



Ethnopharmacological profile of brahmi (*Bacopa monnieri*)

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Abstract

Brahmi (*Bacopa monnieri*) is a small creeper belongs to a family called Scrophulariaceae which grows in dank and waterlogged places. The herb is embraced with several medicinal properties like anti-oxidative, antitumor, analgesic, anti-inflammatory and so on. An attempt has been made to recapitulate the features of Brahmi in medicinal uses. Many review papers had been searched to reveal the alleviating effects of this wonder drug. This review suggests that there is a requisite for further clinical studies to confirm the effects of Brahmi and use it in different ailments, to circumvent the aftermath of conventional panacea and achieve a safe and natural management of many diseases leading to a healthy nation. Brahmi has been recorded to be used as *Muqawwi Damagh* (brain tonic), *Muqawwi Asaab* (nervine tonic), *Musakkin* (sedative), *Muqawwi Hafiza* (strengthen to memory).

Keywords: brahmi, *Muqawwi damagh*, *Muqawwi asaab*, *Musakkin*, *Muqawwi hafiza*

Introduction

Bacopa monnieri (Brahmi) is a small creeper belonging to a family called Scrophulariaceae which grows in dank and waterlogged places. The herb is embraced with several medicinal properties like anti-oxidative, antitumor, analgesic, anti-inflammatory and so on. The plant is used in various health ailments like in Epilepsy, Dermatitis, Alzheimer's disease, Nervous disorders etc. Pre-clinical studies have reported Brahmi to be efficient in increasing the T4 concentration in male mice and increasing both T3 and T4 concentration, acting as thyroid stimulating agent, hence it can be used in underactive thyroid disorder. In the traditional system of medicine Brahmi is used as diuretic, cardiac and nervine tonic, aperient and to expel phlegm. Brahmi is reported to act as anti-fertility in male mice.

In Unani System of Medicine Brahmi has been a stardom among other drugs used in enhancing cognitive functions and memory due to its natural makeup. This natural Herbaceous plant obtained the interest of scientists to explore its biologically active constituents to produce evidenced based documents for further use of this herb in medical up gradation.

Brahmi has been recorded to be used as *muqawwi damagh* (brain tonic), *muqawwi asaab* (nervine tonic), *musakkin* (sedative), *muqawwi hafiza* (strengthen to memory). For *muqawwi damagh wa hafiza* it is use in powder form with milk and local application on head by mixing with other oils. Due to its nervine tonic effect, it is use in nervous disorders like *Nisyan* (Amnesia), *Sudaa* (Headache), *Junoon* (Mania) *Iktinaaq ur raham* (Hysteria). In *Sudaa* (Headache) and *Iktinaaq ur raham* (Hysteria) Brahmi is used in the form of *Joshanda* and along with other suitable drugs in *Jiryani mani* (Premature Ejaculation) [1]

In Ayurveda Brahmi has been known for its nervine tonic and memory boosting agent, for this reason it has been used in a number of mental disorders like insanity, amnesia,

anxiety, epilepsy. Brahmi has also been used as anti-inflammatory, analgesic, antipyretic and sedative. Now a number of clinical and preclinical studies had been carried out to validate its effectiveness and to reveal its active compounds which are responsible for prevention and management of various disorders leading to a healthy life. But these validations are not enough, some more randomised clinical trials are needed to confirm its safety and dose adjustment according to age. It has been mistaken for *Hydrocotyle Asiatic* because of its name same as Brahmi in Hindi [2]

The taxonomy of Brahmi (*Bacopa monnieri*) has been described in table-1

Habitat and distribution: Damp places, banks of fresh water streams, plain districts in India [3].

Vernacular names

Assam, Hindi, Mal. & Ori: Brahmi

Beng: Brijhmi-sak

Eng: Thyme leaved gratiola

Guj: Neerbrahmi, Bamanavari

Kan: Nirubrahmi, Valabrahmi

Mar: Jalnam, Brahmi, Birami

Punj: Brahmibuti

Tam: Nirabrahmi, Brahmi, Vazhukkai

Tel: Sambarenu, Sambarani

Ethno botanical description:

Roots: Cylindrical, off-white colour

Stem: noded, glabrous, purplish

Leaf: Decussate, sessile, obovate-oblong, faint green colour

Fig 1

Flower: Pale blue or pinkish white, stigma bilobed

Fruit: ovoid, glabrous capsule, purplish

Seed: irregular, minute, numerous [3]

Table 1: Taxonomy of Brahmi (*Bacopa monnieri*)

Kingdom	Plantae
Phylum	Tracheophyta
Class	Magnoliopsida
Order	Lamiales
Family	Plantaginaceae
Genus	<i>Bacopa</i>
Species	<i>Monnieri</i> ^d

Parts Used: Whole plant

Temperament: Hot 2° & Dry 2° or Cold 2° & Dry 2°^[5]

Functions: Cardiac and nervine tonic, Diuretic, Aperient, Expectorant of phlegm

Substitute: *Darchini* (Cinnamon), *Kababa* (Cubeb), *Taj* (Cassia bark)

Dose: 3-5 grams

Adverse effects: Hot temperament people

Compound formulations: *Majun barhmi*



Fig 1: Brahmi-*Bacopa monnieri* (Courtesy: NRIUM-SD, Hyd)

Evidence based scientific studies

In the Unani system of medicine Brahmi has been affirmed to improve behavioural and cognitive functions and act as nerve tonic along with some other qualities. This perspective has been scientifically tested through multiple clinical trials which are as follows.

Analgesic/antinociceptive and anti-inflammatory activity

- A preclinical study revealed inhibition of writhing by 37.37% at 250 mg/kg and 46.46% at 500 mg/kg body weight in writhing induced mice with methanol soluble extract of *Bacopa monnieri* as compared to diclofenac sodium with 62.22% at 25mg/kg^[6]
- Another preclinical study comparing morphine, diclofenac and hydroethanolic extract of *Bacopa monnieri* suggests consequential results as antinociceptives^[7]
- Another study in chronic constriction injury model of neuropathic pain in Male Sprague-Dawley rats recommends the presence of pronounced antinociceptive properties in bacosides rich fraction of *Bacopa monnieri*^[8]
- Studies revealed anti-inflammatory properties of various extracts of *Bacopa monnieri*. Mainly extracts of methanol and aqueous fractions (100 mg/kg) manifests a markable reduction in the oedema volume of carrageenan induced edema in rat's hind paw. The anti-inflammatory activity was assayed using Human red blood cell (HRBC) membrane stabilization method. Also, it revealed that methanolic extract produced membrane stabilization much better than diclofenac

sodium. The triterpenoids and bacosides present in BM impede pro-inflammatory cytokines like TNF-alpha and IL-6^[9]. The mechanism of reduction in inflammation is depicted through the flowchart below.

- The acetic acid induced writhing effect in mice after treated with ethanol extract of *Bacopa monnieri* at 250 mg/kg and 500mg/kg of dose manifested significant writhing inhibition as compared to diclofenac sodium^[9]
- *Bacopa monnieri* has been documented in an animal study to protect the organs and distant organs directly from ischemia reperfusion (I/R) injury through its anti-inflammatory and anti-nitrosative activities^[10]. An *in vitro* cell line study on activated N9 microglial cells elaborated the effect of *Bacopa monnieri* as anti-inflammatory agent, which inhibits pro-inflammatory cytokines TNF-alpha and IL-6 (Fig-2). Also, the extracts of bacopa effectively impedes caspase 1 and 3 along with matrix metalloproteinase-3 in the cell free assay which concludes that bacopa contains favourable source of compounds which can limit the inflammatory process in CNS^[11]

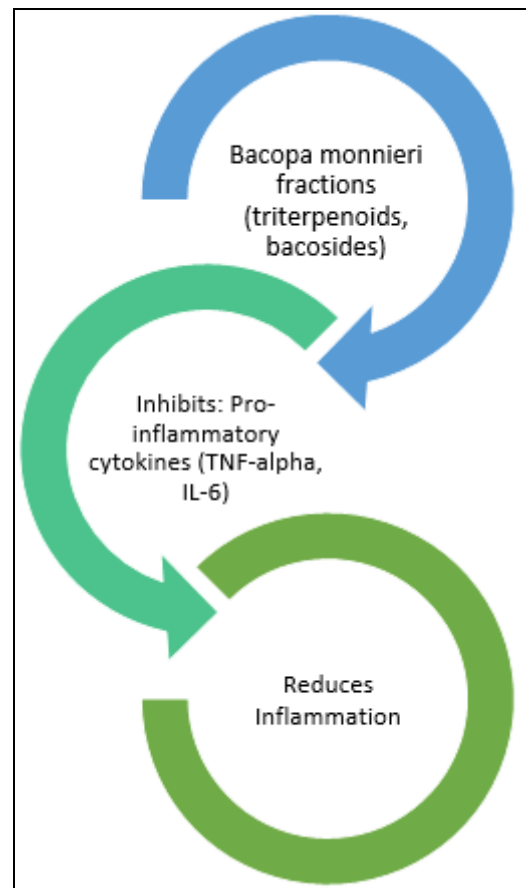


Fig 2: Anti-inflammatory mechanism of Brahmi (*Bacopa monnieri*)

Thyroid stimulating activity

- A relative efficacy of three medicinal plants *Bacopa monnieri*, *Aegle marmelos* and *Aloe vera* were experimented in male mice. The results signify an increase in T4 level by Bacopa and serum T3 and T4 were inhibited by *A. marmelos* and *Aloe vera* extracts at 200mg/kg, 1.00g/kg, 125mg/kg dose respectively thus indicating the use of *Bacopa monnieri* in Hypothyroidism and *A. marmelos* and *Aloe vera* in Hyperthyroidism^[5]

- *Bacopa* in the ancient era, used in various disorders. In thyroid gland it is suggestive to stimulate the production of T4 without enhancing T3 levels. Therefore, further clinical studies needed to summarise the dose and effectiveness of this herb in thyroid ailments. A preclinical trial proved the stimulation and release of T4 hormone in mice without affecting T3 synthesis^[5, 9]
- The extracts of *Bacopa monnieri* manifests conquering effects on motility of spermatozoa, depletion in number of spermatozoa count and their viability and morphology. Thus, revealing the antifertility effect of bacopa in male mice. However, the effects showed as anti-fertility are proved to be reversible^[9]
- A recent case study has proved the efficacy of Brahmi along with Asgand (*Withania somnifera*) in the management of Hypothyroidism thus suggesting its use as thyroid stimulating agent^[12]

Nootropic activity

- A placebo-controlled trial in 40 mentally retarded children administered the standardised extract of CDRI-08 signify the enhancing effect on learning and controlled abnormal behaviour^[13]
- A randomized double-blind placebo controlled non-crossover; parallel clinical trial was conducted among 60 medical students of either sex who were given 150mg of standardised extract of bacopa (bacognize) for six weeks. This study reported markable augmentation in cognitive functions. Also, it revealed a surge in the levels of serum calcium (still within normal range)^[14]
- Another randomised, double-blind placebo-controlled clinical trial was conducted in 36 attention deficit hyperactivity disorder (ADHD) affected children, in which freshly prepared extract of Brahmi were given in the dose of 50mg twice a day for 12 weeks. Recovery was observed at 12 weeks through cognitive function tests^[12]
- Another study in which 23 healthy adults were given BacominTM capsules 300 mg once a day for first 15 days and 450 mg once a day for next 15 days showed improved mental ability^[13]
- Baghel *et al* 2020 certified their result of a preclinical trial using BM (0.05-01% p. o) in swiss albino mice in ethanol extract withdrawal state and in sucrose diet as control group in which marble burying behaviour of mice were studied. Two-way ANOVA test revealed a remarkable effect in ethanol withdrawal mice^[15]
- Another clinical study in which healthy elderly subjects as well as people diagnosed with senile dementia of Alzheimer's type (SDAT) were recruited, their behavioural and biochemical parameters like learning abilities, inflammatory markers and oxidative stress were measured after 90 days of treatment with Brahmi which showed enhanced memory function in patients with SDAT and also markable reduction in the levels of inflammatory markers like homocysteine-reactive protein and tumour necrosis factor alpha, oxidative stress markers like glutathione peroxidase, glutathione, thiobarbituric acid reactive substances and SOD were noticed^[13]
- Micheli *et al* intervene into the effects of *Bacopa monnieri* to evaluate the efficacy of this wonder drug in

a new dimension of psychology i.e., anhedonia, a condition in which there is inability to feel pleasure. They conducted both preclinical and clinical studies for the same. A standardized extract of *B. monnieri* was administered at the dose of 50-200 mg/kg-1 p.o. for 1 week to a lipopolysaccharide (LPS) induced depressive like syndrome mice. Whereas in clinical trials 42 subjects (two groups) of marked degree of anhedonia were recruited and treated with citalopram of 40 mg and citalopram associated with *Bacopa monnieri* 300 mg bid for 4 weeks. Both studies confirmed its efficacy in anhedonia, however further controlled trials are necessary to use it as therapeutic agent in anhedonia^[16]

- One more clinical study of similar kind was conducted which was multi-centred using similar criteria corroborated the efficacy of Brahmi in improving cognitive function^[17]
- Another clinical trial validates its effects in elevating mood and minimising stress by lowering the levels of cortisol in 17 healthy individuals who were given 320 and 640 mg of Brahmi. This was a double-blind placebo-controlled trial suggesting the use of Brahmi to treat various ailments^[18]
- A randomized double-blind placebo controlled clinical study recruited 76 adults of age between 40 and 65 years reported the efficacy of Brahmi in retaining the new information whereas rate of learning, attention, verbal and visual short-term memory were unaffected^[19]
- Gupta *et al* reported their results of a preclinical study on HPTLC analysis for evaluating the efficacy of *Bacopa monnieri*, *Evolvulus alsinoides*, *Tinospora cordifolia*, both in combination and separate. In scopolamine induced amnesic rat, the treatment was given at 200mg/kg, the observations were noted using mean latency time (in seconds) in the Morris water maze test and latency to reach shock free zone (SFZ), mistakes in 15 minutes on the Passive-avoidance test, this unveil a bacoside A in *Bacopa monnieri* extract, flavonoid glycoside in EAE and unknown compounds in TCE. Also, combination of these three herbs shows significant synergistic effects in behavioural assessment in scopolamine induced amnesia rat^[20]
- A preclinical study was conducted in adolescent male mice of 4 weeks old, which has been treated with *Bacopa monnieri* extract for 1 week. RNA seq analysis showed marked increase in hippocampal incorporation and expression of genes involved in neurogenesis. Its histochemistry showed non-significant cell death. After 4 weeks of terminating BME treatment a tweak in the spatial working memory was retained. Bacopaside I is the active component of BME responsible for boosting hippocampal neurogenesis^[21]
- Another study of its kind conducted on *Drosophila melanogaster* flies known as fruit flies. These photopositive fruit flies are edified to avoid light using quinine as aversive stimulus. This is called Aversive phototaxic suppression (APS) assay. This conditioned behaviour is recognized to impede by sleep deprivation. APR was assayed in two tests groups sleep deprived and non-sleep deprived fruit flies administered *Bacopa monnieri* extract at 4.62×10^{-4} g/ml, 4.62×10^{-3} g/ml, and 4.62×10^{-2} g/ml concentrations. This trial reported to enhance, learning and short-term memory which was

accessed through average pass rates (APR) in both sleep deprived and non-sleep deprived subjects after BM supplement as compared to subjects without BM supplementation thus suggesting the efficacy of *Bacopa monnieri* in learning and memory retaining ability^[22]

- A clinical study enrolling 35 adults were given 12 grams of Brahmi syrup for 30 days results in enhancement of nervousness, concentration and memory^[13]
- Sharma *et al* in 1987 verifies the similar observations in children, where 350 grams of Brahmi in the form of syrup were given to 20 primary school children, thrice a day for 90 days. This proved to enhance the learning ability, memory and reaction times in them^[23]
- Anand *et al* in 2016 reported the results of a randomized placebo-controlled, double blind clinical study indicating the ameliorating effect of Brahmi on memory. In this trial 40-65 years old, 76 adults were enrolled and they were administered 300 mg of Brahmi. This study finally suggests the only long-term use of Brahmi shows memory enhancing effects^[13]
- Another placebo-controlled double blind clinical study was conducted in which 46 healthy individuals aged between 18 to 60 years were given 300mg of CDRI-08 for 12 weeks. Then a series of cognition function tests were conducted which showed a remarkable increase in verbal learning and concentration. Like this a number clinical trials were conducted which suggests that Brahmi can be used as potent memory enhancer as mentioned by^[24, 25, 26]
- Peth Nui *et al.* in 2012 conducted a trial which proves the efficacy of Brahmi in enhancing, memory, cognitive processing and attention in 60 healthy adults of around 60 years of age^[27]

Anti-alzheimer activity

- A phase 2 randomized active controlled double blind parallel group single centred clinical trial was conducted to evaluate the efficacy of Brahmi in subjects with Alzheimer's Disease. Donepezil was used as an active control agent, the treatment (bacopa 300 mg OD and donepezil 10mg OD) was given for 12 months. The study was terminated with a sample size of 34 due to high dropout rate. The results validated that there is no significant difference between two groups and suggested to conduct large phase 3 trials preferably multicentric to find its efficacy over donepezil^[28]
- Brahmi has been included in an evidence-based approach for the management of Alzheimer's disease according to Unani system of medicine in a recent article by Bashir *et al* in 2019^[29]
- Another *in silico* analysis, conducted by S.L. talapathra.*et.al* in 2019 predicted the presence of phytocompounds bacopa saponin G and bacopa saponin N2 in *Bacopa monnieri* which could be used individually or in combinations as preventive agents against Alzheimer disease. However further *in vitro* and *in vivo* analysis are required to validate the prediction^[30]

Antifungal activity

- Tinea capitis a common skin disorder of scalp, for its restriction molecular docking-based screening tests of some phytochemicals was done that proved the

presence of phytochemicals with active site of sterol14-alpha-demethylase of trichophyton sp in *Bacopa monnieri*, thus suggesting its use as preventive and therapeutic agent in tinea capitis^[31]

Anti-diabetic activity

- Tirtha Ghosh. al (2010) reported an *in vitro* and *in vivo* potential of ethanolic extract of *Bacopa monnieri*. This study validates the antihyperglycemic activity, antioxidant, potential effect on glycosylated hb of BM. They also estimated the level of glycogen content in liver and peripheral glucose utilization of bacosine, a triterpenoid from ethanolic extract of BM^[32]

Anti-cancer activity

- Various extracts of *Bacopa monnieri* like ethanol, methanol, DCM, hexane, acetone, alcohol, water had been experimented to reveal their potential components. It has been evinced its efficacy against different cancer cell lines either by modulating specific signalling pathways resulting in cell death or by simply remitting cytotoxicity which leads to activation of autophagic pathway by sparing healthy tissues. DCM extract of BM is documented to execute anticancer cell activity more among other extracts. *Bacopa monnieri* was found to be sensitive for specific cancer cells like neuroblastoma, colon cancer, prostate cancer. The HPTLC analysis of DCM extract of BM verified the presence of bacoside A and B along with cucurbitacin B, D, E and betulinic acid. The components of BM bac I and bac II proclaim efficacious effects in triple breast cancer cell line MDA-MB-231, ER β cell line MCF-7, T47D (both ER β and PR β) and HER2 β breast cancer cell line BT474. Thus, directing to a new stream and providing a ray hope for the still untreatable diseases^[33]

Cytotoxic activity

- Hemayet hossain described the results of a study conducted by Elangovan *et al.* 1995 revealing the cytotoxic effects of saponin fractions of *Bacopa monnieri* for sarcoma-180 cells and this might be due to inhibition of DNA replication in CA cells. He also signifies the potency of ethanolic extract of *Bacopa monnieri* against brine shrimp nauplii by using brine shrimp lethality bioassay^[34]

Anti-parkinson activity

- Standardized extract of *Bacopa monnieri* at 200 mg/kg/day for 3 weeks in PQ mice shows enhanced PQ-induced reduction of exploratory behaviour, abnormalities of gait and motor impairment. Also halted the reduction of dopamine and restoration of mitochondrial succinate dehydrogenase activity and MTT reduction were noted^[35]

Vasorelaxant activity

- In 2019^[37], K chootip. *et.al* published their research on the efficacy of *Bacopa monnieri* in vasodilation. The preclinical study validated the effect of *Bacopa monnieri* as vasorelaxant along with mechanisms of actions of its compounds (saponins and flavonoids) in rat isolated mesenteric arteries by using organ bath technique. This signifies that, the flavonoids luteolin and apigenin showed double the potential in

vasorelaxant effects than saponins-backsides A and Bacopaside I^[36]

Antimicrobial activity

- An in silico-analysis of *Bacopa monnieri* along with *Andrographis paniculata* conducted by J.S. Eswari and M. Yadav in 2019^[37] proved the presence of phytochemicals-Bacoside, Bacopa saponin, andrographin and β -sitosterol possessing antimicrobial activity against methicillin resistant staphylococcus aureus (MRSA)^[37]

Anti diarrhoeal activity

- The ethanolic extract of *Bacopa monnieri* manifests antidiarrheal effect in castor oil induced in Swiss albino mice with a dosage of 250mg/kg and 500mg /kg p.o. respectively as compared to loperamide. Thus, suggesting further evaluation^[34]

Other effects

- Ethanolic extract is similar in effect on the heart as quinidine.
- In different experimental animals bacopa manifested relaxant effects on pulmonary arteries, aorta, trachea, ileal and smooth muscles of bronchus by inhibiting calcium ion influx to cell membranes.
- Ethanol extract of Bacopa exhibit cardiac depressive activity in left ventricular contractility, heart rate and coronary flow in rabbit heart^[9]

Adverse effects

Studies have been conducted to evaluate the safety of Brahmi in male volunteers in both single (20-30) and multiple doses (100-200mg) which validates its safety. Another study in rats evince the safety of both aqueous (5g/kg) and alcohol extracts (17g/kg) of *Bacopa monnieri*^[9]

Table 2: Chemical constituents

<ul style="list-style-type: none"> Dammarane type triterpenoid saponins 	<ul style="list-style-type: none"> Jujubogenin or pseudo-jujubogenin moieties as aglycon units
<ul style="list-style-type: none"> Bacopasides I-XII 	<ul style="list-style-type: none"> Hersaponin
<ul style="list-style-type: none"> Apigenin 	<ul style="list-style-type: none"> D-mannitol
<ul style="list-style-type: none"> Monnierasides I-III 	<ul style="list-style-type: none"> Plantainosides B
<ul style="list-style-type: none"> Cucurbitacin 	<ul style="list-style-type: none"> Alkaloid-brahmine, herpestine and nicotine
<ul style="list-style-type: none"> Most potent constituents are bacosides A3, bacopasaponin C, Bacopaside II and Bacopaside X^[12] 	<ul style="list-style-type: none"> Bacosides A [3-(α-L-arabinopyranosyl)-O-β-D-glucopyranoside-10
<ul style="list-style-type: none"> 20-dihydroxy-16-keto-dammar24-ene] 	<ul style="list-style-type: none"> Saponins A, B and C
<ul style="list-style-type: none"> Betulinic acid 	<ul style="list-style-type: none"> Stigmastanol
<ul style="list-style-type: none"> Stigmasterol^[9] 	<ul style="list-style-type: none"> Asiatic acid; asiaticoside
<ul style="list-style-type: none"> Beta. -Sitosterol; betulinic acid; brassinolide 	<ul style="list-style-type: none"> Vitamin E
<ul style="list-style-type: none"> Flavonol 3-O-beta-D-glucosyl-(1-2)-beta-D-glucosyl-(1-2)-beta-D-glucoside, 	<ul style="list-style-type: none"> L-Arginine, L-Cladinose, melampodin, microcystin LR,
<ul style="list-style-type: none"> Oligomycin A, B, C and D, ononin, 	<ul style="list-style-type: none"> Silanol, ethyl dimethyl, sinapyl aldehyde, stanolone benzoate, stearic acid, stigmastanol, stypanol, verapamil
<ul style="list-style-type: none"> chikusetsusaponin IV, chlorophyll b, chlorthiophos, cholesterol sulfate, citric acid, coniferin, cucurbitacin I, A, B, C, D, E and H, curcumin monoglucoside, deltonin, fexaramine^[38] 	

Active components

Active components of Brahmi have been described with their functions in table-3

Table 3: Active components of Brahmi

Active components	Functions
<ul style="list-style-type: none"> Triterpenoid saponins 	<ul style="list-style-type: none"> Repairs damaged neurons by upregulating neuronal synthesis and kinase activity Restores synaptic activity Maintains neurotransmitter balance^[39, 40, 41]
<ul style="list-style-type: none"> Bacopaside E, B, VII 	<ul style="list-style-type: none"> Anti-tumor^[42]
<ul style="list-style-type: none"> Bacopaside A 	<ul style="list-style-type: none"> Chemoprotective, Hepatoprotective, Neuroprotective^[42]

Dosage

- Nonstandard power:** 5-10 grams
- Infusion:** 8-16 ml
- Syrup:** 30 ml
- 1:2 Fluid extracts:** 5-12 ml/day for adults 2.5-6 ml/day children

- 20% extracts Standardized to bacosides A and B:** 200-400 mg/day for adults and 100-200 mg/day for children^[9]

Conclusion

In this review an attempt has been made to summarise the preclinical and clinical trials until date on the safety and efficacy of *Bacopa monnieri*.

This suggests that there is a need for concentration of scientists to show interest in this regard to use this wonderful drug in the management of various ailments which would help in overcoming the burden of expensive and lengthy treatments for the same.

Most of the studies reported above indubitably showed a new purview in therapeutic approach to nervous disorders. From this review we can conclude that more emphasis should be done to get scientific results by conducting randomised, controlled, clinical trials on various aspects in general and CNS in specific regarding Brahmi. All the preclinical data should be used to get clinical data on various health disorders. With this, newer and safer drug regimen can be obtained.



Fig 3: Pharmacological activities of Brahmi (*Bacopa monnieri*)

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