

# Meta-Analysis Report of *Convolvulus Pluricaulis* extract: Demonstrating Neurodisorders Impairment with respect to Pharmacological Activities

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## ABSTRACT

Shankhpushpi (*Convolvulus pluricaulis*- Family *Convolvulaceae*) is a remedial herb extensively used in the Ayurveda. Its protective efficacy has been recognized in several dermatological as well as non-dermatological diseases including cancer, diabetes and liver disfunctioning. Its protective effect might be attributed due to its anti-oxidant property that has been reported in several studies. In the present study, we investigated the effect of shankhpushpi plant extract against several types of neurodegenerative disorders such as Ischemia, Alzheimer's disease and Neurotoxicity. We also investigated several pharmacological activities of different types of extracts of *C. pluricaulis*. In conclusion, the present meta-analysis supported the fact that Shankhpushpi plant extract might be an effective remedy to protect neurodegeneration.

**Keywords:** *Convolvulus pluricaulis*, toxicity, oxidative stress, neurodegeneration.

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## 1. INTRODUCTION

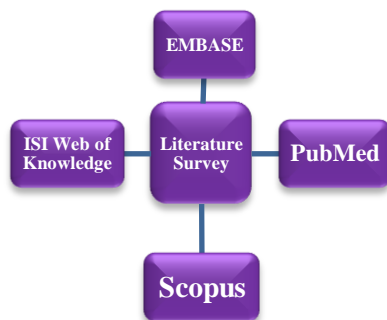
Shankhpushpi acts as an alexiteric and tonic to improve memory and to tone brain. Recently, it has been found effective against several types of neurodegeneration. The present study was carried out with an objective to explore the potential of shankhpushpi plant extract. If the generation of free radicals exceeds the protective effects of antioxidants, this can cause oxidative damage which accumulates during the life cycle, and has been implicated in aging, and age dependent diseases such as neurodegenerative disorders and other chronic conditions. To reduce such a damage, we need to increase the efficacy of enzymes. Some antioxidant food supplements are required to minimize stress and neurodegeneration. We find therapeutic constituents present in shankhpushpi that keep the nervous system active and increase the efficiency of SOD and Catalase.

## 2. MATERIAL AND METHODS

### Search strategy:

We carried out a literature search in the online medical databases PubMed, EMBASE, ISI Web of Knowledge, Scopus and Lilacs. We conducted a systematic review of original articles, which evaluate the effect of shankhpushpi on

neurodevelopment due to different types of neurotoxicity which cause neurodegenerations. These studies were carried out on several animal models as well as on humans.



### Inclusion criteria:

In our review we included studies that met the following criteria: (a) original articles; (b) assessment of pre- or post-natal exposure to toxicants like hydrogen peroxides, scopolamine, aluminum etc. (c) study of neuroprotection and disorders derived from exposure to metallic trace elements.

- 1) Disorders: Ageing induced neurodegeneration, Huntington’s disease and excitotoxic neuronal injury.
- 2) Neuroprotection activity: Antidepressant activity, antioxidant and antianxiety activity of the shankpushpi plant extract which results in communication, cognitive, attention, memory and learning enhancement.

### 3. META-ANALYSIS

We performed a meta-analysis of the results reported by different studies in order to make an overall estimate and summary of the magnitude of the effect of neurotoxicants exposure on neurodevelopment. There were very few studies assessing neurotoxicants exposure to be able to perform a meta-analysis. We find many ameliorative pharmacological activities like antidepressant activity, antioxidant and antianxiety activities of the shankpushpi plant extract.

### 4. RESULTS

#### Under Inclusion Criteria:

#### Neurodisorder impairments by Shankpushpi extract:

Here by description of the articles that were initially identified in the literature search, which met the inclusion criteria and evaluated the ameliorative effects of *Convolvulus pluricaulis* extract on Neuro-degeneration disorders. Table 1 shows the most relevant characteristics of the studies included in the systematic review.

**Table 1: Different Studies showing the impact of Shankpushpi plant extract on neurological disorders.**

Neurodegenerative Disorders	Shankpushpi (dose and time)	Models	Major Findings	References
Excitotoxic Neuronal Injury	28 mg/kg body wt. for 3 weeks	Mice	Reduction in lipid peroxidation and protein carbonyl content in the hippocampus of mice.	<b>Parihar and Hemnani, 2003</b>
Hydrogen Peroxide toxicity	25µg/ml for 24 hrs.	Human Neuro-blastoma Cells	Decrease in the expression level of stress markers mortalin and HSP70 and cytoskeletal marker NF-200 along with increased expression of antioxidant enzymes and Glutathione.	<b>Dhunaet al., 2012</b>
Scopolamine induced	150 mg/kg body	Rat	Reduced scopolamine	<b>Bihaqiet al.,</b>

Toxicity	weight for 7 days		induced memory and learning impairment of spatial memory induced by scopolamine as well as enhancing activity through anti-AChE and antioxidant action.	<b>2011</b>
Ageing induced neurodegeneration	200 mg/kg for 24 hrs	Mice	Increase in memory in aged mice, enhanced AChE activity.	<b>Sharma et al., 2010</b>
Huntington's disease	100 and 200 mg/kg for 20 days.	Rat	Attenuated 3- Nitro-propionic acid induced reduction in locomotor activity, grip strength, memory and oxidative defense.	<b>Malik et al., 2015</b>
Aluminium induced neurotoxicity	150 mg/kg body weight for 3 months.	Rat	Preserved the mRNA levels of muscarinic receptor-1, choline acetyl transferase and Nerve Growth Factor-Tyrosine Kinase A receptor and upregulation of protein levels.	<b>Bihaqiet al., 2009</b>
Gamma-radiation induced toxicity	50 µg/ml	Rat	Decrease in lipid peroxidation, protein carbonylation, protein degradation and DNA fragmentation.	<b>Joshi et al., 2003</b>

In the articles studied, we found that exposure to hydrogen peroxide, scopolamine, aluminium and Gamma radiation had a significant negative effect on neurodevelopment. To treat such disorders caused by these toxic compounds, shankpushpi was found to be ameliorative against toxicants.

- More specifically the finding of study by **(Parihar and Hemnani, 2003)** has suggested that phytochemicals present in plant extracts mitigate the effects of excitotoxicity when a dose of shankpushpi 28 mg/kg body wt. was given for 3 weeks.
- **Dhuna et al., (2012)** observed cytoprotective effect of CP-Mex against hydrogen peroxide induced toxicity when a dose of 25 µg/ml for 24 hrs on Neuroblastoma cell was supplemented.
- **Bihaqiet al., (2011)** observed ameliorative effect of shankpushpi as a significant dose of 150 mg/kg body wt. was given for 7 days which enhanced antioxidant action.
- **Sharma et al., (2010)** observed when a dose of shankpushpi 200 mg/kg was supplemented for 24 hrs. Reduced ageing induced neurodegeneration.
- A study conducted by **Malik et al., (2015)** revealed a standardized dose of 100 or 200 mg/kg for 20 days treated Huntington's disease.
- **Bihaqiet al., (2009)** protective effect of the herb against Aluminum induced neurotoxicity when a dose of 150 mg/kg body weight for 3 months was supplemented. It decreased the elevated enzymatic activity of acetylcholine esterase which resulted from aluminum intake.
- As observed by **Joshi et al., (2003)** the CP (50 µg/ml assay) showed significant protection against the gamma radiation induced toxicity.

#### Ameliorative pharmacological activities of shankpushpi extract

Study conducted from the literature survey also showed several pharmacological activities of different types of extracts of shankpushpi. Evidences suggest that toxicants reaches the central nervous system directly, which would cause a

neurotoxic effect and have an impact on neurodevelopment. *C. pluricaulis* was found to be protective as it exert various pharmacological activities like antidepressant activity, antianxiety activity etc. as shown in tabular form (Table 2).

**Table 2. Major findings of pharmacological activities of *C.pluricaulis***

Types of Activity	Plant part used	Extract	Major Findings	References
Antidepressant Activity	Whole part	Ethanolic	The results showed that only chloroform fraction in this dose significantly reduced the immobility time in both FST & TST.	<b>Dhingra and Volecha, 2007</b>
Antianxiety activity	<i>Ayurvedic</i> formulation	Aqueous	The result demonstrated the experimental group showed reduced anxiety than the control group.	<b>Indurwade and Biyani, 2000</b>
Memory and learning enhancement activity	Root part	Ethanolic	The result shown that higher retentions was observed with plant extract as compared with standard drug.	<b>Dubey et al., 1994</b>
Learning behavior improvement by Brain protein	Whole part	Ethanolic	An increase in brain protein was found in all treatments which resulted that shankpushpi extract exhibited potent memory enhancing effects and learning behavior improvement.	<b>Prakash and Sinha, 1988</b>
Antioxidant Activity	Whole part	Methanolic	The <i>C. pluricaulis</i> extract demonstrated significant free radical scavenging effect.	<b>Sethiyaet al., 2013</b>
Anti-neurohumoral activity	Aerial parts	Alcoholic	Shankpushpi treated groups showed decline in level of acetylcholine and histamine and significantly lower levels of all the three neurohumors than control.	<b>Mudgalet al., 1977</b>

These studies estimated several neuroprotective activity which were assessed by various research papers in the literature survey.

- **Dhingra and Volecha, (2007)** evaluated the antidepressant-like activity of *Convolvulus pluricaulis* as the plant elicited a significant antidepressant-like effect in mice by interaction with the adrenergic, dopaminergic, and serotonergic systems.
- **Indurwade and Biyani (2000)** found that shankpushpi showed a safe and effective remedy for anxiety. The findings showed that the experimental group experienced reduced anxiety than the control group.
- **Dubey et.al., (1994)** observed improvement in memory when ethanolic extract of *Convolvulus pluricaulis* was supplemented to the model organism.
- **Prakash and Sinha (1988)** observed ethanolic extract increased the brain protein thus possess learning power improvement activity.
- **Sethiyaet. al., (2013)** concluded shankpushpi possesses antioxidant activity as antioxidants are attributed for their beneficial role in age-related cognition decline.
- **Mudgalet.al., (1977)** observed anti-neuro-humoral activity when alcoholic extract was supplemented. A direct influence of shankpushpi on the central nervous system by strengthening the way of neurohumoral responses, thus shankpushpi was chosen as best neural tonic.

### Result of Meta-analysis

#### Neuroprotection caused by Shankpushpi

We conducted separate meta-analysis on the results of the articles that assessed neurotoxicants exposure on neurodevelopment. We find many ameliorative pharmacological activities like antidepressant activity, antioxidant and antianxiety activity of the shankpushpi plant extract as shown in figure below.

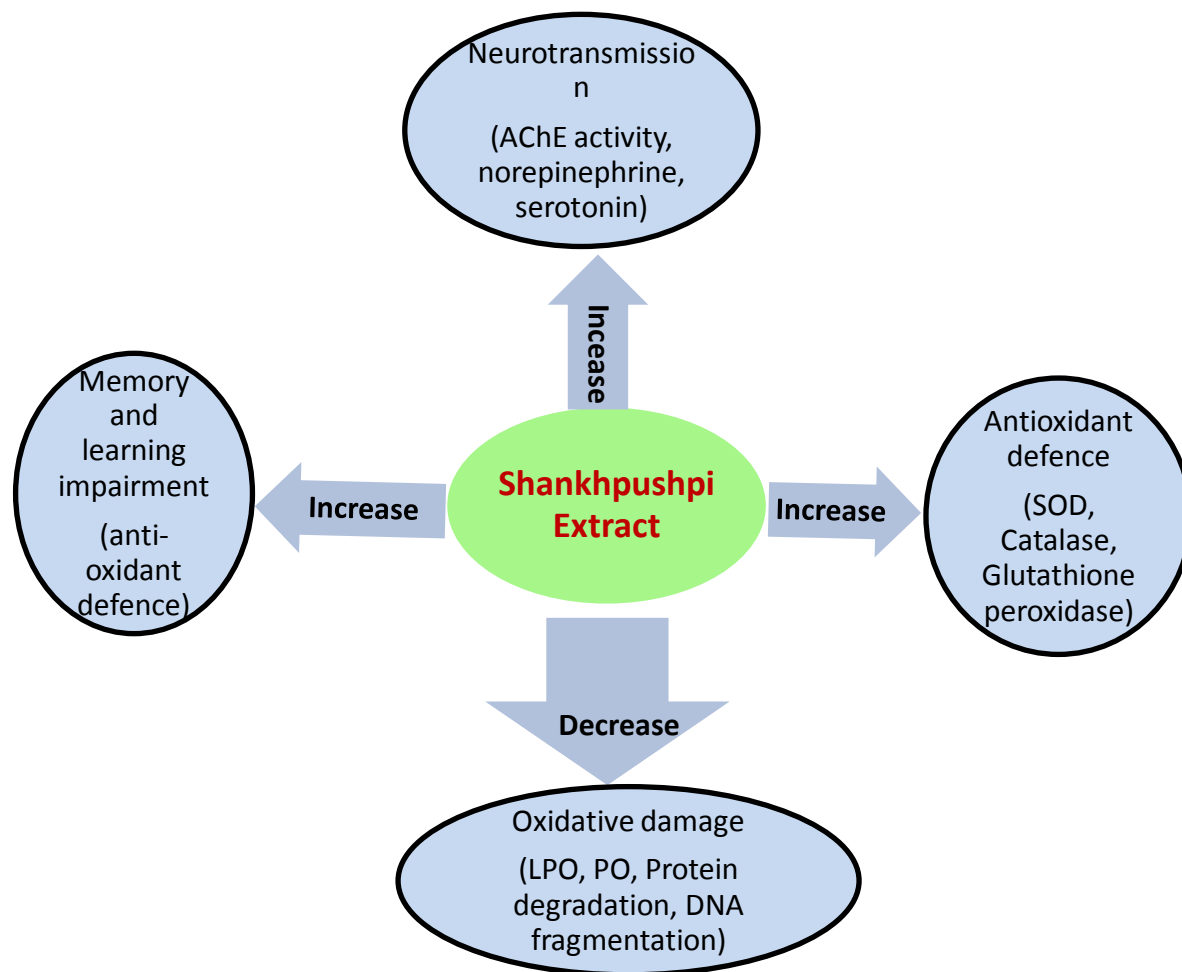


Figure 1: Showing Meta-analysis report of shankhpushpi extract.

### Antioxidant defence

The literature survey from various studies revealed that the shankhpushpi extract increases antioxidant defence; the several enzymes play a key role against antioxidant defence such as superoxide dismutase (SOD). Shankhpushpi increases Superoxide dismutase which protect against oxygen radical damage to aerobic cells. The level of catalase is also enhanced by the extract to prevent damage to cells and tissues. Catalase is frequently used by cells to rapidly catalyze the decomposition of hydrogen peroxide into less-reactive gaseous oxygen and water molecules. Shankhpushpi extract was also found to increase glutathione peroxidase to protect the organism from oxidative damage as oxidative damage increases due to nervous system deterioration during ageing.

### Neurotransmission

Shankhpushpi extract enhanced neurotransmission thereby improving memory performance as the acetylcholine level was found to be increased which enhanced cognition ability. The level of stress hormone like norepinephrine was also found to be increased due to ameliorative activity of shankhpushpi to overcome depressive systems in the brain. The serotonin level was increased by the *C. pluricaulis* extract to enhance memory power.

### Memory and learning impairment

Shankhpushpi extract showed memory and learning impairment due to increase in antioxidant defence by its various pharmacological activities like antidepressant activity and anxiety activity. Thus, shankhpushpi was analyzed as ameliorative due to impairment in learning and memory power.

## Oxidative damage

Various studies demonstrated that the shankpushpi decreases oxidative damage by decreasing lipid peroxidation (LPO); a factor in free radical damage. Shankpushpi extract may help in scavenging free radicals generated during the initiation and progression of this disease. The extract reduced the apoptosis and DNA fragmentation induced by chemicals and radiations.

## 5. DISCUSSION

The results of this review showed that there is evidence in the recent scientific literature that relates neurotoxicant exposure with neurodevelopmental problems. This meta-analysis showed that there are evidences in the recent scientific literature showing Shankpushpi as a well-known medicinal herb and is believed to enhance certain aspects related to intellect and memory improvement. In the present study, various types of neurodegenerative disorders were impaired by the medicinal plant shankpushpi. For this *Convolvulus pluricaulis* extract in several forms was used for neuroprotection. Few studies have evaluated neurodegeneration disorders due to neurotoxicants available in the environment. Pharmacological studies carried out on crude extracts of *Convolvulus pluricaulis* which revealed this herb to be a valuable source for medicinally important molecules. Animal experiments have shown that toxicants mostly affects brain metabolism and also inhibiting enzymes. These evidences suggest that toxicants reaches the central nervous system directly, which would cause a neurotoxic effect and have an impact on neurodevelopment. Since, all studies included in the meta-analysis summarized the relation between neurodegeneration and neuroprotection. After pooling and synthesizing the results of published studies, there are also many other pharmacological aspects of this particular plant which were considered to be very useful because of its neuroprotective activity. As evident from in vitro and in vivo studies, shankpushpi extract can be a promising source in pharmaceutical, medicinal as well as in nutraceutical industries. The evidence of ameliorative effects of *Convolvulus pluricaulis* may emerge as a new perspective for therapeutic interventions against toxicant induced neurotoxicity.

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