CAHIERS MAGELLANES-NS
Volume 06 Issue 1
2024

ISSN:1624-1940
DOI10.6084/m9.figshare.25998085
http://magellanes.com/

SARAWATA CHURNA TREATMENT AMELIORATES THE COGNITION IMPAIRMENTS IN LITHIUM-PILOCARPINE INDUCED EPILEPTIC RATS

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Abstract:

The purpose of this study was to see how Saraswata Churna (SC) affected the cognition of 4 month old adult male Wistar rats who had epilepsy. One of the most common epilepsy symptoms is memory impairment. The elevated plus maze (EVPM) and Morris water maze (MWM) tests were used to assess the effect of SC on rat learning and memory. Pilocarpine (270 mg/kg BW, i.p.) was used to induce epilepsy.Saraswata Churna's effect on pilocarpine-induced epilepsy was evaluated. Saraswata Churna (300 mg/kg b.w. orally) improved the rats' cognitive performance, as shown by reduced latency in the EVPM, decreased escape latency during training, and more time spent in the target zone during recovery in the MWM. Saraswata Churna (300 mg/kg b.w.

ISSN:1624-1940
DOI10.6084/m9.figshare.25998085
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oral) has memory-enhancing action comparable to phenytoin (30 mg/kg b.w. i.p.). Saraswata Churna demonstrated memory-improving efficacy in rats, most likely because to its phytoconstituents, which have anti-inflammatory, antioxidant, and anticonvulsive properties.

Keywords: Saraswata Churna, Epilepsy, Dementia, Cognition, Neurocognitive illness, acetylcholine esterase inhibition,

Introduction:

Epilepsy is a brain illness defined by recurrent paroxysmal occurrences unprovoked by any immediate triggering stimulus and characterised by stereotyped behavioural abnormalities, all of which have neurobiologic, cognitive, psychologic, and social repercussions(Pradhan 2006).Epilepsy is the third most common neurological condition in the old, behind stroke and neurodegenerative diseases. It affects roughly 10 people out of every 1,000 people worldwide. Epilepsy affects people of all ages, but it is most frequent in the elderly(Fodjo, Makoy et al. 2019). Dementia is a significant neurocognitive illness in the elderly in which cognitive processes are the primary clinical deficiency. Dementia is a condition that worsens with age, increasing exponentially in the elderly(Beghi and Beghi 2020). The proportion of people experiencing seizures accompanied with cognitive loss is projected to rise as both clinical disorders become more common as they age.Both dementia and epilepsy are linked to a number of negative effects. Attention, alertness, and psychomotor speed are the major cognitive impacts. Comorbid medical disorders are more common, with depression being particularly prominent(Gualtieri, Johnson et al. 2006). Epilepsy and dementia patients are more prone to have postoperative complications, with stroke being a major concern(Gualtieri, Johnson et al. 2006, Subota, Pham et al. 2017).

The Morris water maze (MWM) and Elevated Plus Maze (EVPM) are two extensively used models for investigating the cognition behaviour in rats. The MWM test examines spatial learning and memory in particular. This task has the advantage of being learned quickly without any prior training or dietary restrictions(Vorhees and Williams 2006, Dhingra and Kumar 2012). Furthermore, by changing the testing technique, learning, memory, and elements that influence these behaviours, such as visual acuity, motor function, and motivation, can be separated Pellow et al.(Pellow, Chopin et al. 1985)used rats in the elevated plus-maze, while Lister et.al., used in mice(Lister 1987). The EVPM, which has two uncovered and two enclosed arms, is used to measure anxiety in rats and is based on rats' natural sensitivity to exposed and elevated areas.Because they abhor open arms, animals spend more time in enclosed arms than open arms. Pellow et al. (1985) found that the open arms' unpleasant character is not obvious until the rats enter them. As a result, we hypothesised that if the animal had already entered the open arms, transfer latency (the time it takes for the animal to go from the open arms to the enclosed arms) would be reduced. If this is the case, the reduced transfer latency could be linked to memory. According to this theory, the EVPM approach may be useful in finding nootropic drugs because

ISSN:1624-1940
DOI10.6084/m9.figshare.25998085
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it is simple, rapid, and does not require modifying appetitive behaviours or the introduction of aversive stimuli(Itoh, Nabeshima et al. 1990).

Preventive health principles and Ayurvedic rasayana (rejuvenative) herbs are being studied intensively for their usefulness in dementia. Saraswata Churna is a unique mixture of Medhya medicines with a high quantity of Brahmi, which has been well-known for its Nootropic and Memory boosting effects via different experiments and clinical trials (Kaushik, Jain et al. 2021). The Churna also contains medications including Kustha, Vacha, Saindhava, Pippali, Guduchi, Shankhapushpi, and Ashvagandha, which have antiinflammatory, anti-amyloidogenic, anticholinesterase, hypolipidemic, and antioxidant properties. These anti-dementia herbs are described together with pertinent research updates(Radheyshyam, Tripathi et al. 2011).As a result, Saraswata Churna has the potential to help people with dementia. Using behavioural models, the current study was conducted to explore the influence of Saraswata Churna on rat learning and memory.

Materials and Methods:

Methods:

Animals:

Four-months-old male Albino rats of the Wistar strain (n=24) weighing 180g - 250g were acquired from the Manipal Academy of Higher Education's Central Animal House Facilities in Karnataka, India after receiving the ethical approval. All of the animals were housed in the animal cage in a controlled environment (22°C and 1212 light-dark cycle, lights on at 7 a.m.). The animals were provided with pellet meal and water. All protocols for animal research were compliant with the CPCSEA.

Experimental Design:

All the animals (n=24) were divided into four experimental groups (n = 6 per group), Normal Control group (NC), Pilocarpine group (PI), Phenytoin group (PHE), Saraswata Churna group (SC), and the control group (n=6) was maintained in the home cage under normal conditions.Epilepsy model was created by a single intraperitoneal injection (270mg/kgbw) of pilocarpine 18-24 hours after Lithium chloride (127 mg/kg.b.w.) injection. At the end of 24 hours and 48 hours post first seizure occurrence (as per the Raccine Scale), Phenytoin (30mg/kgbw.i.p.) and SC (308 mg/kgbw oral) were given to the respective groups. After 14 days of inducing seizure MWM Test and EVPM Test were done for all the animals in four groups.

MWM Test to Assess Spatial Learning and Memory:
A circular polypropylene pool with a diameter of 110 cm and a depth of 20 cm was used to construct the Morris water maze (MWM) Test for rats. At room temperature, a 1.5 m diameter,

ISSN:1624-1940
DOI10.6084/m9.figshare.25998085
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45 cm deep MWM was filled with water to a depth of 26.5 cm. A harmless white coloured dye was used to make the water opaque.With the help of two threads fixed at right angles to each other on the lip of the pool, the tank was divided into four equal quadrants/zones (Z1, Z2, Z3, and Z4). A submerged platform (top surface 6 cm x 6 cm and painted white) was put 1 cm below the water's surface inside the target quadrants (Z4 in this investigation). The platform's position was maintained throughout the training session.Each animal was given four daily trials spaced by five minutes (beginning on the 8th day of drug administration and finishing on the 11th day), following which they were set free out on to the hidden platform and stay around for 20 seconds.The rat was gently placed in the water between quadrants, facing the pool wall, with the drop location changing for each trial, and given 60 seconds to locate the submerged platform throughout the training period. If the rat did not discover the platform within 60 seconds, it was gently guided onto it and left there for 20 seconds.The time it takes the animal to get from the beginning quadrant to the hidden platform in the target quadrant is known as escape latency (EL). Each animal's EL was recorded from the eighth to the eleventh day. Each animal were subjected to four days of training trials, with the starting position changing with each session as indicated below, but the target zone (Z4 in this case) remaining unchanged throughout. On the 5^{th}day (the 12th day of drug treatment), the platform was removed, and the rat was placed in one of the three quadrants and given 45 seconds to explore the target quadrant. The average time spent in each of the three quadrants, Z1, Z2, and Z3, was kept track of. The water maze's position in respect to other laboratory objects was carefully monitored.

Elevated Plus Maze (EVPM) Test:

This apparatus is shaped like a cross and stands at a height of 40 cm off the ground. The apparatus has two unclosed arms that are 50 x 10 x 59 cm in size. Two further arms, perpendicular to the unclosed arms, are closed by walls. The test takes 5 minutes per animal in total. The rat was positioned in the maze's centre, facing an open arm. Height and open areas frighten anxious rats. A rat exploring the device's unclosed arms was labelled "less worried," while a rat confined to the device's closed arms was labelled "anxious."

The variables that had been measured were a) the duration the rats spent in the unclosed arm and b) the number of times the rats enters into the closed arm.

Statistical analysis:

Version 16.0 of IBM's Statistical Packages for the Social Sciences (SPSS) was used to analyse the data and the data are displayed as Mean ± SEM(standard error of mean). Tukey's for the post-hoc analysis was done to report significance between the groups, if any found.Statistical significance was assumed at $P \leq 0.05$. Note that, * indicates $P<0.05$; ** indicates $P<0.01$; *** indicates $P<0.001$.

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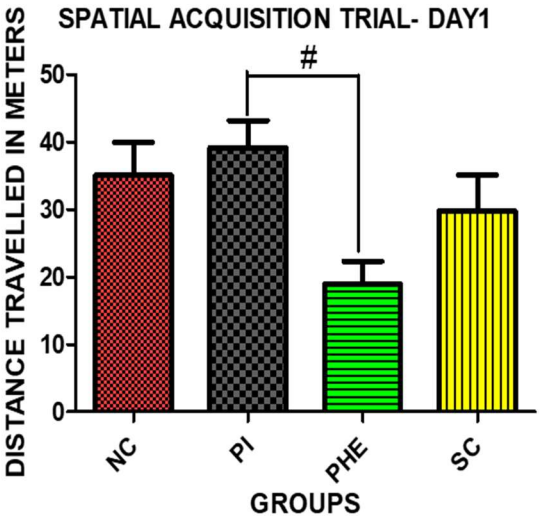
Results:

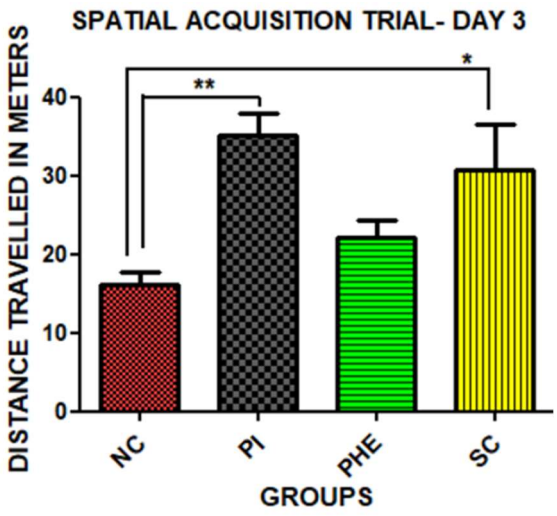
a. Morris Water Maze Test - Analysis of Spatial Learning:

The spatial acquisition learning shows significant differences between the animals in all the groups during day1 to 4 of training sessions in MWM Test. On Day 1, $p < 0.05$ between the phenytoin (18.92 ± 8.40)* and Saraswata Churna group (29.77 ± 13.22)* Graph.01; day 3, $p < 0.01$ between the Pilocarpine (35.18 ± 6.52)** and Normal Control group (16.13 ± 4.08) as well as $p < 0.05$, between Saraswata Churna (30.80 ± 14.05)* and Normal Control group (16.13 ± 4.08) Graph.02; day 4, $p < 0.05$between the Pilocarpine (28.28 ± 9.76)* and Normal Control (14.48 ± 3.03) group as well as $p < 0.05$, between Saraswata Churna (26.68 ± 5.37)* and Normal Control group (14.48 ± 3.03), Graph.03. The Tukey's Post Hoc test revealed there were no significance on the Day 2 of the 5 days experimental period, Graph.04.

On the 4thday of training, the Saraswata Churna (15.83 ± 0.91)# and Phenytoin (15.70±5.10)# groups had significantly greater latency (p0.05) than the Pilocarpine group, Graph.05.



Graph: 01. The above graphs show the distance travelled (in meters) during the spatial acquisition trials on day 1 by the animals in all the four groups: Normal Control (NC), Pilocarpine group (PI), Phenytoin treated group (PHE), and the drug Saraswata Churna (SC)



Graph: 02. The above graphs show the distance travelled (in meters) during the spatial acquisition trials on day 3 by the animals in all the four groups: Normal Control (NC), Pilocarpine group (PI), Phenytoin treated group (PHE), and the drug Saraswata Churna (SC) treated groups.

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DOI10.6084/m9.figshare.25998085
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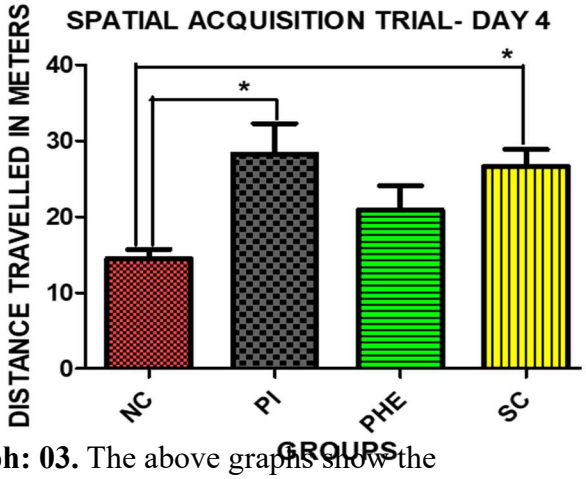
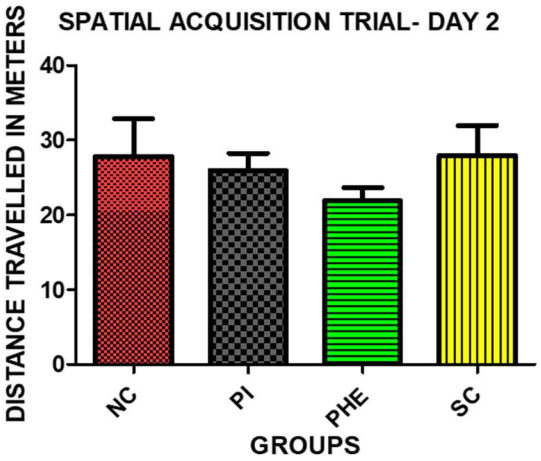
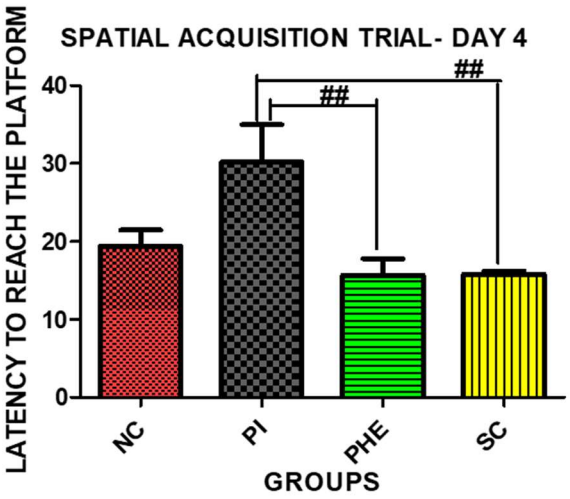


Graph: 03. The above graphs show the distance travelled (in meters) during the spatial acquisition trials on day 4 by the animals in all the four groups: Normal Control (NC), Pilocarpine group (PI), Phenytoin treated group (PHE), and the drug Saraswata Churna (SC) treated groups.



Graph: 04. The above graphs show the distance travelled (in meters) during the spatial acquisition trials on day 2 by the animals in all the four groups: Normal Control (NC), Pilocarpine group (PI), Phenytoin treated group (PHE), and the drug Saraswata Churna (SC) treated groups.



Graph: 05. The above graphs show the Latency to reach the platform (in seconds) during the spatial acquisition trials on day 4 by the animals in all the four groups: Normal Control (NC), Pilocarpine group (PI), Phenytoin treated group (PHE), and the drug Saraswata Churna (SC) treated groups.
NC- Normal Control Group, PI- Pilocarpine Group, PHE- Phenytoin Group, SC- Saraswata Churna Group
*- In Comparison with NC Group, #- In Comparison with PI Group, @- In Comparison with Phenytoin Group

b. Probe Trial - Memory Retention Test:

On the Day 5, a probe trial was conducted. There was no escape platform in the maze at the time. Each animal completed a 45-second trail. Each rat was dropped into the maze

ISSN:1624-1940
DOI10.6084/m9.figshare.25998085
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from one of four starting points and was allowed to explore the pool freely. The following measurements were recorded during the probe trial.

i. The distance travelled (in meters) by the rats from a zone (Z1, Z2, Z3, Z4) to the island zone
ii. Time it takes to reach the target quadrant
iii. Duration spent in the target quadrant

i. The distance travelled (in meters) by the rats from a zone (Z1, Z2, Z3, Z4) to the island zone:

On Day 5 of the five days experimental period, the Saraswata Churna treatment group (12.27± 0.96) *** showed a significant ($p < 0.001$) decrease in the distance travelled to reach the platform, Graph.06, in comparison to the pilocarpine group (17.17± 1.07), when compared to the Phenytoin (14.85± 2.27)* ($p<0.05$) and Normal Control groups.

ii. Latency to reach target quadrant:

The Saraswata Churna treated group (10.07 ± 4.25)* showed significant decrease in the latency, $p < 0.05$ when compared with the Phenytoin (12.37 ± 4.90) and Normal Control group (10.78 ± 1.60) to get into the escape platform, i.e. took less time to reach the platform, compared to the Pilocarpine and Phenytoin treated group in the memory retention test, with removal of platform, Graph.07.

iv. Duration spent in (Island) target quadrant:

The rats of Saraswata Churna group (25.52 ± 4.79)* stayed for longer duration in the target quadrant and group showed significant difference $p < 0.05$ in comparison to the pilocarpine group and Phenytoin treated group (20.68 ± 6.58). The pilocarpine induced group (13.70 ± 6.25)* showed significant decrease in the time spent in the target quadrant ($p < 0.05$) in comparison to the Phenytoin and Saraswata Churna treated group Graph.08. This results suggest that the Saraswata Churna treated group shows good memory retention.

ISSN:1624-1940
DOI10.6084/m9.figshare.25998085
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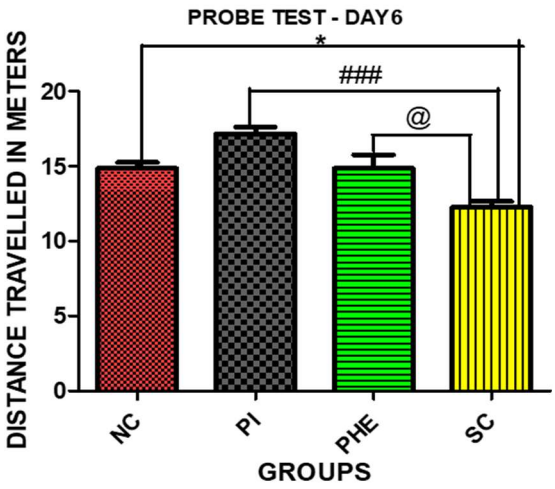
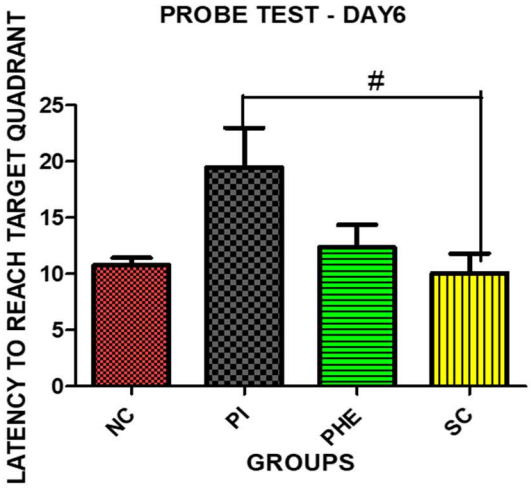
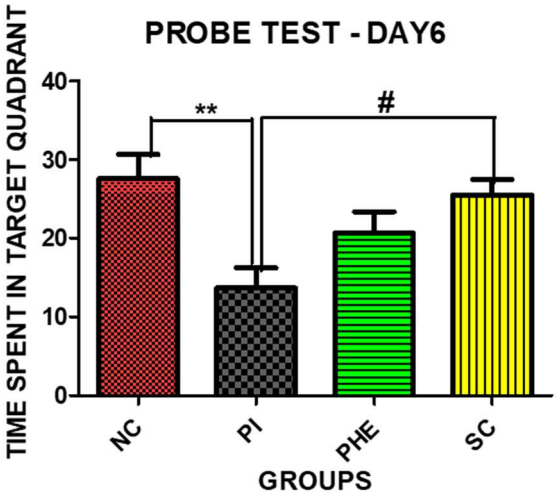


Graph: 06. The above graphs show the distance travelled (in meters) during the probe test on day 5, by the animals in all the four groups: Normal Control (NC), Pilocarpine group (PI), Phenytoin treated group (PHE), and the drug Saraswata Churna (SC) treated groups.



Graph: 07. The above graphs show the Latency (in seconds) to reach the target quadrant during the probe test on day 5, by the animals in all the four groups: Normal Control (NC), Pilocarpine group (PI), Phenytoin treated group (PHE), and the drug Saraswata Churna (SC) treated groups.



Graph: 08. The above graph shows the time spent (in seconds) in the target quadrant during the probe test on day 5, by the animals in all the four groups: Normal Control (NC), Pilocarpine group (PI), Phenytoin treated group (PHE), and the drug Saraswata Churna (SC) treated groups.

NC- Normal Control Group, PI- Pilocarpine Group, PHE- Phenytoin Group, SC- Saraswata Churna Group
*- In Comparison with NC Group, #- In Comparison with PI Group, @- In Comparison with Phenytoin Group

ISSN:1624-1940
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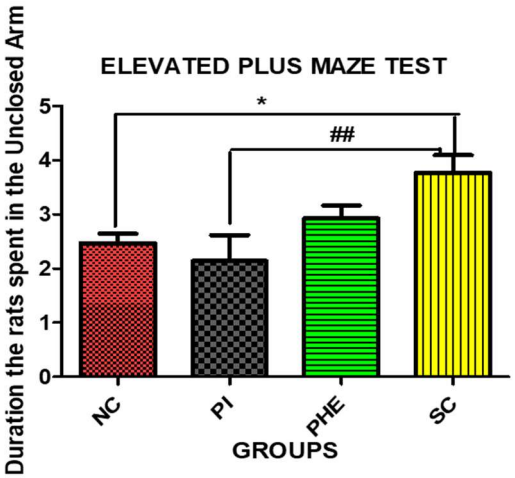
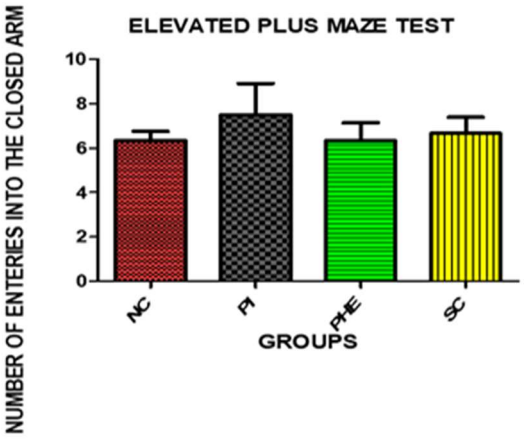
Elevated Plus Maze (EVPM) Test:

a) The duration the rats spent in the unclosed arm:

The duration spent in the unclosed arm of the EVPM apparatus by the animals are: Normal Control (NC) group (49.4%, 2.47 ± 0.43), Pilocarpine Group (PI) group (42.8%, 2.14 ± 1.17), Phenytoin (PHE) treated group (58.6%, 2.93 ± 0.58), and the drug Saraswata Churna (SC) treated group (75.4%, 3.77± 0.79)**. This result shows that SC group showed significant difference ($p \leq 0.01$) in spending more time in unclosed arm in comparison to the PI and ($p \leq 0.05$) in comparison to the PHE group which shows the cognitive effect of SC is significant in reducing the memory deficit Graph.09.



Graph: 09. The above graph shows the time spent by the animals of all the four groups in the open arm: Normal Control (NC), Pilocarpine group (PI), Phenytoin treated group (PHE), and the drug Saraswata Churna (SC) treated groups.



Graph: 10. The above graph shows the number of times entered by animals of all four groups into the closed arm: Normal Control (NC), Pilocarpine group (PI), Phenytoin treated group (PHE), and the drug Saraswata Churna (SC) treated groups.

NC- Normal Control Group, PI- Pilocarpine Group, PHE- Phenytoin Group, SC- Saraswata Churna Group

*- In Comparison with NC Group, #- In Comparison with PI Group, @- In Comparison with Phenytoin

b) The number of times the rats enters into the closed arm

Number of entries attempted by the rats in all the four groups are: Normal Control group (38 times, 6.33 ± 1.03), Pilocarpine Group (45 times, 7.50 ± 3.45), Phenytoin treated group (39 times, 6.33 ± 1.97), and the drug Saraswata Churna treated group is (40 times, 6.67 ± 1.75). This result suggests that the animals in the PHE treated group and SC treated groups' showed less number of entries into the closed arm and is significant when compared to PI group Graph.10.

ISSN:1624-1940
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Discussion:

Epilepsy and Dementia Association Mechanisms:

Epilepsy that begins in the elderly can be a symptom of a central nervous system structural disorder or injury. Several disorders, including stroke, traumatic traumas, metabolic and toxic states, result in the accumulation of brain damage with epileptogenic potential(Liu, Yu et al. 2016).Alzheimer's disease and Parkinson's disease are two neurodegenerative disorders that are frequently implicated. There are various factors that could describe why persons with dementia have seizures(Chin and Scharfman 2013). Cerebrovascular illness, for example, is a common mechanism in both vascular dementia and Alzheimer's disease.Deposition of amyloid owing to mutations in the amyloid precursor protein/ or mutations in the presenilin-1 gene are two more possibilities(Wirths, Multhaup et al. 2002).There is mounting evidence that amyloid plaque deposition and epilepsy share some similarities, implying common underlying processes for both disorders and supporting the concept that amyloid induces an increase in excitatory synaptic transmission, at least at low concentrations(Palop and Mucke 2010).

Possible mechanism of enhancing the cognition by Saraswata Churna:

Due to their antioxidant and trace element concentration, Saraswata Churna ingredients including Kustha, Vacha, Saindhava, Pippali, Guduchi, Shankhapushpi, and Ashvagandha have neuroprotective and ameliorative qualities.Guduchi (Tinospora cordifolia), Shankhapushpi (Convolvulus pleuricaulis Chois), and Vacha (Acorus calamus) are known to be high in trace elements (Zinc and Copper), which function as antioxidants and protect cells from the detrimental effects of oxygen radicals produced during immunological activation and also possess anti-stress, antioxidant properties as well as improves learning and memory(Sharma and Pandey 2010).In the Hebb William maze and the passive avoidance task, Guduchi improved cognition in normal and cognition-deficient rats(Agarwal, Malini et al. 2002). Immune stimulation and increased acetylcholine production are the mechanisms of cognitive enhancement; choline supplementation improves cognition(Singh, Banerjee et al. 2006). Apart from anti-oxidant action, acetylcholine esterase inhibition, (N-Methyl-D-aspartate) NMDA antagonism, Dopaminergic activity, and elimination of amyloidal plaques are all variables that aid in anti-dementia and neuro protection(Patil, Patki et al. 1997, Agarwal, Malini et al. 2002, Yalla Reddy, Mohana Lakshmi et al. 2010, Sangeetha, Balaji Raghavendran et al. 2011).

Conclusion:

Various plants and their separated phytochemicals have been utilised in traditional medicine for the treatment of various learning and memory issues. Saraswata Churna has a great potentiality for demonstrating activities that can be used in conditions like Alzheimer's and dementia. Finally, Sasraswata Churna demonstrated memory-enhancing activity in rats, most likely due to its antioxidant activity and inhibition of brain acetylcholinesterase activity.

ISSN:1624-1940
DOI10.6084/m9.figshare.25998085
http://magellanes.com/

Funding:
No targeted funding was reported.

Availability of data and materials:
All data and materials are presented in this manuscript. No additional materials are available.

Ethics Approval:
All experimental procedures in this study were approved by the Institutional Animal Ethics Committee (IAEC) of Kasturba Medical College, Manipal Academy of Higher Education, India.
Ethics Approval Number - IAEC/KMC/25/2019.

Authors' contributions:
a. Study planning: Sudarshan S., Pugazhandhi.B
b. Literature search: Sudarshan S., Pugazhandhi.B, Aul Amuthan, Rajesh Thangarajan,Venu Madhav Nelluri, R Huban Thomas
c. Manuscript writing: Sudarshan S., Pugazhandhi.B
d. Manuscript revision: Sudarshan S., Pugazhandhi.B, Arul Amuthan, Rajesh Thangarajan,Venu Madhav Nelluri, R Huban Thomas
e. Final approval: Sudarshan S., Pugazhandhi.B, Arul Amuthan, Rajesh Thangarajan, Venu Madhav Nelluri, R Huban Thomas

Acknowledgment:
Not Applicable

Competing interests:
Authors declare no competing interest

References:

Agarwal, A., et al. (2002). "Effect of Tinospora cordifolia on learning and memory in normal and memory deficit rats." Indian journal of pharmacology**34**(5): 339-349.

Beghi, E. and M. Beghi (2020). "Epilepsy, antiepileptic drugs and dementia." Current opinion in neurology**33**(2): 191-197.

Chin, J. and H. E. Scharfman (2013). "Shared cognitive and behavioral impairments in epilepsy and Alzheimer's disease and potential underlying mechanisms." Epilepsy & Behavior**26**(3): 343-351.

Dhingra, D. and V. Kumar (2012). "Memory-enhancing activity of palmatine in mice using elevated plus maze and Morris water maze." Advances in Pharmacological Sciences**2012**.

Fodjo, J. N. S., et al. (2019). "Epilepsy prevention." The Lancet**394**(10214): 2072.

ISSN:1624-1940
DOI10.6084/m9.figshare.25998085
http://magellanes.com/

Gualtieri, C. T., et al. (2006). "Neurocognition in depression: patients on and off medication versus healthy comparison subjects." The Journal of neuropsychiatry and clinical neurosciences**18**(2): 217-225.

Itoh, J., et al. (1990). "Utility of an elevated plus-maze for the evaluation of memory in mice: effects of nootropics, scopolamine and electroconvulsive shock." Psychopharmacology**101**(1): 27-33.

Kaushik, R., et al. (2021). "Studying the Ethno-Pharmacological Basis of Antiepileptic Activity of Medhya Rasayanas-A Nootropic Package From Ayurveda." Current Traditional Medicine**7**(5): 87-98.

Lister, R. G. (1987). "The use of a plus-maze to measure anxiety in the mouse." Psychopharmacology**92**(2): 180-185.

Liu, S., et al. (2016). "The causes of new-onset epilepsy and seizures in the elderly." Neuropsychiatric Disease and Treatment**12**: 1425.

Palop, J. J. and L. Mucke (2010). "Amyloid-β–induced neuronal dysfunction in Alzheimer's disease: from synapses toward neural networks." Nature neuroscience**13**(7): 812-818.

Patil, M., et al. (1997). "Antistress activity of Tinospora cordifolia (wild) miers." Indian drugs**34**(4): 211-215.

Pellow, S., et al. (1985). "Validation of open: closed arm entries in an elevated plus-maze as a measure of anxiety in the rat." J Neurosci Methods**14**(3): 149-167.

Pradhan, P. (2006). Investigation of Psychiatric Diagnoses in Clinical Populations with Non-epileptic Attack Disorder and Epilepsy, The University of Manchester (United Kingdom).

Radheyshyam, T., et al. (2011). "Pharmaceutical and clinical studies on compounds ayurvedic formulations, Saraswatha churna." International Research Journal of Pharmacy**2**: 77-84.

Sangeetha, M. K., et al. (2011). "Tinospora cordifolia attenuates oxidative stress and distorted carbohydrate metabolism in experimentally induced type 2 diabetes in rats." Journal of natural medicines**65**(3): 544-550.

ISSN:1624-1940
DOI10.6084/m9.figshare.25998085
http://magellanes.com/

Sharma, V. and D. Pandey (2010). "Protective role of Tinospora cordifolia against lead-induced hepatotoxicity." Toxicology international**17**(1): 12.

Singh, R., et al. (2006). "Tinospora cordifolia induces enzymes of carcinogen/drug metabolism and antioxidant system, and inhibits lipid peroxidation in mice." Phytomedicine**13**(1-2): 74-84.

Subota, A., et al. (2017). "The association between dementia and epilepsy: A systematic review and meta-analysis." Epilepsia**58**(6): 962-972.

Vorhees, C. V. and M. T. Williams (2006). "Morris water maze: procedures for assessing spatial and related forms of learning and memory." Nature protocols**1**(2): 848-858.

Wirths, O., et al. (2002). "Intraneuronal APP/Aβ Trafficking and Plaque Formation in β-Amyloid Precursor Protein and Presenilin-1 Transgenic Mice." Brain Pathology**12**(3): 275-286.

Yalla Reddy, Y., et al. (2010). "Review on effect of natural memory enhancing drugs on dementia." Int J Phytopharmacol**1**: 1-7.