Exploration of Neuroscience

Open Exploration

Open Access Mini Review

Neuroprotective compounds from three common medicinal plants of West Bengal, India: a mini review

Suvendu Ghosh[1], Partha Sarathi Singha[2], Debosree Ghosh[3*]

[1]Department of Physiology, Hooghly Mohsin College, Chinsura, Hooghly Pin 712101, West Bengal, India
[2]Department of Chemistry, Government General Degree College, Kharagpur II, Paschim Medinipur Pin 721149, West Bengal, India
[3]Department of Physiology, Government General Degree College, Kharagpur II, Paschim Medinipur Pin 721149, West Bengal, India

***Correspondence:** Debosree Ghosh, Department of Physiology, Government General Degree College, Kharagpur II, Paschim Medinipur Pin 721149, West Bengal, India. ghoshdebosree@gmail.com
Academic Editor: Marcello Iriti, Milan State University, Italy
Received: October 27, 2023 **Accepted:** December 9, 2023 **Published:** December 26, 2023

Cite this article: Ghosh S, Singha PS, Ghosh D. Neuroprotective compounds from three common medicinal plants of West Bengal, India: a mini review. Explor Neurosci. 2023;2:307–17. https://doi.org/10.37349/en.2023.00030

Abstract

Neural disorders refer to conditions of the nervous system due to infection or degeneration of the neurons leading to either neurodegenerative disorder or neuropsychiatric disorder. Some such disorders of the nervous system include Parkinsons's disease, depression, amnesia, dementia, Alzheimer's disease, schizophrenia, cerebrovascular impairment, epilepsy, seizure disorders, etc. In conventional medical system, some medicines belonging to the class of psychodelic drugs, sedatives, neurotransmitters, neuro-stimulants, etc. are in extensive use. Unfortunately, most of these drugs either delay the progression of the neural disorder or leave the patient with prominent adverse side effects. Several potent bioactive compounds with neuroprotective potential have been reported from medicinal plants and some of them have been found to be highly effective. Belonging from natural sources, mostly, the plant derived compounds exhibit minimum or no cytotoxicity at a prescribed standardised dose against a particular health ailment. Many such phytocompounds from plant sources with potent neuroprotective activities have been in use in Ayurvedacharya, Unani, and Chinese medicine for ages. The compounds if isolated chemically, modified to make more potent neuroprotective derivatives and utilised to make highly effective neuroprotective pharmaceutical formulations with minimum side effects, may open new revolutionary doorways in neuropharmacology. In this review, it has been briefly discussed about the neuroprotective compounds isolated from certain indigenous plants of West Bengal, India, and their mechanism of action.

Keywords

Neuroprotection, phytocompounds, Ayurvedacharya, Alzheimer's disease, Parkinsons's disease

Introduction

Plants are sources of myriads of potent bioactive compounds with medicinal properties [1, 2]. Studies show that plants growing under the ocean are also a rich source of bioactive phytochemical and are of immense medicinal importance [3]. Plants have been medicinally important since the beginning of civilization and various medicines used in Ayurveda, Unani, etc. have their sources from plants. Many of the drugs of modern day owe their roots to plant origin. Potent bioactive compounds derived from plant sources are used as potent lead molecules for developing drugs with minimal side effects [4]. Plants of every region have their unique phytochemical. The composition of the phytochemicals is known to vary in quality and quantity depending on the geographic region and soil composition on which the plant grows [5]. Natural products have been in use as drug candidates since ages [6]. Plants growing in a particular region by default find their use in local folk medicine. Mother nature has gifted mankind with a vast reserve of different kinds of plants all around. Most of these plants are rich source of potent bioactive phytochemical. The plants like *Murraya koenigii*, *Moringa olefera*, *Ocimum sanctum*, *Terminalia arjuna*, *Azadirachta indica*, and *Coriendrum sativum* are some of the very common popular potent medicinal plants found in almost all regions of South-East Asia including India [7–11]. Several hundreds of medicinal plants growing in the Indian Sub-continent have been identified to have potent neuroprotective activity. Some of these are *Bacopa monnierae*, *Withania somnifera*, *Hypericum perforatum*, *Allium sativum*, *Centella asiatica*, *Nicotiana tabaccum*, *Celastrus paniculatus*, *Enhydra fluctuans*, *Ricinus communis*, *Ginkgo biloba*, *Angelica sinensis*, *Uncaria tomentosa*, *Terminalia chebula*, *Salvia officinalis*, *Physostigma venosum*, *Acorus calmus*, *Curcuma longa*, *Huperiza serrata*, *Glycyrrhiza glabra*, *Crocus sativus*, and *Valeriana wallichii*, etc. [12].

Neuroprotection refers to the mechanism of protection of neurons from injuries or degenerations and conserving their normal physiological functions [13, 14]. Most common neurodegenerative diseases affect the aging population around the globe. Several plants derived traditional medication are there in use for ages for treating neurodegenerative situations, improving memory and learning as well as delaying the process of ageing [15, 16].

More than one hundred and twenty plants are known to be in use to address neurological ailments in the Asian countries [16]. These plants are rich sources of phytocompounds which have been studied to have potent neuroprotective activities [12]. Thus, the bioactive compounds and their derivatives with neuroprotective potential from these plants are used as lead compounds for developing neuro-psychopharmacological drug formulations. In this review, the neuroprotective compounds and their mechanism of action from four major indigenous plants grown in the state of West Bengal, India has been discussed.

Neuroprotective compounds from *Withania somnifera* (Aswagandha)

Withania somnifera (Ashwagandha) is a very common medicinal plant of India and has been in extensive use in Ayurveda for ages. The plant has several medicinal properties. Neuroprotective potential of Aswagandha is one of the most important and significant medicinal properties of the plant. It is known to be used as a nerve tonic in Ayurveda [17]. Studies show that *Withania somnifera* has cognition promoting impact [17]. It is reported to be effective in treating memory deficit in children and is also known to improve memory in aged people [17]. *Withania somnifera* is useful and effective in treating neurodegenerative diseases like Alzheimer's, Parkinson's and Huntington's diseases [17]. *Withania somnifera* is commonly known as the "Indian Ginseng" and "Indian Winter Cherry" [18]. The plant is known to have γ-aminobutyric acid (GABA) mimetic effect and is reported to promote dendrites formation [19]. The plant is also known to improve energy levels. It has positive effects on mitochondrial health. The plant is also reported to have anxiolytic and antidepressant effects [20]. This effect of *Withnia somnifera* is reported to be by virtue of the glycowithanolides present in *Withania somnifera* [20]. Alkaloids like anaferine, isopelletierine, anahygrine, cuseohygrine have been reported to be present in *Withania somnifera* (Table 1). The plant has been known to be a source of saponins and steroidal lactones like withaferins, and withanolides [21]. Other bioactive compounds reported to be present in *Withania*

somnifera are acylsterylglucosides, Withaferin A and sitoindosides (Table 1). These compounds have anti-stress effects [22]. Compounds like 5-dehydroxy withanolide-R and withasomniferin-A have been isolated from the aerial parts of the plant [23].

Table 1. Some neuroprotective phytochemicals from the medicinal plants *Withania somnifera*, *Bacopa monnieri*, and *Centella asiatica*, their actions and the mechanisms of their actions

Plant	Neuroprotective phytochemicals		Neuroprpotective action	Mechanism of action
	Phytochemicals	Chemical nature		
Withania somnifera	Anaferine	Alkaloids	Protection against neurodegenerative diseases like Huntington's disease, Parkinsonism, Alzheimer's disease [24]	GABA mimetic action that promotes dendrites formation [19]
	Withanolides	Steroidal lactones		
	Anahygrine	Alkaloids		
	Cuseohygrine	Alkaloids		
	Isopelletierine	Alkaloids		
	Withaferin A	Steroidal lactones		
	Sitoindosides	Acylsterylglucosides		
	5-Dehydroxy withanolide-R	Steroidal lactones		
	Withasomniferin-A	Steroidal lactones		
Bacopa monnieri	Bacopaside III	Bascosides	Restoration of memory related disorders, restoration of nerve transmission, defensive role in schizophrenia [25]	NMDAR1 receptor turnover, stimulates certain kinases activity essential for normal neural transmission activity [26]
	Bacopaside X	Bascosides		
	Bacoside A3	Bascosides		
	Bacopasaponin C	Bascosides		
	Apigenin	Flavonoid		
	Jujubogerin	Saponin glycosides		
	Pseudojujubogenin	Saponin glycosides		
	Cucurbitacin	Tetracyclic terpenes		
	Hersaponin	Alkaloids		
	Brahmine	Alkaloids		
	Monnierasides I–III	Phenylethanoid glycosides		
	D-Mannitol	Sugar alcohol		
	Nicotine	Alkaloids		
	Herpestine	Glycoside		
	Ebelin lactone	Lactone		
Centella asiatica	Eugenol derivatives	Phenylpropanoid derivatives	Enhances cognition, improves memory. Anxiyolytic, anticonvulsant, protects against beta amyloid toxicity [27]	Improves antioxidative signaling pathways like Nrf2 and HO-1 pathways Impacts other signal transduction pathways like ERK1/2 and PKB pathway [27]
	Flavonoids	Phenylpropanoid derivatives		
	Caffeoylquinic acids	Phenylpropanoid derivatives		
	Plant sterols	Isoprenoids		
	Sesquiterpenes	Isoprenoids		
	Pentacyclic triterpenoids	Isoprenoids		
	Saponins	Glycoside compounds		

NMDAR1: *N*-methyl-*D*-aspartate receptor 1; Nrf2: nuclear factor erythroid 2-related factor 2; HO-1: heme oxygenase-1; ERK1/2: extracellular signal-regulated protein kinases 1 and 2; PKB: protein kinase B

Neuroprotective compounds from *Bacopa monnieri* (Brahmi)

Bacopa monnieri popularly known as Brahmi is a common medicinal herb grown abundantly in parts of West Bengal, India [28]. It is a small succulent herb grows naturally in wet soil. The herb was used by the ancient Vedic scholars to memorize lengthy scriptures and sacred hymns. A phytochemical namely Bacosides, is known to be present in Brahmi (Table 1), and causes an increase in the cerebral blood flow. This compound is extensively used as brain health supplement and is remarkably used in the treatment of

Alzheimer's disease [28]. The herb is primarily composed of bioactive compounds like dammarane-type triterpenoid saponins that are called Bacosides and they have jujubogenin or pseudo-jujubogenin moieties as their aglycone units [29]. Bacosides have been reported to promote nerve impulse transmission, repair damaged neurons by stimulating kinase activity and also stimulate neuronal synthesis [29]. Bacosides are also reported to restore nerve impulse transmission [29]. Studies conducted on murine model of schizophrenia reveals that administration of Brahmi resulted in restoration of the memory impairment by decreasing NMDAR1 in certain brain areas in the rats [30]. Another study shows that memory impairment induced by streptozoticin is restored by Brahmi in murine model [31]. Studies report that Brahmi has the ability to enhance the expression of 5-hydroxytryptamine type 3A (5-HT3A) receptors, the level of serotonin, and also the level of cyclic adenosine monophosphate response element binding protein (CREB) in hippocampus of postpartum rats and these facilitates the learning abilities of the experimental animals [32]. The fact that Brahmi has the potential to bring improvements in cognitive abilities, has now been well established with supporting experimental and clinical data [33, 34]. Studies show that during clinical trials using Brahmi, there has not been any toxicity in the human subjects [34]. The studies reveal that Brahmi has the ability to improve nervousness, concentration and memory in adult subjects [34]. A study using 60 healthy human adults, reveals that Brahmi improves cognitive processing, attention, and working memory partly through the decrease in acetylcholinesterase (AChE) activity [35].

Bacoside A (dammarane-type triterpenoid saponins), the primary neuroprotective compound group recognised from Brahmi is composed of bacopaside III, bacopaside X, Bacoside A3, and bacopasaponin C (Table 1) [33–35]. Through structural analysis, 12 analogues derived from the Bacosides have been reported, different saponin types have also been identified as essential ingredients which are known as bacopasides I–XII [36]. Other components of *Bacopa* are apigenin, monnierin, cucurbitacin, hersaponin, azlkaloids brahmine, monnierasides I–III, D-mannitol, nicotine and herpestine [37, 38].

Studies show that Bacosides have the potential to prevent amyloid beta peptide (Aβ) aggregation, and formation of fibrils [38] and also protect neurons from toxicity induced by Aβ [39]. The compounds are reported to directly interact with the neurotransmitter and thus bring changes in memory and learning [40, 41]. Bacosides isolated from Brahmi, are non polar glycosides in nature and they easily cross the blood brain barrier [42–44]. This has been confirmed by radiopharmaceuticals biodistribution studies [45]. Thus, the Brahmi, rich in Bacosides have potent neuroprotective potentials and may be explored for utilizing the phytocompounds as lead molecules for developing more potent and effective neuroprotective drugs. Computational study predicts ebelin lactone as the most important compound from *Bacopa monnieri*. The study claims ebelin lactone as the most promising drug candidate and that it can be utilised to develop a drug against Alzheimer's disease, post pre-clinical and clinical validations [46]. The herb has also been found to have potent neuroprotective and neurorescuing effects against neurodenerative disese like Parkinsons's disease [47].

Neuroprotective compounds from *Centella asiatica*

Centella asiatica is a small perennial plant that grows abundantly in hot humid tropical and sub-tropical regions around the globe. The plant grows extensively in West Bengal, India [48] (Figure 1). Some of the primary bioactive phytocompounds identified and reported from *Centella asiatica* are phenylpropanoid derivatives (eugenol derivatives, flavonoids, and caffeoylquinic acids) and isoprenoids (plant sterols, sesquiterpenes, saponins, and pentacyclic triterpenoids) (Table 1) [49].

Several studies have been conducted in rodent models and some in human models to investigate the neuroprotective potentials of *Centella asiatica* [49]. The medicinal plant *Centella asiatica* is traditionally known for enhancing the cognition and improving memories [50]. The plant is also known in folk medicine as an anxiolytic agent and anticonvulsant [51]. In Ayurveda the plant is known as "medhyarasayana" by virtue of its ability to improve memory and cognition [52]. *Centella asiatica* is reported to have neuroprotective effect and it has also been established in several *in vitro* models. Administration of *Centella asiatica* has been reported to improve antioxidant status, inhibit pro-inflammatory enzyme namely

Figure 1. *Centella asiatica*

phospholipase A2 and protect against beta amyloid toxicity [49]. *Centella asiatica* is known to impose its neuroptropic effects by modulations of the signal transduction pathways including ERK1/2 and PKB pathway [53]. Increased dendritic arborization and synaptogenesis are the prime neuroptopic effects of *Centella asiatica* [53]. Most of these neurotropic and neuroprotective potentials of *Centella asiatica* are due to the potent phytocompounds present in the plant which include triterpene compounds asiaticoside, asiatic acid, and madecassoside [54]. The new group of compounds reported from *Centella asiatica* are caffeoylquinic acids and these have the potential of inducing the Nrf2-antioxidant response pathway and HO-1 signaling [55]. Studies show that by virtue of its ability to improve the antioxidative signaling pathway, the plant *Centenella asciatica* improves memories in experimental rats [55].

Other medicinal properties of *Withania somnifera*, *Bacopa monnieri* and *Centella asiatica*

All these three plants are known to possess several other medicinal properties besides that of neuroprotective actions. The plant *Withania somnifera*, popularly known as Aswagandha and the phytocompounds namely Withaferin A, withanolide A, withanolide D, and withaniamides are known to play significant pharmacological roles. Glycoproteins from *Withania* and lectin like-protein are reported to possess potent antimicrobial, anti-snake venom poison and antimicrobial therapeutic potentials [56]. In folk medicine, the plant *Withania* is known to be in use for treating ailments like hypothermia, diabetes, cancer, hepatitis, arthritis, asthma, ulcer, eyesores, heart problems, haemorrhoids, etc. The plant *Withania* is known to have anticancer, antimicrobial, and muscle strengthening activities. It is also reported to have potential in treating low back pain [57]. Several important secondary metabolites like steroids, alkaloids,

phenolics, flavonoids, saponins, and glycosides have been reported from the *Withania* and these have potent medicinal properties [57]. Phytocompounds from different parts of the plant *Withania*, specially the roots have been extensively explored for their medicinal properties like treating male infertility, antianxiety, obsessive-compulsive disorder, etc., and several of these experimental studies have been evaluated successfully for clinical trials [56, 57]. A bitter alkaloid named Somniferin has been isolated from *Withania somnifera* and is known to have hypnotic activity [58].

The plant *Bacopa monnieri*, is also known to be a rich source of medicinal phytocompounds with various medicinal properties. Memory enhancing ability of the plant is well documented [59]. The plant is known to add years to life and also promotes rejuvenation [59]. Several potent medicinal phytochemicals namely triterpenoid saponins, monnierinalkaloids flavonoids, glycosides and other phytochemicals namely betulinic acid, betulic acid, oroxindin, wogonin, stigmasterol, beta-sitosterol, sapogenin, Brahmic acid, brahminoside, brahamoside, isobrahmic acid, etc., have been isolated from the leaves of the plant *Bacopa monnieri* [59]. Studies reveal broad therapeutic potentials of the *Bacopa monnieri* that include analgesic, anxiolytic, antioxidant, anti-inflammatory, anti-microbial, anti-depressant, anti-convulsant, adaptogenic, hepatoprotective, immunostimulatory, anti-ulcerative and anti-neoplastic, etc. [60–70]. Extracts of the plant *Centella asiatica* are reported to have extensive use in folk medicine in China and India and has potentials in boosting memory, preventing cognitive deficits and improving brain functions [71]. Certain potent phytochemicals namely pentacyclic triterpenoid glycosides, madecassoside and asiaticoside have been reported from the plant. Corresponding aglycones, asiatic acid and madecassic acid of the mentioned compounds have also been reported to have potent medicinal properties. Asiaticoside and madecassoside are reported as marker compounds of *Centella asiatica* and are known to have wide pharmacological potentials. The triterpene compounds, asiaticoside and madecassoside have been reported to have anti-inflammatory, antioxidant, anti-allergic, wound healing, cardioprotective, hepatoprotective, neuroprotective, anxyiolytic, anti-fibrotic, antibacterial, anti-arthiritic, anti-tumor, anti-ulcerative properties. The compounds are also widely used for addressing issues of skin abnormalities and for treating burn injuries, asthma, lupus, psoriasis and scleroderma, etc. [71–76].

Conclusions

Neurological diseases are usually long term disturbances that may occur in any stage of life. The common degenerative neural diseases includes Alzheimer's disease, Parkinson's disease, Huntington's disease, insomnia, loss of cognitive ability, etc. The primary causes of these diseases are stress, ageing, inflammation, compromised immunity and neural injury. The chief neurotransmitter systems disabled in such illness are cholinergic, GABAergic, dopaminergic transmitter pathways. The plants discussed in this review work on several target molecules effecting these neurotransmitters, metabolism of the brain or checks oxidative stress mediated neural damage. The potent phytocompounds from these plants are also known to be affecting various signaling pathways and all together they have been found to be potent neuroprotective agents. There are extensive literature revealing *in vitro*, *in vivo*, and *in silico* studies and also successful clinical trials of some of the potent bioactive neuroprotective compounds from the plants namely *Withania somnifera*, *Bacopa monnieri* and *Centella asiatica*. These studies taken together, show that these indigenous West Bengal, India may be explored to utilise their rich source of bioactive neuroprotective compounds for developing new potent, effective and affordable neuropharmacological formulations and drugs which are expected to have minimum or no side effects.

Abbreviations

ERK1/2: extracellular signal-regulated protein kinases 1 and 2

HO-1: heme oxygenase-1

NMDAR1: *N*-methyl-*D*-aspartate receptor 1

Nrf2: nuclear factor erythroid 2-related factor 2

PKB: protein kinase B

Declarations

Author contributions

SG: Writing—original draft, Investigation. PSS: Writing—review & editing, Investigation. DG: Conceptualization, Writing—original draft, Writing—review & editing, Investigation.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical approval

Not applicable.

Consent to participate

Not applicable.

Consent to publication

Not applicable.

Availability of data and materials

Not applicable.

Funding

Not applicable.

References

1. Ghosh D, Firdaus SB, Mitra E, Dey M, Bandyopadhyay D. Protective effect of aqueous leaf extract of Murraya Koenigi against lead induced oxidative stress in rat liver, heart and kidney: a dose response study. Asian J Pharm Clin Res. 2012;5:54–8.
2. Atanasov AG, Waltenberger B, Pferschy-Wenzig EM, Linder T, Wawrosch C, Uhrin P, et al. Discovery and resupply of pharmacologically active plant-derived natural products: a review. Biotechnol Adv. 2015;33:1582–614.
3. Ghosh D, Parida P. Drugs from the Ocean: a review. World J Pharm Pharm Sci. 2014;3:1437–42.
4. Kinghorn AD, Pan L, Fletcher JN, Chai H. The relevance of higher plants in lead compound discovery programs. J Nat Prod. 2011;74:1539–55.
5. Ghosh D, Mitra E, Firdaus SB, Dey M, Ghosh AK, Chattopadhyay A, et al. *In vitro* studies on the antioxidant potential of the aqueous extract of Curry leaves (*Murraya koenigii L.*) collected from different parts of the state of West Bengal. Ind J Physiol Allied Sci. 2012;66:77–95.
6. Cragg GM, Newman DJ. Natural products: a continuing source of novel drug leads. Biochim Biophys Acta. 2013;1830:3670–95.
7. Ghosh D, Firdaus SB, Mitra E, Chattopadhyay A, Pattari SK, Dutta S, et al. Aqueous leaf extract of *Murraya koenigii* protects against lead-induced cardio toxicity in male wistar rats. Int J Phytopharm. 2013;4:119–32.
8. Mahleyuddin NN, Moshawih S, Ming LC, Zulkifly HH, Kifli N, Loy MJ, et al. *Coriandrum sativum* L.: a review on ethnopharmacology, phytochemistry, and cardiovascular benefits. Molecules. 2021;27:209.
9. Milla PG, Peñalver R, Nieto G. Health benefits of uses and applications of *Moringa oleifera* in bakery products. Plants (Basel). 2021;10:318.

10. Mitra E, Ghosh D, Ghosh AK, Basu A, Chattopadhyay A, Pattari SK, et al. Aqueous Tulsi leaf (Ocimum sanctum) extract possesses antioxidant properties and protects against cadmium-induced oxidative stress in rat heart. Int J Pharm Pharm Sci. 2014;6:500–13.
11. Paul S, Ghosh AK, Ghosh D, Dutta D, Mitra E, Dey M, et al. Aqueous bark extract of Terminalia arjuna protects against phenylhydrazine induced oxidative damage in goat red blood cell membrane protein, phospholipid asymmetry and structural morphology: a flow cytometric and biochemical analysis. J Pharm Res. 2014;8:1790–804.
12. Gong X, Sucher NJ. Stroke therapy in traditional Chinese medicine (TCM): prospects for drug discovery and development. Trends Pharmacol Sci. 1999;20:191–6.
13. Elufioye TO, Berida TI, Habtemariam S. Plants-derived neuroprotective agents: cutting the cycle of cell death through multiple mechanisms. Evid Based Complement Alternat Med. 2017;2017:3574012.
14. Iriti M, Vitalini S, Fico G, Faoro F. Neuroprotective herbs and foods from different traditional medicines and diets. Molecules. 2010;15:3517–55.
15. Kumar GP, Khanum F. Neuroprotective potential of phytochemicals. Pharmacogn Rev. 2012;6:81–90.
16. Kumar V. Potential medicinal plants for CNS disorders: an overview. Phytother Res. 2006;20:1023–35.
17. Singh N, Bhalla M, de Jager P, Gilca M. An overview on ashwagandha: a Rasayana (rejuvenator) of Ayurveda. Afr J Tradit Complement Altern Med. 2011;8:208–13.
18. Sharma CG. Ashwagandharishta--rastantra sar evam sidhyaprayog sangrah--krishna--gopal ayurveda bhawan (dharmarth trust). Nagpur; 1938. pp. 743–4.
19. Yin H, Cho DH, Park SJ, Han SK. GABA-mimetic actions of *Withania somnifera* on substantia gelatinosa neurons of the trigeminal subnucleus caudalis in mice. Am J Chin Med. 2013;41:1043–51.
20. Bhattacharya SK, Bhattacharya A, Sairam K, Ghosal S. Anxiolytic-antidepressant activity of *Withania somnifera* glycowithanolides: an experimental study. Phytomedicine. 2000;7:463–9.
21. Mishra LC, Singh BB, Dagenais S. Scientific basis for the therapeutic use of Withania somnifera (ashwagandha): a review. Altern Med Rev. 2000;5:334–46.
22. Bhattacharya SK, Goel RK, Kaur R, Ghosal S. Anti-stress activity of sitoindosides VII and VIII, new acylsterylglucosides from *Withania somnifera*. Phytother Res. 1987;1:32–7.
23. Atta-ur-Rahman, Abbas S, Dur-e-Shahwar, Jamal SA, Choudhary MI. New withanolides from Withania sp. J Nat Prod. 1993;56:1000–6.
24. Dar NJ, MuzamilAhmad. Neurodegenerative diseases and *Withania somnifera* (L.): an update. J Ethnopharmacol. 2020;256:112769.
25. Sekhar VC, Viswanathan G, Baby S. Insights into the molecular aspects of neuroprotective bacoside A and Bacopaside I. Curr Neuropharmacol. 2019;17:438–46.
26. Hiren Kumar Bose. Medicinal herb ushers prosperity for Sagar Island farmers [Internet]. Village Square; 2023 [cited 2023 Oct 26]. Available from: https://www.villagesquare.in/medicinal-herb-ushers-prosperity-for-sagar-island-farmers/
27. Newall CA, Anderson LA, Phillipson JD. Herbal medicines. A guide for health care professionals. London: The Pharmaceutical Press; 1996.
28. Mathur D, Goyal K, Koul V, Anand A. The molecular links of re-emerging therapy: a review of evidence of Brahmi (*Bacopa monniera*). Front Pharmacol. 2016;7:44.
29. Singh H, Dhawan B. Neuropsychopharmacological effects of the Ayurvedic nootropic Bacopa monniera Linn. (Brahmi). Ind J Pharmacol. 1997;29:359.
30. Piyabhan P, Wetchateng T. Neuroprotective effects of Bacopa monnieri (Brahmi) on novel object recognition and NMDAR1 immunodensity in the prefrontal cortex, striatum and hippocampus of sub-chronic phencyclidine rat model of schizophrenia. J Med Assoc Thai. 2014;97:S50–5.

31. Khan MB, Ahmad M, Ahmad S, Ishrat T, Vaibhav K, Khuwaja G, et al. *Bacopa monniera* ameliorates cognitive impairment and neurodegeneration induced by intracerebroventricular-streptozotocin in rat: behavioral, biochemical, immunohistochemical and histopathological evidences. Metab Brain Dis. 2015;30:115–27.
32. Rajan KE, Singh HK, Parkavi A, Charles PD. Attenuation of 1-(*m*-chlorophenyl)-biguanide induced hippocampus-dependent memory impairment by a standardised extract of *Bacopa monniera* (BESEB CDRI-08). Neurochem Res. 2011;36:2136–44.
33. Singh R, Ramakrishna R, Bhateria M, Bhatta RS. *In vitro* evaluation of Bacopa monniera extract and individual constituents on human recombinant monoamine oxidase enzymes. Phytother Res. 2014;28: 1419–22.
34. Singh RH, Singh L. Studies on the anti-anxiety effect of the medhya rasayana drug brahmi (Bacopa moniera Wettst), part I. J Res Ayur Siddha. 1981;1:133–48.
35. Peth-Nui T, Wattanathorn J, Muchimapura S, Tong-Un T, Piyavhatkul N, Rangseekajee P, et al. Effects of 12-week *Bacopa monnieri* consumption on attention, cognitive processing, working memory, and functions of both cholinergic and monoaminergic systems in healthy elderly volunteers. Evid Based Complement Alternat Med. 2012;2012:606424.
36. Rauf K, Subhan F, Al-Othman A, Khan I, Zarrelli A, Shah MR. Preclinical profile of bacopasides from Bacopa monnieri (BM) as an emerging class of therapeutics for management of chronic pains. Curr Med Chem. 2013;20:1028–37.
37. Kapoor R, Srivastava S, Kakkar P. *Bacopa monnieri* modulates antioxidant responses in brain and kidney of diabetic rats. Environ Toxicol Pharmacol. 2009;27:62–9.
38. Blázquez-Sánchez MT, de Matos AM, Rauter AP. Exploring anti-prion glyco-based and aromatic scaffolds: a chemical strategy for the quality of life. Molecules. 2017;22:864.
39. Holcomb LA, Dhanasekaran M, Hitt AR, Young KA, Riggs M, Manyam BV. Bacopa monniera extract reduces amyloid levels in PSAPP mice. J Alzheimers Dis. 2006;9:243–51.
40. Limpeanchob N, Jaipan S, Rattanakaruna S, Phrompittayarat W, Ingkaninan K. Neuroprotective effect of *Bacopa monnieri* on beta-amyloid-induced cell death in primary cortical culture. J Ethnopharmacol. 2008;120:112–7.
41. Anand T, Prakash KB, Pandareesh MD, Khanum F. Development of bacoside enriched date syrup juice and its evaluation for physical endurance. J Food Sci Technol. 2014;51:4026–32.
42. Deepak M, Amit A. The need for establishing identities of 'bacoside A and B', the putative major bioactive saponins of Indian medicinal plant *Bacopa monnieri*. Phytomedicine. 2004;11:264–8.
43. Chakravarty AK, Sarkar T, Masuda K, Shiojima K, Nakane T, Kawahara N. Bacopaside I and II: two pseudojujubogenin glycosides from *Bacopa monniera*. Phytochemistry. 2001;58:553–6. Erratum in: Phytochemistry. 2002;59:365.
44. Pardridge WM. Blood-brain barrier biology and methodology. J Neurovirol. 1999;5:556–69.
45. De K, Chandra S, Misra M. Evaluation of the biological effect of brahmi (Bacopa monnieri Linn) extract on the biodistribution of technetium-99m radiopharmaceuticals. Life Sci J. 2008;5:45–9.
46. Ahmad F, Abiha U, Ahmad SR, Patel N. Ebelin lactone as the most promising neuroprotective compound from Bacopa monnieri extract targeting microtubule affinity regulation kinase-4 involved in Alzheimer's disease: a computational study. Research Square [Preprint]. 2023 [cited 2023 Dec 15]. Available from: https://www.researchsquare.com/article/rs-2879310/v1
47. Singh B, Pandey S, Rumman M, Kumar S, Kushwaha PP, Verma R, et al. Neuroprotective and neurorescue mode of action of *Bacopa monnieri* (L.) Wettst in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine-induced Parkinson's disease: an *in silico* and *in vivo* study. Front Pharmacol. 2021; 12:616413.
48. Mondal B, Khatua DC. White rot of *Centella asiatica* and two weeds in West Bengal, India. J Crop and Weed. 2015;11:225–6.

49. Gray NE, Alcazar Magana A, Lak P, Wright KM, Quinn J, Stevens JF, et al. *Centella asiatica*: phytochemistry and mechanisms of neuroprotection and cognitive enhancement. Phytochem Rev. 2018;17:161–94.
50. Kapoor LD. Handbook of Ayurvedic medicinal plants. 1st Edition. Boca Raton: CRC Press; 1990.
51. Shinomol GK, Muralidhara MMB. Exploring the role of "Brahmi" (Bacopa monnieri and Centella asiatica) in brain function and therapy. Recent Pat Endocr Metab Immune Drug Discov. 2011;5:33–49.
52. Nadkarni KM. Indian materia medica. In: Popular Prakashan. Bombay; 1976. p. 1142.
53. Cichon N, Saluk-Bijak J, Gorniak L, Przyslo L, Bijak M. Flavonoids as a natural enhancer of neuroplasticity—an overview of the mechanism of neurorestorative action. Antioxidants (Basel). 2020;9:1035.
54. Bandopadhyay S, Mandal S, Ghorai M, Jha NK, Kumar M, Radha, et al. Therapeutic properties and pharmacological activities of asiaticoside and madecassoside: a review. J Cell Mol Med. 2023;27: 593–608.
55. Matthews DG, Caruso M, Murchison CF, Zhu JY, Wright KM, Harris CJ, et al. *Centella Asiatica* improves memory and promotes antioxidative signaling in 5XFAD mice. Antioxidants (Basel). 2019;8:630.
56. Dar PA, Singh LR, Kamal MA, Dar TA. Unique medicinal properties of Withania somnifera: phytochemical constituents and protein component. Curr Pharm Des. 2016;22:535–40.
57. Saleem S, Muhammad G, Hussain MA, Altaf M, Bukhari SNA. *Withania somnifera* L.: insights into the phytochemical profile, therapeutic potential, clinical trials, and future prospective. Iran J Basic Med Sci. 2020;23:1501–26.
58. Umadevi M, Rajeswari R, Rahale CS, Selvavenkadesh S, Pushpa R, Kumar KPS, et al. Traditional and medicinal uses of Withania somnifera. Pharma Innovation. 2012;1:102–10.
59. Walker EA, Pellegrini MV. Bacopa monnieri. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023.
60. Mathew J, Gangadharan G, Kuruvilla KP, Paulose CS. Behavioral deficit and decreased GABA receptor functional regulation in the hippocampus of epileptic rats: effect of *Bacopa monnieri*. Neurochem Res. 2011;36:7–16.
61. Sairam K, Dorababu M, Goel RK, Bhattacharya SK. Antidepressant activity of standardized extract of *Bacopa monniera* in experimental models of depression in rats. Phytomedicine. 2002;9:207–11.
62. Russo A, Borrelli F. *Bacopa monniera*, a reputed nootropic plant: an overview. Phytomedicine. 2005; 12:305–17.
63. Ghosh TR, Maity TK, Das M, Bose A, Dash DK. *In vitro* antioxidant and hepatoprotective activity of ethanolic extract of Bacopa monnieri Linn. aerial parts. IJPT. 2007;6:77–85.
64. Elangovan V, Govindasamy S, Ramamoorthy N, Balasubramanian K. *In vitro* studies on the anticancer activity of Bacopa monnieri. Fitoterapia. 1995;66:211–5.
65. Jain P, Khanna NK, Trehan N, Pendse VK, Godhwani JL. Antiinflammatory effects of an Ayurvedic preparation, Brahmi Rasayan, in rodents. Indian J Exp Biol. 1994;32:633–6.
66. Abbas M, Subhan F, Mohani N, Rauf K, Ali G, Khan M. The involvement of opioidergic mechanisms in theactivity of Bacopa monnieri extract and its toxicological studies. Afr J Pharm Pharmacol. 2011;5: 1120–4.
67. Bhattacharya SK, Ghosal S. Anxiolytic activity of a standardized extract of *Bacopa monniera*: an experimental study. Phytomedicine. 1998;5:77–82.
68. Chowdhuri DK, Parmar D, Kakkar P, Shukla R, Seth PK, Srimal RC. Antistress effects of bacosides of *Bacopa monnieri*: modulation of Hsp70 expression, superoxide dismutase and cytochrome P450 activity in rat brain. Phytother Res. 2002;16:639–45.
69. Shukla A, Rasik AM, Jain GK, Shankar R, Kulshrestha DK, Dhawan BN. *In vitro* and *in vivo* wound healing activity of asiaticoside isolated from *Centella asiatica*. J Ethnopharmacol. 1999;65:1–11.

70. Aguiar S, Borowski T. Neuropharmacological review of the nootropic herb *Bacopa monnieri*. Rejuvenation Res. 2013;16:313–26.
71. Mato L, Wattanathorn J, Muchimapura S, Tongun T, Piyawatkul N, Yimtae K, et al. *Centella asiatica* improves physical performance and health-related quality of life in healthy elderly volunteer. Evid Based Complement Alternat Med. 2011;2011:579467.
72. Wu F, Bian D, Xia Y, Gong Z, Tan Q, Chen J, et al. Identification of major active ingredients responsible for burn wound healing of *Centella asiatica* herbs. Evid Based Complement Alternat Med. 2012;2012: 848093.
73. Hengjumrut P, Anukunwithaya T, Tantisira MH, Tantisira B, Khemawoot P. Comparative pharmacokinetics between madecassoside and asiaticoside presented in a standardised extract of *Centella asiatica*, ECa 233 and their respective pure compound given separately in rats. Xenobiotica. 2018;48:18–27.
74. Gohil KJ, Patel JA, Gajjar AK. Pharmacological review on Centella asiatica: a potential herbal cure-all. Indian J Pharm Sci. 2010;72:546–56.
75. Somchit MN, Sulaiman MR, Zuraini A, Samsuddin L, Somchit N, Israf DA, et al. Antinociceptive and antiinflammatory effects of *Centella asiatica*. Indian J Pharmacol. 2004;36:377–80.
76. Babu TD, Kuttan G, Padikkala J. Cytotoxic and anti-tumour properties of certain taxa of Umbelliferae with special reference to *Centella asiatica* (L.) Urban. J Ethnopharmacol. 1995;48:53–7.