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Original article

Anti-Alzheimer's potential of extracts of *Sterculia foetida* seeds and aerial parts of *Chenopodium album*

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Abstract

Objective: Memory impairment is one of distinctive traits related to Alzheimer's disease. The Ayurveda prioritizes herbs for managing memory impairment. The phytoconstituents contained in *Sterculia foetida* and *Chenopodium album* have proved their ability against pathology, including oxidative stress and acetylcholine degradation, involved in memory loss. Therefore, the present study focused on evaluation of seeds of *S. foetida*, and aerial sections of *C. album* in the rat model, along with related biochemical parameters, for anti-Alzheimer potential.

Materials and methods: The plant materials were collected and authenticated, followed by extraction, fractionation, and identification of the chemical constituents. The exteroceptive behavioral models were chosen to evaluate memory impairment, and therefore, impact of the extracts on improvement of Alzheimer. Biochemical parameters, and histopathological changes were also observed.

Results: The study identified alkaloids, flavonoids, saponins, glycosides, steroids, amino acids, and proteins as the phytoconstituents contained in the plant material. Ethanolic extract of both the plant parts significantly improved memory in animal model, during object recognition, Morris water maze test, and elevated plus maze tests. The results of biochemical assays suggested inhibition of acetylcholinesterase activity, lipid peroxidation, and serum total cholesterol levels by the plant materials. Also, serum glucose, reduced glutathione and superoxide dismutase activities were elevated, and the histopathological reports clearly demonstrate decreased abnormalities in the hippocampus region of the test animal.

Conclusion: The study concludes that the aerial sections of *C. album* and the seeds of *S. foetida* displayed potential in a dose dependent manner, and therefore, were effective in alleviating Alzheimer's-related memory and recognition disorders.

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Introduction

The term memory refers to the mental capability to encode and hold evidence, imitations, actions and subsequently recollecting earlier happenings and practices (Amin and Malik 2013; Vicuna and Vicuna 2024). Dementia, an age-related mental problem is characterized by gradual memory loss, decline in the ability to perform routine tasks, deterioration and difficulty in learning, loss of language skills, and impairments of judgement and personality change. The group of symptoms is caused by the depletion of specific neurotransmitter-acetylcholine, and neuronal apoptosis (Health 2007; Hendriks et al. 2023). Dementia is a characteristic trait related to Alzheimer's disease (AD), a progressive neurodegenerative disorder that primarily affects people aged 65 years or older. It is featured by cerebral plaques, made up of amyloid beta (Aβ) protein (Sin et al. 2021) along with impaired and dead neurons (Imbimbo et al. 2005). AD involves reduction in choline acetyltransferase, and cholinergic markers. Globally 4.7 million people in their sixth decade of life or later have AD dementia. The figure may reach to 130 million by the year 2050 worldwide (Lopez and Kuller 2019). As the rate of AD cases increases with aging, requirement of drugs which might alleviate the degeneration, becomes more and more urgent.

A nootropic is any substance having a positive action on cognition (Chiroma et al. 2019; Patel et al. 2024). Nootropic agents along with anti-cholinesterase drugs including galantamine, rivastigmine and donepezil are clinically used for symptomatic improvement, but the resulting side-effects associated with them have made their utility limited (Joe and Ringman 2019). Therefore, a requirement has been emerged to find more effective compounds which have fewer side effects in managing memory impairment. The medicinal plants are one of the excellent natural sources of therapeutic agents that can be used for management of common health conditions (WHO 2002). Various phytoconstituents such as quercetin, trigonelline, rosmarinic acid, anthocyanins, and 6-shogaol are reported to have protective effects in memory impairments. These phytoconstituents possess anti-oxidant property, and have the ability to prevent degradation of acetylcholine by inhibiting acetylcholinesterase enzyme (AChE) (Fonteles et al. 2016; Gabriel et al. 2020; Khalili et al. 2018). The primary factors involved in memory impairment in AD, include acetylcholine deficiency, and oxidative stress which are required to be combated in order to manage AD (Fukui et al. 2001; Huang et al. 2022; Lee et al. 1993). In the recent years, many plants have been explored for their therapeutic potential against scopolamine-induced AD model in rats including *Sterculia guttata, Verbesina encelioides, Ficus racemosa, Centratherum anthelminticum, Psidium guajava* and *Gentiana lutea* (Abdul et al. 2024; Pasam et al. 2024; Rani et al. 2025; Rashmi et al. 2025; Tagad et al. 2025; Verma et al. 2025).

Chenopodium album (*C. album*; Family: Chenopodiaceae) commonly called "bathua", contains trigonelline, flavonoids, phenolic acids and β-carotene (Poonia and Upadhayay 2015). Among these, phenolic acids, β-carotene and trigonelline are reported to possess anti-cholinesterase activity (Ali Hassan and Abu Bakar 2013). In addition, flavonoids (quercetin and kaempferol), phenolic glycosides (chenoalbuside) and free phenolic acids obtained from fruits and leaves of *C. album* exhibit anti-oxidant action (Al-Joufi et al. 2022; Kumar and Kumar 2009; Laghari et al. 2011). Both anti-cholinesterase activity and anti-oxidant activities act as key factors for treatment of AD (Fukui et al. 2001; Huang et al. 2022; Lee et al. 1993).

Sterculia foetida (*S. foetida;* Family: Sterculiaceae) commonly recognized as "jangli badam" contains phosphatidylcholine and phosphatidylethanolamine which can be catalyzed to acetylcholine by action of enzyme phospholipase D, and choline

acetyltransferase, thereby supporting cholinergic neurotransmission. Furthermore, flavonoids found in *S. foetida* seeds show anti-oxidant activity (Nhân and Trinh 2019), while sterculic acid have been reported to reduce adrenomedullin and stearoyl-CoA desaturase expression, both of which provoke memory failure. Additionally, sterculic acid is associated with inhibition of inflammatory, and cytotoxic responses of 7-ketocholesterol, an oxysterol related to neurodegenerative diseases like AD (Mahalakshmi et al. 2021; Wang et al. 2024).

Both *C. album* and S. *foetida* have demonstrated phytochemical profiles and promising biochemical indications against oxidative stress, AChE and other pathological factors involved in AD, yet neither has been comprehensively evaluated for its therapeutic effects against using standardized models. Therefore, this study aimed to evaluate and compare extracts and fractions of *S. foetida* seeds and aerial sections of *C. album* for their anti-oxidant potential, and effects on AD pathologies. Previous studies involving another species, namely *Chenopodium murale* primarily investigated its antioxidant and neuroprotective activities in streptozotocin (STZ)-induced diabetic model where memory impairment was assessed only as a secondary outcome of metabolic dysfunction. The STZ model mainly represents metabolic or insulin-resistance–related neurodegeneration**,** rather than direct cholinergic impairment (Ahmed et al. 2022)**.** This model involves oxidative stress and neuroinflammation, but does not directly target cholinergic dysfunction (Salkovic-Petrisic and Hoyer 2007). However, scopolamine-induced model was selected in the current study as it is based on cholinergic deficit, a characteristic hallmark of AD and one of the earliest and most critical pathological events,)—thus providing a relevant framework to assess the early neuroprotective efficacy of both plant extracts. This makes it a mechanistically valid and time-efficient model for studying compounds targeting the "cholinergic hypothesis" of AD (Klinkenberg and Blokland 2010; Rani et al. 2025) and provides a more disease-relevant and mechanistically specific evaluation of plants potential against Alzheimer's-type cognitive deficits (Ebert and Kirch 1998; Hasselmo 2006). In contrast, the Aβ model, though pathologically relevant, is technically demanding, costly, and time-intensive**,** and typically represents late-stage irreversible neurodegeneration**,** which may obscure the evaluation of early neuroprotective or cholinergic effects. The current study is primarily aimed to assess the early-stage neuroprotective and memory-enhancing potential of *C. album* and *S. foetida*. The scopolamine model provided an appropriate and reproducible platform for this purpose.

Materials and Methods

Collection, authentication, extraction and fractionation of the plants

The aerial sections of *C. album*, and the seeds of *S. foetida* were obtained from Indira Gandhi Botanical Garden, Raebareli, and surrounding areas of Lucknow, India. The plant voucher specimens were deposited to the National Botanical Research Institute, Lucknow, India for authentication, with herbarium numbers 101141 (*C. album*) and 101102 (*S. Foetida).*

The plant materials were cleaned and dehydrated in shade for a week, then powdered, and stored in airtight box at 25ºC. They were extracted in a microwave synthesizer (Bagade and Patil 2021) at a power of 350 W for 20 min, using ethanol as the solvent. The solvent: sample loading ratio was 10:1, and pre-leaching time was 10 min. The crude extract was collected, and concentrated using a vacuum rotary evaporator. An aqueous preparation of the crude extract concentrate was fractionated with *n*-butanol (ratio 1:100). The *n*-butanol layer was separated, and concentrated to

obtain ~~*n*-butanol~~ the fraction. The remaining layer was further fractionated using ethyl acetate, and the ethyl acetate layer was collected, and concentrated to obtain ethyl acetate fraction. The remaining solid from this fraction was fractionated with water, and the fraction was concentrated for aqueous fraction. The percentage yields of crude extracts and all the fractions of plants were calculated.

Preliminary phytochemical screening

The ethanolic extracts and fractions (ethyl acetate, *n*-butanol and aqueous) of both plant materials were examined for the active phytoconstituents present (Evans 2009; Harborne 1998).

Drugs and chemicals

Scopolamine hydrobromide, piracetam and sodium carboxy methyl cellulose (CMC) were procured from Merck, Germany. Other analytical grade reagents and chemicals were obtained from SD Fine-Chem Ltd., India.

Pharmacological activity

Male Albino Wistar rats (150-200 g; 6-8 weeks age) were procured from Animal House of BBDNIIT, Lucknow. Animals were provided with pellet diet and water *ad libitum*. Animals were housed at 25^{o}C under controlled environmental conditions (55% relative humidity, 12:12 hr dark/light cycle). The study was approved by the institutional animal ethics committee (IAEC) vide protocol number BBDNIIT/IAEC//001/2015.

Experimental design

A total of 66 animals were used in this study. All animals were randomly assigned to eleven groups of six animals each using a computer-generated randomization schedule in Microsoft Excel to ensure unbiased allocation. The groups were: control [Sodium CMC (0.3% w/v per oral; *p.o.*)]; positive control [Scopolamine (1 mg/kg intraperitonial; *i.p.*)]; standard treatment [Piracetam (200 mg/kg *p.o.*)] (Bhattacharjee et al. 2015; Kailas et al. 2021); test treatments [*C. album* ethanolic extract 200 mg/kg b. wt. *p.o.* (CAE200), *C. album* ethyl acetate fraction 200 mg/kg b. wt. *p.o.* (CAF200), *C. album* ethanolic extract 400 mg/kg b. wt. *p.o.* (CAE400), *C. album* ethyl acetate fraction 400 mg/kg b. wt. *p.o.* (CAF400), *S. foetida* ethanolic extract 300 mg/kg b. wt. *p.o.* (SFE300), *S. foetida n*- butanol fraction 300 mg/kg b. wt. *p.o.* (SFF300), *S. foetida* ethanolic extract 600 mg/kg b. wt. *p.o.* (SFE600), and *S. foetida n*-butanol fraction 600 mg/kg b. wt. *p.o.* (SFF600)]. The respective *n*-butanol and ethyl acetate fractions of *S. foetida* and *C. album* were taken on the basis of percentage yield obtained. *C. album* doses (200 and 400 mg/kg) were selected based on previous reports demonstrating its antidiabetic, antiulcer, hepatoprotective, and antioxidant activities at doses ranging from 200–500 mg/kg, with no toxic effects (Ahmed et al. 2022; Choudhary et al. 2021; Hussain et al. 2022; Padarthi et al. 2013). Similarly, *S. foetida* has been reported to exhibit dose-dependent anti-inflammatory and antinociceptive activity at single oral doses of 200 and 400 mg/kg (Alam et al. 2021). To validate these doses in the scopolamine-induced amnesia model**,** we conducted pilot studies. For *C. album* (extracts and fractions), 200 and 400 mg/kg were tested over eight days of oral treatment. The pilot results showed dose-dependent improvement in memory impairment induced by scopolamine. Therefore, these doses were selected for the final study. For *S. foetida* (extracts and fractions), doses of 200, 300, and 400 mg/kg were tested over eight days. In the pilot study, no significant difference in memory improvement was observed between 300 and 400 mg/kg, whereas 200 mg/kg showed no effect. Based on these findings, we selected 300 mg/kg (medium effective dose) and 600 mg/kg (higher dose) for the final experiment.

Available literature suggests that the ethanolic extract and ethyl acetate fraction of *C. album* did not produce any signs of

toxicity or mortality up to 2000 mg/kg body weight (OECD Test Guidelines 425, Up-and-Down Procedure), and were considered relatively safe (Jain and Singhai 2012). Similarly, oral administration of crude leaf extracts in mice up to 5 g/kg body weight showed no mortality or toxic signs (Magama and Asita 2017). For *S. foetida*, the methanolic extract (MESF) administered orally at 500–2000 mg/kg in mice did not result in any mortality or visible behavioral changes within 72 hr post-administration (Alam et al. 2021).

The selected doses for both plants were guided by literature evidence, pilot experiments, and observed efficacy in improving scopolamine-induced memory deficits, ensuring both safety and mechanistic relevance for the final study.

Exteroceptive behavioural model and dosing schedule

The animals were trained for maze task performance by conducting daily training trial for 15-30 min time interval. Also, the animals were trained daily for object recognition tests, during which, animals did not receive any drug. The trained animals were chosen for experiments and dosed once a day with the respective drug for 8 days. On the 8th day, 45 min after administration of the drug/extract, scopolamine was injected to all the groups, except the control. The positive control group received only one dose of 1 mg/kg b. wt. *i.p.* scopolamine on the 8th day. Following this, all exteroceptive behavioural tests were conducted to evaluate the learning and memory behavior of animals at the times mentioned in respective tests (Bhattacharjee et al. 2015).

Morris water maze test includes two phases, including maze acquisition and maze retention phases. The retention latency was recorded on the 8th day as time taken to detect the hidden platform (Alikatte et al. 2012). For elevated plus maze test, after 45 min of scopolamine injection on the 8th day, transfer latency was recorded in the animals for acquisition phase. After 24 hr, i.e. on day 9th, transfer latency was monitored again, and recorded as a marker of memory retention (Kulkarni et al. 2010). During object recognition tests, the retention trial was performed on day 8, 30 min after a single dose of scopolamine or vehicle, and the discrimination index (D) was recorded (Ozarowski et al. 2013). Importantly, the investigators conducting the behavioral assessments were blinded to the treatment groups throughout the experiment to minimize observer bias and ensure the reliability of the data.

Biochemical estimations and histopathology

The animals were fasted for 18 hr prior to blood withdrawal. After 24 hr of scopolamine administration (on the 9th day), 100 μL blood was collected from the retro-orbital plexus under mild anesthesia, using 2-3% isoflurane in oxygen. The animals were observed for 48 hr after the procedure for any distress in the ocular region.

The serum was separated from the blood sample. The total cholesterol and glucose levels in serum were analyzed by autoanalyzer with GOD-POD (glucose oxidase-peroxidase) and CHOD-PAP (cholesterol oxidase phenol 4-aminoantipyrine peroxidase) kits, respectively. The animals were sacrificed by cervical decapitation, and their brain was removed. Then, histopathological study of the hippocampus section of the brain stained with haematoxylin and eosin was performed (Fischer et al. 2008; Morroni et al. 2019). The freshly isolated brains were homogenized with ice cold phosphate buffer, and estimation of AChE, malondialdehyde (MDA), reduced glutathione (GSH), and superoxide dismutase (SOD) activities was carried out as per the previously described methods, with slight modifications (Ellman 1959; Ellman et al. 1961; Nandi and Chatterjee 1988; Oyedemi et al. 2010; Patil et al. 2014; Srikumar et al. 2004; Waisundara et al. 2008).

Statistical analysis

The results are given as mean ± SEM (standard error of mean). The behavioral parameters were analyzed using repeated measures of two-way ANOVA, followed by post-hoc Bonferroni test, except for the discrimination index. This as well as remaining datasets was analyzed with one-way ANOVA followed by post-hoc Student Newman-Keuls test. $p<0.05$ was considered statistically significant for data analysis. The GraphPad Prism 9.0 software was employed for the statistical analysis.

Results

The novel feature of the study includes the exploration of nootropic potential of aerial parts of *C. album* and *S. foetida* seeds. The respective fractions of ethyl acetate and *n*-butanol of *C. album* and *S. foetida* showed highest percentage yield, as given in Table 1. The phytochemical screening concluded alkaloids, flavonoids, saponins, glycosides, amino acids, polyphenols, proteins and steroids as the phytochemicals present in *S. foetida* seeds and aerial sections of *C. album* (Table 2).

Table 1. Percentage yields of extracts and fractions of *S. foetida* seeds and *C. album* aerial parts

S. No.	Extract/ Fraction	Weight (gm)		Percentage Yield (w/w)	
		C. album	*S. foetida*	*C. album*	*S. foetida*
1	Ethanolic Extract	18.50	16.76	7.20	7.20
2	*n*-butanol Fraction	4.19	7.51	1.67	3.00
3	Ethyl acetate Fraction	6.50	1.19	2.51	0.48
4	Aqueous Fraction	0.68	0.52	0.27	0.21

Table 2. Preliminary phytochemical screening of extracts and fractions of *S. foetida* seeds and *C. album* aerial parts.

S. No.	Class of Compounds	Ethanolic Extract		*n*-butanol Fraction		Ethyl acetate fraction		Aqueous Fraction	
		C. album	*S. foetida*	*C. album*	*S. foetida*	*C. album*	*S. foetida*	*C. album*	*S. foetida*
1	Alkaloids	+	+	+	+	+	+	+	+
2	Flavonoids	+	+	+	+	+	+	+	+
3	Saponins	+	+	+	+	+	─	+	─
4	Glycosides	+	+	─	+	+	─	─	─
5	Polyphenols	+	+	+	─	+	─	+	─
6	Steroids	+	+	+	─	+	─	─	─
7	Amino acids	+	+	─	+	+	+	─	+
8	Protein	+	+	─	+	─	─	─	─
9	Carbohydrate	─	+	─	+	─	+	─	+
10	Fixed oils	─	+	─	+	─	+	─	+

+ Present; ─ Absent.

Effect of *C. album* and *S. foetida* extracts and fractions on Morris water maze test

Repeated-measures two-way ANOVA revealed significant differences in escape latency across treatment groups and training days ($p<0.05$). Both *C. album* (aerial parts) and *S. foetida* (seeds) extracts and fractions significantly reduced escape latency in a dose-dependent manner compared to the scopolamine-treated group, indicating improved learning and memory performance in the Morris water maze test. The effects were more pronounced at higher doses, and comparable to the standard drug piracetam (Figure 1a–b).

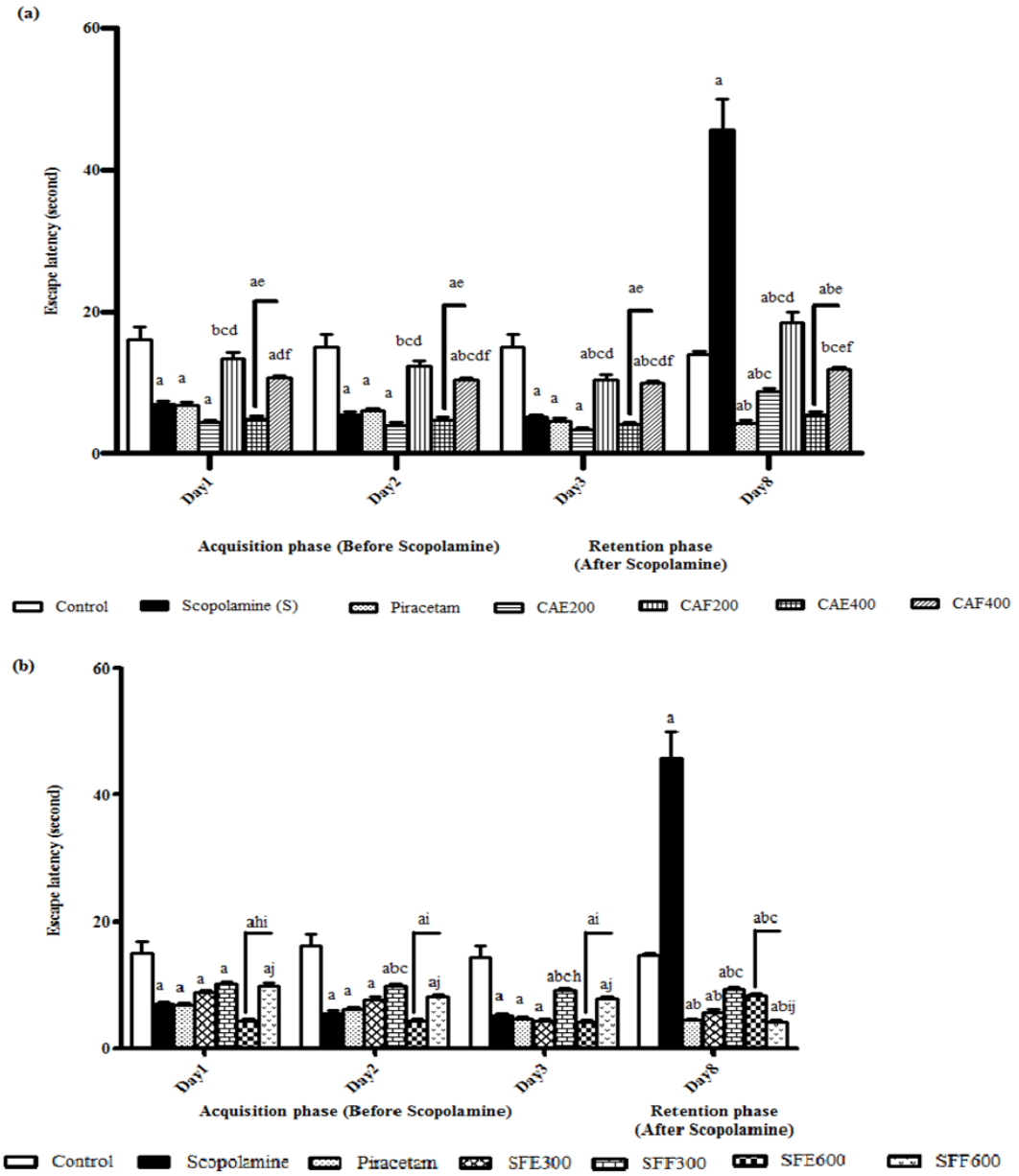


Figure 1. Effect of fractions and extracts of aerial sections of *C. album* (a) and seeds of *S. foetida* (b) on learning performance by Morris water maze model. All values are mean ± SEM; n=6; [a]p<0.05 compared to control; [b]p<0.05 compared to scopolamine; [c]p<0.05 compared to piracetam; [d]p<0.05 compared to CAE200; [e]p<0.05 compared to CAF200; [f]p<0.05 compared to CAE400; [h]p<0.05 compared to SFE300; [i]p<0.05 compared to SFF300 and [j]p<0.05 compared to SFE 600 [Repeated measures of two-way ANOVA followed by Bonferroni test].

Effect of *C. album* and *S. foetida* extracts and fractions on elevated plus maze test

Repeated-measures two-way ANOVA revealed significant effects of treatment groups, training phases, and their interaction on transfer latency ($p<0.05$; Figure 2). Scopolamine administration markedly increased transfer latency during both the acquisition and retention phases, confirming impaired learning and memory. In contrast, treatment with *C. album* and *S. foetida* extracts and fractions significantly reduced transfer latency in a dose-dependent manner compared to the scopolamine group. Notably, *C. album* extract (400 mg/kg b.w.) and *S. foetida* extract (300 mg/kg b.w.) demonstrated the most pronounced improvement in retention performance, comparable to the standard drug piracetam.

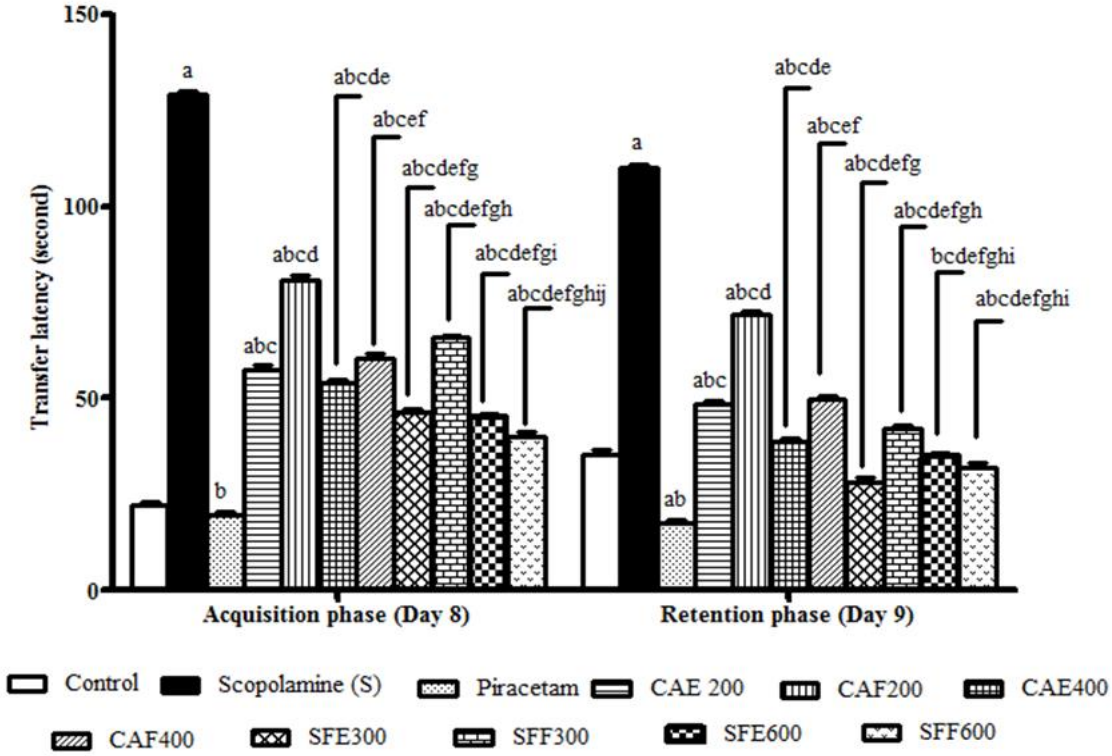


Figure 2. Effects of fractions and extracts of aerial sections of *C. album* and seeds of *S. foetida* on transfer latency by elevated plus maze test. All values are mean ± SEM; n=6; [a]p<0.05 compared to control; [b]p<0.05 compared to scopolamine; [c]p<0.05; compared to piracetam; [d]p<0.05 compared to CAE200; [e]p<0.05 compared to CAF200, [f]p<0.05 compared to CAE400, [g]p<0.05 compared to CAF400, [h]p<0.05 compared to SFE300, [i]p<0.05 compared to SFF300 and [j]p<0.05 compared to SFE600 [Repeated measures of two-way ANOVA followed by Bonferroni test].

Effect of *C. album* and *S. foetida* extracts and fractions on object recognition test

One-way ANOVA revealed significant differences in the discrimination index among treatment groups (p<0.05; Figure 3). Similarly, repeated-measures two-way ANOVA showed significant differences in exploration times for familiar *versus* new object, confirming improved recognition memory in the treated groups (p<0.05; Figure 4a–b). Both *C. album* and *S. foetida* extracts and fractions significantly restored recognition ability in scopolamine-induced amnesic rats in a dose-dependent manner. Higher doses of *C. album* (400 mg/kg) and *S. foetida* (300 and 600 mg/kg) produced marked improvements, showing reduced exploration time for familiar objects and enhanced preference for novel objects—comparable to the standard drug piracetam.

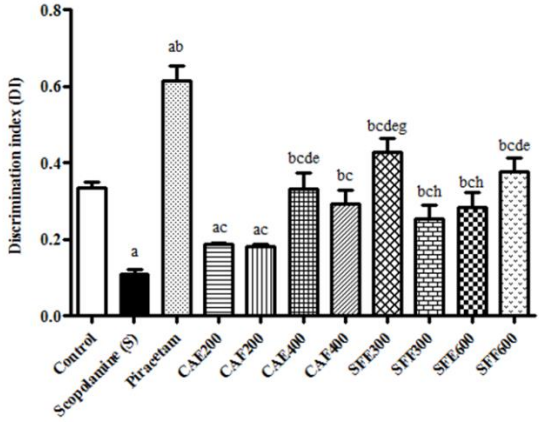


Figure 3. Effect of fractions and extracts of aerial sections of *C. album* and seeds of *S. foetida* on discrimination index by object recognition test. All values are mean ± SEM; n=6; [a]p<0.05 compared to control; [b]p<0.05 compared to scopolamine; [c]p<0.05; compared to piracetam; [d]p<0.05 compared to CAE200; [e]p<0.05 compared to CAF200, [f]p<0.05 compared to CAE400, [g]p<0.05 compared to CAF400 and [h]p<0.05 compared to SFE300 [One way ANOVA followed by Student Newman-Keuls Post-hoc test].

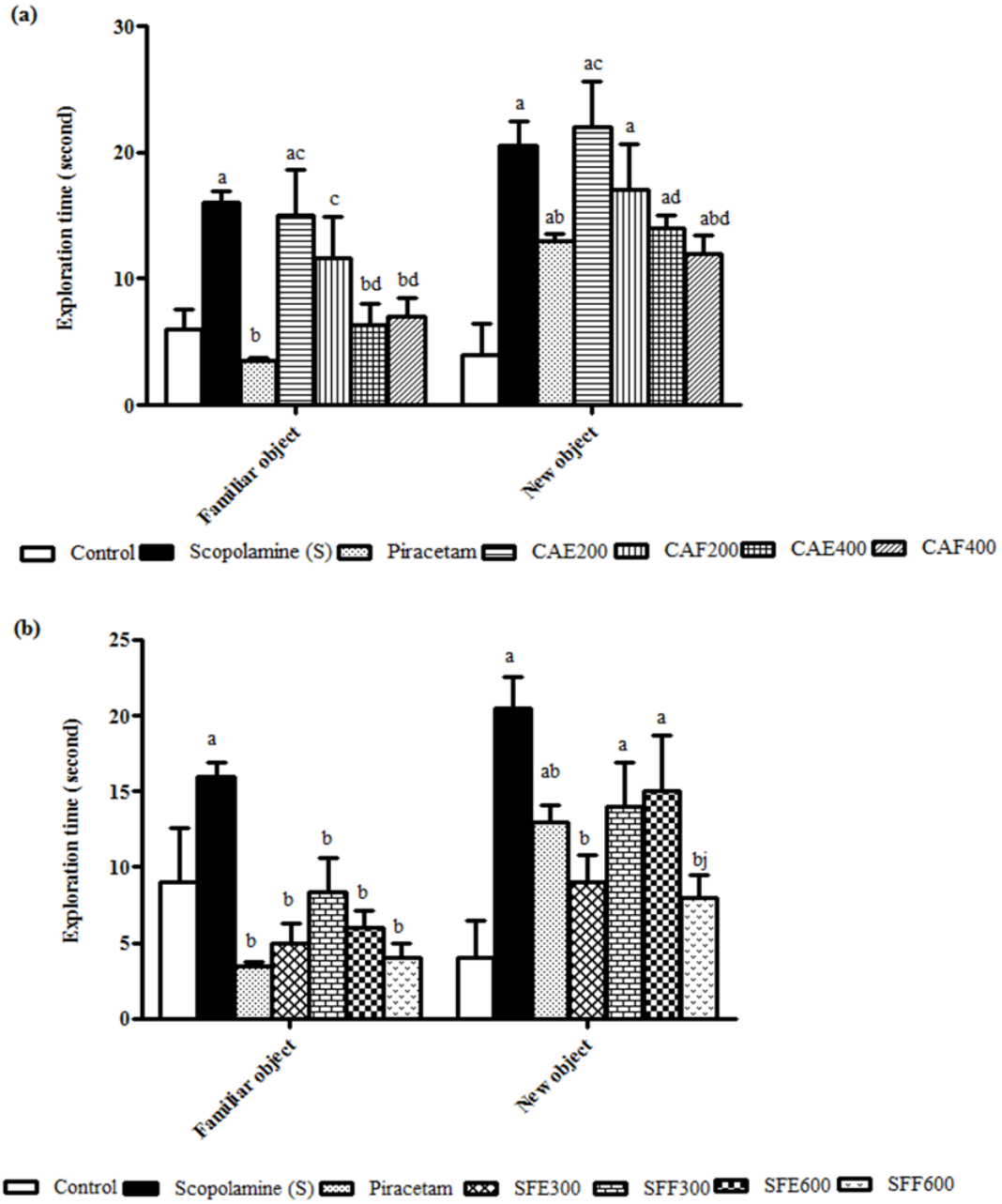


Figure 4. Effects of fractions and extracts of aerial sections of *C. album* (a) and seeds of *S. foetida* (b) on exploration time in object recognition tests. All values are mean ± SEM; n=6; [a]p<0.05 compared to control; [b]p<0.05 compared to scopolamine; [c]p<0.05 compared to piracetam; and [d]p<0.05 compared to CAE200 and [j]p<0.05 compared to SFE600 [Repeated measures of two-way ANOVA followed by Bonferroni test].

Effect of *C. album* and *S. foetida* extracts and fractions on serum total cholesterol and serum glucose levels

One-way ANOVA revealed significant differences among groups in serum glucose and total cholesterol levels (p<0.05; Figure 5a–b). Both *C. album* and *S. foetida* extracts and their respective fractions markedly reduced serum cholesterol levels in a dose-dependent manner. Among them, the 400 mg/kg dose of *C. album* extract showed greater efficacy than the 200 mg/kg dose, Additionally, both plant treatments improved serum glucose levels compared to the scopolamine-treated group, indicating potential metabolic benefits alongside their neuroprotective effects.

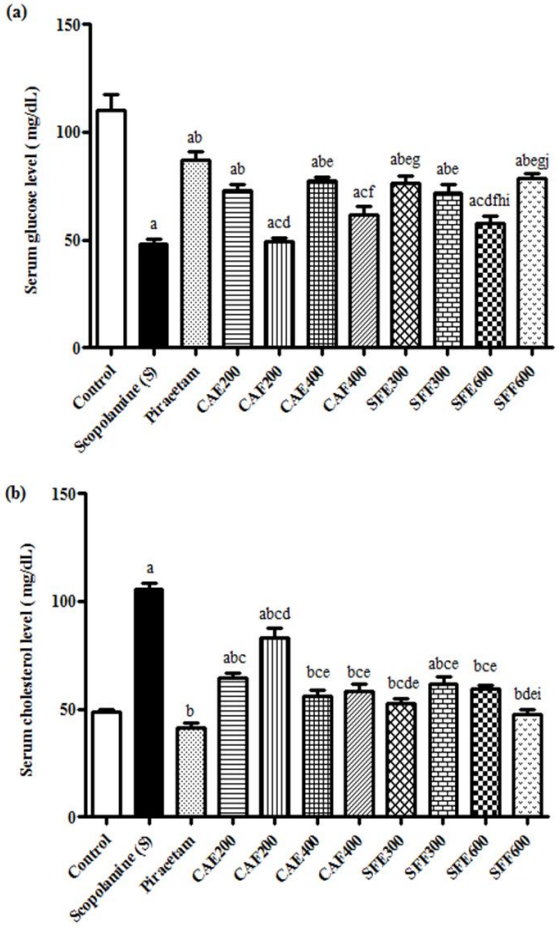


Figure 5. Effects of fractions and extracts of aerial sections of *C. album* and seeds of *S. foetida* on serum glucose (a) and total cholesterol (b) levels. All values are mean ± SEM; n=6; [a]p<0.05 compared to control; [b]p<0.05 compared to scopolamine; [c]p<0.05; compared to piracetam; [d]p<0.05 compared to CAE200; [e]p<0.05 compared to CAF200, [f]p<0.05 compared to CAE400, [g]p< 0.05 compared to CAF400, [h]p<0.05 compared to SFE300, [i]p<0.05 compared to SFF300 and [j]p<0.05 compared to SFE600 [One way ANOVA followed by Student Newman-Keuls Post-hoc test].

Effect of *C. album* and *S. foetida* extracts and fractions on brain AChE activity

Treatment with *C. album* and *S. foetida* extracts and fractions significantly reduced AChE activity in a dose-dependent manner compared to the scopolamine-treated group, indicating restoration of cholinergic function. These findings suggest that both plants may enhance memory and cognitive performance by modulating cholinergic neurotransmission (Figure 6a).

Effect of *C. album* and *S. foetida* extracts and fractions on oxidative stress

Treatment with *C. album* and *S. foetida* extracts and fractions significantly attenuated oxidative stress in the brains of scopolamine-treated rats. Both plants reduced lipid peroxidation (MDA) and enhanced antioxidant defenses (GSH and SOD) in a dose-dependent manner, demonstrating their neuroprotective potential (Figure 6b, 7a, and 7b).

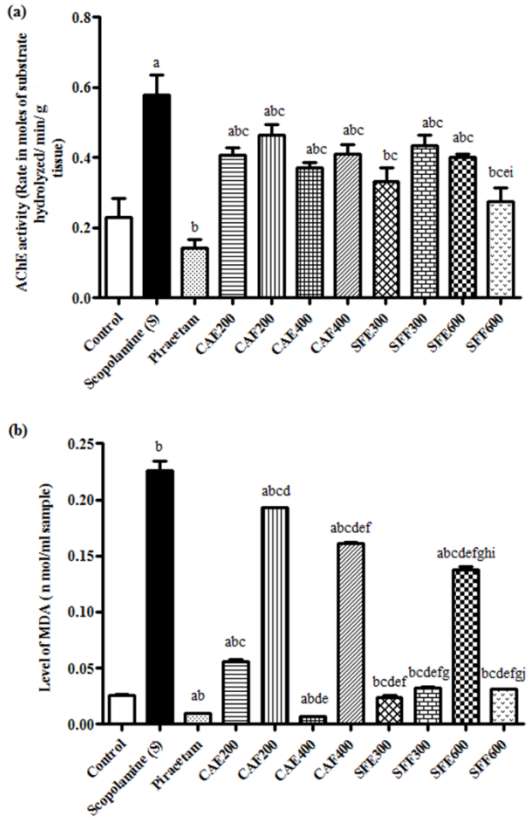


Figure 6. Effects of fractions and extracts of aerial sections of *C. album* and seeds of *S. foetida* on brain AChE activity (a) and MDA levels (b). All values are mean ± SEM; n=6; [a]p<0.05 compared to control; [b]p<0.05 compared to scopolamine; [c]p<0.05; compared to piracetam; [d]p<0.05 compared to CAE200; [e]p<0.05 compared to CAF200, [f]p< 0.05 compared to CAE400, [g]p<0.05 compared to CAF400, [h]p<0.05 compared to SFE300, [i]p<0.05 compared to SFF300, and [j]p<0.05 compared to SFE600 [One way ANOVA followed by Student Newman-Keuls Post-hoc test].

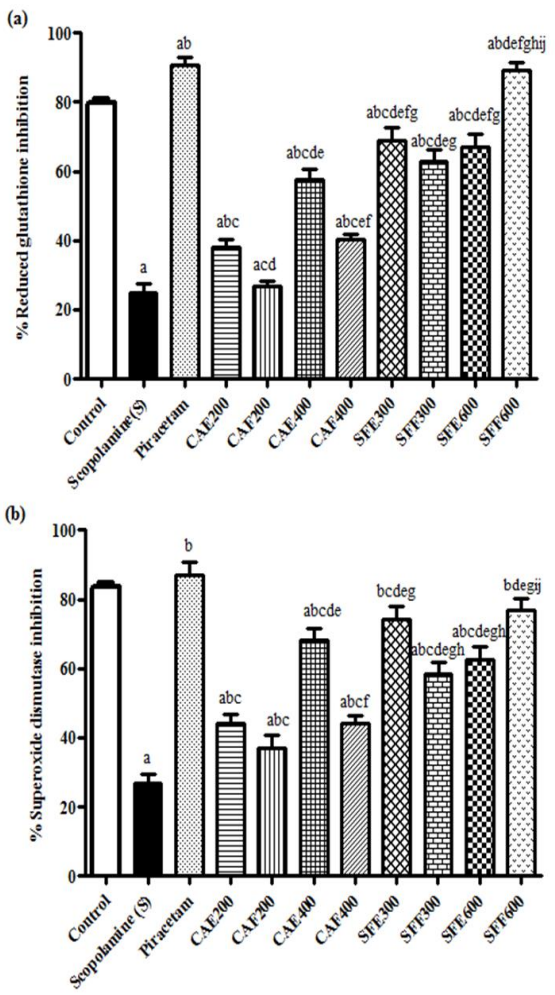


Figure 7. Effects of fractions and extracts of aerial sections of *C. album* and seeds of *S. foetida* on brain GSH (a) and SOD (b) activities. All values are mean ± SEM; n=6; [a]p<0.05 compared to control; [b]p<0.05 compared to scopolamine; [c]p<0.05; compared to piracetam; [d]p<0.05 compared to CAE200; [e]p<0.05 compared to CAF200, [f]p<0.05 compared to CAE400, [g]p<0.05 compared to CAF400, [h]p<0.05 compared to SFE300, [i]p<0.05 compared to SFF300, and [j]p< 0.05 compared to SFE600 [One way ANOVA followed by Student Newman-Keuls Post-hoc test].

Effect of *C. album* and *S. foetida* extracts and fractions on hippocampal protection

Normal neuronal morphology with intact nuclei and well-organized cortical layers was observed in control group, with no signs of inflammation or degeneration, evident neuronal shrinkage, pyknotic nuclei, and vacuolation. Disruption of cortical architecture and increased cell loss suggest scopolamine-induced neurotoxicity. Reduced vacuolation and fewer pyknotic cells compared to scopolamine groups, indicating moderate neuroprotective effect of piracetam group. For CAE 200 and 400, dose-dependent improvement in tissue morphology was observed. CAE400 showed better preservation of neuronal structure, reduced inflammation, and near-normal cortical layering. However, CAF200 and CAF400 showed mild to moderate neuroprotection. CAF400 showed reduced neuronal damage compared to CAF200, though less effective than CAE counterparts. SFE600 demonstrated substantial neuroprotection with minimal vacuolation and preserved neuronal architecture. SFE300 showed moderate improvement. SFF600 exhibited notable reduction in scopolamine-induced damage, with improved cell density and morphology. SFF300 showed partial recovery (Figure 8). This altogether proved the protective property of *S. foetida* seeds and aerial sections of *C. album*, and their potential to treat AD.

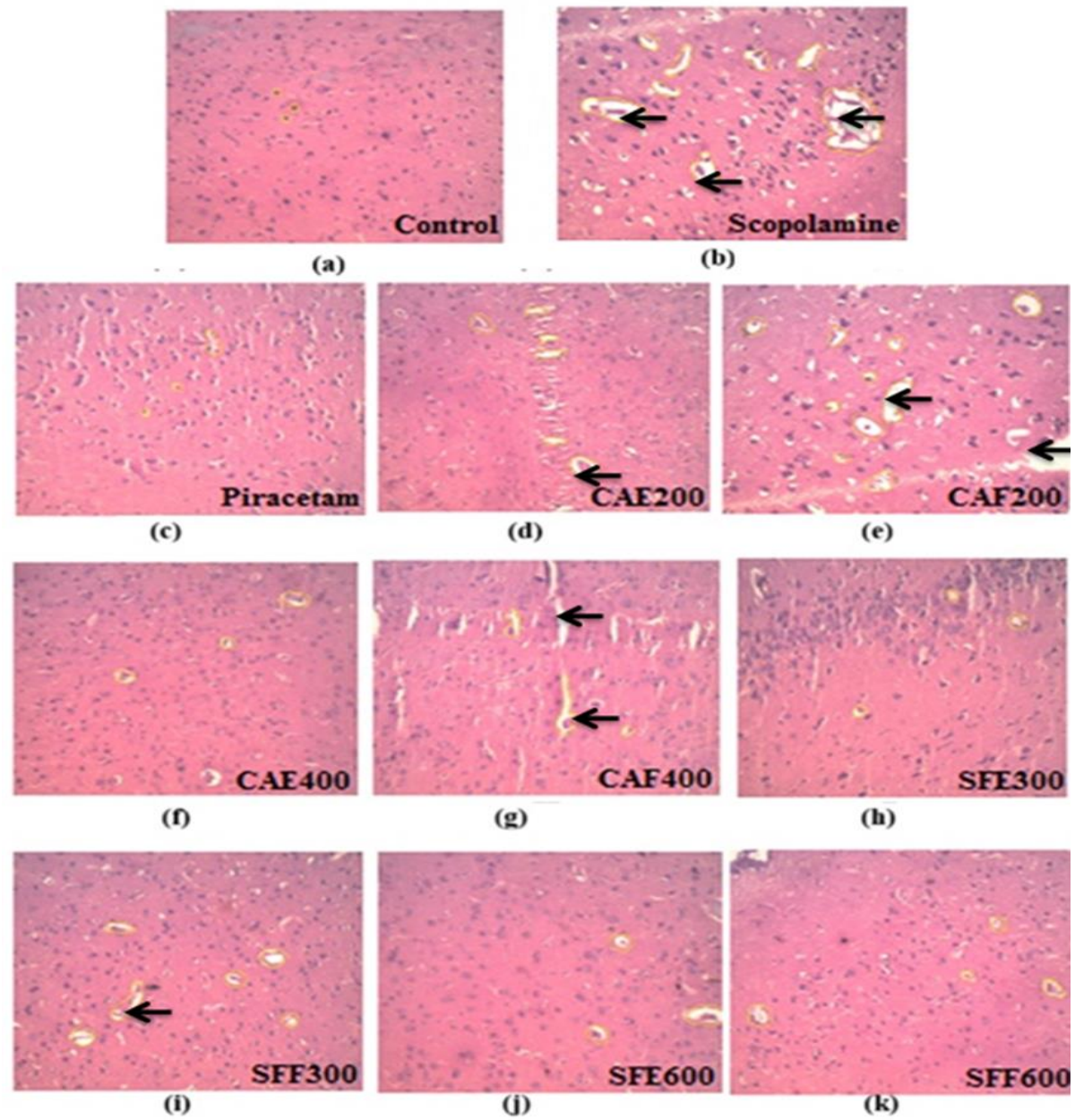


Figure 8. Histopathological observation of hippocampus tissues stained with Haematoxylin and eosin (observed at 10X and scale bar 200μm) in different groups. The arrows indicate shrunken neurons at different treatment. Control (a), Scopolamine (b), Piracetam (c), CAE200 (d), CAF200 (e), CAE400 (f), CAF400 (g), SFE300 (h), SFF300 (i), SFE600 (j), SFF600 (k).

Discussion

This study is the first to systematically assess and compare the extracts and fractions of *S. foetida* seeds and *C. album* aerial parts in an AD–relevant model (scopolamine-induced amnesia). Furthermore, the study evaluated acetylcholinesterase inhibition, oxidative stress modulation, and behavioral outcomes within a unified experimental framework, thereby providing novel insights into their cholinergic and neuroprotective mechanisms that have not been addressed in previous literature. The novelty of the present work particularly lies in the use of the scopolamine-induced amnesia model to investigate the neuroprotective and memory-enhancing potential of *C. album* and *S. foetida*. The scopolamine model is considered more appropriate for screening

compounds that act directly through cholinergic mechanisms, as scopolamine—a muscarinic acetylcholine receptor antagonist—induces reversible cognitive impairment by blocking central cholinergic transmission. Scopolamine does not fully mimic pathology of AD. But given that AD is characterized by a pronounced loss of cholinergic neurons and reduced ACh levels, this model effectively reproduces the cholinergic dysfunction underlying cognitive decline and is therefore mechanistically aligned with the "cholinergic hypothesis" of AD (Klinkenberg and Blokland 2010; Rashmi et al. 2025).

Studies have demonstrated that oxidative stress and abnormal cholesterol accumulation may be the cause of formation of Aβ plaques in blood vessels, and intraneuronal neurofibrillary tangles in AD. Additionally, acetylcholine depletion or cholinergic deficiency is a major contributing cause to AD and memory loss. Lipid peroxidation, a commonly used indicator of the production of free radicals, produces MDA as a byproduct. An increased level of MDA in the brain can result from oxidative stress and aging, which can impair memory and learning. However, by shielding the cell from harmful effects of the reactive oxygen species, GSH and SOD make up the anti-oxidant system. Constituents of *C. album* including phenolic acids, β-carotene and trigonelline are reported to possess anti-cholinesterase activity (Ali Hassan and Abu Bakar 2013) and the leaves of *C. album* exhibit anti-oxidant action (Al-Joufi et al. 2022; Kumar and Kumar 2009; Laghari et al. 2011). Both anti-cholinesterase activity and anti-oxidant activities act as key pathological features of AD (Fukui et al. 2001; Huang et al. 2022; Lee et al. 1993). Furthermore, flavonoids found in *S. foetida* seeds show anti-oxidant activity (Nhân and Trinh 2019), while sterculic acid have been reported to reduce adrenomedullin and stearoyl-CoA desaturase expression, both of which provoke memory failure. The current study did not evaluate inflammation. However, the findings about therapeutic effects of the plant extracts are in line with previous studies. Thus, it can be hypothesized that inflammation might be one of the mechanisms behind its neuroprotective potential.

According to the experimental findings of this study, the phytochemicals protected against memory deficits by blocking AChE, which inhibits degradation of acetylcholine. Additionally, the extracts and the fractions were found to increase the GSH and SOD activity, while lowering MDA levels. In comparison to the control, the histological analysis also showed their protective action against abnormalities, and neuronal degeneration. While observing the dose-dependent effects of the fraction, it was found that *C. album* extract (400 mg/kg b. wt.) along with *S. foetida* extract (300 mg/kg b. wt.) was highly effective for retention trial. Additionally, *C. album* fractions and extracts along with *S. foetida* fraction caused dose-dependent reduction in transfer latency against memory impairment. *S. foetida* and *C. album* (400 mg/kg b. wt.) significantly restored the recognition capacity of familiar object by reducing the total time taken in exploration during retention trial. *S. foetida* extract 300 mg/kg b. wt., *S. foetida* fraction 600 mg/kg b. wt. along with *C. album* fraction 400 mg/kg b. wt. was effective for new objects. *C. album* and *S. foetida* extracts and fractions showed a significant reduction in AChE activity and showed anti-oxidant potential in a dose-dependent manner. In histopathology, higher doses of *C. album* extract, *S. foetida* extract, and *S. foetida* fractions showed promising neuroprotective effects. *C. album* extract (400 mg/kg) and *S. foetida* extract (600 mg/kg) were particularly effective in restoring near-normal histoarchitecture. Thus, the study presents the significance of phytochemicals of aerial sections of *C. album*, and of the seeds of *S. foetida* in alleviating the symptoms associated with AD and related neurological disorders.

The aerial sections of *C. album* and seeds of *S. foetida* have significant neuroprotective activity due to inhibitory activity on AChE and oxidative stress. The depletion of acetylcholine by AChE is considered a characteristic hallmark of AD, and both the plant parts inhibited AChE, indicating their role against acetylcholine depletion. Additionally, the plant parts lowered the serum total cholesterol, elevated glucose and protected the hippocampus region of the animal, against scopolamine-induced histopathological abnormalities. It was consistent with earlier reports of its hepatoprotective effects against alcohol-induced toxicity (Nigam and Paarakh, 2011). Pre-treatment with ethanolic extracts and ethyl acetate fractions of aerial parts of *C. album*, and ethanolic extracts and *n*-butanol fractions of *S. foetida* for 8 days improved the neuronal behavior, in a dose-dependent manner. The underlying factors responsible for these protective effects might be due to the presence of phytoconstituents like alkaloids, glycosides, flavonoids, amino acids, saponins, steroids and proteins.

This study demonstrates the early neuroprotective potential of *C. album* and *S. foetida* against scopolamine-induced cognitive impairment. However, several limitations should be acknowledged. First, a comprehensive dose–response evaluation was not performed for all behavioral and biochemical parameters; thus, the precise relationship between dose and effect remains to be determined. Second, formal toxicity studies, including acute and sub-chronic evaluations, were not conducted, limiting conclusions regarding the safety profile of the extracts and fractions. Third, only male rats were used, which may restrict the generalizability of the findings across sexes. Future studies should include dose–response analyses, toxicity assessments, evaluation in both sexes, molecular docking, gene expression studies along with active compound quantification**.** Additionally, these findings could be further validated in an Aβ–induced AD model, which is more pathologically relevant and represents late-stage progressive neurodegeneration.

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Conflicts of interest

The authors have no financial or non-financial interests to disclose.

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None.

Ethical Considerations

The animal study was approved by the Institutional Animal Ethics Committee.

Code of Ethics

Animal ethical approval number BBDNIIT/IAEC/001/2015.

Authors' Contributions

PT: methodology, analysis; GNF: data curation, analysis, writing; AM: analysis, writing; VM: conceptualization, data curation; SKS: conceptualization, review and final draft.

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