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RESEARCH ARTICLE

Nootropic activity of ethanolic extract of *Alangium salvifolium* leaves on Scopolamine mouse model of Alzheimer's disease

Parameshwari K[1], Shashi kumar[2], Priyadharshini Bai G[3], Prathima C[4], Neetha C[2]

[1]Department of Physiology, East Point College of Medical Sciences and Research Centre, Bengaluru, Karnataka, India, [2]Department of Pharmacology, Chamarajanagar Institute of Medical Sciences, Chamarajanagar, Karnataka, India, [3]Department of Pharmacology, Shridevi Institute of Medical Sciences, Tumkur, Karnataka, India, [4]Department of Pharmacology, JSS Medical College, JSS Academy of Higher Education and Research, Mysuru, Karnataka, India

Correspondence to: Priyadharshini Bai G, E-mail: ravi_darshini@yahoo.co.in

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ABSTRACT

Background: *Alangium salvifolium* possesses completely different medicine activities such as antioxidant, anticancer, anti-inflammatory, bactericide, antifungal, and antifertility. It is also employed in the treatment of anxiety. The previous study is revealed significant of antidepressant activity of ethanolic extract of leaves of *A. salvifolium* (EASL) by stress-induced depression through forced swim test and tail suspension test models in Swiss albino mice. **Aims and Objectives:** The present study was designed to explore learning and memory enhancing activity leaves of *A. salvifolium* in Swiss albino mice. **Materials and Methods:** EASL of two divided doses (EASL-100 and 250 mg/kg orally) and scopolamine (0.4 mg/kg i.p.) per kg body weight was administrated for 7 days to individual groups of mice. The sensitivity behavioral models such as Elevated plus maze and Morris water maze were used to appraise learning and memory. However, scopolamine is the natural agent that is elicited cognitive state served as interoceptive models. The results area unit expressed as mean ± S.E.M. Statistical analysis was done by one-way analysis of variance test followed by Dunnett's multiple comparison tests. $P < 0.05$ was measured as statistically significant. **Results:** The results of this study showed that *Alangium salvifolium* at the doses of 100–250 mg/kg significantly ($P < 0.05$) improved abstraction short-term and memory, the exceptional reduction in transfer latency of the 6th and 7th days as a region of learning and memory. Within the elevated maze and reducing the escape latency within the Morris water maze. **Conclusion:** The results concluded, leaves of *A. salvifolium* have revealed as a significant memory enhancing activity altogether the screening models used.

KEY WORDS: *Alangium Salvifolium*; Elevated Plus Maze; Learning and Memory; Morris Water Maze

INTRODUCTION

Alzheimer's disease (AD) may be a liberal and inescapable loss of intellectual perform accompanying with the incidence of senile plaques in the hippocampus area of the brain.[1] It is the foremost necessary sort of dementia, which accounts for 60–80% of cases worldwide.[2] Alois Alzheimer was the first to talk about a case of intellectual deterioration and with histological results of intracellular nodules of neurofibrillary type.[3] However, the exact etiology of AD remains undefined. Dementia in the AD with early onset at 65 years has a relatively rapid course with a multiple marked disorder of a superior cortical function and another with onset after 65 years showed a progression with a greater deterioration of the characteristics of memory.[4]

Pathogenesis of AD is from German neuropathologist, Prof. Alois Alzheimer. The World Health Organization

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reportable this disease within the year 1906 for the first time during a 51-year-old woman affected for the year by heart problems, language dysfunction, and confusion? It is a particular neurodegenerative illness characterized by senile deposit, neuritic twists, and gradual loss of neuron leading to cognitive state, alteration in thinking, and alternative brain perform. The development of the ailment is relaxed and gets worse through additional somatic cell-cell death.[5] Dementia is a disturbance, characterized by defeat of cerebral facility adequately plain as to inhibit through one's activity and communal deeds and it consistently includes weakening of memory. The foremost common validation for dementia is advanced neurodegenerative disorder related to loss of nerve cell in discrete areas.[6]

A medicine survey revealed that dementia or state of mind may be a serious hidden downside in Indian population.[7] The rapidity of dementedness can increase exponentially by aggregate age, and this aging technique in animals is related to a deliberate deterioration of sensory and motor activity at intervals in the region of the brain. The degeneration in sensory and motor activity takes remained accredited toward the oxidative injury to the cellular lipids, proteins, nucleic acids, and disproportion of several compounds level due to oxidative stress. Consequently, various antioxidant therapy and flavonoids elements may also be useful for protecting brain functions and bar the age-related deficits.[8]

At present, there is no cure for Alzheimer's. Clinicians usually prescribe medication to improve symptoms that usually accompany AD, as well as wakefulness, nomadic, nervousness, distress, and depression. The medications presently used are tacrine hydrochloride (HCL) (Cognex),[9] and donepezil HCL (Aricept),[10] rivastigmine (Exelon),[11] and galantamine (Razadyne).[12] They strengthen the effectivity of the nerve cells most affected by Alzheimer's unwellness. Nevertheless, the outcomes are transient and do not treat the unwellness. Scholars have sought for molecules that inhibit the "parent" molecule of the beta-amyloid supermolecule, to cut back the assembly of the proteins.[13] Studies mistreatment has shown little, however, vital enhancements in operating in one cluster of Alzheimer's unwellness sufferers.[14] Investigators are testing a variety of antioxidants to envision if they assist shield nerve cells. Researchers are certain of that beta-amyloid proteins could become ototoxic as they build up. If the accumulated proteins may be reduced, they will be less harmful.[15]

Herbal medicines square measure the exceptional provide for the discovery of the invention of a recent drug, are in use even from the religious text length. It is properly mounted that 80% of drug molecules are herbal merchandise or natural compound inspired.[16] The supply of herbal merchandise as a source of novel human therapeutics reached its height within the western pharmaceutical at some stage in 1970–1980. That end in the pharmaceutical panorama closely aroused with the help of non-synthetic molecules.[17] Herbal remedy compromises various choices to change the event and signs and symptoms of an advert. There has been a replacement trend at intervals the education and advertising of medicine primarily based on therapeutics flowers, and their clinical and industrial significance looks to be amassing momentum in health-applicable regions. Those plant-derived medicines area unit cautiously standardized, and their effectuality and protection for a specific software system were exhibits.[18]

Alangium salvifolium (ankolemara) is one of the foremost valuable plants in a ancient system of the drugs from ancient period. The plant A. *salvifolium* may be a little ligneous plant, or deciduous tree could or might not be armed. Leaves square measure alternate, sometimes unequal, 12.5 cm–17 cm long, 2.5 cm–7.0 cm broad, oblong-lanceolate or oblong-oval, acute or rounded, outstanding below, and obtuse at the apex with 3–6 pairs of oblique veins with white or yellowish-white color and fragrance. It is renowned to contain numerous secondary metabolite such as alkaloids (ipecac and benzopyridoquinolizidine), flavonoids, triterpenoids, saponins, tannins, phenolic resin glycosides, oil, alangine, lamarckinine, salviifosides A-C, salicin, kaempferol, and kaempferol 3-O-b-D-glucopyranoside.[19]

As per the standard privilege, the plant possesses completely different medicine activities such as antioxidant, anticancer, anti-inflammatory, bactericide, antifungal, and antifertility. It is also employed in the treatment of anxiety.6 Our previous study is revealed significant of antidepressant activity of ethanolic extract of leaves of *A*. *salvifolium* (EASL) by stress-induced depression through forced swim test and tail suspension test models in Swiss albino mice.[21] Hence, the present study was carried out for the nootropic activity of EASLs on scopolamine mouse model of AD.

MATERIALS AND METHODS

The experiment was allotted when obtaining due clearance from the Institutional Animal Ethics panel of JSS Medical College, Mysuru.

Animals

Swiss albino mice weighing 25–30 g, of either sex, have been procured from the central animal facility of the institute and maintained underneath the well-known conditions: Room temperature (25 ± 3) is °C, humidity 45–55%, and 12/12 h light/dark cycle. They were fed with commercially.

Animals were divided into 5 groups of and each group consists of 6 mice. Group I treated as vehicle control (normal saline), Group II was treated with standard - (Piracetam

400 mg/kg/i.p.) and Groups III and IV were administered two different doses of EASL 50, 250 mg/kg/per orally, Group V is treated with scopolamine (0.4 mg/kg p.o)., respectively, which were administered up to 7 days. The following tests were employed for the assessment of memory activity, 1 h after the administration of the extract and the animals were used once for each test.

Chemicals

Piracetam (sun pharmaceuticals), scopolamine, normal saline, and ethanol were used.

Plant Materials and Preparation of Drug Solution

A. salvifolium leaves were collected from Hill region (Dimbam), Coimbatore district, Tamil Nadu State, and it had been documented by Dr. Mruthunjaya, Pharmacognosy Department of JSS Pharmacy College, Mysuru. The leaves were subjected to clean with subjected of alcohol and created into coarse powder when a shade dry for 1 week. Concerning 800 g of this powder was subjected to Soxhlet extraction for 12 h victimization ethyl alcohol as a solvent with revered temperature. The extract was more targeted employing a vacuum extractor for complete removal of the ethyl alcohol (absolute, ≥99.5%). The targeted EASL was accustomed to appraise the antidepressant activity. The stock resolution was freshly ready by employing a solvent as traditional saline before dosing from which the different doses were administered by choosing the suitable concentration.

Assessment of Memory Activity

Elevated plus maze

It is involving of two open arms (16 cm × 5 cm) and two enclosed arms (16 cm × 5 cm × 12 cm) was recycled. The maze was elevated to a height of 25 cm. Animals were located associate distinct basis at the tip of associate degree open arm facing removed from central platform and time took by them to move from there to either of the closed arms transfer latency (TL) was documented. If the animal did not arrive into the closed arms at intervals 90 s, it had been slightly pushed into one of the two closed arms, and therefore the chemical element was allotted as 90 s. The animals were permissible to explore the maze for an added 10 s and so originated spinal to its home cage. Retention of this learned - task was examined 24 h when the 1st-day trial. TL when 24 h was expressed as "Inflexion magnitude relation IR" victimization the formula diagrammatical by Jaiswal and Bhattacharya (1992): IR = (L1–L0)/L0 is that the TL once 24 h, and L1 is that the early TL in seconds. Female mice, weight 25–30 g, were divided into seven groups consisting of half-dozen animals. Group I: Saline (10 ml/kg) was administered orally for days, and TL was recorded. Retention of the learned task was examined when 24 h, cluster II: Hyoscine HCL (0.4 mg/kg) was injected before coaching. A metallic element was recorded when 45 min of injection. Retention was examined when 24 h. Groups III and IV: EASL extract (50–100 mg/kg) was administrated orally for 7 days. A TL was noted when 90 min of administration on the 6th and 7th days. Group V: Standard. Group VI received extract with most nootropic activity (50 mg/kg) for 7 days when 90 min of extract treated, scopolamine (HCL (0.4 mg/kg) was given. TL was recorded when 45 min injection and when 24 h. Group VII received Piracetam (100 mg/kg) for 6th and 7th days and on the 7th day when 90 min of administration, hyoscine HCL (0.4 mg/kg) was given. TL stood logged when 45 min of inoculation and once 24 h.

Morris water maze

Morris, 1984; Bejar *et al*., 1999; Frick *et al*., 1995; and Gordon *et al*., 1995: A abstraction take a look at was performed by the tactic of Morris with trivial alteration. The water maze could be a spherical mere (120 cm in diameter and 50 cm in height) with an uninspired internal superficial. The pool was satisfied with complexity of 35 cm with water covering 500 ml of milk (20 ± °C). The pool was alienated into four quadrants of the equivalent part. A snowy stage (6 cm in diameter and 29 cm in height) was then placed in one of the pool quadrants.

The primary trial day was devoted to spinning exercise for 60 s deprived of the flooded platform. Throughout the 5 ensuing days. The mice remained given two daily trials by inter-trial intermission of 30 min in the incidence of the stage, it had been allowable to stay there on for 10 s, if the mouse failed to find the platform inside one 120 s, and it had been located on the platform for 10 s. The animal was taken to its home cage and was allowed to dry up under room temperature. During each trial session, the time taken notice the hidden platform (latency) was recorded. At some point, once the last training trial session, mice were subjected to review trial sessions within which the platform was off from the pool, allowing the mice to swim for 120 s, to go looking for it. A record was continuous to spinning time within the pool quadrant wherever the platform had previously been placed. Memory impairment was evoked in the mice with scopolamine (0.4 mg/kg i.p.) at 60 min once treatment of test samples. Management cluster received normal saline.

Statistical Analysis

Data obtained by elevated plus maze and Morris water maze were scrutinized using one-way analysis of variance monitored by Dunnett's multiple compared test. $P < 0.05$ was considered statistically significant.

RESULTS

Acute Toxicity Study

The acute toxicity was conceded out in Swiss albino mice through static dosage process of organisation for economic co-operation and development guideline No. 423.[23] EASL was given orally up to the dose level of 2000 mg/kg.

Behavioral Studies

Elevated plus maze model

The effects of elevated plus maze are shown in Table 1. Low dose of EASL (50 mg/kg) and greater dose of EASL (250 mg/kg) were anticipated for 7 consecutive days orally treated revealed significant deduction on TL, greater dose produced highly significant ($P < 0.01$) and low dose produced slight significance effect ($P < 0.05$) after associated through scopolamine-induced amnesia as well as normal control group, on 6th–7th days. The animals were administrated with small to high dose showed a significant decline in TL of the 6th–7th days as a part of learning and memory. Scopolamine (0.4 mg/kg i.p) injected prior training considerably increased TL on the 6th–7th days indicating impairment in learning and memory. Piracetam (used as a standard drug) at a dose of 100 mg/kg additionally revealed considerably decrease metal. The impact made by Piracetam was more significant ($P < 0.001$) which has presented greater efficacy on learning and memory as paralleled to standard group and control group. Even though each of the two doses of EASL produced a significant reduction in TL, greater dose was additional effective than lesser dosage [Table 1].

Morris water maze

There is a rise in escape latency in scopolamine evoked animals equated to the standard of each the times [(4, 25) = 66.05] ($P < 0.001$). (F [4.25] = 66) ($P < 0.001$). EASL low dose (50 mg/kg) does not show any significance on the 6th–7th days ($P < 0.8295$), ($P < 0.7727$). Higher dose of EASL (250 mg/kg) indicates slight significance on the 6th day ($P < 0.0238$) and high significance on the 7th day ($P < 0.0024$). The animals administrated with a higher dose of EASL showed remarkable decrease in escape latency of 6th–7th days as part of learning and memory [Table 2].

Table 1: Impact of EASL on TL of mice using elevated plus maze

Treatments	TL on 6th day mean±SEM (*n*=6)	TL on 7th day mean±SEM (*n*=6)
Control	23±0.91	24±0.65
Scopolamine (0.4 mg/kg)	54±2.4	55±2.5
EASL (50 mg/kg)	18±0.7*	19±0.8*
EASL (250 mg/kg)	16±0.54**	17±0.63**
Piracetam 100 mg/kg	5.8±0.7***	5.9±0.61***

EASL: *Ethanolic extract* of *A. salvifolium* leaves; *P<0.05, **P<0.01, ***P<0.001, TL: Transfer latency, SEM: Standard error of mean, *A. salvifolium*: *Alangium salvifolium*

DISCUSSION

The novel focus on existing study, toward demonstrates to nootropic activity of EASL on scopolamine mouse model of Alzheimer's. Scopolamine is an organic compound obtained from the Solanaceae *Datura stramonium,* and that is blights quick-time period and extended time-memory in both animals and humans.[21] Through the interference of neurotransmitter within the brain, hyoscine will cause oxidative stress resulting in cognitive impairment. Hence, scopolamine-induced memory impairment could be an effective model for the assessment of anti-amnesic properties of the most recent pharmaceutical medication. Numerous activity animal models are generally used for the assessment and substantiation of recent medication in contradiction of dementia[2]

In the present study, 7 days pre-treatment of animals with *A. Salvifolium* leaves extract considerably counteracted the reduction of the percentage of spontaneous alternation triggered through scopolamine suggesting significant improvement of area-related short-term memory by the EASL.

In the existing study, 7 days pre-treatment of animals with *A. Salvifolium* leaves extract extensively neutralized the decrease of the proportion of impulsive interchange elicited through scopolamine signifying vital progress of area-related instant memory by the EASL.

The equine protozoal myeloencephalitis (EPM) test was used for the analysis of learning and memory. The EPM relies on the normal natural aversion of rodents to open and excessive areas, and in the beginning, it is far used for measurement of anxiety.[23] Some parameters of the EPM at the side of retention TL (the time taken by suggests that of

Table 2: Impact of EASL on escape latency of mice using Morris water maze

Treatments	Escape latency on 6th-day mean±SEM (*n*=6)	Escape latency on 7th-day mean±SEM (*n*=6)
Control	25±2.2	26±2.5
Scopolamine (0.4 mg/kg)	38±1.6	43±0.85ns
EASL (50 mg/kg)	23±1.2ns	25±0.96
EASL (250 mg/kg)	19±0.92*	19±1.5**
Piracetam 100 mg/kg	11±0.91***	12±0.17***

EASL: Ethanolic extract *A. salvifolium* leaves; *P<0.05, **P<0.01, ***P<0.001, ns: Nonsignificant, SEM: Standard error of mean, *A. salvifolium: Alangium salvifolium*

the animal to move from the open palms to the penned arms) are employed for the analysis of memory. Moreover, an animal that has formerly (acquisition trial) delicate entering the open hands have the shortened switch latency among the retention trial. Modern studies on numerous nootropics associated amnesic agents on elevated and maze have verified this model as an extensively accepted paradigm for training, learning, and memory process in rodents. These results suggest that *A. Salvifolium* has a nootropic impact as a result of it ameliorates the retention of pieces of information in the absence of any memory impairment inducer. In our observe study, management of Piracetam and EASL for 7 days included animals from learning and memory impairment created through interceptive stimuli (scopolamine). The decision cautioned the attainable neuroprotective role for EASL whereas, the boom in IR (inflexion ratio) when 24 h indicated advanced retention of a learned challenge.

Correspondingly, EASL turned into evaluated to illustrate its cognitive improving consequences on spatial memory and studying function of mice toward scopolamine-triggered amnesic defects the usage of Morris water maze take a look at. In this take a look at, EASL and Piracetam treatment at the scopolamine-caused amnesic mice exhibited huge shorter get away latencies in day by day 1st trial than the scopolamine administered firms throughout a 7-consecutive day training periods. The effects reveal that EASL improves spatial mastering and memory characteristic in opposition to scopolamine-triggered amnesia.

As per our previous study, consequences confirmed the phytochemical analysis of EASL exhibited the presence of assorted phytoconstituents which incorporates flavonoids, saponins, and tannins.[20] It is far recognized that saponins complex has nootropic and also antioxidant activities.[29] This fairly explains the mechanism of movement of the extract. Similarly, studies are necessary to isolate the nootropic composite and elucidate the action that underlies spatial gaining knowledge of and memory, age-related modifications in spatial guidance and the capability of nootropic sellers to influence particular cognitive techniques. The neurochemical basis of learning and memory persist poorly understood despite huge experimental and scientific take a glance at. Although the role of the precious cholinergic system is fairly known, the position of the different neurochemical system cannot be ignored.[24] Considering scopolamine prompted amnesia changed into reversed through EASL, it is possible that the beneficial effect on studying and reminiscence changed into because of facilitation of cholinergic transmission in mouse brain

CONCLUSION

The consequences of this examine show that the EASL stabilized scopolamine-prompted memory impairment and also may be oxidative stress. As a consequence, it will be terminated that *A. Salvifolium* might exist a precious herb aid for the management of dementia, in trendy, associate age-related psychological feature deficit of Alzheimer's type principally. Though, larger studies with *A. salvifolium* targeted on totally different hypotheses of advert are needed to clarify the exact mechanism of motion of the plant

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