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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 dysfunction, oxidative stress, cholinergic deficit, and neuronal degeneration. This review focuses on the comparative neuroprotective effects of Bacopa monnieri (Brahmi) and Centella asiatica (Gotu Kola) in experimental models of scopolamine-induced Alzheimer's-like cognitive impairment in rats. Both herbs are traditionally used to enhance memory and intellect, and possess rich phytochemical profiles, including bacosides in Bacopa monnieri and asiaticoside/asiatic acid in Centella asiatica. Experimental findings indicate that both extracts significantly improve learning and memory in behavioral paradigms such as the Morris Water Maze, Y-Maze, and Novel Object Recognition tests. Mechanistically, they attenuate scopolamine-induced oxidative stress by elevating endogenous antioxidant markers (SOD, CAT, GSH) and reducing lipid peroxidation (MDA). Moreover, both extracts exhibit cholinesterase inhibitory activity, thereby restoring acetylcholine levels in the hippocampus. Histopathological studies demonstrate reduced neuronal damage and improved hippocampal integrity following treatment. Comparative studies suggest that while Bacopa monnieri shows stronger cholinesterase inhibition due to its bacoside content, Centella asiatica provides higher antioxidant and neuro-regenerative benefits through asiaticosides. Collectively, the findings support the potent neuroprotective and cognition-enhancing properties of these medicinal plants, highlighting their potential as complementary therapies for Alzheimer's disease prevention and management.

Keywords: Bacopa monnieri; Centella asiatica; Alzheimer's disease; Scopolamine; Cognitive impairment; Neuroprotection.

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.

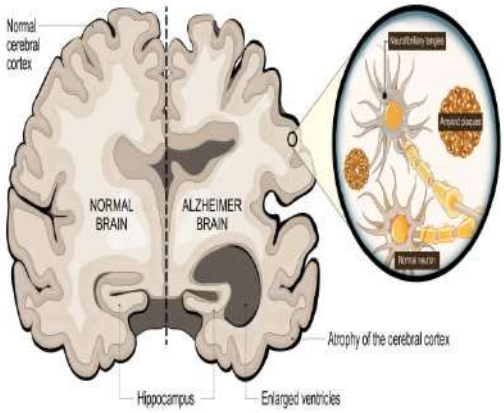

Figure 1: Image of Alzheimer disease (AD)

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.[1]

Need for Alternative Therapeutic Strategies

There is growing interest in multitarget natural therapies, particularly herbal neuroprotectants with antioxidant, anti-inflammatory, and cholinergic modulatory properties. Herbs like Bacopa monnieri and Centella asiatica have gained attention for their ability to enhance cognition and protect against neurodegenerative changes, making them promising candidates for Alzheimer's management.[2]

Advantages of Herbal Neuroprotective Agents[3]

- **Multitargeted Action:** Herbal compounds act on multiple pathological pathways simultaneously.
- **Low Toxicity and Better Tolerability:** Compared to synthetic drugs, most herbal agents have fewer adverse effects.
- **Antioxidant and Adaptogenic Properties:** Enhance neuronal resilience to oxidative and metabolic stress.
- **Blood-Brain Barrier Penetration:** Many phytochemicals are lipophilic, facilitating brain entry.
- **Cognitive Enhancement:** Improve synaptic plasticity and long-term potentiation, crucial for learning and memory.

Plant Profile

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 [4,5]

Plant Profile of Bacopa monnieri

Figure 2: Plant of Bacopa monnier

Table 1: Botanical Classification

Kingdom	**Plantae**
Division	Magnoliophyta
Class	Magnoliopsida
Order	Lamiales
Family	Plantaginaceae(formerly Scrophulariaceae)
Genus	Bacopa
Species	Bacopa monnieri (L.) Wettst.

Morphological Description: Bacopa monnieri is a prostrate, succulent herb that grows in damp or marshy areas. It has fleshy, oblong leaves, small white to pale blue flowers, and creeping stems rooting at nodes. The entire plant has a bitter taste and characteristic odor.[6]

- **Stem:** Creeping, smooth, and branched.
- **Leaves:** Opposite, sessile, obovate-oblong, 0.6–2.5 cm long.
- **Flowers:** Axillary, solitary, five-petaled.
- **Fruits:** Ovoid capsules with numerous small seeds.

Phytochemical Constituents

The principal active compounds are damarane-type triterpenoid saponins, collectively termed bacosides, responsible for neuropharmacological actions.[7]

Table 2:

Category	Constituents	Activities
Triterpenoid saponins	Bacoside A, Bacoside B, Bacopasaponins A–F	Cognitive enhancement, antioxidant, anti-amyloid
Alkaloids	Brahmine, Nicotine, Herpestine	CNS stimulation
Flavonoids	Luteolin, Apigenin	Antioxidant, anti-inflammatory
Sterols	β-sitosterol, Stigmasterol	Adaptogenic
Other	Mannitol, Betulic acid	Osmoregulatory,antioxidant

Pharmacological Activity[8-10]

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

Table 3: Botanical Classification

Kingdom	**Plantae**
Division	Angiosperms
Class	Dicotyledonae
Order	Apiales
Family	Apiaceae (Umbelliferae)
Genus	Centella
Species	Centella asiatica (L.) Urban

Morphological Description[11]

Centella asiatica is a creeping perennial herb with slender stems and reniform (kidney-shaped) leaves. The leaves arise on long petioles and the plant spreads horizontally by stolons.

- **Leaves:** Smooth, rounded, with serrated margins and a characteristic venation pattern.
- **Flowers:** Small, pink to reddish, in axillary umbels.
- **Fruits:** Small, compressed, and ribbed mericarps.

Phytochemical Constituents[12]: The main bioactive compounds are triterpenoid glycosides, collectively known as centellosides, which include asiaticoside and madecassoside.

Table 4:

Category	Constituents	Activities
Triterpenoid saponins	Asiaticoside, Madecassoside, Thankuniside	Wound healing, antioxidant
Triterpenic acids	Asiatic acid, Madecassic acid	Anti-inflammatory, antiapoptotic

Flavonoids	Quercetin, Kaempferol, Catechin	Antioxidant
Phytosterols	Stigmasterol, β-sitosterol	Membrane stabilization
Volatile oils	Caryophyllene, α-humulene	Sedative, CNS depressant

Pharmacological Activity[13-15]

- **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.

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