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Research Article

Comparative Neuroprotective Study on Scopolamine-Induced Alzheimer's-Like Cognitive Deficits in Rats

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Abstract:
Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by memory loss, cognitive impairment, oxidative stress, and cholinergic dysfunction. The present study was designed to evaluate and compare the neuroprotective effects of Bacopa monnieri and Centella asiatica against scopolamine-induced Alzheimer's-like cognitive deficits in rats. Wistar rats were divided into seven groups, including normal control, scopolamine control, standard drug-treated (donepezil), and treatment groups receiving low and high doses of Bacopa monnieri and Centella asiatica. Cognitive function was assessed using the Morris Water Maze (MWM) and Y-Maze tests. Biochemical parameters such as acetylcholinesterase (AChE), lipid peroxidation (MDA), superoxide dismutase (SOD), catalase (CAT), reduced glutathione (GSH), and total protein were estimated. Histopathological examination of brain tissue was also performed. Scopolamine administration resulted in significant cognitive impairment, increased AChE activity and lipid peroxidation, and decreased antioxidant enzyme levels and total protein, confirming induction of Alzheimer-like pathology. Treatment with both plant extracts significantly improved behavioral performance, reduced AChE activity and MDA levels, and restored antioxidant enzymes and protein levels in a dose-dependent manner. Histopathological findings revealed reduced neuronal degeneration and improved brain architecture in treated groups. Comparative evaluation indicated that Bacopa monnieri exhibited superior neuroprotective activity compared to Centella asiatica, particularly at higher doses, with results comparable to the standard drug donepezil. In conclusion, the findings suggest that both Bacopa monnieri and Centella asiatica possess significant neuroprotective and cognitive-enhancing properties, with Bacopa monnieri emerging as a more potent therapeutic candidate for the management of Alzheimer's disease.
Keywords: Alzheimer's disease, Bacopa monnieri, Centella asiatica, Scopolamine, Neuroprotection, Antioxidant, Memory.

Introduction

Alzheimer's disease (AD) is a chronic, progressive, and irreversible neurodegenerative disorder characterized by a gradual decline in memory, cognitive function, and behavioral

abilities that interferes with daily life and social activities. It is the most common form of dementia, accounting for approximately 60–80% of all dementia cases worldwide.

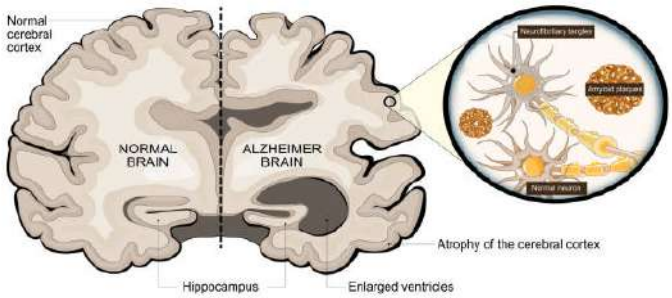

Figure 1: Image of Alzheimer disease (AD)

Epidemiology and Global Burden: Alzheimer's disease poses a major global health challenge. According to the World Health Organization (WHO), more than 55 million people are currently living with dementia, and approximately 10 million new cases occur each year, of which Alzheimer's disease constitutes the majority. The Global Burden of Disease (GBD) 2021 report estimates that the prevalence of Alzheimer's will triple by 2050, mainly due to increasing life expectancy and aging populations.

Plant Profile

Plant of Bacopa monnier

Medicinal plants have long been employed in Ayurvedic and traditional systems of medicine for promoting mental health and cognitive functions.

Among these, Bacopa monnieri (Brahmi) and Centella asiatica (Gotu Kola) are well-recognized as Medhya Rasayanas-rejuvenating herbs for intellect and memory.

Figure 2: Plant of Bacopa monnier

Pharmacological Activity

Antioxidant Activity:

Enhances superoxide dismutase (SOD), catalase (CAT), and glutathione (GSH) activity in brain tissue.

Neuroprotection:

Protects neurons against β-amyloid toxicity and scopolamine-induced oxidative stress.

Adaptogenic and Anxiolytic Effects:

Reduces corticosterone and stress-induced memory impairment.

Plant Profile of Centella asiatica

Figure 3: Plant of Centella asiatica

Pharmacological Activity

Memory Enhancement: Improves long-term potentiation and enhances neuronal dendritic arborization.

Antioxidant and Anti-inflammatory Effects: Protects hippocampal neurons from oxidative injury.

Neurogenesis: Stimulates neurite outgrowth and promotes brain-derived neurotrophic factor (BDNF) expression.

Anti-Amyloidogenic Effect: Inhibits β-amyloid aggregation and tau hyperphosphorylation.

Materials and Methods

Collection and Authentication of Plant Material: Fresh aerial parts of both plants was collected, washed, shade-dried, and pulverized using a mechanical grinder. The specimens was be authenticated, Department of Botany.

Animals: Healthy Adult Male Wistar rats (180–220gm) Obtained from CCSEA approved animal house. Housed at 25 ± 2 °C, 12 h light/dark cycle, with free access to standard diet and water.

Preparation of Extracts: The powdered materials was be subjected to Soxhlet extraction using 95 % ethanol for 24 h. Extracts was filtered and concentrated under reduced pressure in a rotary evaporator at 45°C. The dried extracts was stored at 4 °C in airtight containers until use.

Phytochemical Screening

Phytochemical analysis was carried out to determine the presence of primary and secondary metabolites responsible for the pharmacological activity of the ethanolic extracts of Bacopa monnieri and Centella asiatica. Both qualitative and quantitative methods was be employed according to standard procedures.

Acute Oral Toxicity Study

Conducted per OECD Guideline 425 (Up-and-Down Procedure). Male Wistar rats (n = 6) received single oral doses (300–2000 mg/kg). Animals was be observed for 14 days for behavioral changes and mortality. The LD_{50} cut-off value was estimated, and 1/10th & 1/5th doses were chosen for efficacy studies.

Experimental Animals

- **Species:** Wistar rats
- **Weight:** 180–250 gm
- **Sex:** Either Sex
- **Total number:** 42 rats
- **Housing:** Standard laboratory conditions (12 hr light/dark cycle, 22 ± 2°C, 40–70% humidity)
- **Food and water:** Ad libitum

Grouping and Treatment Design: A total of Seven groups, each containing six rats (n = 6):

Group	Treatment	Dose & Route
I (Normal Group)	Normal Control	Vehicle only (food & water ad libitum) p.o.
II (Disease Group)	Disease Control	Scopolamine Hydrobromide (1 mg/kg, i.p.) Inducer
III (Standard Group)	Standard Drug	Donepezil 1mg/kg, p.o.
IV (Treatment Group)	Bacopa monnieri Extract (Low Dose)	200 mg/kg(p.o.) + Scopolamine Hydrobromide (1 mg/kg, i.p.)
V (Treatment Group)	Bacopa monnieri Extract (High Dose)	400 mg/kg(p.o.) + Scopolamine Hydrobromide (1 mg/kg, i.p.)
VI (Treatment Group)	Centella asiatica Extract (Low Dose)	200 mg/kg(p.o.) + Scopolamine Hydrobromide (1 mg/kg, i.p.)
VII (Treatment Group)	Centella asiatica Extract (High Dose)	400 mg/kg(p.o.) + Scopolamine Hydrobromide (1 mg/kg, i.p.)

Induction of Cognitive Deficit

Scopolamine Hydrobromide (1mg/kg, i.p.) administered 30 min before behavioral testing on each day of evaluation to induce temporary memory impairment mimicking Alzheimer's-like cognitive deficits.

Behavioral Assessment

Morris Water Maze (MWM) Test

The Morris Water Maze was be used to evaluate spatial learning and memory in rats.

Y-Maze Test

The Y-maze test was performed to assess working memory based on spontaneous alternation behavior.

Biochemical Estimations

After completion of behavioral experiments, all animals was sacrificed under light anesthesia. The brain tissues was be immediately excised, washed with ice-cold saline to remove blood, and homogenized (10% w/v) in 0.1 M phosphate buffer (pH 7.4) using a Teflon–glass homogenizer.

The homogenates was centrifuged at 10,000 rpm for 15 minutes at 4 °C, and the clear supernatant was be used for the following biochemical estimations related to oxidative stress and cholinergic function.

- Estimation of Acetylcholinesterase (AChE) Activity
- Estimation of Lipid Peroxidation (MDA/TBARS Assay)
- Estimation of Reduced Glutathione (GSH)
- Estimation of Superoxide Dismutase (SOD)
- Estimation of Catalase (CAT)
- Estimation of Total Protein

Histopathological Examination: In the present study, histopathology was be employed to evaluate the morphological changes in the hippocampus and cerebral cortex following scopolamine-induced cognitive impairment and to assess the neuroprotective effects of Bacopa monnieri and Centella asiatica extracts. Histology helps correlate behavioral and biochemical findings with actual tissue-level alterations, thereby validating the neuroprotective efficacy of the test extracts.

Statistical Analysis: All experimental results was be expressed as Mean ± Standard Error of Mean (SEM) for each group (n = 6). One-way Analysis of Variance (ANOVA) was applied to determine the overall significance among different treatment groups. The level of statistical significance was be set at $p < 0.05$ for all comparisons.

Results

Preliminary Phytochemical Screening

Preliminary phytochemical screening of Bacopa monnieri and Centella asiatica extracts revealed the presence of various bioactive constituents responsible for neuroprotective activity

Table 1: Preliminary Phytochemical Screening

Phytoconstituents	Bacopa monnieri	Centella asiatica
Alkaloids	+	+
Flavonoids	++	++
Tannins	+	+
Saponins	+	++
Glycosides	++	+
Terpenoids	+	++
Phenolics	++	++

(+) = Present, (++) = Strongly Present

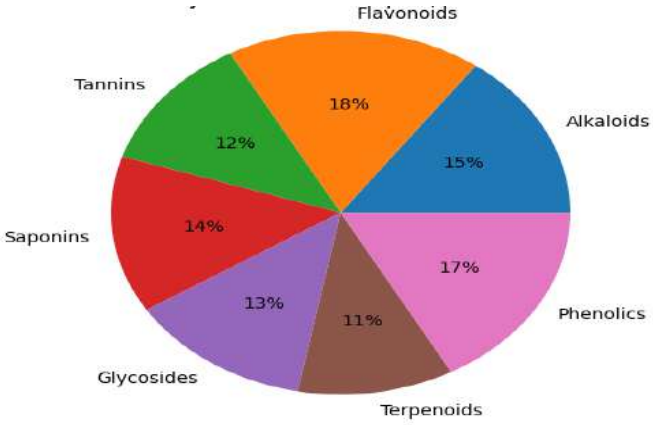

Figure 4: Preliminary Phytochemical Screening

Acute Toxicity Study

An acute toxicity study was performed to evaluate the safety profile of Bacopa monnieri and Centella asiatica extracts in experimental animals. The study was conducted in accordance with OECD Guideline 423. Both Bacopa monnieri and Centella asiatica extracts were found to be safe up to a dose of 2000 mg/kg body weight, indicating a high margin of safety.

Behavioral Studies

Morris Water Maze (MWM) Test

The Morris Water Maze test was used to evaluate spatial learning and memory in experimental rats.

The parameter measured was Escape Latency Time (seconds), which indicates the time taken by the animal to locate the hidden platform.

Table 2: Effect on Escape Latency Time in MWM Test

Group	Treatment	Escape Latency (sec)
Group I	Normal Control	25.3 ± 1.2
Group II	Scopolamine Control	68.5 ± 2.5***
Group III	Donepezil	30.4 ± 1.4###
Group IV	Bacopa Low Dose	45.6 ± 1.8**
Group V	Bacopa High Dose	32.1 ± 1.5###
Group VI	Centella Low Dose	50.2 ± 2.0**
Group VII	Centella High Dose	36.8 ± 1.6###

Values expressed as Mean ± SEM (n = 6) *p < 0.001 vs Normal Control ###p < 0.001 vs Scopolamine Control

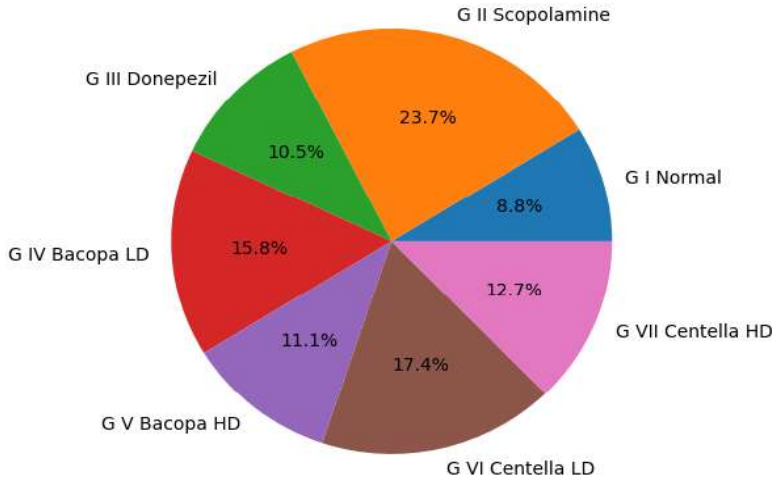

Figure 5: Effect on Escape Latency Time in MWM Test

Y-Maze Test: The results indicate that both extracts possess memory-enhancing and neuroprotective activity**,** with Bacopa monnieri being more effective.

Table 3: Effect on % Spontaneous Alternation in Y-Maze Test

Group	**Treatment**	**% Alternation**
Group I	Normal Control	72.4 ± 2.1
Group II	Scopolamine Control	38.6 ± 1.9***
Group III	Donepezil	68.2 ± 2.3###
Group IV	Bacopa Low Dose	55.3 ± 2.0**
Group V	Bacopa High Dose	66.7 ± 2.2###
Group VI	Centella Low Dose	52.1 ± 1.8**
Group VII	Centella High Dose	63.4 ± 2.1###

Values expressed as Mean ± SEM (n = 6) *p < 0.001 vs Normal Control ###p < 0.001 vs Scopolamine Control

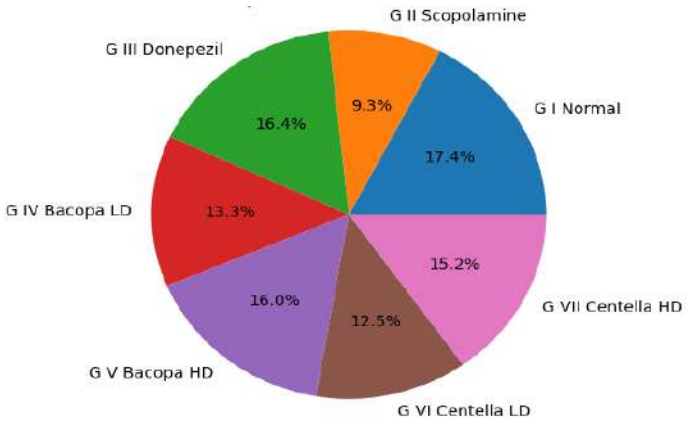

Figure 6: Effect on % Spontaneous Alternation in Y-Maze Test

Estimation of Acetylcholinesterase (AChE) Activity (Ellman's Method): Acetylcholinesterase (AChE) activity was estimated using Ellman's method to evaluate cholinergic function. Increased AChE activity leads to rapid breakdown of acetylcholine, resulting in memory impairment.

Table 4: Effect on AChE Activity

Group	Treatment	AChE Activity (µmol/min/mg protein)
Group I	Normal Control	18.5 ± 1.1
Group II	Scopolamine Control	42.3 ± 2.2***
Group III	Donepezil	22.1 ± 1.3###
Group IV	Bacopa Low Dose	30.4 ± 1.5**
Group V	Bacopa High Dose	24.2 ± 1.4###
Group VI	Centella Low Dose	32.8 ± 1.6**
Group VII	Centella High Dose	26.7 ± 1.5###

Values expressed as Mean ± SEM (n = 6) *p < 0.001 vs Normal Control ###p < 0.001 vs Scopolamine Control

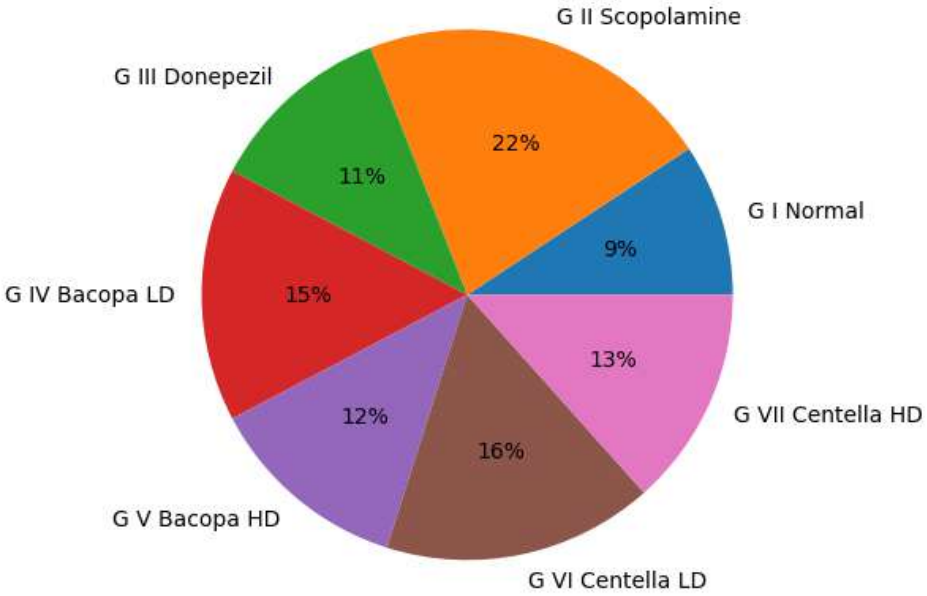

Figure 7: Effect on AChE Activity

Estimation of Lipid Peroxidation (MDA/TBARS Assay): Lipid peroxidation was assessed by measuring Malondialdehyde (MDA) levels using the TBARS (Thiobarbituric Acid Reactive Substances) assay. Increased MDA levels indicate enhanced oxidative stress and neuronal damage.

Table 5: Effect on Lipid Peroxidation (MDA Levels)

Group	Treatment	MDA (nmol/mg protein)
Group I	Normal Control	1.85 ± 0.10
Group II	Scopolamine Control	4.92 ± 0.25***
Group III	Donepezil	2.10 ± 0.12###
Group IV	Bacopa Low Dose	3.20 ± 0.18**
Group V	Bacopa High Dose	2.35 ± 0.14###
Group VI	Centella Low Dose	3.45 ± 0.20**
Group VII	Centella High Dose	2.65 ± 0.16###

Values expressed as Mean ± SEM (n = 6) *p < 0.001 vs Normal Control ###p < 0.001 vs Scopolamine Control

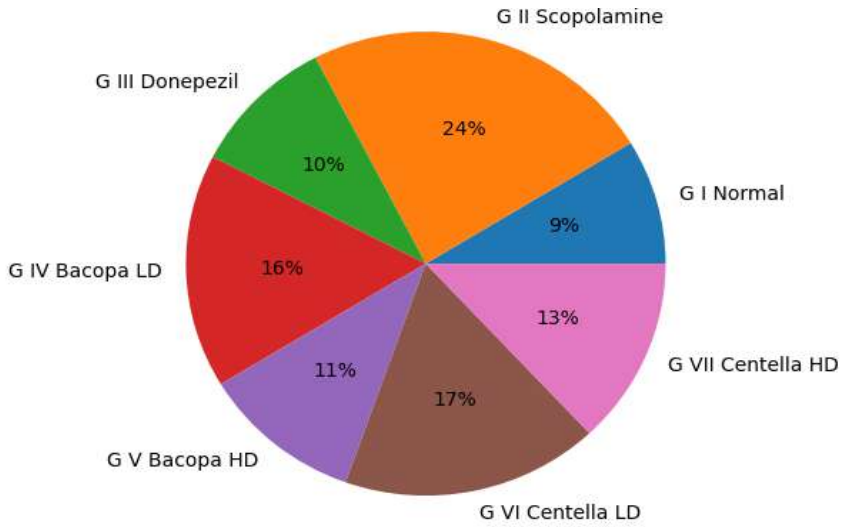

Figure 8: Effect on Lipid Peroxidation (MDA Levels)

Estimation of Reduced Glutathione (GSH): Reduced Glutathione (GSH) is a major intracellular antioxidant that protects neuronal cells from oxidative damage. Depletion of GSH is a key indicator of oxidative stress and is commonly observed in neurodegenerative disorders such as Alzheimer's disease.

Table 6: Effect on Reduced Glutathione (GSH) Levels

Group	Treatment	GSH (µmol/mg protein)
Group I	Normal Control	8.5 ± 0.4
Group II	Scopolamine Control	3.2 ± 0.2***
Group III	Donepezil	7.9 ± 0.3###
Group IV	Bacopa Low Dose	5.8 ± 0.3**
Group V	Bacopa High Dose	7.2 ± 0.3###
Group VI	Centella Low Dose	5.4 ± 0.2**
Group VII	Centella High Dose	6.8 ± 0.3###

Values expressed as Mean ± SEM (n = 6) *p < 0.001 vs Normal Control, ###p < 0.001 vs Scopolamine Control

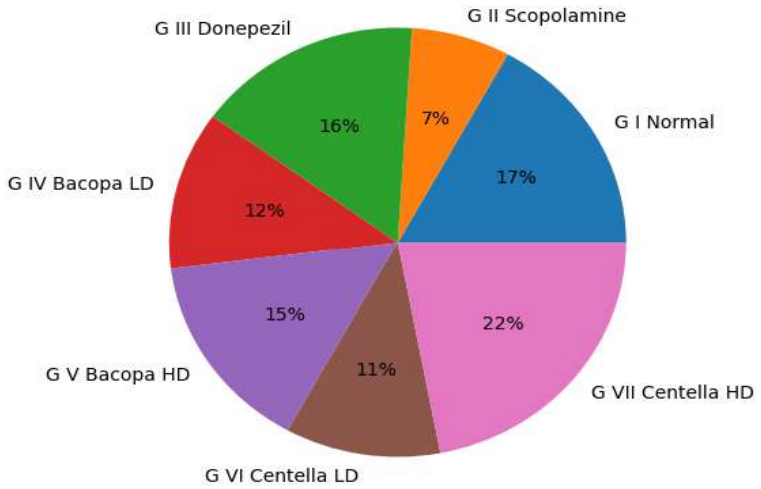

Figure 9: Effect on Reduced Glutathione (GSH) Levels

Estimation of Superoxide Dismutase (SOD): In the present study, the scopolamine-treated group (Group II) showed a significant reduction in SOD activity compared to the normal control group, confirming induction of oxidative stress. Treatment with Donepezil (Group III) significantly restored SOD activity, indicating its neuroprotective and antioxidant effect.

Table 7: Effect on Superoxide Dismutase (SOD) Activity

Group	Treatment	SOD (U/mg protein)
Group I	Normal Control	9.8 ± 0.4
Group II	Scopolamine Control	4.1 ± 0.2***
Group III	Donepezil	9.1 ± 0.3###
Group IV	Bacopa Low Dose	6.8 ± 0.3**
Group V	Bacopa High Dose	8.5 ± 0.3###
Group VI	Centella Low Dose	6.3 ± 0.2**
Group VII	Centella High Dose	7.9 ± 0.3###

Values expressed as Mean ± SEM (n = 6) *p < 0.001 vs Normal Control ###p < 0.001 vs Scopolamine Control

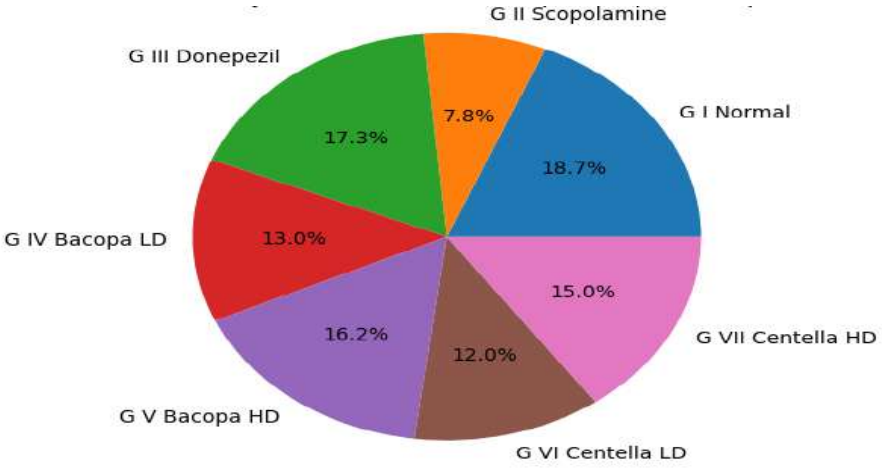

Figure 10: Effect on Superoxide Dismutase (SOD) Activity

Estimation of Catalase (CAT) Activity: In the present study, the scopolamine-treated group (Group II) showed a significant reduction in CAT activity compared to the normal control group, confirming induction of oxidative stress. Treatment with Donepezil (Group III) significantly restored CAT activity, indicating its antioxidant and neuroprotective effect.

Table 8: Effect on Catalase (CAT) Activity

Group	Treatment	CAT (µmol H_2O_2 decomposed/min/mg protein)
Group I	Normal Control	52.4 ± 2.1
Group II	Scopolamine Control	21.6 ± 1.3***
Group III	Donepezil	48.9 ± 1.9###
Group IV	Bacopa Low Dose	36.5 ± 1.6**
Group V	Bacopa High Dose	45.8 ± 1.8###
Group VI	Centella Low Dose	34.2 ± 1.5**
Group VII	Centella High Dose	42.6 ± 1.7###

Values expressed as Mean ± SEM (n = 6) *p < 0.001 vs Normal Control ###p < 0.001 vs Scopolamine Control

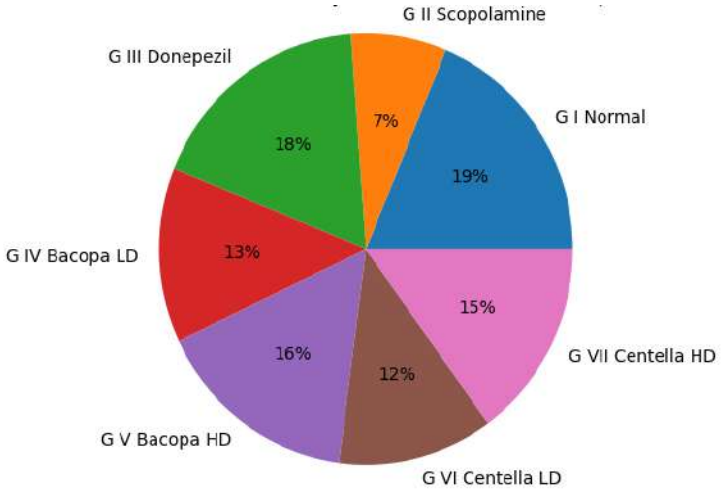

Figure 11: Effect on Catalase (CAT) Activity

Estimation of Total Protein: In the present study, the scopolamine-treated group (Group II) showed a significant reduction in total protein levels compared to the normal control group, indicating neuronal damage and metabolic dysfunction. Treatment with Donepezil (Group III) significantly restored protein levels, confirming its neuroprotective effect.

Table 9: Effect on Total Protein Levels

Group	Treatment	Total Protein (mg/g tissue)
Group I	Normal Control	62.5 ± 2.4
Group II	Scopolamine Control	34.2 ± 1.8***
Group III	Donepezil	58.7 ± 2.1###
Group IV	Bacopa Low Dose	48.3 ± 2.0**
Group V	Bacopa High Dose	55.6 ± 2.2###
Group VI	Centella Low Dose	46.2 ± 1.9**
Group VII	Centella High Dose	52.8 ± 2.1###

Values expressed as Mean ± SEM (n = 6) *p < 0.001 vs Normal Control ###p < 0.001 vs Scopolamine Control

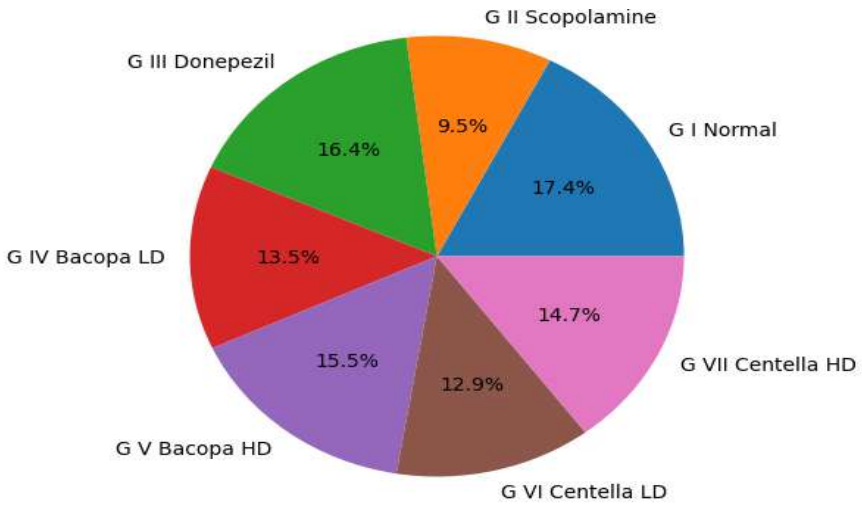

Figure 12: Effect on Total Protein Levels

Histopathological Examination of Brain Tissue: Histopathological examination of brain tissue (hippocampus region) was carried out to evaluate neuronal damage and neuroprotective effects of treatments. The scopolamine-treated group showed marked neuronal degeneration, confirming induction of Alzheimer-like pathology. Treatment groups showed varying degrees of protection, with Bacopa monnieri high dose showing near-normal architecture.

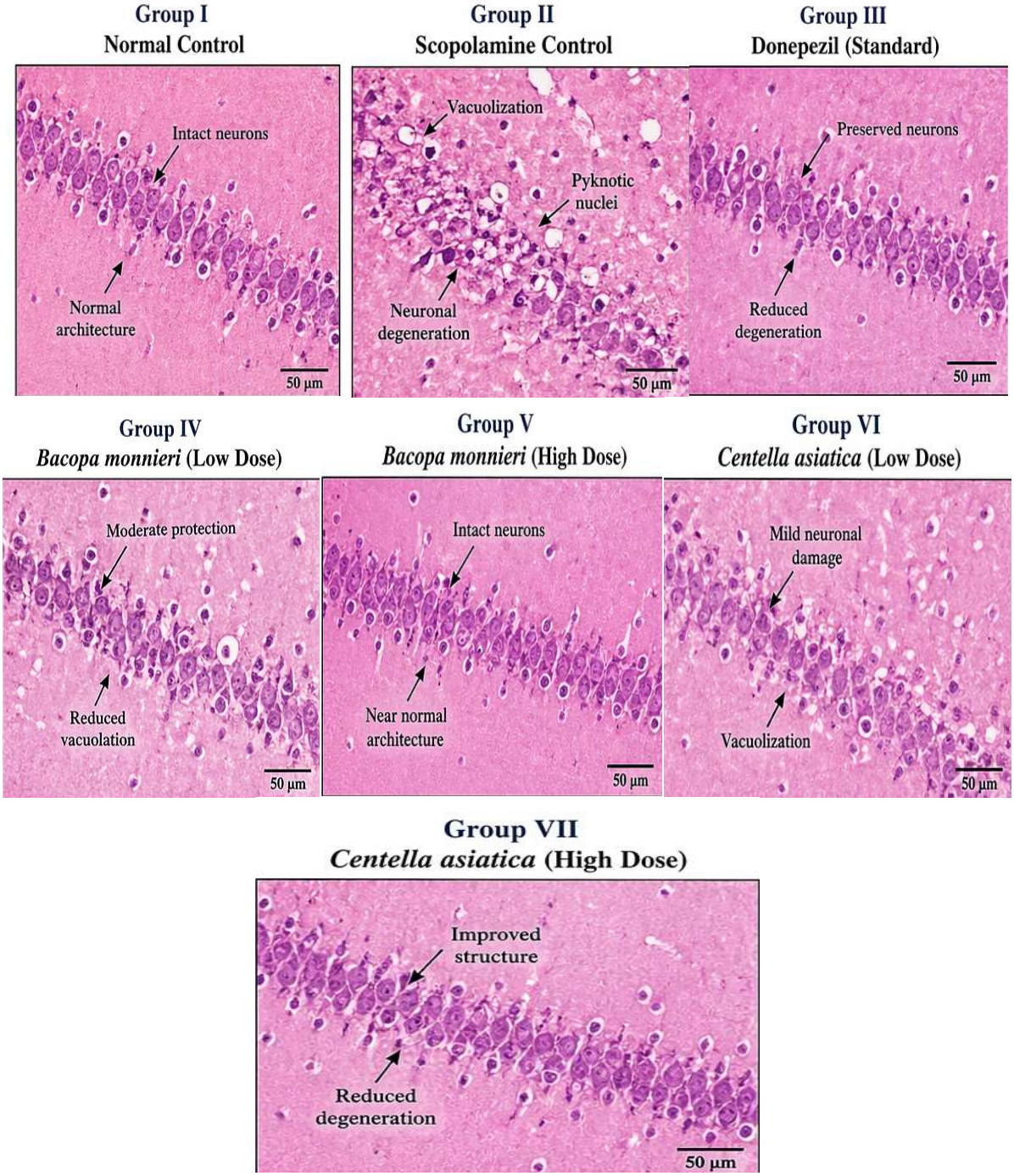

Figure 13: Microscopic Histopathological Observations

Table 10: Histopathological Examination of Brain Tissue

Group	Treatment	Histopathological Findings
Group I	Normal Control	Normal neuronal architecture, intact pyramidal cells, clear nucleus, normal synaptic arrangement
Group II	Scopolamine Control	Severe neuronal degeneration, cell shrinkage, pyknotic nuclei, vacuolization, inflammatory infiltration
Group III	Donepezil	Mild neuronal damage, mostly preserved architecture, reduced degeneration
Group IV	Bacopa Low Dose	Moderate neuronal protection, reduced vacuolation, partial restoration
Group V	Bacopa High Dose	Near-normal architecture, intact neurons, minimal degeneration
Group VI	Centella Low Dose	Moderate neuronal damage, mild improvement compared to disease control
Group VII	Centella High Dose	Mild neuronal protection, improved structure but less than Bacopa high dose

Discussions

All individual results consistently demonstrate that is Scopolamine induces cognitive impairment and oxidative stress.

Both plant extracts provide neuroprotection. Bacopa monnieri exhibits superior efficacy compared to Centella asiatica.

Conclusion

In conclusion, the results of the present study provide strong scientific evidence supporting the traditional use of Bacopa monnieri and Centella asiatica as cognitive enhancers. Among the two, Bacopa monnieri emerges as a more effective neuroprotective agent and holds significant promise as a potential therapeutic candidate for the management of Alzheimer's disease.

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