

## Brahmi (*Bacopa monnieri*): A potent cognition-enhancing drug of unani system of medicine

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### Abstract

In the folklore of Indian medicine, several herbs have been used traditionally as brain or nerve tonics. One of the most popular of these neurotonics is Brahmi (*Bacopa monnieri*), a well-known memory booster. *Bacopa monnieri* (family: Scrophulariaceae) is used in traditional medicine to treat various nervous disorders and as a Brain tonic for enhancing memory, intellect and to provide relief in anxiety or epileptic disorders. It is a small, creeping succulent herb. The leaf and flower bearing stems are 10-30 cm long and arise from creeping stems that form roots at the nodes with pale blue or pinkish white flowers and grown nearly banks of freshwater streams and ponds, paddy fields, and other damp places. Traditionally in Unani system of medicine it has been used since long time to treat various diseases such as Epilepsy, Depression, anxiety, hysteria etc. Modern phytochemical evaluation of *brahmi* revealed that it contains brahmine, herpestine, bacoside A & B and saponins as the chief phytoconstituents. Bacoside A, B are the major constituents present in *Brahmi* plant in the form of saponins other than this D- mannitol, hersaponin and potassium salts are also present. *Bacopa*'s antioxidant properties may offer protection from free radical damage in cardiovascular disease. Neuropharmacological effect have been shown by isolated Bacoside and number of reports are available showing nootropic action.

**Keywords:** bacoside, brahmi, brain tonic

### Introduction

The use of herbal medicine is increasing tremendously in the developed as well as in the developing countries [1]. Mental illness has become a major problem world-wide. The herbal medicine shows hope for such patients suffering from mental illness like depression, insomnia, anxiety, loss of memory, loss of concentration etc [2]. Herbal medicines are traditionally used as nerve and brain tonics. *Bacopa monnieri* is one of the most popularly known drugs used for the treatment of hysteria, anxiety, epilepsy, insomnia, depression etc. [3]. *Bacopa monnieri* Linn. Belongs to Scrophulariaceae family. It is a small creeping herb having light purple flowers and oblong leaves. In summer fruits and flowers appear. The whole plant is used medicinally [4-6]. Traditionally it is known as "Brahmi". It grows at high altitude of about 4,400 feet and grows in wet soil naturally [7]. It improves mental function and enhance memory have been shown by preclinical and clinical studies [8]. The use of the drug is reported as anti-inflammatory, anticonvulsant, cardiogenic, Bronchodilator and used in Epilepsy amnesia, constipation, ulcer, sterility. It also helps in overcoming the problem of depression [4-6, 19]. The component of *B. monnieri* extract believed to help in neuronal synthesis, restoration of synaptic activity and repair of damaged neurons and stress decreasing activity also shown in both acute and chronic stress conditions [9]. The nootropic function has been reported on chronic administration of extract of *B. monnieri* on healthy human subjects [10]. It has been shown to have

anticancer, vasodilator, antiulcer, antiaddictive property [11-16].

### Taxonomical classification [17, 18]

Kingdom: Plantae  
Division: Angiospermae  
Class: Dicotyledonae  
Order: Tubiflorae  
Family: Scrophulariaceae  
Genus: *Bacopa*  
Species: *Monnieri* Linn.

### Vernacular names [19, 20, 83]

Bengali: Adhabirni, brahmisak, dhopchamni, jalanimba  
English: *Bacopa*, thyme-leaved gratiola  
Gujrati: Kadaviluni  
Hindi: Barambhi, brahmi, safedchanmi  
Kannada: Neer brahmi, nirubrahmi  
Malayalam: Brahmi, nirbrahmi, nirubrahmi  
Marathi: Neerbrahmi  
Sanskrit: Brahmi, nira-brahmi  
Tamil: Brahmi, nirbrahmi, nirprimi  
Telgu: Sambrabichettu  
Urdu: Jalanim, nirabrahmi.

### Description of Plant

*Bacopa monnieri* (L.) is a member of family Scrophulariaceae.

B. Monnieri is a small, creeping, glabrous, somewhat succulent herb; rooting at nodes; leaves simple, opposite, obovate-oblong, obtuse, entire, to 2x1cm; flowers pale violet, axillary, solitary on long pedicles; calyx 5-partite, lobes unequal; corolla gamopetalous, funnel-like, white or pinkish with purple blotches<sup>[21]</sup>. The plant is found in wet, marshy and damp places throughout India and, therefore, known as Jalbrahmi or Nirbrahmi<sup>[19, 22]</sup>. It is also found in Nepal, Srilanka, China, Taiwan, Vietnam, Florida and Southern states of USA. It is widely distributed in warmer parts of Asia, Australia, America<sup>[23]</sup>. The herb can be found at an altitude of 4,400 feet, and can easily be cultivated if adequate water is available. Flowers and fruit appear in summer and the entire plant is used for medicinal purpose<sup>[24]</sup>.

### Macroscopic characters

The plant is succulent when fresh but on drying it becomes shriveled. It does not have any characteristic odor but have slightly bitter taste and composed of crumpled, matted broken pieces of roots, branching stems, leaves, flowers, and few tender fruits<sup>[25, 26]</sup>. Dried main roots fragments are cylindrical in shape, about 5 mm in diameter, wrinkled longitudinally.

Leaves are simple, opposite, sessile, obovate oblong to spatulate in shape with length of 0.6-2.5 cm and width of about 3-8mm. The lower surface of the leaf is dotted with minute specks<sup>[27]</sup>. Stems pieces are cylindrical with prominent nodes, at places attached with vertically growing branches and ventrally to cluster of tortuous, brittle roots, internodes about 1-1.5 cm in length and 3-4 mm in diameter, pale yellowish green and with purplish tinge. The flowers are pinkish white or pale blue in color, solitary, axillary and approximately 0.6-3 cm in length. longer than the leaves with two linear bracteoles, pedicel slender, calyx glabrous, deeply 5 partite Corolla gamopetalous, stamens 4, didynamous, anthers 2 celled, pistil carpel, syncarpous ovary two chambered with many ovules, style dilated toward the top, stigma-bilobed<sup>[28, 29]</sup>. Fruits are long purplish when fresh, Globose to ovoid, glabrous capsule, 5 mm in length, enclosed within persistent calyx, ped 1-3 cm. Seeds are very minute <1cm wide, numerous, irregular or oblong.

### Microscopic characters

The root is irregularly circular to angular in shape and show an outermost piliferous layer, parenchymatous cortex with intervening air spaces. The xylem is centrally located encircled by narrow phloem. The piliferous layer is replaced by formation of cork cells, cortex is wide, parenchymatous, traversed with simple and compound starch grain intervened with air spaces, endodermis is distinct, a narrow band of phloem surrounding the located solid core of xylem composed of radially arranged isolated vessels, fibers, and medullary rays<sup>[30]</sup>.

The stem is almost circular, shows outer epidermis, broad aerenchymatous cortex occupying the major area of the section, a distinct endodermis encircling the ring of stellar tissue and central parenchymatous pith with a layer of thick-walled celled epidermis covered with thin cuticle, cortex is very wide, consisting of chlorenchymatous aerenchyma embedded with starch grains, endodermis is distinct, encircling the narrow band of parenchymatous phloem and xylem, the central region being occupied by narrow parenchymatous pith embedded with simple and compound

starch grains. The leaf passing through the midrib is almost cylindrical in outline and a very narrow elevation is present on the upper side of the midrib. Leaf shows upper and lower epidermis, the cells of the upper being bigger in size and at places show striated cuticle, both the epidermis are embedded with stomata and bear sessile-glandular trichomes with multi cellular head. A narrow collenchymatous band is located underneath both the epidermis of the midrib and shows a centrally located conjoint collateral meristele encircled by a parenchymatous sheath. The mesophyll tissue of the lamina is composed of spongy parenchyma, traversed with vascular strands; prismatic and few cluster crystals of calcium oxalate are embedded throughout the parenchymatous cells of the leaf<sup>[29, 31]</sup>.

Powder Shows upper and lower epidermis fragments of leaf in surface view embedded with sessile-glandular trichomes with 4-8 celled head and diacytic to anomocytic stomata, they being more on the lower side and at places shows prismatic, cluster crystals of calcium oxalate ;striated cuticle, starch grains and oil globules scattered as such throughout or embedded in the parenchymatous cells, fragments of longitudinally cut annular and spiral vessels, transversely cut fragments of stem showing papillose marginal cells of the petal, aerenchymatous cortical cells, testa of the seed in surface view and transversely cut fragments of cotyledon<sup>[32]</sup>.

**Mizaj (Temperament):** Hot 2<sup>0</sup> and according to some Unani physicians it is Cold-Dry<sup>[33, 82]</sup>

**Nafa-e-khas (Important Actions):** Mufarrah & Muqawwi e Aaza Raisa (Exhilarant & Tonic for principal organs)<sup>[33, 82]</sup>

**Muzir (Toxic):** Harmful for people with hot temperament<sup>[33]</sup>

**Musleh (Correctives):** Corriandrum sativum (Dhanya khushk)<sup>[33, 82]</sup>

**Badal (Alternative):** Darchini (Cinnamomum zeylanicum), kababa (Zanthoxyhim alatum), Taj<sup>[33, 82]</sup>

**Miqdar-e-Khurak (Dose):** 3-5 g<sup>[33]</sup>

### Pharmacological actions & indications in Unani System of Medicine

1. Mirgi (Epilepsy)<sup>[19, 34, 35]</sup>.
2. Khafkan (Palpitation)<sup>[34]</sup>.
3. Balgami bukhar (Fever)<sup>[34]</sup>.
4. Hazim (Digestive)<sup>[34]</sup>.
5. Increase Quwaat e hafza (Memory Enhancer)<sup>[36, 33]</sup>.
6. Mudir e baul (Diuretic)<sup>[19, 36]</sup>.
7. Aatshak (Syphilis)<sup>[36]</sup>.
8. Muqawwi e dimag (Brain tonic)<sup>[36, 33]</sup>.
9. Decreases Safra and balgam<sup>[36]</sup>.
10. Mudammil e Qurooh (Cicatrizant)<sup>[36]</sup>.
11. Zukam (Coryza)<sup>[36]</sup>.
12. Khansi (Cough)<sup>[36]</sup>.
13. Jiryane Mani (Spermatorrhoea)<sup>[33]</sup>.
14. Muqawi e Aaza e Raisa (Tonic for principal organs)<sup>[33]</sup>.
15. Malekhulia (Depression)<sup>[19, 35]</sup>.
16. Hysteria (Ikhtenaq-ur-Rahem)<sup>[35]</sup>.

17. Insanity (Junoon) [19, 35, 36].
18. Zeeq-un-Nafas (Asthma) [35, 19, 37].
19. Nihayt Mulattif (Demulcent) [38].
20. Qabz (Constipation) [38].
21. Muqawwi e meda (stomachic) [38].
22. Muqawwi jigar (Liver tonic) [38].
23. Musakkin-e- alam (Analgesic) [38].
24. Mufarraah (Exhilarant) [38].
25. Mullayan (Laxative) [19, 37].
26. Muqawwi e Qalb or Aasab (Heart and Nerve tonic) [19, 37].
27. Quba (Dermatosis) [19].
28. Faqr-ud-dam (Anemia) [19].
29. Ziabitus shakri (Diabetes) [19].
30. Su-e-Hazm (Dyspepsia) [19].
31. Waram-e-Mafasil (Arthritis) [19, 37].
32. Muqawwi e Qalb (Cardiac Stimulant) [37].

## Pharmacological Actions

### Anti-asthmatic activity

The extract of *Bacopa monnieri* possess relaxant properties in tracheal muscle of guinea-pigs and rabbit with a partial contribution by prostaglandins and (beta)-adrenoreceptor [39]. In anaesthetized rats it produces broncho dilation [7] supported the traditional use of this plant in various respiratory ailments [13]. The antagonism of carbachol-induced effects reflects bronchodilator property of extract on inspiratory and expiratory pressures. Extract exhibited a dual action on broncho-constriction induced by carbachol. At low doses (25 and 37 mg/kg), predominantly inhibited inspiratory pressure, but at a high dose (50 mg/kg) inhibited only expiratory pressure. This property of the plant extract implies that more than one mechanism of action may be responsible for broncho-dilation. Some of the possible mechanisms include (beta)-adrenoreceptor activation, muscarinic receptor antagonism, prostaglandin release or interference with calcium mobilization.

### Anti-convulsive activity

In Traditional medicine, *Bacopa* has been indicated as a remedy for epilepsy and showed anticonvulsant activity at high doses over extended periods of time. It have also been reported that crude water extract of *BM* controls epilepsy in experimental animals [32]. It naturally exhibited sedative effect and significantly prolonged hypnotic action of phenobarbitone. Those substances which stimulate GABA are known to possess pain relieving, anticonvulsant and sedative effects [40]. It suggests the involvement of GABA-ergic system in mediation of central nervous system [41]. *BM* was evaluated alone and in combination with phenytoin (PHT) for its effect on PA task, maximal electroshock seizures and locomotors activity in mice [42]. Both acquisition and retention of memory showed improvement without affecting PHT anti-convulsive activity.

### Anti-cancer activity

Pretreatment with *BM* significantly reduced the acute stress increase in the ulcer index, adrenal gland weight, plasma glucose, aspartate aminotransferase (AST), and creatine kinase (CK) [9] in cancerous patients. Bacosides present in *BM* have anti-cancerous activity. Methanolic extract exhibited potent mast cell stabilizer activity [43]. *Bacopa monnieri* is also a known hyper accumulator of chromium, cadmium, lead & mercury and used for Phyto remedy [44].

### Antidepressant activity

In a study antidepressant potential of methanolic extract of *BM*, was evaluated in rodents. Oral extract at a dose of 20 and 40mg/kg was given for 5 days and showed significant antidepressant activity in forced swim and learned helplessness models of depression and was comparable to that of imipramine [12].

### Anti-inflammatory activity

*Bacopa monnieri* has the ability to inhibit inflammation through modulation of pro-inflammatory mediator release [45]. In traditional medicine, it possesses significant anti-inflammatory activity are relevant to its effectiveness in the healing of various inflammatory conditions [46]. It also significantly inhibited 5-lipoxygenase (5-LOX), 15-LOX and cyclooxygenase-2 (COX-2) activities [47]. This activity may be due to presence of the bacosides and triterpenoids in it.

### Anti-nociceptive activity

Aqueous extract of *Bacopa monnieri* (AEBM) exhibits analgesic activity through multiple pain pathways [48] i.e. involvement of  $\beta$ 1-adrenergic,  $\alpha$ 2 -adrenergic receptors and 5-HT receptors in analgesic activity. It has also been observed that when AEBM was given in combination with naloxone did not increase the latency for analgesic effect, which indicates involvement of opioid receptors in analgesic activity.

### Antioxidant activity

Alcoholic and hexane extract of *BM* have antioxidant properties [44] by inhibiting lipid peroxidation. A more recent study explored antioxidant effect of *BM* by other mechanism like inhibition of superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPX) activities [49]. It was also observed that the hydro alcoholic extract of the whole *BM* plant exhibited an inhibitory effect on superoxide released from polymorphonuclear cells in nitro blue assay [50].

Methanolic extract *BM* is able to directly inhibit the superoxide anion formation in a dose-dependent manner due to this it reduces concentrations of nitric oxide (NO), generated (enzymatic and non-enzymatic) by activated astrocytes, might be involved in a variety of neurodegenerative diseases, such as ischemia and epilepsy [51, 52].

### Anti-stress activity

*BM* Standardized extract possesses an adaptogenic activity. In low dose of *BM* extract, Pretreatment significantly reversed the changes in ulcer index and plasma AST only, whereas in higher dose, the pretreatment significantly reversed changes in ulcer index, adrenal gland weight, CK, and AST [53].

### Anti-spasmodic activity

*BM* extract have spasmolytic activity in smooth muscles due to inhibition of calcium influx via both voltage and receptor-operated calcium channels of the cell membrane [54].

However, the absence of any modification of either nor-adrenaline or caffeine-induced contractions in the presence of *BM* extract suggests that this natural compound has no detectable effect on mobilization of intracellular calcium.

### Anxiolytic effect

BM extract in higher doses produced significantly greater anxiolytic effects compared to lorazepam (LZP) [55]. However, BM has a distinct advantage over LZP since it does not induce amnesia and has a memory-promoting action in animals and man [56, 57]. These results were also observed by Shanker and Singh and reported that BM extract possessed an anxiolytic effect [58].

### Cardiovascular activity

Ethanol extract of BM, shown cardiac depressant activity on coronary flow, left ventricular contractility and heart rate in isolated rabbit heart [59]. It also demonstrated that protective effect of BM on aorta and pulmonary artery [15].

### Gastroprotective activity

*Bacopa monneri* extract have anti-ulcer and ulcer-healing properties, which may be due to its effects on various mucosal defensive factors such as enhanced mucin secretion, mucosal glycoprotein and decreased cell shedding, rather than on offensive factors such as acid and pepsin [60]. It also have beneficial role in intestinal spasm such as irritable bowel syndrome [13]. It may be due to spasmolytic activity on intestinal smooth muscle, via inhibition of calcium influx across cell membrane channels. Fresh BM juice (BMJ) and BM extract has been reported to have significant anti ulcerogenic activity [61, 62, 63].

### Hepatoprotective activity

The alcoholic extract of BM on morphine treated Rats has been investigated for hepato-protective activity [64]. BM extract has shown to possess a significant protective effect in pretreatment against morphine-induced liver and kidney functions in terms of serum glutamate oxaloacetate transaminase, serum glutamate pyruvate transaminase, alkaline phosphatase, lactate dehydrogenase and gamma-glutamyl transferase activities and urea, creatinine and uric acid level respectively [65]. The elevation of LPO (Lipid Peroxidase) can be prevented by Pretreatment of Bacoside and activity of serum marker enzymes and maintains the antioxidant system and thus protects the rats from Diethyl nitrosamine-induced hepatic toxicity [66].

### Learning and memory

Isolated Bacosides have been investigated for their neuro-pharmacological effects and number of reports are available confirming their Nootropic action. Preliminary studies established that treatment with plant [67] or alcoholic extract of BM plant [68] enhanced learning ability in rats. Subsequent studies indicated that the cognition-facilitating effect was due to presence of Bacosides A and B, in ethanol extract [57]. These active principles inhibit the amnesic effects of scopolamine, electroshock and immobilization stress apart from facilitating learning and memory in normal rats [58]. The mechanism of these pharmacological actions remains conjectural. Bacosides induce membrane dephosphorylation, with concomitant increase in protein and RNA turnover in specific brain areas has also been suggested [69]. Enhanced protein kinase activity of BM in hippocampus have been shown, which could also contribute to its nootropic action [70]. BM administration for two weeks, also reversed the depletion of acetylcholine, the reduction in acetyl cholinesterase activity and the decrease in muscarinic cholinergic receptor binding in the frontal

cortex and hippocampus, induced by neurotoxin, colchicines [71]. It has been suggested that the behavioural effects of cholinergic degeneration can be alleviated by a reduction in noradrenergic function [72]. BM is known to lower norepinephrine and increase 5-hydroxytryptamine levels in the hippocampus, hypothalamus and cerebral cortex [70], thus BM indirectly, modify Ach concentrations.

### Phytochemistry

The systematic chemical examinations of the plant have been carried out by several groups of researchers. Isolation of the alkaloid "*Brahmi*" from *Bacopa monneri* (BM) and other alkaloids like nicotine and herpestine have also been reported [73]. It was found highly toxic, when administered at a dose of 0.5 mg/kg body weight of cat, it produces a fall in the blood pressure. In therapeutic doses its action resembles with action of strychnine chemical. The isolation of D-mannitol, saponins, hirsaponin and potassium salts by Sastri provided further details of the chemical components of BM [74]. The major chemical entity shown to be responsible for the memory-facilitating action of BM, Bacoside A, was assigned as 3-((alpha)-L-arabinopyranosyl)-O-(beta)-D-glucopyranoside-10, 20-dihydroxy-16-keto-dammar-24-ene [75]. It usually co-occurs with Bacoside B, the latter differ to each other only in optical [76]. Bacosides A and B possess haemolytic activity. On acid hydrolysis, Bacosides yield a mixture of aglycones, bacogenin [77], and two genuine saponins, jujubogenin and pseudojujubogenin [78]. In addition, same authors isolated three new saponins from BM, designated as bacopasides III, IV and V [79]. Moreover, three new phenylethnoid glycosides, viz. monnerisides I-III along with the known analogue plantainoside B have been isolated from the glycoside fraction of BM [80]. Analysis of the leaves and stalks exposed, moisture 88.4; protein 2.1: fat 0.6; carbohydrates 5.9; crude fibre 1.05; ash 1.9 g / 100gm, calcium 202.0; phosphorus 16.0; iron 7.8; ascorbic acid 63.0; nicotinic acid 0.3 mg /100 g; and energy 38 cal / 100 g. The leaves contain a sterol C<sub>26</sub> H<sub>46</sub>O.H<sub>2</sub>O, m p 76 0) [81].

### Conclusions

*Brahmi* has long been used in Unani System of Medicine as a remedy for various neurological disorders. Tonic to the vital organs, memory enhancer and exhilarant are some of its potent pharmacological actions mentioned in classical Unani literature. On the basis of these actions it has been used for treating different diseases of brain since antiquity. Most of the recent scientific studies also prove the classical claims. Experimental studies show its anti-convulsive, anti-depressant, anti-nociceptive etc. potential. The major chemical entities shown to be responsible for the memory-facilitating action of *Bacopa monneri* are Bacosides A and B. Despite the fact that lots of works have been done on it but still there is a wide scope to explore its other medicinal and useful properties.

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