

A Comprehensive Overview of *Bacopa monnieri* Taxonomy, Constituents, Bioactivities, Herbal Formulations and Clinical Trials

Vishal Thakur¹, Vishnu Das¹, Shruti Thakur^{1,2,*}, Bharat Kumar¹, Muskan Singh¹

¹School of Pharmaceutical Sciences, Bahra University, Solan, Himachal Pradesh, INDIA.

²Chitkara College of Pharmacy, Chitkara University, Rajpura, Punjab, INDIA.

ABSTRACT

B. monnieri, an herbal plant also referred to as brahmi, is an herb with medicinal and pharmacological active plant in traditional Indian medicinal history which has been broadly used in the an ancient ayurveda for improving memory, cognitive function, and neurological health. Brahmi is an ancient medicinal plant which used to prepare herbal formulations like brahmi ghritam, brahmi rasadi tailam, bacognize®, and bacomind®, which traditionally use in India for enhance memory and cognitive functions. This article provides a complete overview of *B. monnieri* taxonomy, ethnomedicinal uses, phytochemical constituents and their bioactivities, herbal formulation and clinical trials. The review focus on the basic cellular mechanisms responsible for its neuronal protective, antioxidant, oncoprotective, anti-alzheimer, anti-emetic, as well as cardioprotective activities along with major phytochemical constituents present in *B. monnieri* like bacoside A, bacoside B, luteolin, quercetin, β -sitosterol, betulinic acid, and stigmastanol. Recent clinical trial studies identified the cognitive, neurological, and physiological effects of *B. monnieri* which act as the scientific evidence proving its therapeutic potential. Overall, this review combines all information of *B. monnieri* phytochemistry, pharmacological activities, and clinical significance, which help to focus on its importance as a promising medicinal active plant.

Keywords: *Bacopa monnieri*, Bacosides, Medicinal Herb, Neuroprotective, Phytochemical Constituents.

Correspondence:

Ms. Shruti Thakur

Assistant Professor, Department of
Pharmaceutical Chemistry, School
of Pharmaceutical Sciences, Bahra
University, Solan-173234,
Himachal Pradesh, INDIA.
Email: shrutithakur0704@gmail.com

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INTRODUCTION

B. monnieri is a creeper, glabrous and aquatic herb, belongs to family Plantaginaceae.^[1] In Sanskrit it also known as aindri and brahmi. It found in wet lands of India, Indochina, Australia and Sri Lanka at altitude high up to 1500 meters.^[2] It has small oblong leaves and white to purple flowers and green cylindrical stem. It also named as Jalnam, Brahmi buti, Sarasvati, ambarenu, Sambrani Neerbrahmi, Bamaneveri, Mandukaparni, water hyssop and thyme leaved gratiola. Brahmi is known as Medhya rasayana in ayurveda. Medhya rasayana is a special class of medication in ayurveda used for rejuvenation of brain, memory sharpening and to enhance brain functioning.^[3] The taxonomical classification of *B. monnieri* is given in Table 1.

Traditional and ethnopharmacological uses

B. monnieri traditionally used for treating anxiety, epilepsy, insomnia, inflammation, asthma, and skin disorders, with written an ancient text like Charaka Samhita (circa 1000 BCE).^[4] Ethnopharmacologically, it shows activity as a sedative, analgesic, antipyretic, and diuretic in Indian, Sri Lankan, and Southeast Asian traditional medicine.^[5] Ethnomedicinal uses of *B. monnieri* by several native communities in India are classified in Table 2.

Botanical overview

B. monnieri is a creeping herb commonly found in warm and marshy wetland areas including the Indian subcontinent, Australia, East Asia, and the United States. The plant characterized by small leaves and white to pale purple flowers, a maximum height of about 90 cm, thin green stem and root nearly 1 mm thick.^[6,7] The genus *Bacopa* contains more than 100 plant species.^[7] This plant grows to a height of 6 inches and its branches move horizontally and cover the ground.^[8] It has coin shaped green leaves with little marks over them. It grows in the group of two or three on a hairy stem. It has tiny, white and purple in colour flowers, it grows all the year. Because its ability to grow in water it is also called water aquarium plant.^[9]



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Morphology of *B. monnieri*

Leaf - The leaves are arranged in a decussate leaf arrangement and are simple and opposite. They are obovate to spoon shaped (spatulate) in shape of size approximately 0.6 to 2.5 cm in length and 3 to 8 mm in width. The leaves are nearly smooth, hairless and without a stalk and its lower surface showing fine dotted pattern and a light green shade.

Flower - The flowers are single and arises from the leaf axil with pale blue or pinkish white colour. They are generally longer than the leaves and have size of 0.6 to 3 centimetre in length. Each flower consists of a pair of narrow bracteoles, thin and elongated flower stalk, smooth calyx, sympetalous corolla with five deep lobes, four stamens in unequal pairs, and two celled anthers, bilocular fused ovary, numerous ovules and two lobed stigmas.

Fruit - Encased in a persistent calyx, the globose to ovoid, glabrous capsule is 5 mm long and reddish when fresh.

Seed - Many, tiny, oblong or irregular, less than 1 cm across.

Root - The dried bacopa roots are cylindrical in shape, wrinkled, off white in colour and about 5mm in diameter.

Stem - The stem is composed of cylindrical, glabrous pieces with noticeable nodes that are joined to a cluster of brittles, convoluted roots ventrally and at places with vertically developing branches. The stem segments are of size about 1 to 1.5 cm in length and 3 to 4mm in diameter and are light yellowish green in colour with slight purple tint.^[10]

Phytochemical constituent

Triterpenoid saponin and bacosides A and B are the most bioactive components of *B. monnieri*. The most important in between them is Bacoside A. Bacosides A1 and A3 and Bacopasaponin A, Bacopasaponin B, Bacopasaponin C, Bacopasaponin D, Bacopasaponin E, and Bacopasaponin F are the examples of bacopa saponins. Alkaloid like herpestine and brahmin and flavonoids like luteolin 7 glucoside, glucuronyl 7 apigenin, and glucuronyl 7 luteolin are found in minor quantity in *B. monnieri*.^[10] The pharmaceutical constituents and their bioactivities are classified in Table 3. The structural information of all pharmaceutical compounds is shown in Figure 1.

Cellular mechanism

Neuroprotective activity

Bacosides extracted from *B. monnieri* extract successfully demonstrate a healthy antioxidant activity in a variety of human tissue particularly the brain and liver. Bacosides help to achieve the physiological function by suppressing oxidative stress by blocking free radicals, oxidising lipids and promoting antioxidant enzymes. The regulation of mRNA translation and the cell surface expression of neuro receptors including AMPA, NMDA and

GABA receptors in various brain regions is caused by the neuro protective effect of bacosides.^[11]

Antioxidant activity

By using phosphomolybdate assay the relative antioxidant properties of five distinct extract of *B. monnieri* stem were identify using ethanol, acetone, chloroform, petroleum ether and distilled water. In addition to measuring oxidative defence enzymes including superoxide dismutase, catalase, peroxidase, ascorbate oxidase and polyphenol oxidase confirms the fresh stem of *B. monnieri* extract was assessed for chlorophyll and iron content using the thiocyanate method and acetone technique. The studies indicate that the *B. monnieri* has excellent enzymatic defence mechanism and oxidative stress reduction activity deliver a potent preventive effect against illness linked to ROS.^[12]

Anticancer activity

B. monnieri leave extract using different solvent has effective antimetastatic and antiangiogenic and antiproliferated properties.^[13] The ethanol extract of *B. monnieri* contains betulinic acid, cucurbitacins, brahmin and bacoside A and bacoside B. By resulting cell cycle arrest at the G2/M phase cucurbitacins were also known to have potent antitumor and antiproliferative effect.^[14] The terpenoidsaponin bacopaside I and bacopaside II which are present in *B. monnieri* can work in help to block AQP1 biological activity which used to help in the growth of tumor. In breast cancer cell line, it used to stimulate migration, invasion and proliferation via blocking AQP1.^[15]

Anti-emetic activity

The Anti emetic property of *B. monnieri* methanolic and butanolic extract were examined using chemotherapy induced emesis suncus murinus. Cisplatin 30mg per kg is administered into animal to stimulate vomiting. The antiemetic effect of methanolic extract and butanolic extract at multiple doses was tested. Methanolic extract reduced the vomiting by 71% on other hand butanolic extract reduced vomiting by 59.4%.^[16]

Cardioprotective Activity

B. monnieri act as an important cardio protectant and cerebro protectant because its ability to recover the contractile function,

Table 1: Taxonomy classification.^[23]

Taxonomical Rank	Botanical Classification
Kingdom	Plantae
Class	Magnoliopsida
Division	Tracheophyta
Species	<i>Bacopa monnieri</i>
Order	Lamiales
Genus	Bacopa
Family	Plantaginaceae

coronary flow and by reducing infarct volume.^[17] By improving total glutathione levels and antioxidant enzymes it restores the movement of Nrf2, HO-1, and NQO1 which used to maintain the myocardial integrity and cardiac rhythm.^[18]

Herbal formulations

Brahmi ghrita - The 400 g of Puran ghrita was first cooked and then allowed to cool at room temperature. Puran ghrita was blend together to form a homogeneous mixture of fresh brahmi paste and 100 g of *Elettaria cardamomum* powder. In this blend, 1600 mL of water were added. The entire blend was heated until all of the water was evaporated and all the substance get moisture free and ayurvedic testing criteria were fulfilled. Then the mixture was filtered and used in treatment of behavioural and mental illness.^[19]

Brahmi rasadi taila - 1 part of coconut oil is taken as the base and brahmi juice taken 4 times the coconut oil. The fresh juice together is taken as $\frac{1}{4}$ th of oil. Oil cooked till attaining dry hard stage. It is used to promote the hair growth, improve cognitive function.^[20]

BacoMind™- *B. monnieri* commonly referred as brahmi is the source of the structured phytochemical compounds known as BacoMind™. The chemical in the BacoMind™ formulation

contains nine unique bioactive ingredients derived from *B. monnieri*.^[21]

Bacognize® - Bacognize® is the powder made from *B. monnieri* extract that is greenish brown to brown in colour and has a total glycoside content of 12.04%.^[22]

Clinical trials

B. monnieri potential got checked in various clinical trials regarding its properties like overall cognitive enhancement by N100 and P300 modulation, improve short term memory problems, reduce vascular oxidative stress, improve endothelial functions, reduce anxiety and improve ADME profile. The detailed clinical trial studies and their results are classified in Table 4.

DISCUSSION

B. monnieri is an important medicinal herb that have strong potential for future medicinal research due to its broad phytochemical profile and wide range of therapeutical activities. New experiments and clinical studies prove that phytochemical compounds present in *B. monnieri* may help in improvement of plant derived drugs, especially for CNS, chronic dysfunction and cancer. Still, more researches are needed to clearly understand its molecular mechanisms, standardized formulations, and

Table 2: Ethnomedicinal uses of *B. monnieri* by several native communities in India.^[24-29]

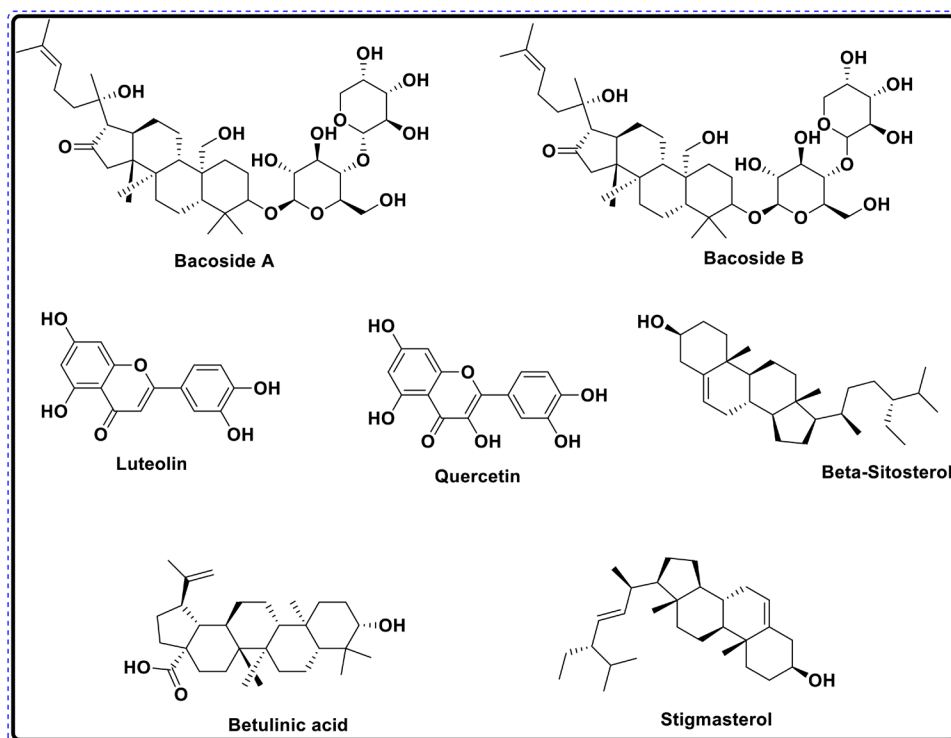
State	Native groups	Parts used	Type of uses	References
Andra Pradesh	Yanadis	Whole plant	Used to treat nervous debility and to make brain tonic	[24]
Chhattisgarh		Whole plant	Used to treat snake bite, nerve tonic and asthma	[25]
Jammu and Kashmir	Gujjar and Bakerwal	Leaves	Used to cure stomach ache	[26]
Jharkhand	Kharia, Savar, Gond, and Kol	Leaves	To treat skin disease	[27]
Kerala	Kattunaikkans	Whole Plant	To treat epilepsy	[28]
Maharashtra	Madhiya and Gond	Whole plant	To treat fever, diarrhea and abdominal diseases	[29]

Table 3: List of pharmaceutical constituents and their bioactivities.^[30-38]

Chemical constituents	Pharmacological activity	References
Bacoside A	Anti-inflammatory, Anti-hypertensive, Anti-tumour activity.	[30,31]
Bacoside B	Neuro-protective and Anti-inflammatory activity and maintains neurotransmitter balance in body.	[30,31]
Luteolin	Anti-inflammatory and analgesic effect	[32]
Quercetin	Anti-inflammatory and anti-hypertensive activity.	[33]
β- Sitosterol	Reduces cholesterol levels in body and Anti-inflammatory activity.	[34]
Betulinic acid	Anti-cancer, anti-inflammatory, and anti-diabetic activity.	[35,36]
Stigmasterol	Anti-tumor, anti-inflammatory.	[37,38]

Table 4: List of clinical trial studies. [39-43]

Study Design	Population and Sample Size	Dose and Duration	Primary Outcomes	Secondary Outcomes	References
Double-blind, randomized controlled trial	7 - 12 years school children	Bacopa extract with multiple micronutrient vs placebo for 4 months	Improve short term memory problem	Over all cognitive enhancement	[39]
Double-blind, placebo controlled	40 Healthy volunteers, 2 groups in which 20 volunteers in each group	<i>B. monnieri</i> 320 mg/day vs placebo for 3 months treatment with 1 month follow up	Reduce vascular oxidative stress	Improve endothelial functions	[40]
Open single site trial	Healthy adults	Bacopa oral tablets (1 tablet a day increased to 2 tablets a day) for 12 weeks	Change in BDNF levels	Improve cognitive performance, depression scores and acceptability	[41]
Controlled study	Students	<i>B. monnieri</i> vs control	Improve working memory	Improve cognitive processing by N100 and P300 modulation	[42]
A Double-blind, placebo controlled, Randomised study	Fit adult volunteers	<i>B. monnieri</i> vs placebo for 12 weeks and 1 month follow up	Improve cognitive function	Reduce anxiety, improve ADME profile	[43]

**Figure 1:** *B. monnieri* derived phytochemical compounds. [30-38]

to confirm its long-term safety and effectiveness profile by well-designed clinical trial studies. Continued research on its phytochemistry, pharmacology, and clinical investigation may help in the development of new pharmaceutical drugs derived from *B. monnieri* to cure various disorder.

CONCLUSION

B. monnieri is an ancient medicinal herb which show neuroprotective, antioxidant and cognitive enhancing properties. There are various clinical trials and research studies that show its potential in improving memory, reducing oxidative stress and maintain overall brain health but to establish its standardised

doses and long-term safety we still need further studies and clinical research.

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ABBREVIATIONS

BCE: Before common era; **AMPA**: α -Amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid; **NMDA**: N-methyl-D-aspartate; **GABA**: Gamma-aminobutyric acid; **ROS**: Reactive oxygen species; **Nrf2**: nuclear factor erythroid 2-related factor 2; **HO-1**: Heme oxygenase-1; **NQO1**: NAD(P)H Quinone dehydrogenase 1; **ADME**- Absorption, distribution, metabolism and excretion; **CNS**: Central nervous system; **AQP-1**: Aquaporin-1; **BDNF**: Brain-derived neurotrophic factor; **mRNA**: messenger ribonucleic acid; **G2/M**: Gap 2/mitosis phase.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS CONTRIBUTION

Vishal Thakur: Conceptualization, literature survey and original draft preparation. **Shruti Thakur and Vishnu Das**: Supervision, conceptual guidance, critical revision and final approval of manuscript. **Bharat Kumar and Muskan Singh**: Literature survey, editing and assistance in manuscript preparation.

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