Journal of Advanced Zoology
ISSN: 0253-7214
Volume 44 Issue 05 Year 2023 Page 1143:1149

Ameliorating Effect Of Myrica Esculenta In Alzheimer's Mice Model

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Article History

Received: 3 Oct 2023
Revised: 8 Nov 3023
Accepted: 5 Dec 2023

Abstract:

Alzheimer disease (AD) is a neurodegenerative ailment that is typified by psychological and behavioral impairment that significantly inhibits a person's capacity to engage in day-to-day living activities. Around one in ten persons who are over the age of 65 and around one third of those who are over the age of 85 are affected by it The practice of phytotherapy, which involves the consumption of herbal remedies, has the potential to serve as a foundational element upon which therapeutic approaches might be simplified. Therefore, the current work was conducted to investigate the anti-alzheimeric effects of plant extract from *Myrica esculenta*. The Morris water maze (MWM), elevated plus maze (EPM), and passive avoidance tests (PAT), Marble burying test were used to examine the impact of *Myrica esculenta* ethanol extracts on scopolamine-induced memory impairment in mice. Ethanolic extract of *Myrica esculenta* obtained from ethanol. In add These extracts, when given orally, were shown to enhance learning and memory in mice as measured by the Morris Water Maze, the Elevated Plus-Maze, and Marble burying test. This research suggests that *Myrica esculenta* might be used as effective therapeutic compounds in the fight against neurodegeneration. Potential therapeutic benefits of the plants may be enhanced by their unique pharmacological activity.

Keywords: Alzheimer's disease, *Myrica esculenta*, Passive avoidance, Elevated plus maze, Morris water maze

1. Introduction

Memory, thinking, emotion, sensation, and the development of motor skills all have their biological base in the synapse Synapses are destroyed by age-related diseases, injuries, and illnesses. In 2009, the World Health Organization projected that 737 million people around the globe will be 60 or older]. By 2050, this figure is expected to rise to 2 billion. There will be 227,032,000 more people in India who are 60 or older by the year 2050. One in nine people in 2009, and one in five by 2050, when expressed as a percentage of the overall population. As the population ages, neurological diseases like Alzheimer's and Parkinson's are expected to become more common. This indicates that age-related diseases are likely to proliferate across the Indian population. [1-4].

When someone has dementia, their brain is unable to operate properly because their neurons have been damaged Dementia comes from the Latin for "madness" (dementia), which combines the prefix de- (meaning "without") and the suffix mens- (meaning "mind"). This condition is characterized by interference in daily living and activities caused by impairments in many cognitive processes, including thinking, reasoning, and behavioral skills. Disruptions in social conduct and emotional regulation often accompany cognitive deficits. The specific dementia symptoms a patient experiences are determined by the specific brain region that has been damaged [5, 6].

Secondary metabolites found in plants provide a natural defense mechanism against disease. These bioactive compounds are formulated and used by humans in numerous traditional medical systems around the globe, including Ayurveda and ethonomedicine. Whether it be a combination of plants or an extract from a single plant, herbal remedies are often used in traditional medicine. However, the mechanistic properties of these medications and plant mixtures, and any historical records detailing their effects, remain unknown. Natural product research has been modified by the science establishment to better explain how these plants work or how their components might be utilized to cure illness. Ayurvedic medicine makes extensive use of the *plant Myrica esculenta*, which belongs to the family Myricaceae and is more widely regarded as Kaiphala or Katphala. Fever may be reduced by consuming an infusion made from the plant. It has also been shown that a decoction made from the plant may be used to successfully treat a cold. Gastrointestinal problems are also treated with bay berry. Asthma sufferers might also benefit greatly from Bay Berry's ability to ease their symptoms. Bronchitis and other lung disorders have also been shown to benefit from it [7-12].

The current study set out to investigate the ameliorative effect against neuroinflammation activity of *M.esculenta* to give a scientific justification for the complementary uses of phytochemicals from *M. esculenta* in the management and treatment of Alzheimer's disease.

2. Materia and Methodos

2.1. Collections, identification and preparation of plant materials

The leaves of *M. esculenta* were collected from Region of Someshwar District Almora (Uttarakhnad) and the plant was authenticated by Patanjali Research Foundation Herbium Haridwar. The leaves of the plant were washed with distilled water (DW) and dried under the shade. The plant material was then pulverized and crushed to powder for extraction.

2.2. Experimental design

In this study, Albino mice weighing between 25 and 30 g. The housing and care of the animals followed all requirements set out by the CPCSEA. Mice were kept in groups of five, with constant access to water and food, and under constant supervision at a temperature of 25 ±1°C and a relative humidity of 60±10%.

The placebo group was given merely saline solution. An intraperitoneal dose of scopolamine (1 mg/kg) was given to all other groups. Donepezil (at 20 mg/kg administered orally) was the standard treatment.

To induce amnesia and brain injury in mice, scopolamine (1 mg/kg, intraperitoneally) was administered. Oral (p.o.) administration of EEME utilizing CMC as the vehicle was done for Groups 3 and 4. In contrast, saline was used as the delivery medium for both scopolamine and donepezil.

The study drug solutions were given orally (p.o.) for 28 days, 90 minutes before the intravenous (i.v.) administration of scopolamine.

On days 21–28, subjects received an injection of scopolamine, and their behavior was studied 45 minutes later. . All the chemicals used are analytical grade and purchased from SD fine chemical limited.

2.3 In vivo study

The effects of plant extracts on the step-down passive avoidance test, MWM elevated plus, maze and the elevated plus mazewere examined..

2.3.1 Passive avoidance test

The experiment was conducted in a rat memory assessor, a custom-built box outfitted with an electrical grid and a shock-free zone (SFZ) at its core. It was decided to bring each mouse on the grid and turn off the device, giving the rodents a full minute to investigate their new environment. The instrument was activated and set to latency mode at that time. After deciding on a suitable voltage current (20V) for foot shock, the mouse was placed on the electric grid, and the test was commenced. The Latency (in s) recorded was the time it took for the mouse to enter the SFZ. Mice that waited longer than two minutes to reach the safety zone were not let in. Each mouse will have three baseline measurements collected. The number of missteps, i.e.,

from the moment the animal touches the electric grid and feels the shock to the end of the 15-minute recording period, was recorded.

2.3.2 Morris water maze:

In the MWM water tank, subjects' spatial and long-term memory may be evaluated by monitoring their reaction times, thigmotaxis times, distances travelled, and speeds. The main advantage of the MWM is that it uses relatively short, uncomplicated trials (often lasting six days) to differentiate between the spatial (hidden-platform) and non-spatial (visible-platform) circumstances. Additionally, odour trails are less likely to be disturbed in a MWM testing environment. Neuroscientists and neuropharmacologists have used this technique to probe the brain's neurological foundations for spatial reasoning. The MWM is essential for the validation of mice models of neurocognitive diseases like AD.

The Morris water maze (MWM) is a circular pool of water. Mice were trained to navigate their way out of the maze by using external visual cues to locate an escape platform submerged under the water's surface. The MWM has a 140-centimeter-diameter tank that holds water at a constant 28±2 degrees Celsius. The pool was divided into quadrants (Q1, Q2, Q3, and Q4), and a platform was set up in the centre. The MWM was located in a large room with several colored landmarks arranged around the perimeter. Four different starting points were used over the four days of training for each mouse. The "Escape latency" is the amount of time it takes to locate the concealed landing platform. The mice were allowed 90 seconds to swim around the pool after the platform was removed on day 5. The average time spent by each mouse in the target quadrant looking for the hidden platform served as a retrieval statistic [13].

2.3.3 Elevated Plus Maze Test

The elevated plus maze for mice included two open arms that were 16 centimetres by 5 centimetres and two covered arms that were 16 centimetres by 5 centimetres by 15 centimetres. These arms stretched from a central platform that was 5 centimetres by 5 centimetres, and the maze was raised to a height of 25 centimetres from the ground. On day one, we separated the mice into groups and put them on opposite ends of open arms, with their backs to the platform in the middle. When measuring how long it took an animal to travel from the open arm to one of the closed arms using all four legs, we called this measure "transfer latency" (TL). Every animal's TL was determined on day 1 (the 27th day after medication delivery). If the rat failed to reach the enclosed arm before 90 seconds, it was cajoled in by hand and given a 90-second TL. After 2 more minutes of maze navigating, the mouse was put back in its cage. Memory for this newly acquired skill was tested 24 hours (on day 28) following the first trial [13].

2.3.4 Marble Burying test:

Mice are known to like digging, both in their natural environments (such as burrows and escape tunnels) and in artificial ones (such as normal cage bedding), and this is used in the marble burying test. In a nutshell, male mice were isolated for 20 minutes in a polypropylene cage (37 x 21 x 14 cm) with 20 glass marbles (10 mm in diameter) spread out over 5 cm deep sawdust. The testing enclosures were isolated from the living area. For this study, we defined obsessive digging as the tendency to bury at least two-thirds of a set of marbles within 20 minutes [14].

2.4 Statistical analysis

Mean ± S.E.M. values are used to represent data. Two groups were compared utilizing Graph Pad Prism 5's one-way analysis of variance (ANOVA) and Tukey's post hoc test for statistical significance. When the value p was less than 0.05, it was judged to be statistically significant.

3. Results

3.1. Step-down passive avoidance test parameters

The step-down latency of the scopolamine-treated group was considerably lower than that of the control group ($p < 0.001$). The delay reduction seen in the step-down condition was reversed in the standard group ($p < 0.001$). The step-down delay significantly increased after EEME 200 and 400 treatments ($p < 0.05$ and $p < 0.001$) as against scopolamine group.

The scopolamine group had a longer escape delay than the control group by a statistically significant margin ($p < 0.001$). When given after scopolamine, donepezil greatly reduced the prolonged escape latencies ($p < 0.001$). EEME 400 considerably reduced escape delay ($p < 0.01$), while EEME 200 could not significantly alter escape latency in comparison to the scopolamine group.

The scopolamine group made significantly more mistakes than the control group ($p < 0.001$), while the

standard medication and EEME 400 reduced mistakes frequency ($p < 0.001$), while EEME 200 could not significantly lessen No. of mistakes in comparison to the scopolamine group

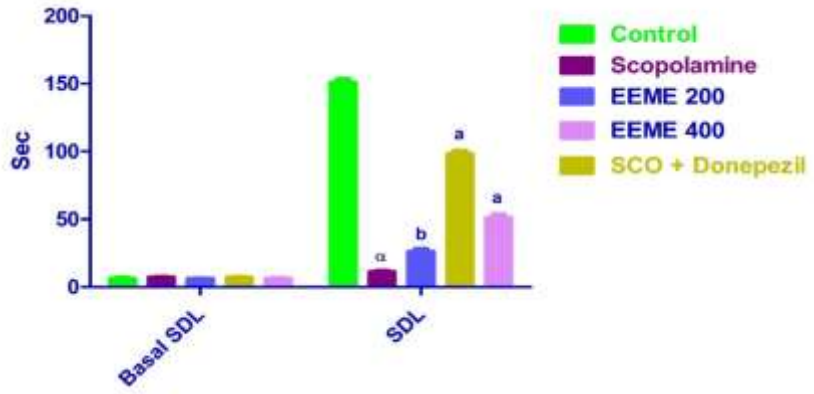

Figure 3.1.: Effect of EEME on SDL in Passive Avoidance Test

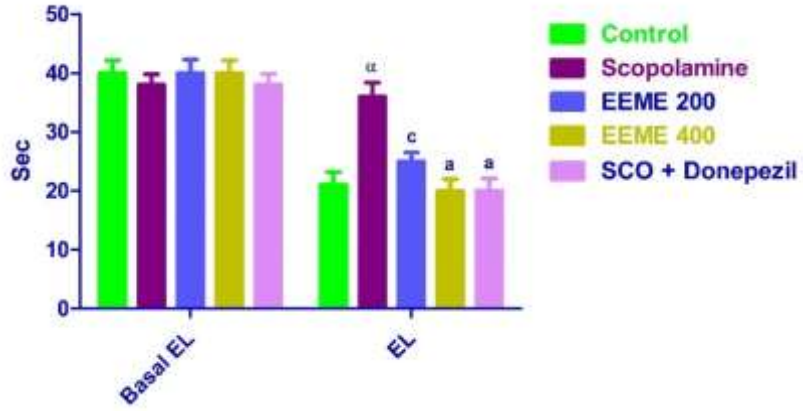

Figure 3.2: Effect of EEME on EL in step down passive avoidance test

3.2. Effect of EEME on behavioral parameters in Morris Water Maze

The Scopolamine group had considerably shorter escape latencies than the control group throughout all five days of testing. ($p < 0.001$). The first day of EEME 200 treatment resulted in a substantial increment in escape latency relative to the scopolamine group ($p < 0.01$), but this effect was attenuated by the fourth and fifth days of testing ($p < 0.001$). On each of the five days of the experiment, the EEME 400 group showed significantly lower levels than the scopolamine group ($p < 0.01$, $p < 0.001$, $p < 0.001$, and $p < 0.001$).

Time spent in target quadrant (TSTQ) was also measured, and it was shown to be considerably lower in the scopolamine group ($p < 0.001$) relative to the control group, while it was found to be significantly higher in all medication treatment groups ($p < 0.001$), relative to scopolamine group

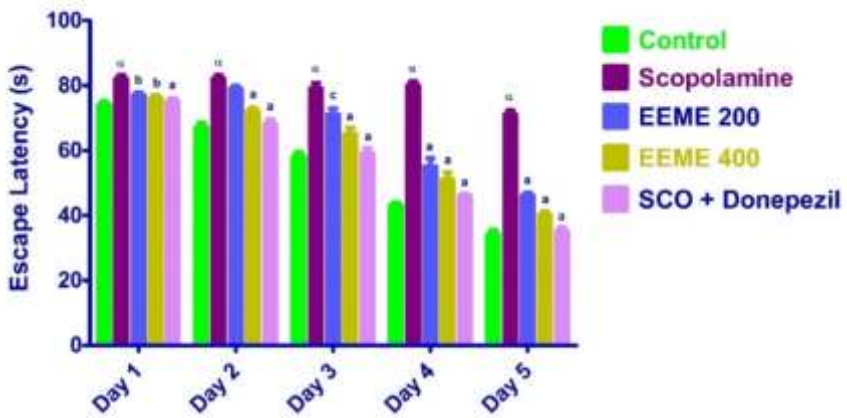

Figure 3.3: Effect of EEME on Escape Latency on Morris Water Maze

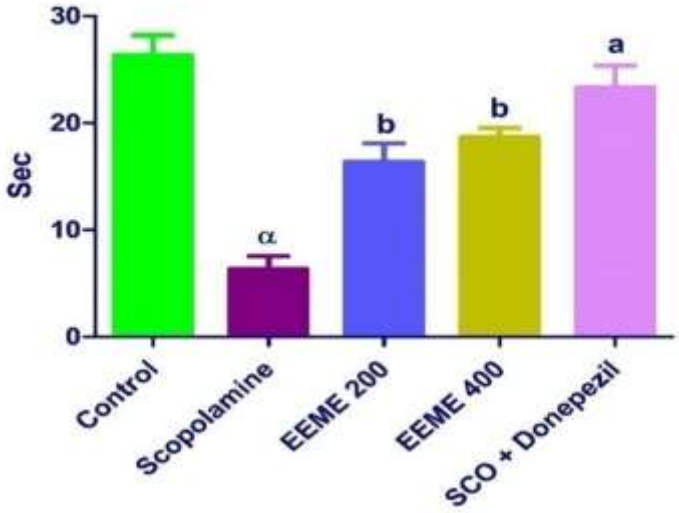

Figure 3.4: Effect of EEME on time spent in target quadrant

3.4. Effect of EEME on transfer latency (TL) of mice using elevated plus maze

The scopolamine group had a significantly longer transfer delay as against the control group ($p < 0.001$). The transfer latency was significantly reduced by EEME 200, 400, and donepezil groups as against the scopolamine group ($p < 0.05$, $p < 0.01$, and $p < 0.001$ respectively), however EEM E200 administration had no effect on transfer latency.

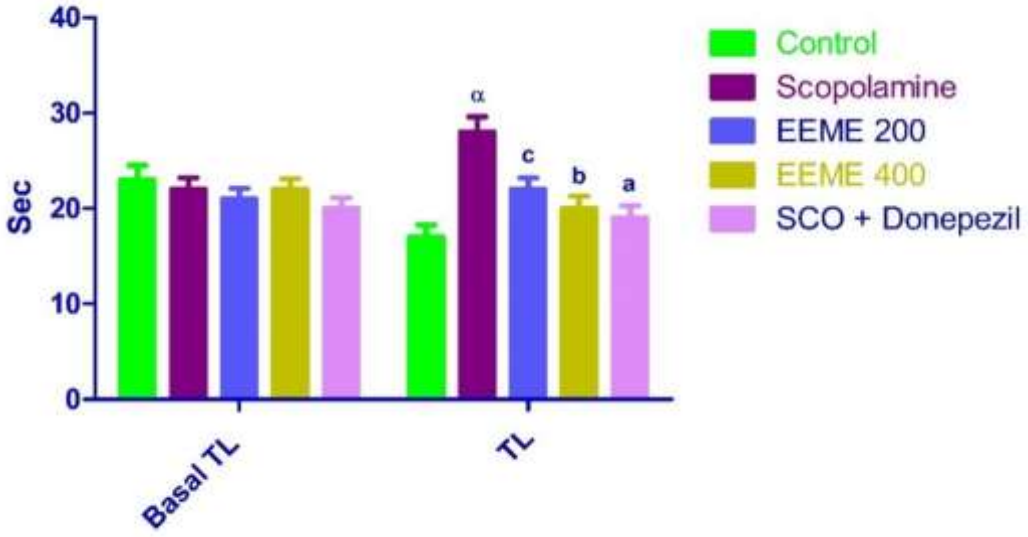

Figure 3.5: Effect of EEME on transfer latency (TL) of mice using elevated plus maze

3.5 Effect of EEME on Marble burying test

Scopolamine-induced Alzheimer's disease led to significantly more marble digging relative to the control group ($p < 0.05$). The frequency of marbles dug decreased after therapy using EEME 400 and Donepezil ($p < 0.01$ and $p < 0.01$), but there was no significant difference between the EEME 200 and scopolamine groups.

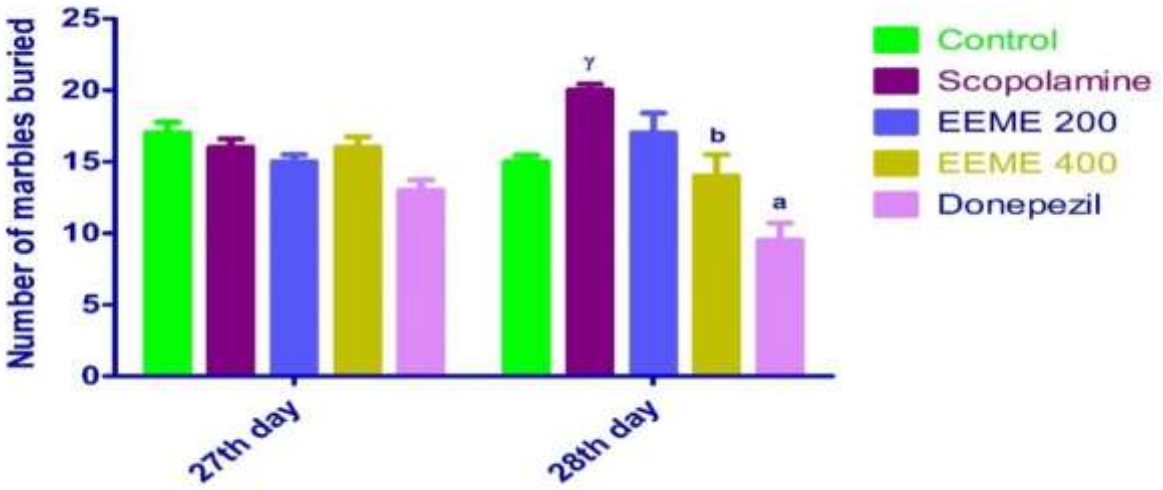

Figure 3.6: Effect of EEFP on MBT

4. Discussion

This study examined whether *Myrica esculenta* improves memory in memory-impaired people via cholinergic pathways. Herbal medicines heal Alzheimer's and memory loss. Ethanolic extracts of *Myrica esculenta* (EEME) were tested on AD mice's memory in the passive avoidance task (PAT), Morris water maze (MWM), and elevated plus maze (EPM).

A brain's cholinergic system controls mental functioning. The muscarinic receptor antagonist scopolamine causes amnesia in animals. This study showed scopolamine dramatically altered mouse memory[15].

Daily extracts for 28 days enhanced mice's scopolamine-induced amnesia. Scopolamine inhibits brain muscarinic cholinergic receptors, affecting learning and memory and causing short- and long-term memory loss. We tested this idea with scopolamine, a mouse memory loss model [16].

Scopolamine immediately after training lowered PAT SDLs. As an amnesic, scopolamine (1 mg/kg) decreased SDL and increased escape delay. Scopolamine preferentially inhibits memory consolidation, according to these findings Scopolamine reduces memory-related protein production in the cholinergic and GABAergic brain systems.Scopolamine shortened step-down latency, whereas 200 and 400 mg/kg EEME i.p. extended it. Donepezil significantly reduced step-down delay compared to the placebo group ($P<0.001$). The extract-treated group had far reduced escape latencies than the scopolamine-treated vehicle group at 200 and 400 mg/kg i.p. Therapy groups made less mistakes, indicating negative reinforcement. Other studies found passive avoidance test results comparable.

After 28 days of extracts, mice's memory improved greatly. Raised plus maze and Morris water maze behavioral models examined learning and memory. These models assess cognition-affecting medications [17,18].

Transfer latency reduced on day 28 of the raised plus maze, suggesting memory gain and vice versa. In the Morris water maze, shorter escape latencies during training and longer target quadrant times during retrieval increased learning and recall. In both behavioural models used to study memory pathways, mice with the greater dose of extracts (400 mg/kg) had superior memory than those with the lower dose (200 mg/kg).

5. Conclusion

These findings suggest that therapeutic compounds obtained from *Myrica esculenta* could be of some assistance in the fight against neurodegeneration. There is a possibility that the pharmacological actions of the plants, both *in vitro* and *in vivo*, contribute to their potential therapeutic usefulness.

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