



Research Article

NEUROPROTECTIVE ACTIVITY OF *SECURINEGA LEUCOPYRUS* AGAINST ETHANOL INDUCED COGNITIVE IMPAIRMENT

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ABSTRACT

Spatial memory, according to neuroscience, is the part of memory, responsible for recording one's environment and its spatial orientation. Learning is a process of acquiring knowledge about the world and memory is retrieval of the knowledge. Among behavioral tests, one of the most suitable devices for measuring spatial learning and memory is the 8 Arm Radial maze. As spatial memory loss is one of the symptoms of Alzheimer's disease, the present study is carried out. It shows the effectiveness of various extracts of *Securinega leucopyrus* on rats to reach the paired arm in radial maze. The results suggest that both the extracts have shown memory enhancement activity as a part of treating Alzheimer's disease.

Keywords: *Securinega leucopyrus*, Alzheimer's, 8 Arm radial maze, Paired arm.

INTRODUCTION

Alzheimer's disease is an irreversible, progressive brain disorder that slowly destroys memory and thinking skills and eventually, the ability to carry out the simplest tasks. In most people with Alzheimer's, symptoms first appear in their mid-60s¹. Alzheimer's disease is a form of brain degeneration in which abnormal particles called neurofibrillary tangles and amyloid plaques form in the brain and destroy healthy neurons (brain cells). These abnormalities tend to settle in brain areas that control the ability to learn a new fact and remember it 30 minutes, or a day later, a skill we refer to as "memory"².

Securinega leucopyrus (Family: Euphorbiaceae), popularly known as Bushweed and Indian Snowberry. It is a commonly found in India, Sri Lanka and Burma. It is a perennial shrub that grows up to 5 m in height. The genus *Securinega* is a native of Madagascar and the Mascarene Islands in Indian Ocean. There are about 45 species present in this genus. In the year 1789, *Securinega* was first described as a genus. *Securinega* was a genus in the family Phyllanthaceae, later it is changed to the family Euphorbiaceae.

It is used topically in paste form for healing of chronic and non-healing wounds³. The leaves of the plant contain germicidal properties. The decoction of leaves is used to dress the cancerous wounds and also used externally in the treatment of piles. The juice or paste of the leaves along with tobacco used to destroy worms in sores. It is used as popular veterinary medicine. The leaves are used to extract the extraneous materials from body tissues without surgery⁴. Leaves are boiled and taken twice a day for stomach aches. The roots are used in the treatment of testicular enlargement and in the cure of oedema. The whole plant is used for the cure of cancer in the sole of the foot. It is also used in the treatment of abdominal lumps and liver hypertrophy and portal hypertension. The bark of stem is used for tooth ache⁵.



Figure 1: Stem of *Securinega leucopyrus*

MATERIAL AND METHODS

Collection and Authentication of Plant Material

The stems of the plant, *Securinega leucopyrus* (Willd.) Muell. were collected from the medicinal garden of Chalapathi Institute of Pharmaceutical Sciences, Guntur. The plant material was identified and authenticated by Dr. M. Raghu Ram, Department of Botany, Acharya Nagarjuna University, Guntur.

Preparation of Extract

The stem of *Securinega leucopyrus* was shade dried and was powdered in a mechanical grinder. The collected powder was extracted with water and methanol by using Soxhlet apparatus. The extraction was carried out for 72 h. Excess solvent was removed by the solvent evaporation.

Experimental Animals

SD rats of either sex (200-300 g) were selected for the study and were maintained for 7 days in the animal house of Chalapathi Institute of Pharmaceutical Sciences, Guntur under standard conditions, temperature (24 ± 10 °C), relative humidity (45-55 %) and 12:12 light: dark cycle. The animals were fed with standard rat pellet and water *ad libitum*. The animals were allowed to

acclimatize to the laboratory conditions 48 h before the start of the experiment. 5 rats/groups were used in all sets of experiments.

Ethical Approval

All the protocols were approved by Institutional Animal Ethical Committee (IAEC) and conducted according to Committee for the Purpose of Control and Supervision of Experimental Animals (CPCSEA) registered no: 1048/PO/Re/S/07/CPCSEA at Department of Pharmacology, Chalapathi Institute of Pharmaceutical Sciences, Guntur.

Behavioral Study

Before starting the behavioural studies 1 week training was conducted. Only food and water was administered during this period.

Radial Arm Maze (RAM)

Rats have an impressive ability to remember locations they have visited⁶. The radial arm maze was developed by Olton and Samuelson (1976) and has become an essential tool for testing memory in rats⁷. The spatial memory was evaluated by the instrument. Open type radial arm maze was used in the study. It had a circular central arena and 8 equally sized arms (20 x 60 cm). Small dishes with animal food was kept at far end inside each arm was mounted. Initially animals were habituated to the environment⁸. In the present study, baited and unbaited arms were fixed throughout the tests. The 1st, 3rd, 5th, and 7th arms were baited while the 2nd, 4th, 6th, and 8th arms were unbaited. The rats was placed in the centre of the maze and allowed to freely explore the maze for 10 minutes on the first day. The rats were required to take the food pellets from each arm without making a re-entry into the arm already visited. The trail was terminated when the animal takes the food reward from all the eight arms or after 10 minutes if all the eight arms were not visited. Correct score was give when the visits an arm and collects the food reward and a maximum score of '8' can be attained per trail. The first entry into the baited arm was recorded as a correct choice. An entry into an unbaited arm was considered a reference memory error (RME). When a rat re-enters an already visited arm it was taken as a working memory error (WMR)⁹.



Figure 2: 8-Arm radial maze

Ethanol- Induced Cognitive Impairment

Ethanol is neurotoxin that able to alter behavioural and cognitive performance in experimental animals in addition to humans. It mainly impairs hippocampus-dependent learning and memory functions. The mechanism of ethanol-induced neurotoxicity is not well understood. Several studies show that free-radical mediated oxidative stress play an imperative role. The brain is extremely susceptible to oxidative stress due to high level of polyunsaturated fatty acids (PUFAs) and catecholamines, large amounts of oxygen (O_2) in relatively small mass and in conjunction with low antioxidant activities. Furthermore, certain regions of the central nervous system (CNS), especially hippocampus and cerebellum, may be more sensitive to oxidative stress because of their low endogenous antioxidant, in relation to other brain regions. Study showed that acetaldehyde dehydrogenase is responsible for the generation of reactive oxygen species (ROS) by converting cytotoxic acetaldehyde produced from oxidation of ethanol to acetate. It has been confirmed that ethanol induces the synthesis of CYP2E1 that lead to oxidative stress. It also increases the ratio of NADH/NAD, responsible for reduction of ferric ion (Fe^{3+}) to ferrous ion (Fe^{2+}) which causes lipid peroxidation by generating hydroxyl radical¹⁰.

Experimental Design

The learning and memory enhancing activity of the aqueous and methanolic stem extracts of *Securinega leucopyrus* was investigated using the ethanol- induced cognitive impairment [Ethanol (20 %) is used to induce dementia like condition in the dose 4.5 mg/kg administered s.c for 21 days). The test animals were randomly chosen and divided into four groups having five rats in each as follows:

Group I: Inducing Group-Ethanol (4.5 g/kg was administered subcutaneously for 21 days).

Group II: Standard Group -Donepezil hydrochloride (2.5 mg/kg was administered orally for 21 days) + Ethanol.

Group III: Test-I -Aqueous stem extract of *Securinega leucopyrus* extract [SLAE- 100 mg/kg was administered orally for 21 days) + Ethanol.

Group IV: Test -II -Methanolic stem extract of *Securinega leucopyrus* [SLME- 100 mg/kg was administered orally for 21 days) + Ethanol.

All the treatment group animals received respective control, standard and test treatment 30 minutes prior to the ethanol administration for 21 days of experimental period.

Statistical Analysis

The values are expressed as mean $\pm$ SEM. The statistical analysis was performed using one way analysis of variance (ANOVA) followed by Dunnett's multiple comparison test. Comparisons were made between haloperidol group and test/standard groups. P-values < 0.05 was considered statistically significant. The statistical analysis was done by using Graph pad prism version no: 6.0.

RESULTS AND DISCUSSION

Effect of Stem Extracts of *Securinega leucopyrus* on Behavioural Parameters

Animals treated with ethanol [4.5 mg/kg] alone for 21 days showed an increase in time taken to reach paired arm and number of entries in baited arms and non-baited arms in 1st, 7th, 15th and 21st days.

Table 1: Effect of stem extracts of *Securinega leucopyrus* on time taken to reach paired arm (ethanol- induced cognitive impairment)

Group	Treatment	Time Taken to reach Paired arm (Sec)			
		1 st day	7 th day	14 th day	21 st day
I	Ethanol	148.4±0.75	139.7±0.93	121.4±2.73	101.4±1.72
II	Standard + ethanol	77.2±0.97	67.6±1.99	58.8±0.86	47.4±2.6
III	SLAE + ethanol	128.8±0.86	122.6±0.93	103.2±0.86	95±1.76
IV	SLME + ethanol	104±0.84	97±0.71	90.6±1.63	76.2±1.46

Table 2: Effect of stem extracts of *Securinega leucopyrus* on number of entries in baited arms and non-baited arms

Group	Treatment	Number of entries in baited arms and non-baited arms							
		1 st day		7 th day		14 th day		21 st day	
		B.A	N.B.A	B.A	N.B.A	B.A	N.B.A	B.A	N.B.A
I	Ethanol	2.4±0.25	2.2±0.2	2.2±0.2	2.6±0.25	2.2±0.2	2.6±0.25	1.6±0.4	0.8±0.2
II	Standard + ethanol	4.6±0.25	4.4±0.25	4.2±0.37	3.2±0.58	6.8±0.37	9.8±0.37	10.4±0.51	13.8±1.16
III	SLAE + ethanol	3.2±0.37	3.4±0.4	3.6±0.25	6.4±0.51	6.4±0.51	7.8±0.8	6.8±1.02	8.2±1.16
IV	SLME + ethanol	7.4±0.51	8±1.30	8±1.30	12.8±0.89	12.4±0.93	10±1.05	9.8±1.16	11.2±1.39

CONCLUSION

Evaluation through mazes is one of the well-known procedures in order to assess memory enhancement in pre-clinical research. Most of the research is ongoing in the area of cognitive impairment and the equipment like 8 arm radial maze, elevated plus maze, Y maze etc plays a major role to evaluate the parameters regarding enhancement or suppression of cognition. The cognition impairment was said to be reduced in our present article based on the anti-oxidant nature of *Securinega leucopyrus* and the presence of saponins and flavonoids.

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