

# Review on ethnomedicinal uses and phyto-pharmacology of memory boosting herb *Convolvulus pluricaulis* Choisy

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*Convolvulus pluricaulis* Choisy: a rasayana drug which is mainly advocated for use in mental stimulation and rejuvenation therapy. It is known as Shankhpushpi by Ayurvedic practitioners in ancient systems of Indian medicine as it was a prominent memory improving drug, a psychostimulant and tranquilliser in traditional Indian medicine. The plant contains several alkaloids, flavanoids and coumarins as active chemicals that bring about its biological effects. Little human research has been published in the Western medical literature regarding this plant. Preclinical (in vivo and vitro) investigations have demonstrated nootropic, anxiolytic, tranquillising, antidepressant, antistress, neurodegenerative, anti-amnesic, antioxidant, hypolipidemic, immunomodulatory, anti-inflammatory, analgesic, antimicrobial, insecticidal, antifungal, antibacterial, antidiabetic, antiulcer, anticatatonc and cardiovascular activity. Clinical studies of its polyherbal formulation justified its potential for the ancient claim of brain tonic. The present review is an attempt to compile information on various ethnomedical aspects of *Convolvulus pluricaulis*, shankhpushpi of Indian traditional medicine.

**Key words:** Shankhpushpi, rasayana, brain tonic, alkaloids

## Introduction

Drugs acting in the central nervous system (CNS) were among the first to be discovered by primitive human and are still the most widely used group of pharmacological agents. The CNS acting drugs are invaluable therapeutically as they can produce specific physiological and psychological effects. From the vast array of materia medica of the indigenous system, many plants have been reported to have activity against CNS disorders and act as very useful remedies for the alleviation of human suffering (Suba 2002).

All critical analyses on commercial and other information available on traditionally known CNS active herbal remedies indicate that the most popular amongst such remedies are those which are clinically and preclinically the most well studied and which are also recommended for therapeutic purposes by the health authorities of many Western and other countries outside the USA (Kumar 2006). Shankhpushpi is a Sanskrit word meaning 'the plant with flowers shaped like a conch'. The conch or Shankha is one of Lord Shiva's sacred instruments often used in ritual worship.

Shankhpushpi of the Ayurvedic Pharmacopeia of India consists of the whole plant of *Convolvulus pluricaulis* Choisy (Convolvulaceae) syn *Convolvulus microphyllus* Sieb. ex Spreng (MHFW 2001). Plants other than *Convolvulus pluricaulis* use the name Shankhpushpi in different parts of the country. These include *Evolvulus alsinoides* Linn, *Clitorea ternatea* Linn and *Canscora*

*decussata* Schult. The Indian Council of Medical Research has given quality standards for *C. pluricaulis* drug in its publication (Gupta 2005).

## Botany

*Convolvulus pluricaulis* Choisy is a prostrate spreading perennial wild herb commonly found on sandy or rocky ground under xerophytic conditions in northern India. *Convolvulus* is known from the margins and within the Sahara and Sind deserts, a distribution that Sa'ad (1967) called Saharo Sindian (Sa'ad 1967). In India it is widely distributed in and grows on the waste land in the plains of Punjab, Bihar and Chhotanagpur. The herb produces flowers during the months of September and October which are white to light pink in colour (Dandiya 1970). The shape of the flower is like a shankh (a marine shell) giving it the name is Shankhpushpi. Different botanical features of *Convolvulus pluricaulis* are shown below.

## Classification (taxonomic)

Kingdom	Plantae, plants
Sub kingdom	Tracheobionta, vascular plants
Super division	Spermatophyta, seed plants
Division	Magnoliophyta, flowering plants
Class	Magnoliopsida, dicotyledons
Sub class	Asteridae
Order	Solanales
Family	Convolvulaceae
Genus	<i>Convolvulus</i>
Species	<i>pluricaulis</i>

**Table 1: Different botanical features of *Convolvulus pluricaulis* Choisy**

(Karandikar 1959, Shah 1961, Sinha 1986, Kapadia 2005)

S. No.	Characters	Evaluated plant characters
1	Habit	Prostrate, perennial herbs
<b>Stem structure</b>		
1	Length	Several prostrate stems (10-30 cm)
2	Surface	Clothed with silky hairs
3	Internodes	10-12 mm
4	Taste	Tasteless
5	Outline in T.S.	Terete, wings absent
6	Cuticle	Striated
7	Trichomes covering	Present, conical, unicellular
8	Glandular trichomes	Present; stalk unicellular; head multicellular (4-cells)
9	Chlorenchyma	Present
10	Collenchyma	Present
11	Endodermis	Indistinct
12	Pericyclic fibers	Present
13	Phloem fibers	Present in old stem only
14	Pith	Often an angular hollow cells pitted in older stem
<b>Leaf structure</b>		
1	Phyllotaxy	Alternate
2	Shape	Linear, lower / Oblanceolate, upper elliptic
3	Size	12-38 × 5-10 mm
4	Apex	Obtuse-murionate
5	Surface	Hairy
<b>Midrib</b>		
1	Outline in T.S.	Concavo-convex
2	Collenchyma	Present beneath upper epidermis
3	Calcium oxalate	Plenty, along veins
<b>Lamina</b>		
1	Lamina	Isobilateral, palisade in 3 and 2 layers beneath upper and lower epidermis respectively
2.	Cuticle	Striated
3.	Trichomes	Present; similar as in stem
4.	Stomata	Both anisocytic and paracytic type on either side
<b>Quantitative analysis</b>		
1	Stomatal number upper surface	202-216-238
	Stomatal number lower surface	184-212-248
2	Stomatal index upper surface	17.0-18.0-19.9
	Stomatal index lower surface	13.8-15.8-16.9

### Ethnomedicinal use

Ethnobotanical research into medicinal plants is becoming an important part of Indian research and has been included in advanced research during recent years. Plants have much relevance to socioeconomic and socioreligious aspects of human life in India. It is herbs that have been used in India for hundreds of years for many disorders such as stress, anxiety and insomnia and to promote longevity and prevent diseases by providing strength and immunity (Handa 1994, Singh 2008).

### Traditional indications

The leaves of Shankpushpi were used to treat chronic bronchitis and asthma. The root was used for childhood fever, and the oil stimulates the growth of hair. The whole herb was used medicinally in the form of a decoction with cumin and milk in fever, nervous debility, loss of memory, syphilis and scrofula.

Shankpushpi is an astringent, hot aphrodisiac and a nervine tonic. It improves strength, digestive power, complexion and voice and cures intestinal worms, animal poisoning, skin disease, cough, dyspnea, diabetes, dysuria and uterine disorder. It is helpful in epilepsy, insomnia, heart disease and hematemesis (Chunekar 1982, Sharma 1983).

*Convolvulus pluricaulis* is a common plant in southern India where the whole plant is used in various formulae as a nervine tonic for improvement of memory and intellect (Adams 2007). The leaves and flowers possess hypotensive properties used for treating anxiety neurosis. It is recommended as a brain tonic to promote intellect and memory, eliminate nervous disorders and to treat hypertension (Bala 1999). It is described as anthelmintic, good in dysentery, a brain and hair tonic, cures skin ailments and reduces high blood pressure by tribals in

Chindwara, Madhya Pradesh, India (Rai 1987). In Gonda Uttar Pradesh, India, the leaves are recommended for depression and mental disturbance (Singh 1996).

*Convolvulus pluricaulis* has been widely used in Ayurvedic medicine to treat nervous disorders, similar to the use of kava kava (*Piper methysticum*) and valerian (*Valeriana officinalis*) is prescribed by American herbalists (Husain 2007). It is only recently that Shankhpushpi has been brought to American stores for medicinal use. Herbalists believe that Shankhpushpi calms the nerves by regulating the body's production of the stress hormones, adrenaline and cortisol (Kumar 2006). *C. arvensis* var. *obtusifolium* Choisy is generally the only variety recognised in North America (Robinson 1908).

### Actions according to Ayurveda

- Medhya - promotes intellectual capacity
- Swarakarini - improves voice
- Grahabhootadi doshaghni - useful in diseases of supernatural origin
- Rasayani - rejuvenates the body
- Kantida - enhances the aura of the body and gives it a healthy look
- Majjadhatu rasayana - rejuvenates the nervous tissue
- Unmadaghna - alleviates insanity and emotional instability
- Vrishya - aphrodisiac
- Pachanbala - increases the strength of the digestive system
- Chedana - laxative
- Nidrajnana - promotes sleep

Shankhpushpi also improves digestion, prevents water retention, borborygmus and constipation. It is specifically beneficial for digestive upsets from nervousness and anxiety.

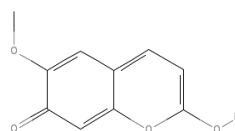
### Chemical constituents

The plant contains carbohydrate-D-glucose, maltose, rhamnose, sucrose, and starch (Deshpande 1969a, 1969b, Bisht 1978, Shah 1989). It contains proteins, amino acids and the alkaloid shankhpushpine ( $C_{17}H_{25}NO_2$ ), having a melting point of 162-164°C. The most notable constituents are tropane alkaloids. Only convolamine has been identified, but other alkaloids (convoline, convolidine, convolvine, confoline, convosine, etc) found in other species from this family are probably present (Basu 1948, Prasad 1974, Lounasmaa 1988, Singh 2000).

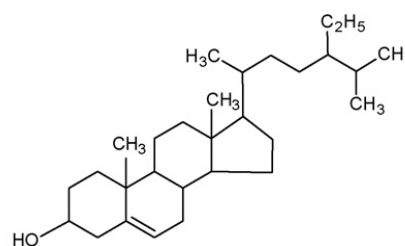
The fresh plant contains volatile oils, fatty acids, fatty alcohols and hydrocarbons i.e. myristic acid (30.9%), palmitic acid (66.8%), linoleic acid (2.3%), and straight chain hydrocarbon hextriacontane (Deshpande 1969a, 1969b-1975). Deshpande and Srivastava (1969) carried out a chemical examination of the whole plant of *C. pluricaulis* and reported the presence of scopoletin,  $\beta$ -sitosterol and ceryl alcohol (Deshpande 1969a, 1969b). The chloroform fraction of this contains 20-oxodotriacontanol, tetratriacontanoic acid and

29-oxodotriacontanol. The flavonoid kampferol and steroids phytosterol,  $\beta$ -sitosterol were also found in major amounts (Singh 2000). Estimation of scopoletin (Nahata 2008a) content was carried by spectrofluorimetry (Zafar 2005) and HPTLC (Kapadia 2006). Structures are presented in Figure 1.

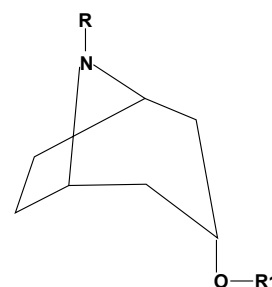
**Figure 1: Chemical structures of isolates from *C. pluricaulis*** (Lounasmaa 1988, Kapadia 2006)



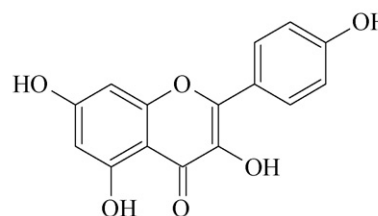
(I) scopoletin



(II)  $\beta$ -sitosterol



(III) tropane alkaloids



(IV) kaempferol

Where convolidine (R-H; R1-vanilloyl)  
 phyllalbine (R-CH<sub>3</sub>;R1-vanilloyl)  
 convolvine (R-H;R1-veratroyl)  
 convolamine N-oxyde (R-CH<sub>3</sub>,O;R1-veratroyl)  
 convolamine (R-CH<sub>3</sub>;R1-veratroyl)  
 convoline (R-OH;R1-veratroyl)  
 convolicine (R-OAc;R1-veratroyl)  
 confoline (R-CHO;R1-veratroyl)  
 convosine (R-OiPr;R1-veratroyl)

## Pharmacology

*Convolvulus pluricaulis* (CP) has been widely screened for its various pharmacological activities. It has relatively well documented neuropharmacological actions such as nootropic, antistress, anxiolytic, antidepressant, anticonvulsant, tranquilising and sedative activities which justify its use in CNS diseases in the Ayurvedic system of medicine. It has antimicrobial, antipyretic, anti-inflammatory, analgesic, diuretic, antidiabetic and insecticidal properties. The various reported pharmacological activities of CP highlight the therapeutic potential of CP and limitations in our knowledge of its claimed traditional Indian usage.

### Effect of CP on learning and memory

Nootropic activity using Cook and Weidley's Pole Climbing Apparatus, passive avoidance paradigms and active avoidance tests were used to test learning and memory. The ethanolic extract of CP and its ethyl acetate and aqueous fractions were evaluated for their memory enhancing properties. Two doses (100 and 200 mg/kg/p.o.) of ethyl acetate and aqueous fractions of the ethanolic extract were administered in separate groups of animals. Both the doses of all the extracts of CP significantly improved learning and memory in rats (Nahata 2008b).

### Anxiolytic, antidepressant, antistress, neurodegenerative and anti-amnesic activity

An alcoholic extract of CP was found to cause an antagonist effect against amphetamines and tremorine, a potentiation of the acetylcholine effect of pentobarbitone induced hypnosis and morphine analgesia, without having own sedative properties. A protective action on muscle against electroshocks has been shown (Sharma 1965, Barar 1966, Mudgal 1975). The chloroform fraction of the total ethanolic extract of *Convolvulus pluricaulis* elicited a significant antidepressant like effect in mice by interaction with the adrenergic, dopaminergic, and serotonergic systems (Dhingra 2007a, 2007b). A methanolic extract of the whole plant produced alterations in the general behaviour pattern, reduction in spontaneous motor activity, hypothermia, potentiation of pentobarbitone sleeping time, reduction in exploratory behavioural pattern and suppression of aggressive behaviour (Pawar 2001). Ethyl acetate and aqueous fractions of the ethanolic extract showed an anxiolytic effect as evidenced by an increase in the time spent in open arms and the number of open arm entries compared with the control group.

The ethyl acetate fractions at doses of 200 mg/kg p.o. significantly reduced the neuromuscular coordination indicative of the muscle relaxant activity at a higher dose (Nahata 2009). A nitrogen containing active principle of the drug produced marked reduction in I-131 uptake, PBI and acetylcholine suggesting its effect on various

glands through neurohumors particularly acetylcholine (Prasad 1974). Upadhyay (1986) studied the therapeutic role of Ayurvedic herbs in mental disorders and classified CP as a brain tonic (Upadhyay 1986). CP in a dose of 100 mg/100 g body weight has a barbiturate potentiation effect in albino rats; this effect was weaker than that of diazepam, but stronger than that of *Centella asiatica* Linn, urban *Hydrocotyle asiatica* Linn. This plant has also been reviewed and reported for its potent anxiolytic, neurodegenerative and antistress activity by various researchers (Singh 1977, Shukla 1981a, 1981b, Sinha 1989, Dandiya 1990, Dubey 1994, Sharma 2009).

### Anticonvulsant activity

The water soluble portion of an alcoholic extract abolished spontaneous motor activity and the fighting response, but did not affect the escape response; electrically induced convulsive seizures and tremorine induced tremors were antagonised by the extract (Sharma 1965). It was observed that the animals treated with the methanolic extracts of stem callus, leaf callu and whole plant (200 mg/kg oral) of CP showed significant protection against tonic convulsion induced by transcorneal electroshock, which was also comparable with that of the standard drug phenytoin (Ahmad 2007). CP has also been shown to possess a potent anticonvulsant activity (Shukla 1981a).

### Antioxidant activity

An ethanolic extract of CP possesses significant antioxidant activity when tested in vitro (Nahata 2009).

### Hypolipidemic

An ethanolic extract of the whole plant when administered to cholesterol fed gerbils, reduced serum cholesterol, LDL cholesterol, triglycerides and phospholipids significantly after 90 days (Chaturvedi 1997).

### Effect on thyroid function

The root extract of CP (0.4 mg/kg/day for 30 days) administered to L-thyroxine induced hyperthyroid mice (n = 7 in each group) decreased serum concentrations of T3 and hepatic 5-D activity. These results indicate that the plant extract induced inhibition in thyroid function is primarily mediated through T4 to T3 conversion (Panda 2001). Potent effect was found with CP for the management of thyrotoxicosis (Gupta 1981).

### Analgesic activity

The CP extract caused a reduction in the fighting behaviour in mice but was devoid of analgesic activity although it potentiated morphine analgesia (Sharma 1965).

### Antimicrobial, insecticidal, antifungal, antibacterial and anthelmintic activity

The whole plant was bioassayed by the leaf disc method by feeding deterrence using *Spilosoma oblique* walker as a test insect. A new compound, 29-oxodotriacontanol isolated from the chloroform fraction of this plant was shown to be a

potent antifeedant constituent under laboratory evaluations, whereas another compound, tetratriacontanoic acid was found for the first time in this plant. The azadirachtin and crude neem extracts were taken as standard. A new compound (29-oxodotriacontanol) produced 85.74% inhibition at 8000 ppm concentration (Bhakuni 1996). The alcoholic extract of *Convolvulus pluricaulis* possessed potent antifungal activity (Gupta 1974).

### Antiulcer and antitumor activity

The antiulcerogenic effect of CP was found to be due to augmentation of mucosal defensive factors such as mucin secretion, lifespan of mucosal cells and glycoprotein rather than on the offensive factors such as acid pepsin (Sairam 2001).

### Antidiabetic activity

CP was found to be an effective remedy for treatment of diabetes (Alam 1990).

### Effect on reproductive system and immunomodulation

The juice of the whole plant prevents excessive menstruation. The fine paste made by grinding the plant is helpful for the cure of abscesses (Singh 2005).

### Cardiovascular activity

A total water soluble fraction of the plant caused a marked and prolonged hypotension in dogs and inhibited the frog myocardium (Rakhit 1958, Chaturvedi 1966). An ethanolic extract of the entire plant exerted a negative inotropic action on amphibian and mammalian myocardium. It also exerted spasmolytic activity on smooth muscles (Sharma 1965).

### Drug interactions

An unexpected loss of seizure control and reduction in plasma phenytoin levels was noticed in two patients who were taking Shankhapushpi (SRC), an Ayurvedic preparation of CP. It was found that a single dose of SRC and phenytoin (oral/i.p.) co administration did not have any effect on plasma phenytoin levels but decreased the antiepileptic activity of phenytoin significantly. The multiple dose co administration of SRC reduced not only the antiepileptic activity of phenytoin but also lowered plasma phenytoin levels (Dandekar 1992).

### Activity of polyherbal formulation: clinical studies

Maharishi Amrit Kalash (MAK) is a herbal formulation composed of two herbal mixtures, MAK-4 and MAK-5. These preparations are part of a natural health care system from India known as Maharishi Ayurveda. MAK-4 and MAK-5 are each composed of different herbs including *Convolvulus pluricaulis* and are said to have a maximum benefit when used in combination. MAK was found to have a cancer inhibiting effect in vitro and in vivo when both were used in combination (Penza 2007).

Thyrocap is a herbal preparation containing solid extracts of *Bauhinia variegata*, *Commiphora mukul*, *Glycyrrhiza glabra* and *Convolvulus pluricaulis* (100 mg of each extract per capsule). This drug was prepared and tried in 50 patients with simple diffuse goiter at a dose of one capsule three times a day for 3 months. After 3 months of treatment a marked improvement was noticed in weakness, fatigability, dyspnea and reduction in neck swelling. A significant increase in serum T4 and T3 concentration ( $p < 0.001$  and  $< 0.02$  respectively) and a decrease in serum cholesterol concentration ( $p < 0.02$ ) confirmed its thyroid stimulating property (Pandit 1992).

### Activity of convolvine, an isolated alkaloid

The specific pharmacological action of convolvine has been found to block M2 and M4 cholinergic muscarinic receptors. It was also found that convolvine potentiates the effects of arecoline, a muscarinic memory enhancer that ameliorates cognitive deficits in Alzheimer's disease (Asthana 1996, Mirzaev 1998).

### Toxicological assessment

The LD50 of the whole extract of *C. microphyllus* by oral administration was found to be 1250 (1000–1400) mg/kg. Mice treated with the extract showed a sedative effect at doses greater than 200 mg/kg and reflected a moderate to marked decrease in locomotor activity which lasted 1–2 h. The decrease in motor activity due to spontaneous motor activity was observed during the study. At a higher dose (more than 1 g/kg) animals died due to respiratory distress (Pawar 2001).

### Current Ayurvedic formulations

There are many medicines currently available in India mixing numerous plant extracts or powders with two or three medhya plants including *Convolvulus pluricaulis*. These formulations are complex preparations of compound medicines and involve a number of processes. Some preparations have been subjected to clinical trials. Examples include:

Remem (Zydus Industries, India): syrup, tablets. 10 species: *Centella asiatica*, *Celastrus paniculatus*, *Convolvulus pluricaulis*, *Asparagus racemosus*, *Acorus calamus*, *Embelia ribes*, *Tinospora cordifolia*, *Achyranthes aspera*, *Terminalia chebula*, *Saussurea lappa*.

Tirukati: 13 species: *Bacopa monnieri*, *Convolvulus pluricaulis*, *Centella asiatica*, *Asparagus racemosus*, *Valeriana wallichii*, *Rueraria tuberosa*, *Saussurea lappa*, *Embelia ribes*, *Tinospora cordifolia*, *Operculina turpethum*, *Pavonia odorata*, *Caryophyllus aromaticus*, *Foeniculum vulgare*.

Ayumemo (Welexlabs, India): 5 species: *Centella asiatica*, *Convolvulus pluricaulis*, *Celastrus paniculatus*, *Withania somnifera*, *Asparagus racemosus*.

Abana (The Himalaya Drug and Co, India): syrup, tablets. 19 species: *Centella asiatica*, *Convolvulus pluricaulis*, *Celastrus paniculatus*, *Balsamodendron*

*mukul*, *Ocimum sanctum*, *Nardostachys jatamansi*, *Piper longum*, *Carum copticum*, *Zingiber officinalis*, *Cyperus rotundus*, *Acorus calamus*, *Embelia ribes*, *Syzygium aromaticum*, *Santalum album*, *Elettaria cardamomum*, *Foeniculum vulgare*, *Rosa damascena*, *Cinnamomum cassia*, *Crocus sativus*.

Tejras (Sandu Brothers, India): syrup. 12 species: *Centella asiatica*, *Convolvulus pluricaulis*, *Celastrus paniculatus*, *Eclipta alba*, *Cynodon dactylon*, *Asparagus racemosus*, *Withania somnifera*, *Nardostachys jatamansi*, *Acorus calamus*, *Zingiber officinalis*, *Vetiveria zizanioides*.

Shankhapushpi (Unjha Pharmacy, India): syrup. 6 species: *Convolvulus pluricaulis*, *Centella asiatica*, *Nardostachys jatamansi*, *Nepeia hindostana*, *Nepeia elliptica*, *Onosma brateatum*.

## Conclusion

*Convolvulus pluricaulis* is one of the traditional ethnomedicines used in Ayurvedic medicine in India as a controversial source of shankhpushpi for various brain related disorders. This plant has been shown to have scientific potential for CNS depression for its anxiolytic, tranquillising, antidepressant, antistress, neurodegenerative, anti-amnesic, antioxidant, hypolipidemic, immunomodulatory, analgesic, antifungal, antibacterial, antidiabetic, antiulcer, anticatonic and cardiovascular activity. It is reported to contain several types of alkaloids, flavanoids and coumarins as active chemicals that bring about its biological effects.

We have previously reported the existence of four plants named shankhpushpi (Sethiya 2009). Since herbal products are prepared in India using the powder drug or extracts of plants known for a particular activity, the controversial source sometimes leads to an inefficacious preparation. Parameters based on characterisation and identification of chemicals and biomarkers using modern methods (such as UV, TLC, HPLC, HPTLC, GC, spectrofluorimetric) may provide a solution to this problem. Their biological efficacy needs to be evaluated to justify the indications of the polyherbal formulations. There is still a lack of clinical data for its efficacy and clinical trials are warranted to justify its traditional use.

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