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The Neuropharmacological Potential And Pharmacognosy Of *Evolvulus Alsinoides* Linn.; An Overview

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ABSTRACT: The modern treatments for CNS disorders have shown a number of problems in terms of safety, efficacy and side effects. Hence, an alternative to synthetic drugs is required for the benefit of patients suffering from neurological disorders. The prevalence rates of the spectrum of neurological disorders from different regions of the country ranged from 967-4,070 with a mean of 2394 per 100,000 population, providing a rough estimate of over 30 million people with neurological disorders (excluding neuroinfections and traumatic injuries). *Evolvulus alsinoides* L. commonly known as Shankhapushpi is found throughout India. It consists of phenols, glycosides, tri-terpenoides, steroids, volatile oil, fixed oils, fatty acids, alkaloids, proteins and amino acids and carbohydrates with various chemical constituents such as betaine, shankhapushpine, evolvine, scopoletin, scopolin, umbelliferone, piperine, triacontane, penttrioctane, octodeconoic acids, hexadecanoic acid squalene etc. This meticulous herb has neuropharmacological actions such as anti-anxiolytic, learning and memory enhancer, anti-convulsant, anti-depressant, anti-stress, and anti-psychotic. This review gives a keen view on its pharmacognosy, phytochemical studies, chemical constituents and neuropharmacological action of the drug and how this plant is capable of producing potent therapeutic effect in brain disorders. This plant is endowed with potential learning and memory enhancing activity.
KEYWORDS: *Evolvulus*, *alsinoides*, neuropharmacology, marketed formulations

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I. INTRODUCTION

Herbs as medicines are originated naturally so there is a strong belief that they are completely safe for the treatment of various ailments. Due to their low cost, less side effects and acceptability they are used for various treatments nowadays. Since they are originated naturally so there is a strong belief that they are completely safe for the treatment of various ailments.[1] Thus, traditional drug including natural medicine, Chinese herbal medicine or additional treatments like Unani, Siddha and Homeopathy having low costs and side effects are of particularly of great interest now a days. Plants consists of natural ingredients which are having potent activities and the phytochemical investigation of the extracts will provide us with various phytocompounds which are essential.[2] They are used in almost every culture as remedy to cure or prevent various diseases. The Indian ayurvedic medicine system is likely to be 5000 years old and plays a crucial role in our culture. According to the World Health Organization, the traditional medicines will continue to play a important role in health care system as around 80% of the population in the world relies on the use of traditional medicines [3].The CNS acting drugs are valuable therapeutically because they are capable of producing specific physiological and psychological effects and also they are most widely used pharmacological agents. From the vast array of plants of the indigenious system many are reported to have potential activity against CNS disorders [4]. The prevalence rates of the spectrum of different neurological disorders from different regions of the country ranged from 967-4,070 with a mean of around 2394 per 100,000 populations, providing over 30 million people with neurological disorders (excluding neuroinfections and traumatic injuries).

Evolvulus alsinoides L. (Family: Convolvulaceae) is an important plant in Ayurveda known for its therapeutic effects. *E. alsinoides* is commonly known as Shankhapushpi, and it is found throughout India ascending to the 6000ft in the Himalayas. The various other names are; Hind: Sankhahuli, Shankhpushpi, Guj: Shankhavali, Tam: Visnukranti, Mar: Sankhavela. The potential therapeutic effect leads to its use in various disorders like insanity, epilepsy, memory enhancement and nervous debility in Ayurveda system of medicine [5]. Anti-oxidant properties of this plant used to treat low spirits and depression as shown in various *in-vivo* experiments [6]. In various formulations it is used as an important ingredient which is used for the management of various CNS disorders like psychosis, epilepsy and other conditions where brain activities are affected. It is widely used as nervine tonic in various asian countries as it has potent memory enhancing activity. It is also

included as a Medhya drug in the treatises of Ayurveda like CharakaSamhita, SusrutaSamhita and AshtangaHridaya[7] .

Table 1.Taxonomic classification of *E. alsinoides*: [8]

Taxanomic hierarchy	***Evolvulus alsinoides* L.**
Kingdom	Plantae
Sub kingdom	Tracheobionta
Super division	Spermatophyta
Division	Magnoliophyta
Class	Magnoliopsida
Sub-class	Asteridae
Order	Solanales
Family	Convolvulaceae
Genus	*Evolvulus*
Species	*alsinoides*

II. METHODS

The information about the plant *E. alsinoides* L. was gathered using Scifinder and it was then searched for its potential effect in neurological disorders and the phyotochemistry. Data was collected from journals accessible in databases such as ScienceDirect, Medline, PubMed etc.

III. RESULTS

3.1 Pharmacognostical features

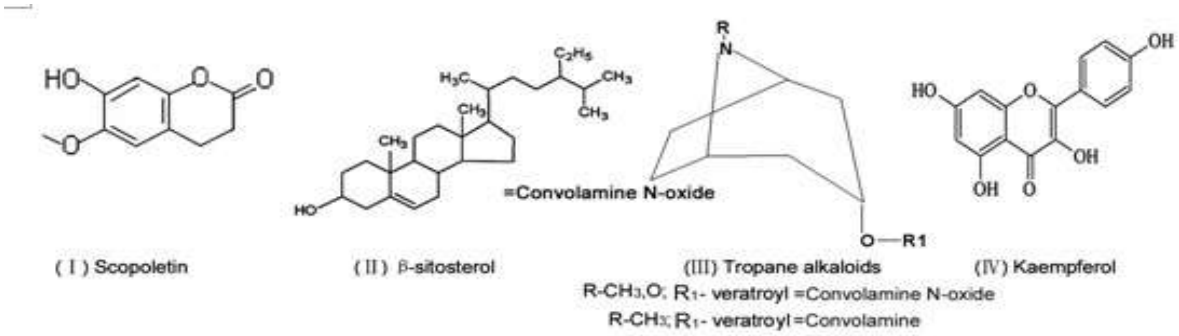
It is a small, procumbent , diffuse, prostate , hairy, perennial herb with around 10-30cm long branches arising from top of the root. It is found wild throughout the plains of India and ascending upto 2,000 m. The pharmacognostical profile of *E. alsinoides* is shown in Table 1. [9]

Table 1:.Different pharmacognostical features of *E. alsinoides.*

Evaluated characterstics	***Evolvulus alsinoides***
Stem structure	
Shape	Slender , wiry, cylindrical
Surface	Pubescent exhibiting scars left by leaf and bud
Internode	0.5 to 1.5 cm in length
Fracture	Splintery
Outline of T.S	Circular , wings absent
Trichomes	Glandular, multicellular stalk and multicellular head
Pericycle fibres	Present, lignified in group of 2 to 3
Endodermis	Distinct in young stem
Pith	Core hollow
Medullary rays	Present, uniseriate
Leaf structure	
Shape	Elliptic oblong to oblong ovate
Phyllotaxy	Alternate
Size	(8-14)mm ×(5-7) mm
Surface	Densely pubescent
Apex	Mucronate
Outline of T.S	Midrib convexly protruding at lower side, flat or concave at upper side
Collenchyma	1-2 layers
Lamina	Narrow , 2-3 rows of palisade cells
Trichomes	Present , similar as in stem
Oil glands	Present, oval to spherical
Stomata	Present, both lower and upper epidermis
Flower, fruits and seed structure	
Colour	Bluish
Inflorescence	Solitary
Calyx	5, lanceolate
Corolla	Rotate or funnel shaped
Fruit	Globose capsule
Seed colour	Brown
Seed surface	Plano-convex with reticulate surface

3.2 Phytochemistry

E. alsinoides contains various secondary metabolites such as glycosides, alkaloids, poly- phenols, amino acids and proteins, saponins, volatile oil, flavonoids and tannins [10,11] Early phytochemical studies of this species resulted in the isolation and identification of chemical constituents such as triacontane, pentatriacontane, β -sitosterol are present in petroleum ether extract[12]and two alkaloids betaine and shankpushpin and evolvine[13] . Bioactivity-guided purification of n-BuOH soluble fraction from the ethanol extract of *E. alsinoides* resulted in the isolation of two new compounds, 2,3,4-trihydroxy-3-methylbutyl 3-[3-hydroxy-4-(2,3,4-trihydroxy2-methylbutoxy)-phenyl]-2-propenoate and 1,3-di-O-caffeoyl quinic acid methyl ester along with six known compounds, caffeic acid , 6-methoxy-7-O-β -glucopyranosidecoumarin, 2-C-methyl erythritol, kaempferol-7-O β-glucopyranoside, kaempferol-3-O-β -glucopyranosideand quecetine-3-O-β -glucopyranoside. The structure of new compounds 1 and 2 were elucidated by spectroscopic analysis, while known compounds were confirmed by direct comparison of their NMR data with those reported in literature. [14]Also the ethanolic extract of *E.alsinoides* contains Ethyl (9Z,12Z)- 9,12 octadecadienoate, Ethyl oleate, Methyl 17-methyl-octadecanoate 2,6,10,14,18,22-Tetracosahexaen, Methyl (2E) - 3- Phenyl - 2- Propeonate , Cholesterol, Cholest-5-en-3-ol (3.beta.), Piperine, Benzenepropanol, Phenol, Naphthalene , Hexadecanoic acid, Ethyl palmiatate (Ethyl ester), 9,12-Octadecadienoic acid (Z,Z), 9-Octadecenoic acid, 1,2,3-propanetriyl ester , Octadecanoic acid.[7] Lupeol (10.79%), Betulin (9.28%), Viridiflorol (8.83%), Glycerol (8.49%), Anthocyanidin (8.24%), 1,2,4-Butanetriol (8.24 %), Quinic Acid (7.83%), 1-[2-(2-Methoxy-1-methylethoxy)-1-methylethoxy]-2-propanol (6.84%), Squalene (6.72%), Phytol (6.70%), Octadecanic acid (5.68%), 9-octadecenoate (4.51%), Copaene (3.86%), terpinolene (3.02%), Conhydrin, (2.79%), Bis(2-ethylhexyl) phthalate (2.30%), Diethyl Phthalate (2.06%), 3,5-Dihydroxy-6-methyl-2,3-dihydro-4H-pyran-4-one (2.06%), Ethyl icosanoate (1.84%), Pyrogallol (1.77%), Triethyl (5-benzoyl-1H-pyrrol-2-yl) methanetricarboxylate (1.76%), Cycloheptatriene (1.72%), 1-(2-Piperidinyl)-1-propanol (1.65%), 3-Methylcyclopentan-1,2-diol (1.09%), 4-(3,6-Dimethyl-3-heptanyl)phenol (1.53 %), Cinnamaldehyde (1.44%), Ethyl 3,7,12 Z trihydroxycholan-24-oate (0.53%). [15]



3.4 Neuro -Pharmacological potential of the drug

The neuropharmacological activities of *E. alsinoides* include following items :

Learning and memory enhancing activity (nootropic)

In the Indian Ayurvedic system of medicine *E. alsinoides* is used for its therapeutic effect on brain disorders such as memory enhancement, insanity, epilepsy and nervous debility. (Chatterjee, 1990).[16]

Nootropic activity of different extracts of this plant has been reported.The ethanol extract of *E. alsinoides* and its ethyl acetate and aqueous fractions prepared were assessed for their memory enhancing properties. Two doses of the all the three extracts were administered in separate groups of animals, compared using piracetam as standard. Two doses of all the extracts of *E. alsinoides* significantly improved learning and memory in rats. Also, these doses reversed the amnesia induced by scopolamine. *E. alsinoides* also exhibited potent memory enhancing effects in the step-down and shuttle-box avoidance paradigms.[17]

The aqueous methanolic extracts of three sources of shankhapushpi in order to determine the true source of the drug. The three plants *Convolvulus pluricaulis, Evolvulus alsinoides* and *Clitoria ternatea* were evaluated at different doses using elevated plus maze and step down avoidance model. The memory enhancing activity was evaluated at 50,100, 200 and 400 mg/kg out of which *E. alsinoides* showed significant results at 200mg/kg and 400mg/kg when compared with vehicle treated animals. It showed maximum activity at 200mg/kg. Out of three plants *E. alsinoides* showed 66% activity (reduction in transfer latency when compared to training days latency). *C. pluricaulis* produced the maximum activity (70%) comparatively followed by *E. alsinoides* (66%) and *C. ternatea*.[18]

The hydroalcholic extract doses of *E. alsinoides* prevented streptozotocin induced cognitive impairement in male rats. It prevents cognitive impairment by reducing oxidative stress, preventing increase in rho kinase expression and by improvement of cholinergic function. Hydro-alcoholic extract of *E. alsinoides*

demonstrated better free radical scavenging activities as compared to aqueous extract and has showed higher cholinesterase, GSK-3-β, ROCK II, PEP COMT and LOX enzyme inhibitory activities. Thus the results demonstrated potential anti- Alzheimer effect of hydro-alcoholic extract of *E. alsinoides*. [19]

Anti- amnesia activity

The crude ethanolic extract *E. alsinoides* for its adaptogenic and memory enhancing properties. The male rats were given acute stress (AS) and chronic unpredictable stress (CUS) which lead to induction of gastric ulceration with increase in adrenal gland weight, plasma creatinine kinase (CK) and corticosterone levels. Rats were treated with different doses of ethanolic extract of *E. alsinoides*, out of the graded doses 200mg/kg p.o was found effective and it reduced stress induced perturbations similar to *Panaxquinquefolium* (PQ) (100mg/kg). Scopolamine induced deficit was decreased at a dose of 100mg/kg. Hence improvement in stress markers and scopolamine induced dementia by *E. alsinoides* indicates its adaptogenic and anti-amnesic properties.[20]

Anti-stress activity

The crude ethanolic extract *E. alsinoides* for its adaptogenic and memory enhancing properties. The male rats were given acute stress (AS) and chronic unpredictable stress (CUS) which lead to induction of gastric ulceration with increase in adrenal gland weight, plasma creatinine kinase (CK) and corticosterone levels. Rats were treated with different doses of ethanolic extract of *E. alsinoides*, out of the graded doses 200mg/kg p.o was found effective and it reduced stress induced perturbations similar to Panaxquinquefolium (PQ) (100mg/kg). Scopolamine induced deficit was decreased at a dose of 100mg/kg. Hence improvement in stress markers and scopolamine induced dementia by *E. alsinoides* indicates its adaptogenic and anti-amnesic properties.[20]

The whole plant extraction of *E. alsinoides* with ethanol and its successive partitioning of the dried extract in $H_2O/CHCl_3$, H_2O/n-BuOH, showed significant anti-stress activity of the n-BuOH fraction. However insignificant anti stress activity showed by $CHCl_3$ soluble fraction while aqueous fraction was found to be inactive. The isolated compunds 2,3,4-trihydroxy-3-methylbutyl 3-[3-hydroxy-4-(2,3,4-trihydroxy2-methylbutoxy)-phenyl]-2-propenoate (1) and 1,3-di-O-caffeoyl quinic acid methyl ester (2) along with six known compounds, caffeic acid (3), 6-methoxy-7-O- β -glucopyranosidecoumarin (4), 2-C-methyl erythritol (5), kaempferol-7-O-β -glucopyranoside (6), kaempferol-3-O-β -glucopyranoside (7) and quecetine-3-O-β -glucopyranoside isolated compounds 1—5 and 8 were screened for anti-stress activity in acute stress induced rats which resulted in significant increase of plasma glucose, adrenal gland weight, plasma creatine kinase (CK), and corticosterone levels. Compound 1 produced most promising anti-stress effect by normalizing stress parameters, while compounds 2 and 3 were also effective, however the compounds 4, 5 and 8 were found ineffective in normalizing these parameters.[14]

Anti-convulsant activity

The anticonvulsant activity using crude methanolic extract of *E. alsinoides* was investigated at graded doses using Pentylenetetrazole (PTZ) induced seizure (chemically induced seizure) and maximal electroshock seizure (electrically induced seizure) models in mice.The extract at doses of 100-400mg/kg increased the latency of PTZ induced seizure and there was a 100% protection against seizure at the dose of 400mg/kg. The MEST test showed dose dependent decrease in the duration of seizure,400mg/kg of the extract and 30mg/kg Diazepam shows the highest activity in this test further these findings suggest that methanol extract of the plant can prove to be beneficial in the treatment of epilepsy.[21]

Antioxidant activity

The Free radical scavenging activity, In-vitro lipid peroxidation and FTIR analysis was studied using ethanolic extract of *E. alsinoides* and the ability of the plant extract to reduce ferric ions was determined in FRAP assay. The results showed that *E. alsinoides* has significant antioxidant activity as compared to that of control ascorbic acid. [7]

The study investigated that the administration of ethanolic extract of *E. alsinoides* at a dose of 200mg/kg for 7 days normalized the chronic in predictable stress induced oxidative chances in blood plasma, hippocampus regions of brain and frontal cortex having efficacy similar to melatonin. Various new compounds were isolated which showed significant In-vitro antioxidant activity. Hence *E. alsinoides* have great potential in preventing deterioration in stress induced oxidative load and disorders related to that. [22]

According to a study correlation between total phenolics and antioxidant activity was observed. The extracts of hexane, chloroform, ethyl acetate, butanol and methanol extracts of fruits of *E. alsinoides* were examined for this study. The study showed that the fruits of *E. alsinoides* have high level of antioxidant potential. [23]

Anti-depressant activity

The anti-depressant activity of *E. alsinoides* was evaluated using forced swim despair test with imipramine as standard showed decrease in immobility period in comparison to control group animals. It produced significant activity at 50 and 100mg/kg doses and increase in mobility period at higher doses. [17]

Anxiolytic activity

E. alsinoides was investigated for its anxiolytic activity and it was observed that at doses of 100,200 and 400 mg/kg the plant showed significant anxiolytic activity, at a dose of 200 mg/kg significant activity was observed (20.4 s in open arm, $p < 0.001$) in comparison to the vehicle-treated group. [17]

Polyherbal formulation on learning and memory enhancing effect

The neuropharmacological effect of a polyherbal formulation (PHF) was investigated for the learning and memory processes in rats. This formulation contained various plants like *Withaniasomnifera* (Ashwagandha), *Nardostachysjatamansi* (Jatamansi), *Rauwolfiaserpentina (*Sarpagandha), *Evolvulusalsinoides* (Shankhpushpi), *Asparagus racemosus* (Shatavari), *Emblicaofficinalis* (Amalki), *Mucunapruriens* (Kauchbij extract), *Hyoscyamusniger* (KhurasaniAjmo), Mineral resin (Shilajit), Pearl (MuktaShukhtiPishti), and coral calcium (Pravalpishti). The learning and memory processes was tested for its effect at the dose of 500mg/kg, p.o and it was studied using passive avoidance learning and elevated plus maze model (EPM) in rats. And it was concluded that the polyherbal formulation produced improvement in passive avoidance and memory retrieval as compared to control. Hence this formulation needs to be further investigated. [24]

IV. CURRENT MARKETED FORMULATIONS

Many medicines are currently available in India, in which after mixing numerous plant extracts or powders with two or three Medhya plants including *E. alsinoides* Ayurvedic formulation is developed. Some preparations have been subjected to clinical trials. Examples include:

1. Memex (vibha naturals, India)
   The 50 gm bottle contains species like Brahmi (*Centellaasiatica*) 25gms.,Shankhapushpi (*Evolvulus alsinoides* Linn.) 15 gms., Harda (*Terminaliachebula*) 10 gms as ingredients in it. It is used to bring down tension and stress and to improve memory.
   Formulation type- powder
2. Shankhapushpi capsules (Baidyanath , India)
   The capsules is formulated using whole plant of *Evolvulus alsinoides*. And it is used to relieve stress and mood changes. It specially pacifies vata, pitta.
   Formulation type- capsules
3. Safe herbs (Vasu Pharma Herbals , India)
   It is a herbal preparation containing *Evolvulus alsinoides* helps in problems related with memory disturbances.
   Formulation type- capsules
4. Banyan Botanicals shankhapushpi powder
   This powder consists of *Evolvulus alsinoides* herb and it is used to boosts memory and concentration, Calms the nerves, Promotes circulation in the brain, Helps promote intelligence and creativity.
   Formulation type- powder

V. CONCLUSION

It can now be concluded that neurological disorders could be reduced by administration of *Evolvulus alsinoides* L. whole plant extract as it has protective effect on various neurological disorders. It is capable of producing various pharmacological effects due to various bioactive constituents. It is endowed with a number of phytoconstituents which shows their effect in various brain disorders such as memory enhancement, insanity, epilipsy and nervous debility. Various marketed formulations present in the market containing the seeds, whole herb of *E. alsinoides*. The bioactive molecules present in *E. alsinoides* can be used for different drug production and play an important role in human health. And it was observed that formulations present in the market are used as stress reliever, memory enhancer. Hence it is concluded that it has potential learning and memory enhancing activity. Therefore it is recommended that future researches should be conducted for other neurological disorders due to the presence of various active constituents, which are having therapeutic potentiality and formulations of the same should be produced and marketed for the treatment of various neurological disorders.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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