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A Review on Pharmaceutically Important Medicinal plant: *Bacopa monnieri*

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ABSTRACT

Bacopa monnieri is an important medicinal plant which has been used in Ayurvedic system of medicine from very long period of time. It belongs to the Scrophulariaceae family and commonly known as Brahmi. It contains various bioactive compounds which include saponins, glycosides, flavonoids and stigmasterols, etc. Due to the presence of various bioactive compounds it possesses wide range of pharmacological properties which include memory and learning enhancer, immunomodulator, adaptogen, cerebral activator, etc. The plant is over exploited due to the preference of natural drugs over synthetic which compelled us for its conservation. The present review aims to summarize the various chemical constituents present in this plant and its pharmacological activity.

Keywords: *Bacopa monnieri,* Chemical constituents, Bacoside, Pharmacological activity

INTRODUCTION

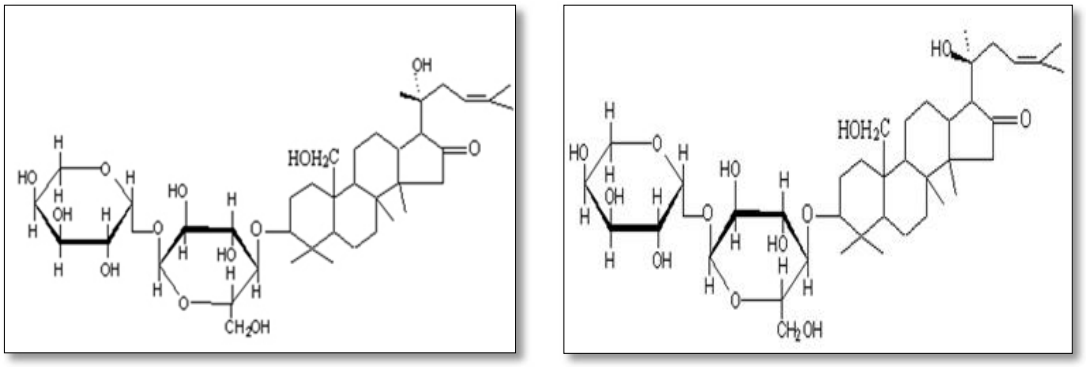
Bacopa monnieri has been used in *Ayurvedic* system of medicine from centuries and classified under *medhyarasayana*, i.e., medicinal plants which rejuvenate memory and intellect (Figure 1). It has been used by Ayurveda in India for almost 3000 years [1]. It is a small perennial creeping herb which belongs to 'Scrophulariaceae' family that has 220 genera and 4500 species. According to National Medicinal Plants Board (NMPB) it is also known as *Herpestis monniera* (L.), *Gratiola monnieria* (L.), *Moniera cuneifolia, Moniera cuneate* locally known as *brahmi*, water hyssop, pan brahmi, jalbuti, jalnim, etc. The name Brahmi is derived from the word 'Bramai' the mythical "creator" in the Hindu pantheon. Genus Bacopa includes more than 100 species of aquatic herbs. It is found in India, Nepal, Srilanka, Vietnam, China, Taiwan, Hawaii, Florida and some other Southern states of USA where it grows in wetland and muddy shores.

Figure 1: *Bacopa monnieri*

The plant has a soft stem which is approximately 10-30 cm long, 1-2 mm in thickness. Leaves are sessile, succulent and they are oppositely arranged on the stem, 0.6-2.5 cm long and 0.2-1 cm wide [2]. Flowers and fruits appear during summer. Flowers are white to pale blue or violet in colour with four or five petals. Fruits of *Bacopa monnieri* are ovoid, 2-celled, 2-valved capsules, acute and tipped with style base [3]. It has no distinct odour and slightly bitter in taste. Growth of plant is faster at30°C to 40°C and 65-80% humidity. In the list of important medicinal plants *Bacopa monnieri* is placed in second position. Whole plant of *Bacopa monnieri* is medicinally useful [4]. *Bacopa monnieri* is enlisted as the most endangered plants due to its overexploitation. According to National Medicinal Plants Board the estimated market demand for *Bacopa monnieri* is around 1,000 tonnes per year.

CHEMICAL CONSTITUENTS

The presence of different pharmacological activities of *Bacopa monnieri* is due to presence of several compounds that include alkaloids, saponins, glycosides, flavonoids and stigmasterols. *Brahmine* was the first alkaloid isolated [5] and later on D-mannitol, herpestine and nicotine was reported from plant leaves [6]. Saponins include hersaponin, monnierin, Bacoside A ([3-(α-L-arabinopyranosyl)-*O*-β-Dglucopyranoside-10,20-dihydroxy-16-keto-dammar-24-ene]) and Bacoside B (Figure 2). Bacoside A is the major component that is responsible for the memory enhancement effect. Bacoside A differs from Bacoside B in optical rotation where Bacoside A is levorotatory and Bacoside B is dextrorotatory. On acid hydrolysis of Bacoside A, it gives bacogenins A1, A2, A3, A4 [7]. Three new phenylethnoid glycosides (monnierasides I to III) were also isolated from glycosidic fraction of *B. monnieri* [8]. Isolation of triterpenoid saponins, i.e., saponins A, B and C and pseudojujubogenin glycoside were also isolatedfrom *B. monnieri*. Saponin A identified as 3-*O*-α-L-arabinopyranosyl-20-*O*-α-L-arabinopyrasonyl-jujubogenin, saponin B 3-*O*-[α-L-arabinofuranosyl (1→2)-α-L-arabinopyranosyl] pseudojujubogenin, and saponin C 3-*O*-β-D-glucopyranosyl(1→3)-{α-L-arabinofuranosyl-(1→2)}-α-Larabinopyrasonyl] pseudojujubogenin and Pseudojujubogenin glycoside as 3-*O*-[α-L-arabinofuranosyl-(1→2)-β-D-glucopiranosyl] pseudojujubogenin [9]. Two peudojujubogenin glycoside bacpoaside I and II were also isolated [10]. Later bacopasides II, IV and V were isolated, which are identified as 3-*O*-α-L-arabinofuranosyl-(1→2)-β-D-glucopyranosyljujubogenin, 3-*O*-β-D-glucopyranosyl-(1→3)-α-L-arabinopyranosyl jujubogenin, 3-*O*- β-D-glucopyranosyl-(1→3)-α-L-arabinofuranosyl pseudojujubogenin [11]. Bacoside A is mixture of four triglycoside that is bacoside A3, Bacoside II, jujubogenin and Bacoside B is mixture of four diglycosidicsaponin that is bacopaside N1, bacopaside N2, bacopaside IV and bacopaside V [12].



Bacoside A Bacoside B

Figure 2: Structure of Bacoside A and B

Pharmacological activity

Figure 3 shows that *B. monnieri* is used to treat variety of diseases which includes epilepsy, skin diseases, leprosy, asthma, depressant, hoarseness of voice, Parkinson's, arthritic, Alzheimer, etc. Behavioural studies show that *B. monnieri* improves motor learning, acquisition, retention and delay extinction of newly acquired behaviour [13]. It was found that *B. monnieri* helps in the improvement of memory functioning in cognitively intact cohorts [14]. *B. monnieri* when administered orally to Wistar rats for different time period it enhances memory [15].

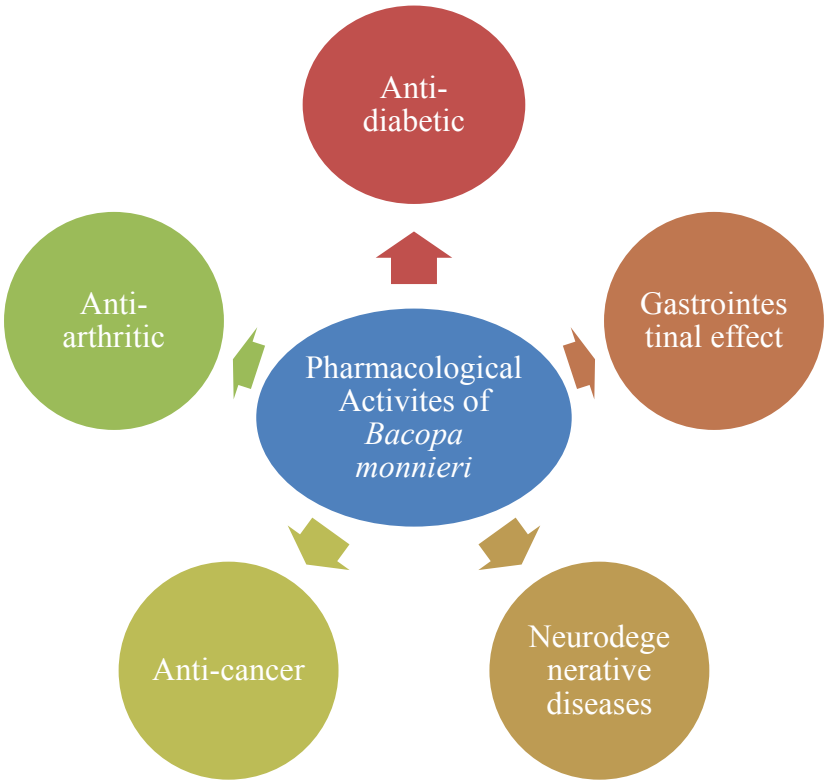


Figure 3: Pharmacological activities of *Bacopa monnieri*

Anti-arthritic

Several people suffer from the problem of rheumatoid arthritis. It was seen that the chances of rheumatoid arthritis in men is three times less than women, so women are more prone to this problem. Rheumatoid arthritis affects several tissues and organs, but especially it affects synovial joints [16]. Extract of *B. monnieri* inhibits arthritic symptom and inhibit cyclooxygenase and lipoxygenase activity [17]. A study reported the effect of various concentration of methanolic extract of *B. monnieri* on the arthritis and its comparison with the standard Diclofenac sodium drug at 2000 µg/ml. The results were found that *B. monnieri* showed 90.34 ± 0.83% inhibition of protein denaturation and 93.67 ± 1.34% membrane stabilisation while for Diclofenac sodium drug showed 96.52 ± 1.25% inhibition of protein denaturation and 98.76 ± 1.67% membrane stabilisation [18].

Anti-cancer

Anticancer property of *B. monnieri* was demonstrated by Elangovan et al. [19]. It was found that *B. monnieri* induces dose and time dependent loss of cell viability Effect of *B. monnieri* against the DNA damage in astrocytes and human fibroblast was also investigated [20]. It was also found that a compound phenylethanoid glycoside of *B. monnieri* shows an inhibitory effect on human colon, breast and lung cancer [21]. DNA replication inhibition in the cancerous cell suggested the anticancer properties of *B. monnieri* extract. In a study ethanolic extract of *B. monnieri* was used to observe the anticancer activity in different cancer cell lines and Sulforhodamine B assay was used to test the activity of extract. It was found that Ethanolic extract was more active in Human breast cancer and anticancer activity may be due to its saponin and flavonoid contents [22].

Anti-diabetic

Diabetes is a type of disorder which occurs due to the abnormal metabolic condition. Treatment for the diabetes is to use insulin or oral hypoglycemic agents, and it was reported that hypoglycaemic agents causes serious side effects. It was reported that ethanolic extract helps in the reduction of weight of diabetic rat and return it to its normal weight [23]. One study reported that hydroalcoholic extract *B. monnieri* was used to treat a group of rats in which diabetes mellitus type II was induced by streptozotocin and it showed a significant myocardial salvaging effect [24]. A study

reported that in alloxan induced hyperglycemic rats; there was a significant decrease in blood glucose level when *B. monnieri* ethanolic extract was used as compared to the standard glibenclamide drug [25]. Pandey reported that extract of *B. monnieri* showed anti-diabetic activity in streptozotocin-induced diabetes mellitus type 2 mice [26].

Anti-microbial

Infection occurs due to variety of microbes. Herbal products are not only less expensive but also have fewer side effects than synthetic drugs. *B. monnieri* shows antimicrobial effect on both the gram positive and gram negative bacteria. A study shows that *B. monnieri* extract (450 µg/ml) was bactericidal against *Salmonella enterica* serovar *typhi* isolates [27]. Another study shows that ether extract of *B. monnieri* have antimicrobial activity against four bacteria *Pseudomonas aeruginosa, Salmonella typhi*, *Vibrio cholera*, *Staphylococcus aureus* and one fungus *Candida albicans*. It was also reports that Bacoside A constituent of *B. monnieri* showed more prominent antimicrobial activity against *Staphylococcus aureus,* i.e., gram positive bacteria than a standard ciprofloxacin drug [28]. It was also reported that in comparison to other extracts like propanolic and ethanolic extract, etc., methanolic extract was the most potent one for antimicrobial activity and its activity showed against *Bacillus subtilis, Klebsiella pneumonia*, *Staphylococcus aureus* and *Pseudomonas aeruginosa.* Aqueous extractof *B. monnieri* shows no activity against any of the microorganisms [29]. The antibacterial effect of leaf extract of *B. monnieri* using different types of solvents, i.e., benzene, petroleum ether, ethyl acetate, methanol and water was done against eleven gram negative bacteria and seven gram positive bacteria and it was found that methanolic and ethyl acetate extracts showed strong antibacterial activity and both extracts were sensitive against all strains of gram positive bacteria [30].

Anti-oxidant

It was reported that *B. monnieri* has an antioxidant activity and anti-stress property. In rats morphine-induced liver and kidney toxicity were inhibited by *B. monneiri*. In a study, it was found that *B. monnieri* induces expression of heat-shock protein 70 and Cytochrome P450 enzymes in all regions of brain and it was found that in response to stress the level of Hsp70 and Cytochrome P450 were increased. Also level of Superoxide dismutase increases when *B. monnieri* was used [31]. In another study, ethanolic extract of *B. monnieri* administered to Wistar albino rats exhibited anti-oxidant property by protecting the liver cell from paracetamol-induced liver damage [32]. In a study DPPH radical scavenging antioxidant activity of four extracts of *B. monnieri* (whole plant) tested and it was found that methanolic extract showed maximum antioxidant activity with IC_{50} values of 46.00 µg/ml and aqueous extract showed IC_{50} values of 43.10 µg/ml [33]. *B. monnieri* plant extract and callus extract shows nitric oxide reduction. Callus extract was able to inhibit nitric oxide 68.94% at the concentration of 100 µg/ml, whereas plant extract was able to inhibit 77.85% [34]. Scavenging activity with IC_{50} value of 0.739 mg/ml by methanolic extract of *B. monnieri* callus was also reported [35]. In a seperate study aqueous extract of *B. monnieri* collected form Thanjavur showed highest antioxidant activity in comparison [36].

Gastrointestinal effect

Several studies showed that *B. monnieri* extract also had an effect on gastrointestinal tract. It was reported that *B. monnieri* shows curative and protective effect on gastric ulcers due to its various mucosa offensive and defensive factors [37]. A study showed that dose of 20 mg/kg *B. monnieri* extract for ten days significantly healed ulcer induced by acetic acid [38]. *B. monnieri* also showed anti-inflammatory effect by inhibiting prostaglandin synthesis and partly stabilizing the lysosomal membrane. Due triterpenoid and bacoside, *B. monnieri* showed anti-inflammatory activity. *B. monnieri* releases pro-inflammatory mediator through which it inhibits inflammation [18].

Neurodegenerative diseases

As *B. monnieri* is known for its treatment in memory loss, so it can be useful for even neurodegenerative diseases.

Parkinson's diseases

Parkinson's disease is a movement disorder in which aggregation of alpha synuclein protein and selective death of dopaminergic neurons occur and therefore in patients it leads to cognitive and motor impairment. Recent evidence shows that there is a link between Paraquat and Parkinson's disease onset. In a study, it was found that pre-treatment with 50 µg/mL of *B. monnieri* significantly protected dopaminergic cell line against both 1-methyl-4-phenyl-pyridinium iodide induced toxicity and Paraquat. *B. monnieri* also prevents the depletion of glutathione, preserved mitochondrial (MT) membrane potential and maintained MT complex I activity [39]. Two different strains of *Caenorhabditis*

elegans were used in a study, where one was a transgenic model which expressing human alpha synuclein and another was pharmacological model which was expressing green fluorescent protein specifically in dopaminergic neurons. Both the strains were treated with selective catecholaminergic neurotoxin 6-hydroxy dopamine (6-OHDA). *B. monnieri* was used to examine the effect of aggregation alpha synuclein, dopaminergic neurons degeneration, lipids content and nematodes longevity. It was found that *B. monnieri* prevents dopaminergic neurodegeneration, reduces alpha synuclein aggregation and restores lipid content in nematodes and therefore provides an anti-parkinson agent [40]. It was reported that ethanolic extract of *B. monnieri* shows protective effects on 6-OHDA induced lesions in rats. 6-OHDA is a neurotoxin which is structurally similar to catecholamines, therefore it is useful in Parkinson's damage modelling. Inside the body 6-OHDA increases lipid peroxidation and generates free radicals. Author administered 12 µg of 6-OHDA on day twenty one into right striatum. Three week later rats were tested and it was observed that both enzyme activity and neurobehavioral deficits significantly restored by *B. monnieri* [41]. One study reported that platinum nanoparticles from *B. monnieri* leaf extract coated with varied phytochemicals shows potential against Parkinson's disease in zebrafish model. Photochemical coated nanoparticle study was done in 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) induced experiment. *B. monnieri* platinum nanoparticles reverse the toxic effect of MPTP by increasing dopamine level and its metabolites, catalase, Glutathione and activities of *Septo-optic dysplasia* and complex I [42]. In a study rats were divided into four groups: group 1 received saline water, group 2 received rotenone for 60 days to induce Parkinson's diseases, group 3 received rotenone for 20 days orally before induction of Parkinson's diseases and group 4 received Levodopa orally. It was seen that levels Dopamine, Serotonin, Epineprine, Nor-epineprine were decreased and Monoamine oxidase activity was increased in different brain regions such as Cerebral cortex , Cerebellum, Mid brain and Pons medulla during induced Parkinson's diseases compared with controls. Ethanolic extract of *B. monnieri* shows reversed result after treatment [43]. Gunduluru et al. also reported the role of *B. monnieri* in rotenone induced Parkinson's diseases in PC 12 cell line and observed that plant extract showed significant morphological damage, cell viability and apoptosis of PC 12 cells [44].

Alzheimer's disease

B. monnieri also shows anti-Alzheimer activity. Alzheimer's disease is a neurodegenerative condition, which mostly affecting elder people. This disease has both short and long term memory affect. It is common cause of dementia in elder people and responsible for approximately 60-80 percent of cases. For Alzheimer's disease researchers are trying to find effective medicines. It was seen that in mice *B. monnieri* reduces the beta-amyloid deposits in cortex and reversed behavioural deficits in brain [45]. In a study effect of alcoholic extract of *B. monnieri* on animal model of Alzheimer's disease induced by ethylcholine aziridinium ion *was used and it was found that extract* improved the escape latency time (p<0.01) in Morris water maze test. Reduction of neurons and cholinergic neuron densities were also mitigated [46]. In a study it was reported that when 300 mg of standardized extract of *B. monnieri* was taken orally two times in a day for a period of six months, there was an improvement in cognitive functions of patients that were suffering from Alzheimer's disease [47]. A study showed that ethanol extract of *B. monnieri* (leaves and stem) have acetylcholinesterase inhibitory property. *In vivo* study of the effect of ethanol extract was done in a male albino rat (225-250 g) where the oral dose of 100 mg/kg of body weight ethanolic extracts given for the fifteen days and it inhibits acetylcholinesterase activity in different brain regions [48]. Another study shows that *B. monnieri* has an endogenic substance that will impact on the components of oxidative stress cascade such as divalent metals reduction, reactive oxygen species scavenging, lipoxygenase activity alteration etc. *B. monnieri* extract contains polyphenols and sulphydryl contents [49]. According to Tembhre *B. monnieri* elicited acetylcholinesterase inhibition in cerebral cortex of rat and kinetic study showed that there was a competitive acetylcholinesterase inhibition in the brain regions [50].

CONCLUSION

The present review shows that *Bacopa monnieri* contains several different phytocompounds like alkaloids, saponins, glycosides, flavonoids, etc. Out of these phytocompounds saponins, i.e., Bacoside A and B are the most important one which are responsible for the different pharmacological activity. It was found that Bacoside A is the main phytocompound which helps in the memory enhancement. *Bacopa monnieri* also helps in the improvement of neurodegenerative disorder as it improves the memory. So it can be utilize as a drugs for the treatment of neurodegenerative disorders. Recently it was seen that *Bacopa monnieri* shows anti-diabetic and anti-arthritic property and it has great potential to treat these diseases.

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