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Convolvulus prostratus Forssk.: A Memory Boosting Herb

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Abstract

Convolvulus prostratus Forssk. aka *C. pluricaulis*, *C. microphyllus* commonly known as 'Shankhpushpi' has been traditionally used for improvement in memory and cognitive function in cases of dementia, epilepsy, depression, anxiety and central nervous system (CNS) disorders. Studies have shown that this herb has potential to enhance memory recall, increase brain plasticity and boost learning ability. The plant species has several active metabolites including alkaloids, flavonoids, phenolic acids and terpenoids that interacts with protein, neurological signaling pathways and demonstrates pharmacological effects, such as, anti-amnesiac, anti-inflammatory, anxiolytic, analgesic, antioxidant, neuroprotective, memory and learning improving, sedative-hypnotic and anticonvulsant activity, which have been linked to brain health and the prevention of neurodegenerative diseases. In the present study, leaf explant of *C. prostratus* were cultured on MS (Murashige and Skoog's) medium supplemented with 1mgL^{-1} 2, 4-D shows optimum callus induction. Moreover, several biotechnological approaches could be used for better understanding of its memory enhancing mechanism, such as, phytochemical analysis for active compounds, *in vitro* and *in vivo* studies for safety and efficacy, metabolomics for potential health benefits and tissue culture for large scale production of this medicinally potent plant species in controlled environment. At present, there are many commercial medicinal products available in the market consisting Shakhapushpi as an ingredient or whole.

Keywords

Convolvulus prostratus, Shankhpushpi, Bindweed, medicinal plant, memory enhancing

Introduction

Human race has been reliant on plants for food, shelter, medicine and other accessories since ancient time. Medicinal plants are a great part of traditional medicine system in Asian and African countries (1). These plants are used by tribal communities for the treatment of several kind of infections and diseases, which show the potential of plants to be used as a base for drug invention and their further investigation can lead to nascent drug discoveries. Medicinal plants are considered as very important source for drug production due to presence of therapeutic phytochemicals. These phytochemicals such as flavonoids and phenolics have been observed to possess considerable effects on vigor and cancer anticipation (2).

Herbs have been used for centuries as natural remedies for a variety of health concerns, including memory loss and cognitive decline. Some herbs

contain active compounds that have been found to boost memory and cognitive function, reduce oxidative stress and improve neurotransmitter levels in the brain. For example, *Ginkgo biloba* and *Bacopa monnieri* are both popular herbs used for their memory-enhancing effects (3, 4), while *Curcuma longa* and *Withania somnifera* have been found to have neuroprotective properties (5, 6).

Convolvulus prostratus Forssk. (CP) is an important medicinal plant belonging to the family *Convolvulaceae* commonly known as bindweed or 'Shankhpushpi'. The plant species has several important medicinal properties such as anti-inflammatory, analgesic, anti-diabetic and anti-ulcer. The whole plant is known to possess pharmaceutically valued compounds like *Convolamine*, *Convoline*, *Convolvine*, *Delphinidine*, *Scopolin* and *Shankhpushpin*. It is a well-known memory enhancing and intellect boosting herb of Ayurveda from time immemorial.

Shankhpushpi is an aboriginal herb commonly found under xerophytic surroundings in northern India (7). The word Shankhpushpi is originated from Sanskrit because the plant has flowers that are conch shaped and it is cited as 'medhya rasayana' (nerve tonic) in Ayurveda (8). The plant has synonyms such as *C. pluricaulis* Choisy and *C. microphyllus* Sieb. ex Spreng (9). It is well-known Indian medicinal plant, extensively used as brain-tonic and also beneficial in chronic bronchitis, asthma as well as in loss of memory. Among all the species of this genus, *C. prostratus* along with *Evolvulus alsinoides* is extensively used in rasayana and is a vital constituent of '*Shankhpushpi*', a well -known memory enhancing drug (Table 1).

In different regions of India some plant species are used and cited under the common name 'Shankhpushpi', mainly comprising of three plants *C. prostratus* Forssk., *Evolvulus alsinoids* L. (both from Convolvulaceae family) and *Clitoria ternatea* L. (Fabaceae). All of these plant species possess nootropic, anxiolytic and CNS-depressant activity but *C. prostratus* is considered as the true source of Shakhpushpi because of its memory-enhancing activity (11).

Numerous research works have been conducted across the world on CP, and its different properties such as neuro-pharmacological, neuro-protective, neuro-modulatory and nootropic have been described. However, there is deficiency of statistics about comprehensive pre-clinical pharmacological profile, mechanism of action studies and biochemical profile of the plant are yet to be accomplished.

Table 1. *Taxonomic position of C. prostratus (10)*

Kingdom	Plantae
Clade	Tracheophyta
Clade	Spermatophyta
Division	Magnoliophyta
Class	Magnoliopsida
Sub class	Asteridae
Order	Solanales
Family	*Convolvulaceae* Juss.
Genus	*Convolvulus* L.
Species	*C. prostratus* Forssk.

The herb is mostly found in open waste lands and it is being depleted in nature because of over exploitation and habitat degradation, therefore it requires protection (12). By exploring the plant and its ecological, economical, ethnomedical, pharmacological and chemical properties, more insight could be given to its diversity of applications in different expanses.

Geographical and taxonomical distribution

The genus *Convolvulus* L. belongs to the bindweed or morning glory family *Convolvulaceae*. The family *Convolvulaceae* comprises of more than 200 species as listed in Plants of World Online, Kew (9). It is a cosmopolitan genus dispersed in tropical and temperate regions worldwide; native to Africa, Europe, America, Arab, Asia and Australia, with some introduced plants in Africa and Asian countries. In India, it is distributed throughout the northern regions, Rajasthan, Punjab, Bihar and Kashmir to Deccan peninsula and Gujarat (13). It is being used in herbal medicine for many centuries. Common species of this genus includes *C. lineatus* L., *C. prostratus* Forssk., *C. althaeoides* L., *C. arvensis* L. and *C. pilosellifolius* Desr. (14) (Table 2).

Ethnomedicinal and Pharmacological Properties

It is a classic memory and intellect booster herb described in Ayurveda (15). The plant has therapeutic properties, such as anticonvulsant (16), neuroprotective (17), hypotensive (18), anti-phlegmatic, anti-phlogistic, anthelmintic, antianxiety, improves complexion, strengthens intellect, useful in bronchitis, increases appetite, biliousness, epilepsy, teething troubles of infants etc. (19, 20). Its mode of action is by reducing the spontaneous motor activity; it controls the refluxes and frightening responses. It eventually acts as a soporific moiety which initiates a persistent decline in blood pressure and cardiac contraction, in that way managing neurological pathologies, such as anxiety, insanity and epilepsy (21). Moreover, one of the most renowned ancient Indian medical practitioners, *Acharaya Charak* used white flower variety of *C. prostratus* along with several other herbs; *Bacopa monnieri* (Brahmi), *Acorus calamus* (Vacha) and *Saussurea lappa* (Kushtha) for alleviating insanity and epilepsy (22). It is believed by herbalists that "Shankhpushpi" works in a manner that it calms the nerves by regulating the production of stress hormone, adrenaline and cortisol (23). Extracts of the plant were reported to have *in vitro* and *in vivo* antimicrobial properties against certain strains of bacteria such as *E. coli*, *S. aureus* and *B. subtilis* (24). Ethanolic extract of callus depicts significant antibacterial activity against *Klebsiella pneumoniae* and antifungal activity against *Penicillium chrysogenum* and *Tricophyton rubrum* (25).

Besides Ayurveda, *C. prostratus* has also been used in Siddha medicine systems as an oil obtained from the plant possess keratogenic activity and promotes hair

Table 2. *Taxonomical description of C. prostratus*

Sl. No.	Description	*C. prostratus*
1	Habit	Perennial herb
2	English Name	Bindweed
3	Vernacular Name	Shankh Pushpi
4	Leaves	Nearly stalkless, alternately arranged, linear to oblong, lance-shaped or invert lance-shaped, velvety to hairy
5	Inflorescence	Axillary solitary
6	Flowers	Monoecious, 1-3 together, 2 small bracts
7	Calyx	Lance-shaped, long-pointed, unequal, hairy
8	Corolla	White or pale pink, funnel-shaped, mid-petaline areas velvety
9	Androecium	Stamens 5
10	Gynoecium	Ovary 2 celled, glabrous
11	Style	2-4 mm long
12	Stigma	Stigmas 2, lobed
13	Fruit	Capsule, round or globose, 3-4 mm diameter
14	Seeds	Seeds 2-4, dark brown
15	Flowering	November to January

growth (26); paste prepared from roots and flowers has anti-aging effects indicating antioxidant properties (27). As well as in Unani medicinal system, syrup prepared from *C. prostratus* and *Piper nigrum* is prescribed in bleeding piles and venereal diseases (22).

Shakhapushpi has a wide-ranging commercial application in pharmaceuticals, cosmeceuticals and nutraceuticals. Patanjali Divya Shankhpushpi Churna™, Dabur Shankhpushpi Syrup™, Biotrex Shankhpushpi™, Maxmind capsule™ etc. are some of the pharmaceutical formulations used for the treatment of neurodegenerative disease, stress and gastric ulcers. Likewise, in the cosmeceutical industry it is used as a tonic for hair and skin related ailments. There are food grade products of the nontoxic wonder herb, like powder and syrup available in the market for being utilized as nutraceutical nootropic supplements (19).

Chemical Profile and Secondary Metabolite Composition

Plants belonging to *Convolvulus* genus comprise various complex chemical compounds including flavonoids, carbohydrates, amino acids, anthraquinones (28), alkaloids, anthocyanidins, caffeoylquinic acid derivatives (29), coumarins, essential oils (30), lignans, lipids, saponins (31), resins (32), steroids, tannins, terpenoids etc.

The major secondary metabolites observed in the plant are alkaloids (*convolamine*), glycosides, flavonoids (*kaempferol*), phenolics (*scopoletins*, *β-sitosterol* and *ceryl alcohol*), steroids and saponins (15, 24). (Fig. 1, Fig. 2) An experiment was conducted to quantify the content of *scopoletin* by HPLC using different solvent systems, from that they observed highest *scopoletin* content in hydro-alcoholic extract (0.1738 %) followed by methanolic extract (0.0932 %) and aqueous extract (0.0435 %). *Shakhapuspine*, an alkaloid, has also been isolated from the plant and is used as a chemotaxonomic marker for this particular species (33, 34) (Table 3).

In a comparative genetic and chemical profile analysis of *C. pluricaulis* population obtained from different sites of India, declared that the plant contains more *scopoletin* in comparison of *kaempferol* and it can be manipulated with further investigation using tissue culture and transformation studies (12).

Neuroprotective activities of CP metabolites

The herb is being used as a traditional ailment for neurological disorders, such as anxiety, dementia, and depression, in Ayurveda, Siddha and conventional Chinese medication. These indicate the pharmacological potential of the herb, such as anticonvulsant, antioxidant, and immunomodulatory properties. The presence of certain chemical compounds could be responsible for such

Table 3. *Phytochemicals found in C. prostratus and their therapeutic functions*

Sl. No.	Metabolite Name	Type of metabolite	Function	References
1	*Kaempferol*	Flavonoid	Chemo-preventive properties, inhibits cell growth, pro-teasome activity and induce apoptosis	35-38
2	*Convolamine*	Alkaloid	anti-inflammatory, Antihypoxic and immune-modulating activity	39
3	*Scopoletin*	Coumarin	anti-allergic, anti-aging, Antifungal and hypouricemic activities	40, 41
4	*β-sitosterol*	Phytosterol	pro-apoptotic, anti-proliferation; anti-pyretic and Anti-inflammatory activity	42, 43
5	*Convoline*	Alkaloid	Anti-epileptic activity	44
6	*Convolvine*	Alkaloid	blocks the M-receptors; exhibits nootropic, cytotoxic and sedative activity	45, 46

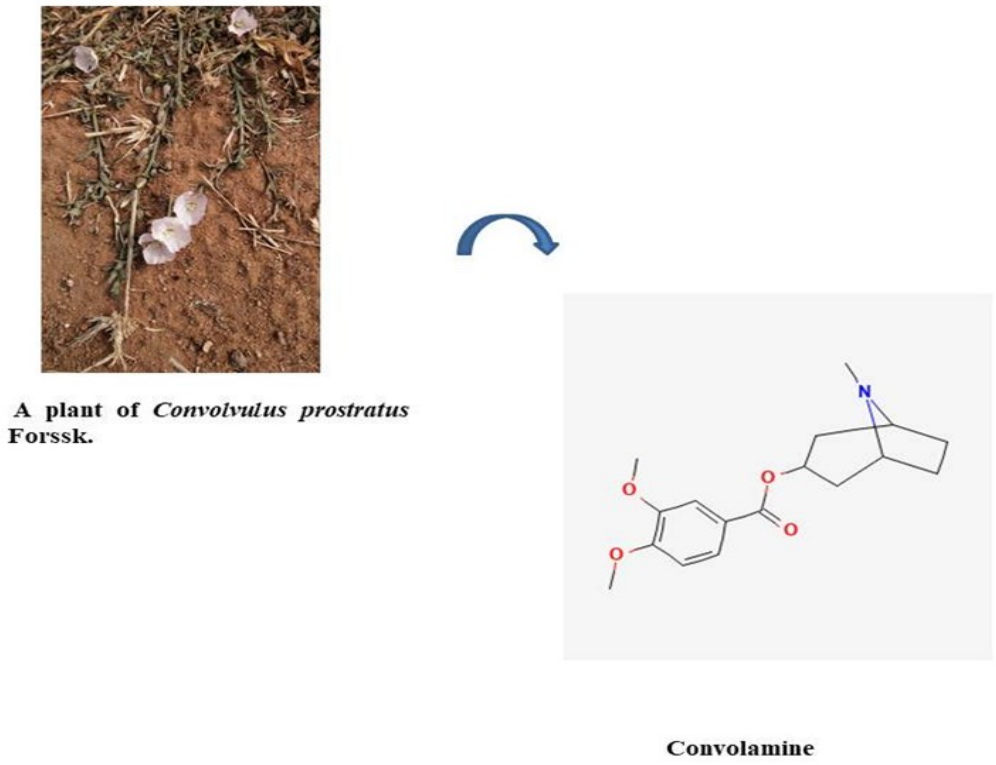

Fig. 1. A plant of *C. prostratus* in field conditions and structure of *Convolamine*: an important alkaloid obtained from it.

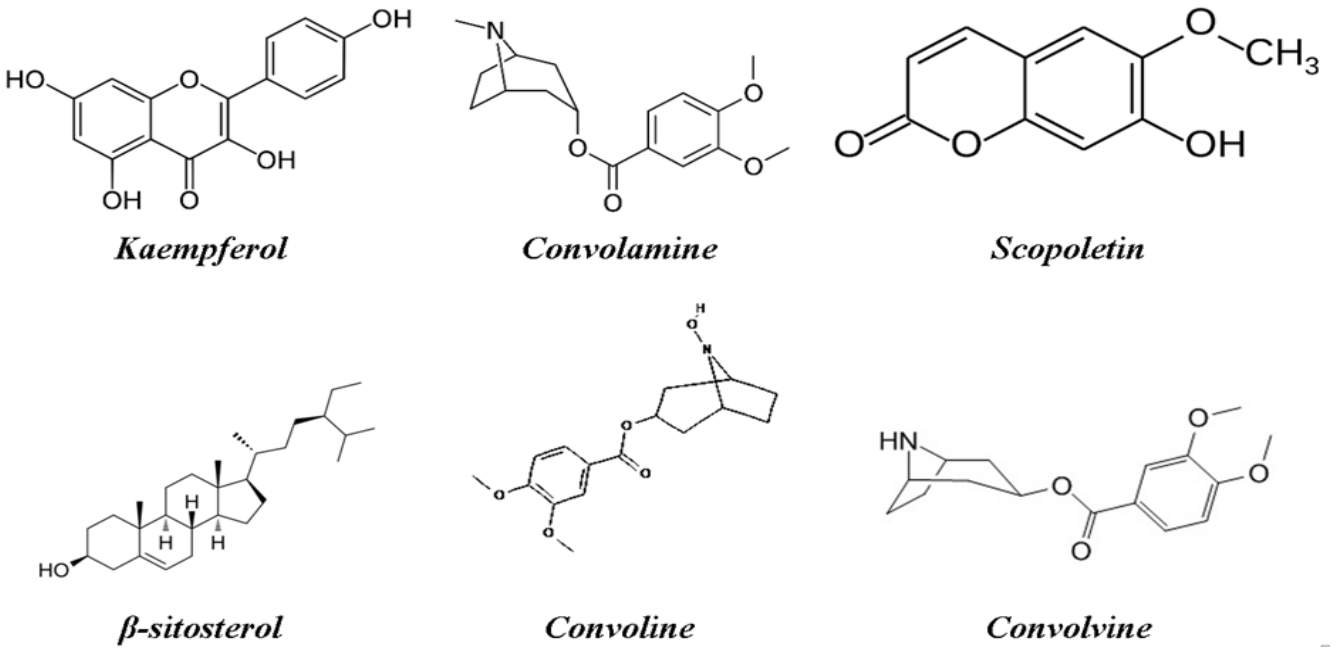

Fig. 2. Chemical structure of some important phytochemicals found in Shankhpushpi (*Convolvulus prostratus* Forssk.).

neuroprotective activities.

An experiment in silico analysis of CP metabolites depicts that *scopoletin, 4-hydroxycinnamic acid, kaempferol, quercetin* and *ayapanin* are the major bioactive compounds that target several neurological pathways viz. PI3K/Akt signaling pathway, the neurotrophin signaling pathway and the insulin signaling pathway with several other molecular targets viz. PTGS1, PTGS2, NOS3, INSR, HMOX1, ACHE, PPARG, MAOA, MAOB and TRKB (47). Rats treated with scopolamine were administered an oral extract of CP (150 mg/kg) that reduced the increased protein and mRNA levels of tau and AβPP levels followed by a reduction in Aβ levels indicating the neuroprotective effects of CP (48). This reduction in the tau protein expression leads to amelioration in amyloid β-induced deficits in the instance of neurodegenerative disorders such as Alzheimer's disease (49). *Taraxerol*, extract from roots of CP, had an IC50 at 20 µM concentration against AngII-induced cardiac hypertrophy in H9c2 cells, indicating that it suggestively increased the cell viability (50).

In another study, combined and individually,

aqueous extracts of CP roots and scopolamine are proposed as potential inhibitors of acetylcholinesterase for their ability to regulate cognitive deficit (51). It suggested that the two active metabolites (*scopoletin* and *kaempferol*) were bound with Human AchE at both active as well as allosteric sites and exhibits inhibitory activity. Combined effects of CP and Omega (1)-3 fatty acid on learning and memory demonstrate more extraordinary significance as compared to alone and to the standard drug (donepezil). In this experiment, Wistar rats were orally administered with whole plant powder of CP and Omega (1)-3 fatty acid in a dose-dependent manner and showed significant memory enhancement (52).

In vitro conservation studies

Convoluvuls prostratus has no significant study in this particular field of research with only a few studies conducted on callus production and organogenesis. The whole plant is known to possess therapeutic properties and active metabolites involved in diverse ethnomedicinal usages. Every part of the herb can be evaluated for detection of certain metabolites and further biotechnological approaches could be implemented for the enhancement of the therapeutic properties.

An experiment was performed culturing leaf as explant on MS basal medium supplemented with different combinations of 2, 4-Dichlorophenoxyacetic acid (2, 4-D) (kinetin) to raise callus. In another research, CP was cultured on MS medium supplemented with 2,4-D, 6 Benzyl Adenine (BAP), Indole-3-Acetic Acid (IAA) and Kinetin (1 ppm each) (53). Methanolic extracts were prepared from leaf and stem callus raised by this procedure, when subjected to Swiss albino mice reflected potential anticonvulsant activity against standard drug phenytoin (16).

To establish the *in vitro* morphogenesis protocol *of C. prostratus* shoot and leaf segments were used as explant for initiation of culture in MS medium. Different concentrations of BAP, 2,4-D and 1-Naphthaleneacetic acid (NAA) were used for initiation of culture. Leaf segments were found optimum for callus induction on MS medium augmented with 1mg/L 2,4-D and 3% sucrose. The obtained callus would be used for extraction, identification and purification of secondary metabolites found in this important medicinal plant (Fig. 3). Similar studies have also done on many medicinal plants like *Caralluma edulis*, *Ceropegia bulbosa*, *Glossonema varians*, *Stevia rebaudiana* etc (54-60).

Toxicological activities

The herb has been evaluated for acute oral toxicity in albino Wistar rats with ethanolic and aqueous administration. The subject reflected no toxic effects or change in behavior up to the dose of 5000 mg/Kg (61). Likewise, the iron oxide nanoparticles when administrated up to the dose of 2000 mg/kg in Swiss albino mice, exhibited no sign of clinical toxicity (62).

Conclusion

Shankhpushpi is used from ancient times in India as a memory booster and it has the well-known written documentation in Ayurveda. There are some valuable pharmaceutically active compounds found in the herb making it a competent source for novel drug manufacturing and pharmaceutical applications due to its various therapeutic properties. However, further research is needed to fully understand the mechanism of action and the dose-response relationship of these compounds. CP has great potential in the treatment of neurological disorders such as Alzheimer's disease and Parkinson's disease. Biotechnological approaches have the potential to improve the quality, consistency and availability of CP

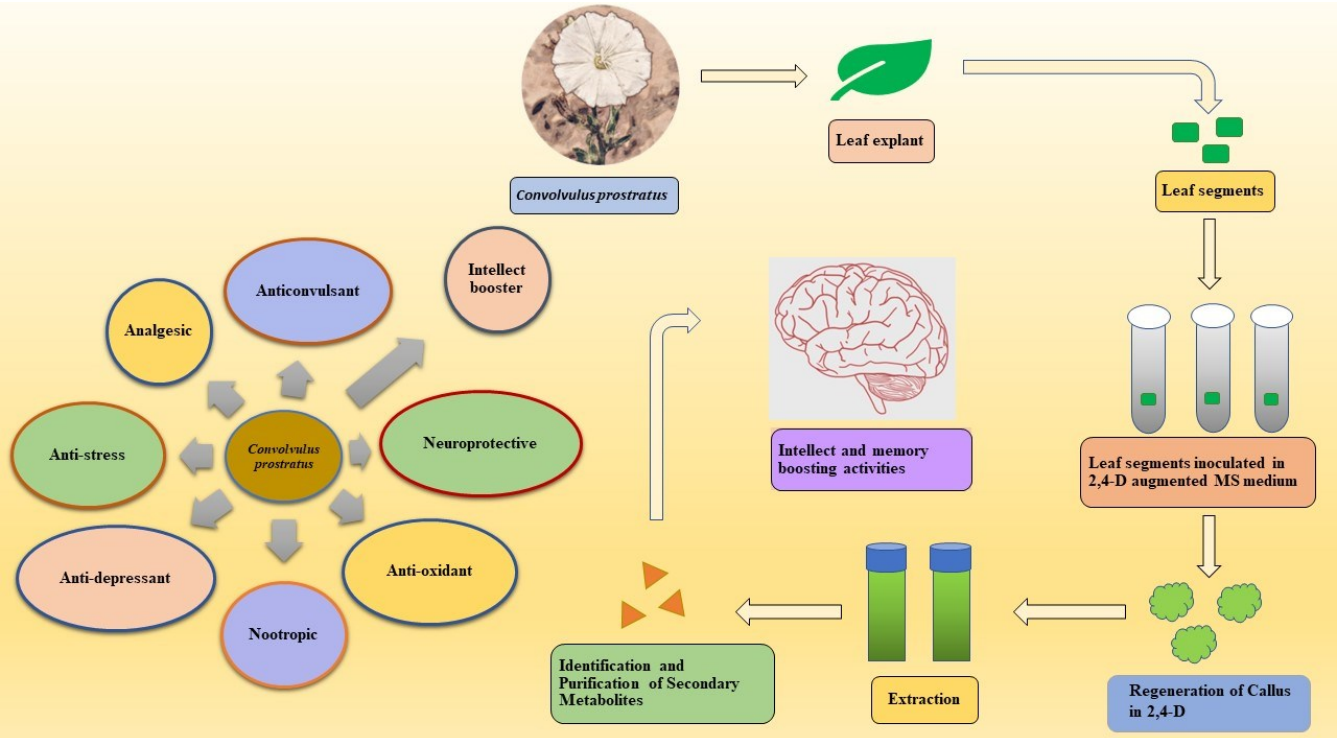

Fig. 3. Diagrammatic representation of *in vitro* production protocol of phytochemicals found in *C. prostratus* and their properties.

extracts for use as memory-enhancing supplements. There is limited information available on the phytochemical profile of CP, therefore, further studies and research are needed to determine the specific phytochemicals found in this herb.

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Authors contributions

GC and NS prepared the manuscript; SP and GSS did corrections in the manuscript.

Compliance with ethical standards

Conflict of interest: Authors declare that they have no competing interests.

Ethical issues: None.

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