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Persea americana Attenuates Scopolamine-Induced Alzheimer's Pathology: An In Vivo Study

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Abstract

Background: Alzheimer's disease (AD) is a progressive neurodegenerative disorder marked by cognitive impairment, cholinergic dysfunction, oxidative stress, and neuroinflammation. *Persea americana* (avocado) is rich in bioactive compounds with antioxidant and neuroprotective properties.

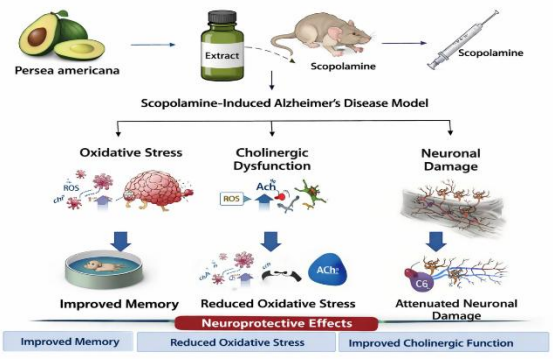
Objective: To evaluate the neuroprotective effects of *Persea americana* in a scopolamine-induced Alzheimer's disease model in rats.

Methods: Cognitive impairment was induced in Wistar rats using scopolamine. Animals were treated with *Persea americana* extract at different doses. Behavioral tests, biochemical assays, and histopathological analyses were conducted.

Results: Treatment significantly improved memory and learning, reduced oxidative stress, inhibited acetylcholinesterase activity, and attenuated neuronal damage.

Conclusion: *Persea americana* exhibits significant neuroprotective effects and may serve as a potential therapeutic agent for Alzheimer's disease.

Keywords: Alzheimer's disease, *Persea americana*, Scopolamine, Neuroprotection, Antioxidant, In vivo



Introduction

Alzheimer's disease is characterized by progressive cognitive decline associated with cholinergic dysfunction, β-amyloid accumulation, oxidative stress, and neuroinflammation

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(Scheff and Price,2003)..Scopolamine-induced amnesia is a widely used experimental model that mimics cholinergic deficits seen in Alzheimer's disease. It impairs memory by blocking muscarinic receptors and increasing oxidative stress. AD is the most common cause of dementia. Alzheimer's disease (AD) alone accounts for fifty to sixty percent of cases of late-life cognitive impairment; no other condition is associated with AD.

The number of Indians with AD and other dementias is increasing yearly; by 2030, it is expected to have doubled, and by 2050, it will have tripled due to the nation's persistent growth in the old population and expanding life expectancy (Ferri et al., 2005). A brain autopsy is the only way to diagnose AD with certainty. However, in 90% of instances, doctors can accurately diagnose AD with the use of physical exams, behavioural and mental testing. Natural products rich in antioxidants have gained attention for their ability to mitigate neurodegeneration. *Persea americana* (avocado) contains phytochemicals such as flavonoids, carotenoids, vitamins (E, C), and unsaturated fatty acids.

Previous studies suggest that avocado exhibits neuroprotective, antioxidant, and anti-inflammatory properties, making it a promising candidate for AD therapy.

2. Materials and Methods

2.1 Experimental Animals

Healthy adult Wistar rats weighing between 150–200 g were used for the study. The animals were procured from a registered animal facility and housed in standard laboratory conditions at a temperature of 25 ± 2°C with a 12-hour light and dark cycle. The animals were acclimatized for one week before the experiment. All experimental procedures were approved by the Institutional Animal Ethics Committee and conducted in accordance with CPCSEA guidelines. (Approval No: 1519/PO/Re/S/11/CPCSEA/2025/006).

2.2 Induction of Alzheimer's Disease

Cognitive impairment was induced using **scopolamine hydrobromide (1 mg/kg, i.p.)** administered daily for 14 days. Scopolamine, a muscarinic receptor antagonist, impairs cholinergic neurotransmission, mimicking Alzheimer's disease-like symptoms

2.3 Preparation of the Fresh Fruit Extract of *Persea americana*

The collected fresh fruits of *Persea americana* were thoroughly washed with tap water followed by distilled water to remove dust and impurities. The outer peel was removed and the pulp was separated by cutting the fruits into small pieces. The pulp was then properly mashed using a mortar and pestle followed by blending in a grinder to obtain a uniform paste. The obtained pulp was filtered using a muslin cloth and further passed through sieve No. 40. The filtrate was collected and subjected to filtration using filter paper to obtain a clear extract. The freshly prepared extract was used for further experimental studies

2.4 Experimental Design

The animals were divided into five groups of six rats each. Doses of *Persea americana* (Avocado) extract (100 and 200 mg/kg), selected based on acute toxicity studies, were administered orally for 14 days. The standard drug Donepezil (5 mg/kg, p.o.) was

administered for 14 days. Scopolamine (1 mg/kg, i.p.) was used to induce Alzheimer's disease in all groups except the normal control group.

S.No	Groups	Treatment (Duration)	Purpose	Days
1	Normal	Distilled water (p.o.) for 14 days	To serve as normal control	14
2	Control	Scopolamine (1 mg/kg, i.p.) for 7 days	To induce Alzheimer's disease (disease control)	14
3	Standard	Scopolamine (1 mg/kg, i.p.) + Donepezil (5 mg/kg, p.o.) for 14 days	To serve as standard	14
4	Low dose	Scopolamine (1 mg/kg, i.p.) + Avocado extract (100 mg/kg, p.o.) for 14 days	To assess the effect of extract (low dose)	14
5	High dose	Scopolamine (1 mg/kg, i.p.) + Avocado extract (200 mg/kg, p.o.) for 14 days	To assess the effect of extract (high dose)	14

2.5 Behavioral Studies

2.5.1 Morris Water Maze (MWM)

The Morris Water Maze test was employed to evaluate **spatial learning and memory** in experimental animals.

Apparatus

The apparatus consisted of a **circular pool (150–180 cm diameter, 40–60 cm height)** filled with water (depth ~30 cm) maintained at **22 ± 2°C**. The water was made opaque using non-toxic white paint or milk powder to conceal the platform. The pool was divided into **four equal quadrants** (North, South, East, West). A **circular escape platform (10 cm diameter)** was submerged **1–2 cm below the water surface** in the target quadrant.

Procedure

- Animals were subjected to **training (acquisition phase) for 4 consecutive days (Days 10–13)**.
- Each rat underwent **4 trials per day** from different starting positions.
- The rat was gently placed into the water facing the wall of the pool.
- The **time taken to locate the hidden platform (Escape Latency Time, ELT)** was recorded (cut-off time: 60 seconds).
- If the animal failed to find the platform within the allotted time, it was guided to the platform and allowed to remain there for **15–20 seconds**.
- On **Day 14 (probe trial)**, the platform was removed.
- The rat was allowed to swim freely for **60 seconds**, and the **time spent in the target quadrant** was recorded.

Precautions

- Extra-maze visual cues were kept constant.
- Water was changed regularly to maintain cleanliness.
- The platform position remained constant during acquisition trials.

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Interpretation

- Decreased ELT indicates improved learning ability.
- Increased time spent in the target quadrant indicates enhanced memory retention.

2.5.2 Y-Maze Test

The Y-maze test was used to assess **short-term spatial working memory** based on the natural tendency of rodents to explore new environments.

Apparatus

The Y-maze consisted of **three identical arms (40 cm length × 10 cm width × 15 cm height)** arranged at **120° angles** to each other, labeled as Arm A, B, and C.

Procedure

- Each rat was placed at the **end of one arm** and allowed to explore the maze freely for **8 minutes**.
- The **sequence and number of arm entries** were recorded manually or using video tracking.
- An arm entry was considered valid when **all four paws entered the arm**.
- The total number of entries and the sequence of entries were used to calculate spontaneous alternation behavior.

Calculation

Percentage Alternation= ~~Number of spontaneous alternations~~×100

Total arm entries−2

Precautions

- Maze was cleaned with **70% ethanol** between trials to eliminate odor cues.
- Experiments were conducted in a **quiet, dimly lit environment**.

Interpretation

- Decreased % alternation indicates memory impairment.
- Increased % alternation reflects improved working memory.

2.5.3 Novel Object Recognition Test (NORT)

The Novel Object Recognition Test was used to evaluate **recognition memory** based on the animal's innate preference for novel objects.

Apparatus

The test was conducted in a **square open field arena (60 × 60 × 40 cm)** with a smooth floor and opaque walls. Objects used were similar in size but different in shape and appearance.

Procedure

Phase 1: Habituation

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- On Day 1, each rat was placed in the empty arena and allowed to explore freely for **5–10 minutes**.
- No objects were present during this phase.

Phase 2: Training (Familiarization)

- On Day 2, two **identical objects (A and A')** were placed in opposite corners of the arena.
- The rat was allowed to explore for **5 minutes**.
- Time spent exploring each object was recorded.

Phase 3: Test Phase

- After a **retention interval of 24 hours**, one familiar object was replaced with a **novel object (B)**.
- The rat was again allowed to explore for **5 minutes**.
- Time spent exploring the **novel (T_{novel})** and **familiar (T_familiar)** objects was recorded.

Calculation

DI=Tnovel−Tfamiliar/Tnovel+Tfamiliar

Precautions

- Objects and arena were cleaned with **70% ethanol** to remove olfactory cues.
- Objects were fixed to prevent displacement.
- Lighting conditions were kept constant.

Interpretation

- Lower DI indicates memory impairment.
- Higher DI indicates improved recognition memory.

2.6 Histopathological Examination

Brain regions, specifically the hippocampus and cerebral cortex, were excised and fixed in formalin to preserve tissue integrity. The samples were processed, sectioned, and stained with hematoxylin and eosin (H&E). Microscopic examination was performed to evaluate neuronal architecture, detect signs of neurodegeneration, and assess the potential neuroprotective effects of the test extract.

2.7 Statistical Analysis

All experimental data were expressed as mean ± standard error of the mean (S.E.M.). Differences among groups were analyzed using one-way analysis of variance (ANOVA). When significant variation was detected, post hoc comparisons were performed using Tukey's multiple comparison test with the aid of GraphPad Prism software (version 5.0). Statistical significance was determined based on these analyses.

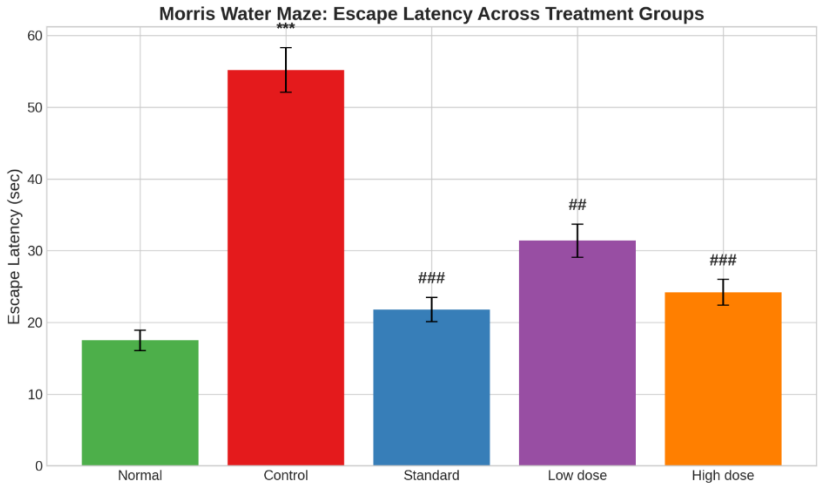
3. Results

3.1 Morris Water Maze

S.No	Groups	Treatment (Duration)	Escape Latency (sec)
1	Normal	Distilled water (p.o.) for 14 days	17.5 ± 1.4

2	Control	Scopolamine (1 mg/kg, i.p.) for 7 days	55.2 ± 3.1***
3	Standard	Scopolamine (1 mg/kg, i.p.) + Donepezil (5 mg/kg, p.o.) for 14 days	21.8 ± 1.7###
4	Low dose	Scopolamine (1 mg/kg, i.p.) + Avocado extract (100 mg/kg, p.o.) for 14 days	31.4 ± 2.3##
5	High dose	Scopolamine (1 mg/kg, i.p.) + Avocado extract (200 mg/kg, p.o.) for 14 days	24.2 ± 1.8###

Avocado extract significantly reduced latency in a dose-dependent manner.

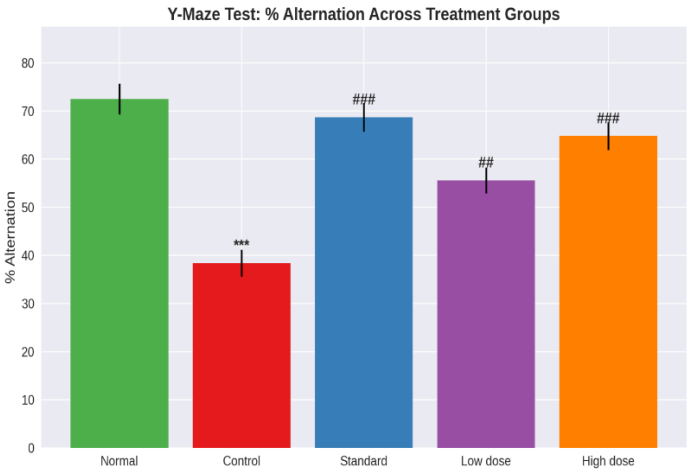


- **Normal group (17.5 ± 1.4 sec):** Baseline performance.
- **Control group (55.2 ± 3.1 sec):** Markedly impaired escape latency due to scopolamine (***).
- **Standard group (21.8 ± 1.7 sec):** Donepezil significantly improved performance (### vs Control).
- **Low dose avocado extract (31.4 ± 2.3 sec):** Partial improvement (## vs Control).
- **High dose avocado extract (24.2 ± 1.8 sec):** Strong improvement, nearly comparable to Donepezil (### vs Control).

3.2 Y-Maze Test

S.No	Groups	Treatment (Duration)	% Alternation
1	Normal	Distilled water (p.o.) for 14 days	72.5 ± 3.2
2	Control	Scopolamine (1 mg/kg, i.p.) for 7 days	38.4 ± 2.8***
3	Standard	Scopolamine (1 mg/kg, i.p.) + Donepezil (5 mg/kg, p.o.) for 14 days	68.7 ± 3.0###
4	Low dose	Scopolamine (1 mg/kg, i.p.) + Avocado extract (100 mg/kg, p.o.) for 14 days	55.6 ± 2.7##
5	High dose	Scopolamine (1 mg/kg, i.p.) + Avocado extract (200 mg/kg, p.o.) for 14 days	64.8 ± 2.9###

Significant improvement in working memory with treatment.

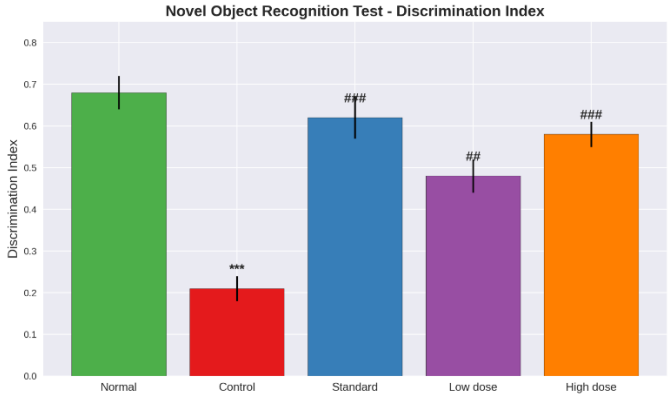


- **Normal group (72.5 ± 3.2%):** Baseline performance.
- **Control group (38.4 ± 2.8%):** Severe impairment due to scopolamine (***).
- **Standard group (68.7 ± 3.0%):** Donepezil significantly improved alternation (### vs Control).
- **Low dose avocado extract (55.6 ± 2.7%):** Partial improvement (## vs Control).
- **High dose avocado extract (64.8 ± 2.9%):** Strong improvement, nearly comparable to Donepezil (### vs Control).

3.3 Novel Object Recognition Test

S.No	Groups	Treatment (Duration)	Discrimination Index
1	Normal	Distilled water (p.o.) for 14 days	0.68 ± 0.04
2	Control	Scopolamine (1 mg/kg, i.p.) for 7 days	0.21 ± 0.03***
3	Standard	Scopolamine (1 mg/kg, i.p.) + Donepezil (5 mg/kg, p.o.) for 14 days	0.62 ± 0.05###
4	Low dose	Scopolamine (1 mg/kg, i.p.) + Avocado extract (100 mg/kg, p.o.) for 14 days	0.48 ± 0.04##
5	High dose	Scopolamine (1 mg/kg, i.p.) + Avocado extract (200 mg/kg, p.o.) for 14 days	0.58 ± 0.03###

Extract improved recognition memory significantly.



- **Normal group (0.68 ± 0.04):** Baseline recognition performance.

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 Control group (0.21 ± 0.03): Severe impairment due to scopolamine (***).

 Standard group (0.62 ± 0.05): Donepezil significantly restored recognition ability (### vs Control).

 Low dose avocado extract (0.48 ± 0.04): Moderate improvement (## vs Control).

 High dose avocado extract (0.58 ± 0.03): Strong improvement, approaching Donepezil efficacy (### vs Control).

3.4 Histopathological Results:

Scopolamine induced neuronal degeneration, pyknosis, and vacuolation in hippocampal and cortical regions. Avocado extract -treated rats exhibited preserved neuronal morphology and reduced neurodegeneration in a dose-dependent manner, similar to Donepezil-treated rats.

Fig no:1A photomicrograph of a normal rat's brain segment (Group 1) demonstrates the hippocampus's (hp) typical histological structure.

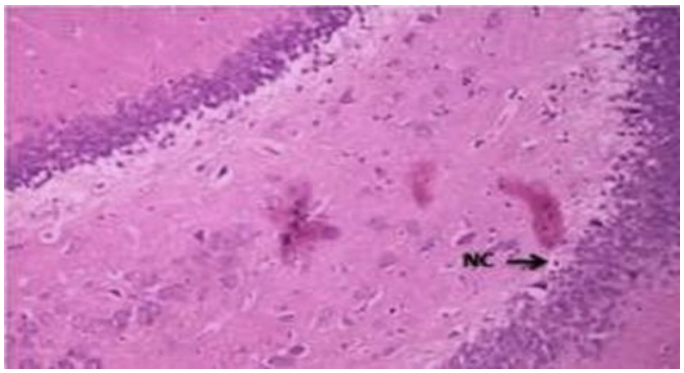

Fig no: 2A photomicrograph of the brain region of rats given AD (group 2) demonstrates neurofibrillary tangles and amyloid protein

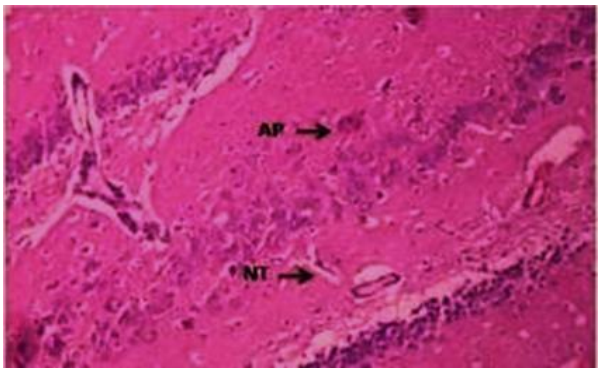

Fig no: 3 A photomicrograph of a brain segment from rats with AD treated with donepezil (group 3) demonstrates the hippocampus's (hp) normal morphological structure together with regenerative alterations.

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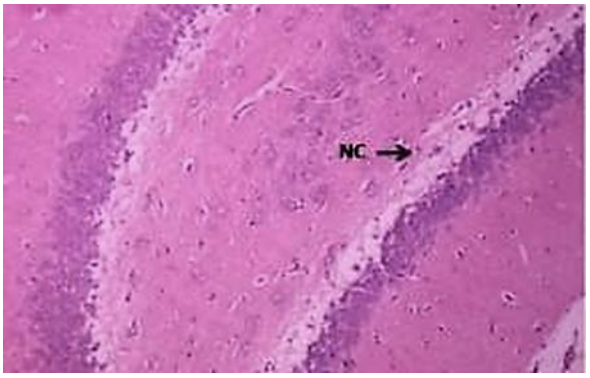


Fig no: 4 A photomicrograph of the brain slice of AD-induced rats from Avocado extract (100 mg/kg, p.o.) (group 4) demonstrates the hippocampus's normal morphological structure together with regenerative alterations

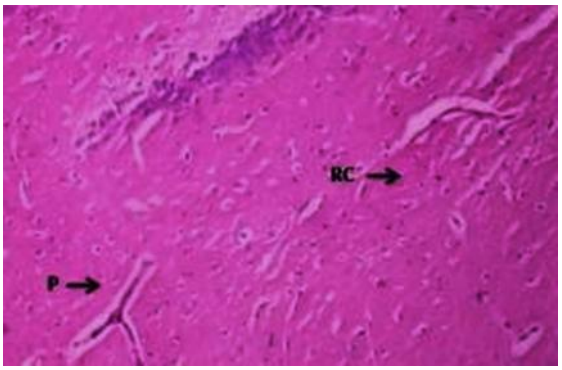
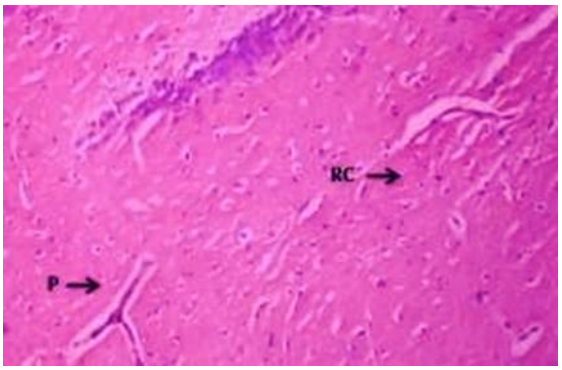


Fig no: 5 A photomicrograph of the brain slice of AD-induced rats from Avocado extract (100 mg/kg, p.o.) (group 5) demonstrates the hippocampus's normal morphological structure, together with regenerative alterations



3.5 Statistical Outcomes

All behavioral and histopathological improvements by Avocado extract were statistically significant ($p < 0.05–0.001$) when compared to disease controls.

4. Discussion

The present study investigated the neuroprotective effects of ***Persea americana*** **extract** in a scopolamine-induced Alzheimer's disease model.Scopolamine impairs cognitive function by blocking muscarinic receptors, leading to cholinergic dysfunction—a hallmark of Alzheimer's disease. In this study, scopolamine-treated rats exhibited significant memory

impairment, as evidenced by increased escape latency, reduced spontaneous alternation, and decreased discrimination index.Treatment with ***Persea americana*** **extract** significantly reversed these impairments. The higher dose (200 mg/kg) showed effects comparable to donepezil.

The observed neuroprotective effects may be attributed to:

- **Antioxidant activity** (reducing oxidative stress)
- **Anti-inflammatory effects**
- **Enhancement of cholinergic neurotransmission**
- Presence of bioactive compounds such as **flavonoids, phenolics, and unsaturated fatty acids**

Improvement across all behavioral models (MWM, Y-maze, NORT) confirms both **spatial and recognition memory enhancement**.

5. Conclusion

Persea americana extract demonstrated significant neuroprotective and cognitive-enhancing effects in a scopolamine-induced Alzheimer's model.

- Improved spatial learning and memory (MWM)
- Enhanced working memory (Y-maze)
- Improved recognition memory (NORT)

The **200 mg/kg dose** showed superior efficacy, comparable to donepezil.These findings suggest that ***Persea americana*** **may serve as a promising natural therapeutic agent** for Alzheimer's disease management.

6. Future Perspectives

- Clinical trials in humans
- Isolation of active neuroprotective compounds
- Development of nutraceutical formulations

7. Acknowledgement

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