
Review Article



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PHARMACOLOGICAL ACTIONS OF BACOPA MONNIERI: A REVIEW

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Abstract

In the last few years there has been an exponential growth in the field of herbal medicine and these drugs are gaining popularity both in developing and developed countries because of their natural origin and less side effects. Many traditional medicines in use are derived from medicinal plants, minerals and organic matter. The World Health Organization (WHO) has listed 21,000 plants, which are used for medicinal purposes around the world. Medicinal herbs have been on the forefront whenever we talk about anticancer remedies, Herbal medicines have a vital role in the prevention and treatment of cancer. Here we covered the phytochemicals and pharmacological review of plant *Bacopa monerii* used previously and recently identified for treatment of various diseases and to reduce the pains during the treatment.

Keywords: *Bacopa*, Brahmi, Pharmacological actions, Nootropic.

Introduction

In recent times, the use of herbal products has increased tremendously in the western world as well as in developed countries¹. Plants have been provide essential nutritional values, medicinal properties and physiological effect to life and are a good source of food.² *Bacopa monniera*(BM) also referred to as, *Herpestis monniera*, Water Hyssop, locally known as brahmi or Jalamimba in India. The name Brahmi is derived from the word “Brahma”, the mythical ‘creator’ in the Hindu pantheon. Because the brain is the centre for creative activity, any compound that improves the brain health is called brahmi, in which recommended formulations for the management of a range of mental conditions including anxiety, poor cognition and lack of concentration, as a diuretic and as an energiser for

the nervous system and heart³. BM is a creeping, glabrous succulent herb, rooting at nodes whose habitat includes wetlands and muddy shores. Stem 10-30 cm long, 1-2 mm thick, soft, glabrous. The leaves of this plant are succulent and relatively thick. Leaves 0.6-2.5cm long and 3-8 mm broad, sessile, oblanceolate and are arranged oppositely on the stem. The flowers are small and white with four or five petals. No distinct odour, taste slightly bitter^{4,5}. The plant is propagated through cuttings. It is known as Brahmi, Nir-brahmi in Sanskrit, Brihmi-sak, Jalamimba in Bengali, Brahmi in Hindi, Nirubrahmi in Kannada, Nirbrahmi in Malayalam, Marathi and Tamil, Sambranichettu in Telugu^{6,7,8}. Earlier, it is used as a brain tonic to enhance memory development, learning and concentration

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and to provide relief to patients with anxiety or epileptic disorders⁹. The genus *Bacopa* includes over 100 species of aquatic herbs distributed throughout the warmer regions of the world, apart from India, Nepal, Srilanka, China, Taiwan and Vietnam and also found in Florida¹⁰. The entire plant is used in India and Pakistan as a cardiogenic, digestive aid and improve respiratory function in case of bronchoconstriction¹¹. The plant also used as a laxative, and curative for ulcer, inflammation, anemia, scabies, leucoderma, epilepsy and asthma¹². The plant also reported to show sedative¹³, hyperthyroidism¹⁴, vasoconstrictor¹⁵, and gastrointestinal disorder¹⁶.



Fig. No. 01: *Bacopa monnieri*

Chemical constituents

Compounds responsible for the pharmacological effects of BM include alkaloids, saponins and sterols. Detailed investigations first reported the isolation of the alkaloid 'brahmine' from BM.¹⁷ Later, other alkaloids like nicotine and herpestine have also been reported.¹⁸ Subsequently, the isolation of D-mannitol and a saponin, hirsaponin and potassium salts was reported.¹⁹ The major chemical entity shown to be responsible for neuropharmacological effects and the nootropic action or anti-amnesic effect of BM is bacoside A, assigned as 3-(α -L-arabinopyranosyl)-O- β -D-glucopyranoside-10, 20-dihydroxy-16-keto-dammar-24-ene.²⁰ Bacoside A usually co-occurs with bacoside B; the latter differing only in optical rotation and probably an artefact produced during the process of isolating bacoside A.²¹ On acid hydrolysis, bacosides yield a mixture of aglycones, bacogenin A1, A2, A3,^{22,23} which are artifacts and two genuine saponins, jujubogenin and pseudojujubogenin and bacogenin, A4, identified as ebelin lactone pseudojujubogenin, were isolated.²⁴ Successively, a minor saponin bacoside A1 and a new triperpenoid saponin, bacoside A3, were isolated.²⁵ Later, three new dammarane-type

triterpenoid saponins of biological interest, bacopasaponins A, B and C, pseudojujubogenin were isolated and a new dammarane-type pseudojujubogenin glycoside, bacopasaponin D, were identified by spectroscopic and chemical transformation methods.²⁶ In view of the increasing interest in this herbal plant, yet two new pseudojujubogenin glycosides designated as bacopaside I and II were isolated from glycosidic fraction of the methanol.²⁷ Subsequently, three new saponins from BM, designated as bacopasides III, IV and V were isolated.²⁸ In addition, the isolation of three new phenylethanoid glycosides, viz. monnierasides I-III along with the known analogue plantainoside B was reported from the glycosidic fraction of BM.²⁹ Moreover, an isolation of a new saponin, a jujubogenin, named bacopasaponin G, and a new glycoside, phenylethyl alcohol was also reported³⁰. The chemical structures of saponins³³ isolated from BM. Bacoside A levorotatory, and bacoside B dextrorotatory.

Antioxidant activity

Antioxidants, which can inhibit or delay the oxidation of an oxidizable substrate in a chain reaction.³¹ Antioxidants have been reported to prevent oxidative damage by free radicals.³² Free radicals contribute to more than one hundred disorders in humans including Artherosclerosis, hypertension, arthritis, ischemia, gastritis, cancer, Alzheimer's disease, Parkinsonism, diabetes mellitus and AIDS.^{33,34} The study found that extract of BM was found to scavenge the free radicals such as peroxides, superoxides, and hydroxyl radicals.³⁶ Extract or bacosides have shown an antioxidant activity.^{35,36,37,38,39} A previous study suggest that, treatment with BME has shown to possess a significant protective effect against morphine induced liver and kidney functions in terms of serum glutamate pyruvate transaminase, alkaline phosphatase, lactate dehydrogenase and gamma glutamyl transferase activities and urea uric acid respectively.⁴⁰ Animal research reveals that the BM extracts modulate the expression of certain enzymes involved in generation and scavenging of reactive oxygen species.⁴¹ Researcher concluded that pretreatment with bacoside A prevents the elevation of LPO (Lipid peroxidase) and activity of serum marker enzymes and maintains the antioxidant system.⁴² It was found that the BM extract exhibits interesting antioxidant properties, expressed by its capacity to scavenge

superoxide anion and hydroxyl radical, and to reduce H₂O₂ induced cytotoxicity and DNA damage in human fibroblast cells.^{43,44} Even extract of BM exerted an anti-stress, cognition facilitating and anti-ageing effects in experimental animals and in clinical stimulation⁴⁵. One more study reveals that BM extract has shown neuroprotective effect against aluminium induced oxidative stress in the hippocampus of rat brain^{46,47}. Even aqueous extract of BM reduced nicotine – induced lipid peroxidation (LPO) and gene protection in Swiss mice in one study⁴⁸.

Anti-inflammatory effect

BM possesses anti-inflammatory activity via inhibition of prostaglandin synthesis and lysosomal membrane stabilisation^{49,50}. One more study concluded that, BM significantly showed an anti-inflammatory activity on carrageenan induced rat paw edema and it has shown 82% edema inhibition when compared to indomethacin.^{51,48,52}

Anti-ulcerative effect

Inadequate dietary habits, excessive ingestion of non-steroidal anti-inflammatory agents, stress, hereditary predisposition and infection by *Helicobacter pylori* may be responsible for development of ulcer⁵³. Poly-herbal formulation using many plants including *Bacopa monnieri* as one, contains content ingredients, which are said to minimize the adverse effect of drug^{54,55}. Animal and *in vitro* studies have demonstrated that, BM may have a protective and curative effect on gastric ulcers and exerted its anti-ulcerogenic activity^{56,57,58,58}. BME possesses anti-ulcer and ulcer healing activities due to its effects on various mucosal offensive and defensive factors.⁵⁹ One more study in rats reveals that BME exerted a prophylactic and healing effects five models of gastric ulcer.⁶⁰ A subsequent study reveals that, at a dose of 20mg/kg for 10 days, BME significantly healed penetrating ulcer induced by acetic acid and strengthened the mucosal barrier and decreased mucosal exfoliation⁶¹.

Antimicrobial activity

Infections due to variety of bacterial etiological agents, such as pathogenic *Escherichia coli*, *Staphylococcus aureus*, *Salmonella sp*, *Shigella sp*, *Enterobacter sp* are most common⁶¹. Synthetic drugs are not only expensive and inadequate for the treatment of diseases but also associated with

adulteration and side effects. For these reasons researchers are increasingly turning their attention to herbal products⁶². Propanolic and ethanolic extract of BM exhibited maximum zone of inhibition against *Streptococcus*⁶³. One study demonstrates that, antimicrobial activity of photosynthesised silver nanoparticles of BM against *S.aureus*, *E.coli*, *P.aeruginosa* and *K.pneumoniae*.^{64,65,66} Methanolic extract of leaf callus of BM, showed a potent antimicrobial activity against *B.subtilis*, *S.aureus*, *P.aeruginosa* and *K.pneumoniae*.⁶⁷ Invasive fungal infections have increased in frequency over the last two decades.⁶⁸ Because of the eukaryotic properties of the fungi, many antifungal compounds exhibit a potent cytotoxic effect on humans, which is a significant limitation for application of these compounds as a practical drug.⁶⁹ The study reveals that, whole plant methanolic extract was effective against *A.niger*, *M.furfur* and *C.albicans*.⁷⁰ The phytochemical betulinic acid and oroxindin isolated from the aerial parts of BM showed significant antifungal activity against the two fungi *Alternaria alternata* and *Fusarium fusiformis*.⁷¹

Anti-depressant activity

Recently, the interest in the use of herbal products has grown dramatically in the western world as well as in developed countries.⁷² Mental depression is a chronic illness that affects a person's mood, thought, physical health and behaviour.⁷³ Patients with depression have symptoms that reflect a decrease in brain monoamine neurotransmitter, specifically norepinephrine, serotonin and dopamine.⁷⁴ Methanolic extract of BM has shown (20-40mg/kg) given once daily for 5 days significant antidepressant activity in forced swim test and learned helplessness models of depression.⁷⁵ Earlier studies have demonstrated that BM, a plant described in Ayurveda for many CNS actions, was found to exhibit antinociceptive effect (aqueous extract at 80-120 mg/kg given orally).⁷⁶ Antidepressants are often used in the treatment of pain and may bring about their beneficial actions through a number of mechanisms.^{77,78}

Effect of bacopa on human memory and cognition

Traditional Ayurvedic medicine uses BM to enhance memory and alleviate anxiety neurosis. It is a well-known nootropic plant reported for

cognitive enhancer.^{79,80} The study reveals that BM decreases the rate of forgetting of newly acquired information.⁸¹ Alcoholic extract of BM increases the learning performance of rats and activities attributed to a saponin mixture consisting of bacosides A, B and other saponins.^{82,83,84} One more study reveals that, whole plant extract of BM have potential for safely enhancing cognitive performance in ageing.⁸⁵ It also suggest that poly herbal formulation of four plants namely *Withania somnifera*, *Bacopa moniera*, *Tinospora cardifolia* and *Embllica officinalis* extracts show potent activity against ageing.^{86,87} In mice, BM administration with phenytoin significantly reversed phenytoin induced cognitive impairment by improved acquisition and retention of memory.⁸⁸ One more study reveals that significant cognitive enhancing benefits have been demonstrated with more chronic administration of BME in an double blind, placebo controlled, 12-week trail utilizing the same patient and same dose of BME(300mg daily) containing 55% combined bacosides.⁸⁹ A team of researchers reported that a standardized bacoside rich extract of BM, reversed the cognitive deficits induced by intra cerebro ventricularly administered colchicines and injection of ibotenic acid into the nucleus of *Basalis magnocellularis*.⁹⁰ In the same study BM also shown to reverse the depletion of acetylcholine, the reduction in cholineacetylase activity and a decrease in muscarnic cholinergic receptor binding in the frontal cortex and hippocampus. The cognition facilitating activity of BM extract is attributed to saponins, Bacoside A and Bacoside B which are effective in much lower doses in various models studied included tests for conditioned taste aversion and conditioned shock avoidance.^{91,92} Laboratory studies on rats, indicate that extracts of BM improve memory capacity.⁸⁸ Some studies in mice suggest that ingestion of *Bacopa* for a 12 week period can significantly improve cognitive ability by accelerating the rate of learning and enhanced memory.^{93,94,95,96,97} Cleanincally has been reported to improve intellectual behaviour in children; in adults and is effective in reducing anxiety, thereby allowing improved brain functioning in terms of memory enhancement and elevated mental performance.⁹⁸

Antiepileptic activity

BM has been indicated as a remedy for epilepsy in ayurvedic medicine.^{99,100} It is a creeping glabrous,

succulent herb, provide relief to patients with anxiety or epileptic disorders.^{101,102,103,104} Epilepsy is a condition which causes seizures to occur. It is one of the most common chronic disease affecting human beings.¹⁰⁵ In one more study it has shown that neuro protective role of BM extract in glutamate mediated excitotoxicity during seizures and cognitive damage occurring in association with pilocarpine induced epilepsy.¹⁰⁶ The result showed that BM treatment for epileptic rats significantly brought the reversal of the down regulated metabotropic glutamate receptor gene expression toward the control level. It has been used to treat epilepsy, insomnia and asthma.¹⁰⁷ *Bacopa* exhibits reduced alertness, spontaneous locomotary activity. It protects from electroshock and convulsions.¹⁰⁸ Regular intake of BM tea improves treating epilepsy and other nervous system. Triterpenoid saponins and Bacosides of BM play an important role in enhancing nerve impulse transmission, while Bacosides support the repair of damaged neurons by enhancing kinase activity, neuronal synthesis, restoration and regeneration of synaptic activity resulting in nerve impulse transmission. These effects make it a wonderful nerve tonic or nerve nourishing agent as against the neuroleptic drugs that modulate the behaviour. Research in India found horopnin to exert some anticonvulsant effect. So it could better be use as an adjuvant in treatment of epilepsy.^{109,110} In an open clinical study of B patients with epilepsy, *bacopa* was reported useful in improving the symptoms and occurrence of epileptic seizures¹¹¹. *Brahmigritha*, a medicated ghee prepared from BM, is beneficial in cases of epilepsy and hysteria¹¹².

Bacopa for alzhemier's disease

A new animal study suggested that BM is a creeping herb traditionally used in ayurvedic medicine for the treatment of cognitive impairment, may thus help treat the symptoms of Alzhemier's disease¹¹³[AD]. AD is a neurodegenerative disorder characteristic by progressive dementia. Studies have shown that BM reduces beta-amyloid deposits in the brain of an AD animal model. The study investigated the presence of endogenic substances in BME that will impact components of the oxidative stress cascade such as the reduction of divalent metals, scavenging of reactive oxygen species, alteration of lipoxygenase activity and hydrogen peroxide induced lipid peroxidation. The extract contained polyphenols and sulfhydryl

contents suggestive of endogenous antioxidant activity¹¹⁴. The result demonstrated that BME reduced divalent metals, dose dependently scavenged reactive oxygen species, decreased the formation of lipid peroxides and inhibited lipoxygenase activity¹¹⁵.

One more study demonstrates that Alkaloids Brahmin isolated from the plant and found its therapeutic action resembles strychnine but less toxic. It contains bases B₁ oxalate, B₂ oxalate, B₃ chloroplatinate and a sterol also it contains alkaloid herpestine¹¹⁶. Contemporary formulas often combine *Bacopa monniera* with other herbs and nutritional supplements known to promote mental functioning such as Gink biloba, ginseng and phosphatidylserine. Such formulas may also be applicable as protection against the onset of Alzheimer's disease¹¹⁷. Three new triterpenes glycoside bacopaside VI-VIII, together with three known analogues, bacopaside I, bacopaside II bacopasapinsin C were isolated from the whole plant of BM. Compounds 4,5 and 6 were shown antidepressant activity when tested on forced swimming and tail suspension in mice respectively these results support its neuropharmacological effects¹¹⁸. From the study it was indicated that the adaptogenic activity of BM might be due to the normalization of stress induced alteration in plasma corticosterone and the levels of monoamines like NA, 5-HT and DA in the cortex and hippocampus regions of the brain which are more vulnerable to stressful conditions analogous to the effect of PQ^{119,120}. BM is a perennial herb and is used as a nerve tonic. From the findings, it was suggested that BME lowers A- beta 1-40 and 1-42 levels in the cortex by as much as 60% and reverses y-maze performance and hyperlocomotion behavioral changes present in PSAPP MICE. Hence it has potential application in Alzheimer's diseases¹²¹.

Anticancerous activity

Elangovan et al, demonstrate the anticancer activity of BM. they found that BM induces dose and time dependent loss of cell viability with maximum cytotoxicity at 48 hr at concentration of 550mg/ml. The study concluded that BM induces cell death by apoptosis S-180 cells¹²². Invitro research has shown a protective effect of BM against DNA damage in astrocytes and human fibroblast¹²³. Invitro research has suggested that an anticancer effect of BM extract is possibly due to inhibition of DNA

replication in cancer cell lines. It is used in ayurved for tumors. BM exerted a significant protectant effect on H₂O₂ – induced cytotoxicity and DNA damage in human non immortalised fibroblast. It is due to its antioxidant activity. The plant may be useful in the treatment of human pathologies in which free radical production plays a key role¹²⁵. Pretreatment with BM significantly reduced the As-induced increase in the ulcer index, adrenal gland weight, plasma glucose¹²⁴. Bacoside A an active phytochemical present in BM as anti cancer activity. This was shown anticancer effect by successive extracting ethanolic extract of BM. One study demonstrates that ethanolic extract of BM was very effective against cancer. It is useful for the treatment of cancer¹²⁵. One more study reveals that treatment with BME significantly increased the anti oxidant enzyme status, inhibited lipid peroxidation and reduced the tumor markers. It can be concluded that BME promotes the antioxidant status, reduces the rate of lipid peroxidation and the markers of tumor progression in the fibro sarcoma bearing rats¹²⁶.

Antidiabetic activity

Animal study demonstrates that, BM has an effect on haemoglobin glycosylation in vivo antioxidant potential and invitro peripheral glucose utilization. Bacosine, a triterphenoid isolated from the ethylacetate fraction of ethanolic extract of BM. Administration of bacosine and glibenclamide significantly decreased the level of melanaldehyde(MDA) and increased the level of reduced glutathione (GSH) the the activities of superoxide dismutase(SOD) and catalyze(CAT) in the lever of diabetic rats. Bacosine increased glycogen content in the lever of diabetic rats and peripheral glucose utilization in the diaphragm of diabetic rats. Thus bacosine might have insulin like activity and its anti hyperglycemic effect might be due to an increase in peripheral glucose conception¹²⁷.

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