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Bacopa Monnieri - A Review

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ABSTRACT

In recent times, the use of herbal products has increased enormously across the globe. Numerous natural products such as those isolated from plants have been evaluated as therapeutics for the treatment of variety of diseases. *Bacopa monnieri* also referred to as water hyssop and "Brahmi," has been used in the Indian system of medicine since time immemorial. It belongs to the family Scrophulariaceae and is an annual creeping plant found in wet, damp, and marshy areas. Phytochemical analysis of *Bacopa monnieri* extracts revealed the presence of various biochemical compounds such as alkaloids, bacosides, flavonoids, glycosides, triterpenoids and saponins etc. The major therapeutic chemical constituents of this plant identified through various researches are the triterpenoids saponins, bacosides. Bacoside A has been recognized as the chief component responsible for therapeutic effects. *Bacopa monnieri* is conventionally used for diverse ailments, but is best known as memory enhancer. A vast range of studies using methanolic and ethanolic extracts of *Bacopa monnieri* have shown its effect in treatment of wide range of diseases like diabetes, depression, cancer, inflammation etc. *Bacopa monnieri* appears to demonstrate low toxicity in various rat, mice models including humans however, long term studies of toxicity in humans still need to study in great details. This review focuses on the studies that have traced both pharmacological and phytochemical properties of plant *Bacopa monnieri* covering wide range of its effect on antidepression, anti epileptic, anti oxidative amongst many others which can surely help in betterment of mankind.

KEYWORDS: *Bacopa monnieri, Pharmacological study*

INTRODUCTION

Bacopa Monniera (L.) Pennell is a plant of scrofulariaceae family that is commonly known as Brahmi, thyme leafed gratiola, water hyssop, herb of grace, Indian pennywort. Bacopa has been used in traditional Ayurvedic treatment for epilepsy and asthma[1]. It is one of the ingredients of many Ayurvedic formulations used for ulcers, tumors, ascitis, spleenomegaly, inflammatory disorders, leprosy, anemia and gastroenteritis. Brahmi is also the name given to Centella asiatica, particularly in North India and Kerala where it is also identified in Malayalam as muttil or kodakan. This identification of brahmi as Centella asiatica has been in use for long in northern India, as Hemadri's Commentary on Astanghridya treats mandukparni (Centella asiatica) as a synonym of brahmi,[2-4] although that may be a case of mistaken identification that was introduced during the 16th century[5]. Bacopa monnieri was initially described around the 6th century A.D. in texts such as the Charaka Samhita, Atharva Veda, and Sushruta Samhita as a medhya rasayana class herb taken to sharpen intellect and attenuate mental deficits. Ancient Vedic scholars to memorize lengthy sacred hymns and scriptures allegedly used the herb. Traditionally it is known as Soumya, Divyateja, Mahousadhi, Kapotavega, Brahmasuvarcala, Sarasvati, Soma, Satyahva, Divya, Kapotavitaka, Munika, Lavanya, Somavallari, Kapotavanka, Somavalli, Surasrestha, Suvarcala, Vaidhatri, Svayambhuvi, Somalata, Surejya, Matsyaksi, Surasa, Medhya, Vira, Bharati, Vera, Parameshthini, Saradi, Brahmacharini, Chaidhatri, vallari. Acharya Charaka described this plant under Balya, Prajasthapana mahakashya, [6] while Bavprakasha mentioned it in Guduchiadi gana.[7]

It is a scattering, evergreen, fleshy herb. Its branches multiply on moist ground and forms dense pad. Roots are found growing at nodes. The leaves are small, club shaped, stalk less, and fleshy which is bitter in taste. The long stalk flowers are found single at the axis of the leaves. Flowers are pale blue or whitish, axillary, solitary, arranged on long slender pedicels. Fruits are ovoid, acute, 2-celled, 2-valved capsules and tipped with style base. Seeds are minute and numerous.[8]

Bacopa monnieri contains compounds as dammarane-type triterpenoid saponins that known as bacosides, with jujubogenin or pseudo-jujubogenin moieties as aglycone units[9]. Bacosides comprise a family of 12 known analogs [10], other saponins called bacopasides I–XII have been identified more recently[11]. The alkaloids brahmine, nicotine, and herpestine have been catalogued, along with D-mannitol, apigenin, hersaponin, monnierasides I–III, cucurbitacin and plantainoside B[12-14]. The constituent most studied has been bacoside A that was found to be a blend of bacoside A3, bacopacide II, bacopasaponin C, and a jujubogenin isomer of bacosaponin C[15].These assays have conducted using whole plant extract and bacoside concentrations may vary depending upon the extracted part. In one Bacopa monnieri sample, Rastogi et al. found this bacoside profile—bacopaside I (5.37%), bacoside A3 (5.59%), bacopaside II (6.9%), bacopasaponin C isomer (7.08%), and bacopasaponin C (4.18%) [16, 17].

Fig -1: Bacopa Monniera

(I) Flower

(II) Dry leafs

(III) Powder formation of brahmi

The plant belongs to Kingdom – Plantae, Division – Angiospermae, Class – Dicotyledonae, Subclass – Gamopetalae, Series – Bicarpellatae, Order – Personale, Family – Scrophulariaceae, Genus – *Bacopa* and Species – *monnieri.* Genus *Bacopa* comprises of 146 species of aquatic herbs distributed throughout the warmer regions of the world[18]. Apart from India, Nepal, Sri Lanka, China, Taiwan and Vietnam, it is also found in Florida and other southern states of USA. In United States, the herbs are recognized as weeds in rice fields and found growing abundantly in marshes and wetlands of warmer regions. In India, it grows in damp, marshy places and on the banks of slow flowing rivers and lakes, ascending up to an attitude of 1,320 m.[19]

Botanical Description

Bacopa monnieri is a small creeping, spreading, succulent herb with numerous branches and small fleshy, oblong leaves. Flowers and fruits appear in summer and the whole plant is medicinally important. The salient botanical features are: Stem - prostrate, (sub) succulent, herbaceous; Leaves - decussate, simple, oblong, 1 × 0.4 cm, succulent, punctate, penninerved, margin entire, apex obtuse, sessile; Flower(s) - axillary, solitary, bracteate, linear, purple, pink or white in colour; Calyx - 5 lobes (unequal); outer 2 lobes larger, oval, 7 × 3.5 mm; inner 2 lobes linear, 5.5 × 0.7 mm; median 1 lobe oblong, 5.5 × 2 mm, imbricate, (sub) succulent, punctuate, obtuse, acute; Corolla - white with violet and green bands inside the throat, 0.8 cm across, 5 mm tube; 5 lobes, obscurely 2-lipped, obtuse or emarginated; Stamens - 4, didynamous; filament pairs 1 and 2.5 mm anthers oblong, contiguous, 1.5 mm; Ovary - oblong-globose, 2 mm; style slightly deflexed, 5.5 mm; Stigma - flat capsule, oblong-globose, 5×2.5 cm septicidal or locilicidal or 4 valved; Seed - oblong, testa striate; Fruit - small, capsule form, less than 0.5 inch in length.[20]

Pharmacological Studies

Compounds responsible for the pharmacological effects of *Bacopa monnieri* include alkaloids, saponins and sterols. Detailed investigations first reported the isolation of the alkaloid 'brahmine' from *Bacopa monnieri* [21]. Later, other alkaloids like nicotine and herpestine have also been reported[22]. Subsequently, the isolation of D-mannitol and a saponin, hersaponin and potassium salts was reported[23]. The major chemical entity shown to be responsible for neuropharmacological effects and the nootropic action or antiamnestic effect of BM is bacoside A, assigned as 3-(a-L-arabinopyranosyl)-O-b- D-glucopyranoside-10, 20-dihydroxy- 16-keto-dammar- 24-ene[24], 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[25]. On acid hydrolysis, bacosides yield a mixture of aglycones, bacogenin A1, A2, A3,[26-28]which are artefacts, and two genuine sapogenins, jujubogenin and pseudojujubogenin and bacogenin, A4, identified as ebelin lactone pseudojujubogenin, were isolated.[29] Successively, a minor saponin bacoside A1 and a new triperpenoid saponin, bacoside A3, were isolated. Later, three new dammarane type triterpenoid saponins of biological interest, bacopasaponins A, B and C, pseudojujubogenin were isolated and a new dammaranetype pseudojujubogenin glycoside, bacopasaponin D, were identified by spectroscopic and chemical transformation methods [30]. 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[31].Subsequently, three new saponins from BM, designated as bacopasides III, IV and V were isolated[32].In addition, the isolation of three new phenylethnoid glycosides, viz. monnierasides I–III along with the known analogue plantainoside B was reported from the glycosidic fraction of *Bacopa monnieri* [33].Moreover, an isolation of a new saponin, a jujubogenin, named bacopasaponin G, and a new glycoside, phenylethyl alcohol was also reported[34-36].

Central Nervous System:

Memory enhancement:

Behavioral studies in animals have shown that Bacopa improves motor learning, acquisition and retention, and delay extinction of newly acquired behavior [37]. The methanol extract and different fractions of *B. monniera* were evaluated for antidepressant activity in the forced swimming test (FST) and tail suspension test (TST) in mice. The results showed that the methanol extract, ethanol and butanol fraction significantly reduced the immobility times both in FST and TST in mice after being administrated orally for 5 consecutive days. All tested samples, in the effective doses for FST and TST, showed no inhibitory effect against locomotor activity. (LA) in mice [38]. On the other hand, it was found that bacosides facilitates anterograde memory and attenuate anterograde experimental amnesia induced by scopolamine and sodium nitrite possibly by improving the acetylcholine level and hypoxic conditions, respectively. In addition, bacosides also reversed BN52021 (a platelet-activating factor receptor antagonist) induced retrograde amnesia, probably due to increase in platelet activating factor synthesis by enhancing cerebral glutamate level[39]. Memory deficits following cholinergic blockade by scopolamine were reversed by Bacopa treatment. Bacopa improved memory functioning in cognitively intact cohorts, with Pycnogenol improving working memory [40].

Benzodiazepines are known to produce amnesia by the involvement of GABAergic system and by the interference of long term potentiation. The behavioral study showed that Bacopa monniera significantly reversed the diazepam induced amnesia[41]. Bacopa administration with phenytoin significantly reversed phenytoin-induced cognitive impairment, as noted by improved acquisition and retention of memory[42]. A clinical trial was carried out to assess the effects of 12 weeks administration of *Bacopa monnieri* (300mg/day) on memory performance in people over the age of 55- years. Bacopa significantly improved memory acquisition and retention in older persons [43]. Significant cognitive enhancing benefits have been demonstrated with chronic administration of Bacopa extracts. A double-blind, placebo-controlled, 12-week trial utilizing the same patient selection criteria and the same dose of Bacopa extract (300 mg daily) containing 55% combined bacosides, was carried out. Forty six healthy volunteers (ages 18-60) were randomly and evenly divided into treatment and placebo groups. The same series of tests administered in the acute dosage trial were administered at baseline, five, and 12 weeks after treatment began. At the end of the 12 week study, results indicated a significant improvement in verbal learning, memory consolidation, and speed of early information processing in the treatment group compared to placebo. These effects were not observed at baseline or at five weeks [44].The Bacopa supplement was commercially available as KeenMind (Flordis).

This product is manufactured from the stems, leaves and roots of Bacopa and is extracted with 50% ethanol. It is standardized to contain active bacosides at levels of 55% ± 5%. KeenMin help develop novel preventative health practices and nutritional/pharmacological targets in the elderly for cognitive and brain health. Bacopa appeared to have multiple modes of action in the brain, all of which may be useful in ameliorating cognitive decline in the elderly. These include: (i) direct pro-cholinergic action; (ii) anti oxidant (flavonoid) activity; (iii) metal chelation; (iv) anti-inflammatory effects; (v) improved blood circulation; (vi) adaptogenic activity; and (vii) removal of b-amyloid deposits[45]. However , in a double blind randomized, placebo control study performed on 76 adults aged between 40 and 65 years, in which various memory functions were tested and levels of anxiety was measured , the rate of learning was unaffected by *Bacopa monnieri* suggesting that *Bacopa monnieri* decreases the rate of forgetting of newly acquired information. Tasks assessing attention, verbal and visual short term memory and the retrieval of pre-experimental knowledge were unaffected. Questionnaire measures of everyday memory function and anxiety levels were also unaffected.[46]

Anti depression:

Research using a rat model of clinical anxiety demonstrated that a BM extract containing 25% bacoside a exerted anxiolytic activity comparable to lorazepam, a common benzodiazepine anxiolytic drug, and it was attentively noted that the BM extract did not induce amnesia, side effects associated with lorazepam, but instead had a memoryenhancing effect [47-49]. The antidepressant potential of BM has been evaluated in an earlier study, wherein it showed a significant antidepressant activity in the most commonly used behaviour paradigms in animal models of depression, namely, forced swim test and learned helplessness tests. In the study, the BM extract in the dose range of 20-40 mg/kg was given once daily for 5 days and it was found comparable to standard anti depressant drug imipramine in antidepressant activity in rodent animals. The same study has postulated the role of serotonin and GABA (gamma amino butyric acid) in the mechanism of action attributed for its antidepressant action along with its anxiolytic potential, based on the compelling evidence that the symptoms of anxiety and depression overlap each other.[50]

Anti oxidiant:

Antioxidants have been reported to prevent oxidative damage by free radicals that are responsible for number of human disorders such as artherosclerosis, hypertension, arthritis, gastritis, ischemia, Alzheimer's disease, diabetes mellitus and AIDS. Bacosides are reported to scavenge free radicals such as peroxides, superoxides and hydroxyl radicals.

Antioxidant activity of alcoholic and hexane extract of *B. monnieri* on lipid peroxidation by ferrous sulphate and cumene hydroperoxide in rat liver homogenate is documented. Based on animal studies, bacosides were shown to have antioxidant activity in the hippocampus, frontal cortex and striatum and found to modulate the expression of certain enzymes involved in generation and scavenging of reactive oxygen species in the brain and demonstrated that Bacoside A3 in the hydroalcoholic extract of the whole plant exhibited an inhibitory effect on superoxides released from polymorphonuclear cells in a nitroblue tetrazolium assay. Sumathy investigated the hepatoprotective activity of its alcoholic extract, administered orally, on the liver antioxidant status of morphine-treated rats. The same research group (Sumathy) reported the protective effect of the plant extract on morphine-decreased brain mitochondrial enzyme activity in rats.

Russo showed the protective role of methanolic extract against the toxicity induced by the NO donor (S-nitroso-N-acetyl-penicillamine, SNAP) in culture of rat astrocytes, consequently preventing DNA damage. The neuroprotective effect of the herb against aluminium induced oxidative stress in the hippocampus of rat brain has also been proved by Janani. Sharan reported the free radical scavenging activity of the methanolic extract of the plant provided protection against DNA damage in human non-immortalized fibroblasts.[51,52]

Anti Epileptic:

Khan reported the neuroprotective role of BM extract in epileptic rats. The experiment showed the glutamate mediated excitotoxicity occurring during seizures and cognitive damage along with pilocarpine induced epilepsy. The study also involved morris water maze experiment. A clinical study by Dhanasekaran [53] reported the effectiveness of alcoholic extract of *Bacopa monnieri* in decreasing symptoms of epileptic seizures. Mathew in another experiment investigated temporal lobe epilepsy, a common epileptic syndrome. The effect of *Bacopa monnieri* on Gamma amino butyric acid (GABA) binding and gene expression was reported in cerebral cortex region of epileptic rats. BM and bacoside-A treatment showed therapeutic effect in this study [54,55] .

Dosage:

Daily doses of Bacopa are 5-10 g of non standardized powder, 8-16 mL of infusion, and 30 mL daily of syrup. Dosages of a 1:2 fluid extract are 5-12 mL per day for adults and 2.5-6 mL per day for children ages 6-12. For Bacopa extracts standardized to 20-percent bacosides A and B, the dosage is 200-400 mg daily in divided doses for adults, and 100-200 mg daily in divided doses for childrens.

Conclusion

It is concluded by above literature that Bacopa Monniera (L.) Pennell (Brahmi) is highly potential medicinal plant that is using in Ayurveda since a long time. Lots of experimental & clinical trial certifies its ancient claims of its therapeutic values on cognition, learning disorders, epileptic seizures, memory, free radical scavenger activity, anxiety, depression, thyroid gland and carcinogenic activity. However, numbers of research are required in future to validate its effectiveness in various disorders.

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