± SEM (n=6). a = p<0.05 when compared to Vehicle (Normal) group, b = p<0.05 when compared to disease control (Scopolamine treated) group. ITL: Initial transfer latency, RTL: Retention transfer latency

Table 3: Effect of *Artocarpus altilis* extract on the number of arm entries.

Treatment	Total arm entries 8th day	Total arm entries 9th day
Normal (Vehicle)	20.67±1.33	18.33±1.60
Scopolamine (1mg/kg)	25.16±3.00	26.83±0.74
Piracetam (200mg/kg)	8.50±0.76[a,b]	8.33±0.88[a,b]
Extract (800mg/kg)	10.16±1.62[b]	9.16±0.79[a,b]
Piracetam (200mg/kg) + Scopolamine (1mg/kg)	9.83±1.68[b]	8.66±.071[a,b]
Extract (200mg/kg) + Scopolamine (1mg/kg)	14.00±1.63	18.66±1.80
Extract (400mg/kg) + Scopolamine (1mg/kg)	15.83±3.48	15.16±2.27
Extract (800mg/kg) + Scopolamine (1mg/kg)	12.67±1.40[b]	11.33±1.45[b]

The values are expressed as- Mean ± SEM, (n=6). a = p<0.05 when compared to Vehicle (Normal) group, b = p<0.05 when compared to Scopolamine (Treated) group.

RTL as compared to the normal control group. The extract of *Artocarpus altilis* at a different dose level, i.e., 200mg/kg, 400mg/kg and 800mg/kg, showed a dose-dependent decrease in ITL and RTL when compared to the normal group suggesting the positive impact of the extract on learning and memory (Table 1).

Hebb-Williams Maze

Time taken by the animals to navigate through the mazes is an indication of the retention of memory of previous reward earning experience. In our study, the test extract caused a significant decrease in the transfer latency both in the learning phase (ITL) and the memorizing phase (RTL) in experimental animals. The activity was checked at three dose levels (200mg/kg, 400mg/kg and 800mg/kg body weight) and was found to be dose dependant. Predicably, scopolamine caused a significant increase in ITL and RTL (Table 2).

Y-Maze

Y-Maze is assessed based on two parameters, i.e., arm entries and % alterations.

Effect on the Number of Arm Entries

Spatial memory and short-term memory of the rodents of different treatment groups was assessed bases on the number of arm entries and percentage alterations. The number of entries was less in piracetam and extract-treated groups as compared

Table 4: Effect of *Artocarpus altilis* extract on % alteration.

Treatment	% Alteration 8th day	% Alteration 9th day
Normal (Vehicle)	22.38±1.09	26.33±0.82
Scopolamine (1mg/kg)	19.79±2.14	19.89±1.8
Piracetam (200mg/kg)	53.40±9.44[a,b]	51.36±3.86[a,b]
Extract (800mg/kg)	41.91±5.01[b]	44.54±1.85[b]
Piracetam (200mg/kg) + Scopolamine (1mg/kg)	39.54±2.2[a,b]	39.07±4.14[a,b]
Extract (200mg/kg) + Scopolamine (1mg/kg)	25.23±9.27	24.64±3.09
Extract (400mg/kg) + Scopolamine (1mg/kg)	25.97±4.17	27.07±2.27
Extract (800mg/kg) + Scopolamine (1mg/kg)	38.89±4.78[b]	38.23±2.13[b]

The values are expressed as- Mean ± SEM (n=6). a = $p<0.05$ when compared to Vehicle (Normal) group, b = $p<0.05$ when compared to Scopolamine (Treated) group.

Table 5: Estimation of acetylcholinesterase activity by Ellman's method.

Treatment	Acetylcholinesterase enzyme activity (In µMoles/min/g of tissue)
Normal (Vehicle)	2.73±0.06
Scopolamine (1mg/kg)	3.95±0.01
Piracetam (200mg/kg)	2.56±0.04[ab]
Extract (800mg/kg)	2.63±0.02[b]
Piracetam (200mg/kg) + Scopolamine (1mg/kg)	2.85±0.02[b]
Extract (200 mg/kg) + Scopolamine (1mg/kg)	3.32±0.03
Extract (400mg/kg) + Scopolamine (1mg/kg)	3.23±0.02[b]
Extract (800mg/kg) + Scopolamine (1mg/kg)	3.10±0.01[b]

The values are expressed as- Mean ± SEM (n=6). a = $p<0.05$ when compared to Vehicle (Normal) group, b = $p<0.05$ when compared to Scopolamine (Treated) group, c = p<0.05 when compared to Group III.

Table 6: Percentage inhibition of acetylcholinesterase by microplate assay.

Treatment	% Inhibition (In Seconds)				
	0	13	26	39	52
Normal (Vehicle)	31.37±0.40	21.7±2.19	19.23±2.07	12.92±1.55	9.4±0.84
Scopolamine (1mg/kg)	25.75±0.64	17.25±1.69	15.32±0.85	4.3±1.30	7.5±1.37
Piracetam (200mg/kg)	40.42±1.01[ab]	37.21±2.71[ab]	38.97±1.77[ab]	25.12±2.4[ab]	23.12±1.89
Extract (800mg/kg)	38.42±1.91[ab]	34.12±0.80[b]	31.21±1.86[b]	22.63±1.30[b]	15.95±2.34
Piracetam (200mg/kg) + Scopolamine (1mg/kg)	36.45±0.49[b]	30.87±1.39[b]	28.03±2.01[b]	19.93±1.71[b]	19.37±1.20
Extract (200 mg/kg) + Scopolamine (1mg/kg)	31.63±0.68[b]	28.47±2.56	26.4±1.19	18.79±2.50	11.5±2.75
Extract (400mg/kg) + Scopolamine (1mg/kg)	33.63±1.88[b]	27.9±1.54[b]	27.6±3.31[b]	18.88±3.80	15.95±3.07
Extract (800mg/kg) + Scopolamine (1mg/kg)	34.19±1.19[b]	30.21±0.75[b]	27.63±0.9[b]	19.25±2.39[b]	17.31±1.34

The values are expressed as- Mean ± SEM (n=6). a = $p<0.05$ when compared to Vehicle (Normal) group, b = $p<0.05$ when compared to Scopolamine (Treated) group

to normal control and scopolamine treated groups. Most of the entries were random and failed to complete the triads (Table 3).

Effect on % Alterations

Interestingly, we noticed a marked increase in the percentage of alterations in piracetam treated animals. Similar results were seen in *Artocarpus altilis* extract-treated groups indicating learned behavior patterns. An increase in the percentage of alterations on the second day confirmed the memory retention of the previous day's experience. Though the effect is not to the extent of piracetam, our extracts in different concentrations reversed the apathy and sluggishness induced by scopolamine (Table 4).

Biochemical Analysis

Estimation of acetylcholinesterase activity by Ellman's method

Pretreatment with the fruit extract of *Artocarpus altilis* of dose level 200, 400 and 800mg/kg and followed by scopolamine administration shows a comparable reduction of AchE activity with scopolamine group, which is pre-treated with piracetam of 200mg/kg. The group which was treated with the extract alone of dose 800mg/kg also gives a comparably significant result with standard piracetam of 200mg/kg dose. However, in the presence of amnesia, the results show that the highest dose level of extract that is 800mg/kg gives a significant decline in AchE level compared to other lower doses of extract and comparable

with standard drug piracetam. The below results demonstrate the ability of the extract to improve the status of memory and learning (Table 5).

Estimation of Acetylcholinesterase by Microplate Assay

The result obtained from the estimation of % inhibition of AchE by using microplate reader showed that those animals challenged by scopolamine after pretreatment with extract at different doses showed a significant increase in % inhibition when compared to the normal and scopolamine treated groups (Table 6).

DISCUSSION

The gradual loss of memory and other cognitive functions is typically associated with advancing age. Though the presence of neurofibrillary tangles, cortical amyloid plaques are found in the brain, pathogenesis for the loss of neurons is not completely understood. So is the treatment for the condition. However, many drugs and medicinal plants are used for retarding the progression of neurodegeneration with limited success. Plants like *Centella asiatica* are used to enhance memory and intellect (medha).

Artocarpus altilis is a useful tropical plant. Its medicinal and nutritional values have been reported. It contains several flavonoids, phenols, steroids, triterpenes and several amino acids. Jiyauddin *et al.*[17] reported that the plant extract has significant antioxidant activity. Fang *et al.*[18] recorded the anti-inflammatory activity of the plant. Antioxidants and anti-inflammatory agents have a positive impact on retarding the progression of neurodegeneration. Further, flavonoids have significant antioxidant activity and the presence of flavonoids in the fruit of *Artocarpus altilis* has been reported. The present study was planned to see the action of the *Artocarpus altilis* fruit extract on learning and memory.

Acute oral toxicity studies revealed that the extract is safe at a dose of 2000mg/kg. Preliminary qualitative phytochemical analysis of extract showed positive results for alkaloids, carbohydrates, flavonoids, steroids, triterpenoids, saponins, tannins, and proteins.

EPM results revealed that the animals challenged with scopolamine and treated with of 800 mg/kg of the extract were quick to learn (ITL: 25.00±0.68) and retained the memory for the next Day (RTL: 23.34±0.98), which was comparable with piracetam (ITL: 21.66±1.2, RTL: 17.50±2.04). A similar result was observed in animals treated with extract alone. (ITL: 23.67±1.21, RTL: 20.34±1.05) suggesting the efficacy of the fruit extract in normal and amnesic animals.

We observed similar results with the Hebb-William's maze. Both ITL (55.67±4.94) and RTL:

(46.00±4.26) improved significantly in extract-treated animals as compared to the scopolamine treated animals (ITl: 149.6±10.6, RTL: 132.8±9.05). In both the models, the activity was dose dependent and we have tested to a maximum dose of 800mg/kg.

The study was carried out with Y-maze to assess spatial working memory based on two parameters, i.e., number of arm entries and % alterations. The number of entries to the different arms on the first Day and second Day was observed after treating the animals with different dose levels and compared with a standard (Piracetam), normal control and amnesic (scopolamine) group. The entries were significantly less in the extract-treated group (first Day:12.67±1.40, second Day:11.33±1) and piracetam treated animals (first Day:8.50±0.76, second Day: 8.33±0.88) as compared to scopolamine treated animals (first Day: 25.16±3.00, second Day: 26.83±0.74). However, the percentage alterations were significantly better in the treated group (first Day: 38.89±4.78, second Day: 38.23±2.13) as compared to the amnesic group (first Day: 19.79±2.14, second Day: 19.89±1.8). The observations suggest that animals, when treated with the extract, completed more triads indicating improved spatial learning and short-term memory.

Estimation of acetylcholinesterase activity by Ellman's method revealed that the Acetylcholinesterase enzyme activity decreased in dose dependent manner in extract-treated groups. The study using a microplate assay to assess the percentage inhibition of AchE corroborated the above finding. The enzyme was inhibited in a dose and time-dependent manner. This property may contribute to the elevated level of acetylcholine in the brain, thereby improving cognitive functions.

CONCLUSION

Based on the results from the present study, we concluded that the ethanolic extract of the fruit *Artocarpus altilis* has nootropic activity in the experimental animals. The finding suggested cholinergic involvement. However, the present study did not include the test for establishing the exact mechanism of action.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

EFAA: Ethanolic Extract of the Fruits of *Artocarpus altilis*; **ITL:** Initial Transfer Latency; **RTL:** Retention Transfer Latency; **AChE:** Acetylcholine esterase; **CNS:** Central Nervous System; **EPM:** Elevated Plus Maze; **DTNB:** 5,5-dithio-bis-(2-nitrobenzoic acid); **ANOVA:** Analysis of Variance.

SUMMARY

Artocarpus altilis is an evergreen plant consisting of various phytoconstituents and is widely used traditionally for the treatment of various ailments. This study was carried out to evaluate the nootropic potential of ethanolic extract of fruits of the plant *Artocarpus altilis* by using *in vitro* and *in vivo* models. The study reported the nootropic activity of the plant in *in vivo* model involving the cholinergic pathway. The study suggests for further investigations to identify the exact mechanism involved in nootropic activity.

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