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Bacopa monnieri: Phytochemical and Pharmacological updates

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ABSTRACT: Plant drugs have a long history in both traditional and modern societies as crude drugs. The plant drugs have been extensively practiced as traditional medicine since centuries by peoples of almost all countries of the world. The medicinal plants are considered to be the almost exclusive source of primary health care as well as a source of pharmacological active compounds for 80 % of the world's population, herbal medicines have been proven effective in common as well as rare diseases. *Bacopa monnieri* belongs to the family *Scrophulariaceae* is perennial, creeping herb, origin to wetlands of southern and eastern India, Australia, Europe, Asia, north and South America. The major therapeutic chemical constituents of this plant identified through various researches are the Triterpenoids, Saponins, Bacoside, Flavonoids and Glycosides. Bacoside A has been recognized as the chief component responsible for therapeutic effects. The plant is used in traditional Ayurvedic treatment for a range of CNS applications, being considered as a memory tonic. It has been found to possess various CNS actions including nootropic, antidepressant and anxiolytic action. It is also considered to be an important adaptogen. This review shall cover pharmacological properties, chemical constituents and scientific researches supporting not only traditional use of Ayurvedic claims but also other physiological conditions such as anti-inflammatory, cardio tonic and other pharmacological effects of *B. monnieri* extracts.

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INTRODUCTION:

In human culture from days immemorial medicinal plants have assumed a significant function in the avoidance and control of ailments. It has been affirmed by WHO that natural medicines serve the wellbeing needs of around 80 % of the world's population particularly for many individuals in the rural areas of developing countries. Advancement of science and innovation and the adverse reaction of current medication have brought about expanded and viable use of plant-based drugs. Attention to therapeutic plants utilization is a consequence of the numerous long stretches of battles against sicknesses because of which

man figured out how to seek medications in barks, seeds, natural product bodies, and different plant species. India has a rich heritage of traditional medicine and traditional health care systems. *Bacopa monnieri (L.)* is a significant medicinal plant of the family *Scrophulariaceae* used in traditional medicine to treat various CNS disorders and for promoting memory and intellect. It is known as a memory enhancer, and many preparations are now commercially available in the market [1].

CLASSIFICATION, DISTRIBUTION AND HABITAT:

The plant belongs to Kingdom - Plantae, Division - Angiospermae, Class - Dicotyledonae, Subclass - Gamopetalae, Series - Bicarpellatae, Order - Personale, Family - *Scrophulariaceae,* Genus – *Bacopa* and Species - *Monnieri*. Plant includes 146 types of aquatic species distributed all through the warmer regions of the world. Aside from India, Nepal, Sri Lanka, China, Taiwan and Vietnam, it is also found in Florida and other southern parts of the USA. In the US, the herbs are found as weeds in rice fields growing richly in marshes and wetlands of warmer regions [2]. In India, it grows in moist, damp spots and on the banks of moderate flowing rivers lakes, climbing up to an attitude of 1,320 m [3].

BOTANICAL DESCRIPTION:

B. monnieri is a small, creeping and slightly fleshy herb. The leaf and flower bearing stems are 10 to 30 cm long and emerge from creeping stems. The roots are coming out at the nodes. The leaves are simple, obviate, opposite, around 2 cm × 1 cm in dimension, with obtuse edges (Fig 1). Flowers are blue or white with purple veins, singularly on long pedicels in the leaf axils. The corolla is five lobed, white or pinkish with purple blotches. The fruit is an up to 5 mm capsule, which develops in the tenacious calyx [4].

Fig 1. The flowering plant of *Bacopa monniera.*

TRADITIONAL USES:

B. monnieri is commonly cherished in India as an energy booster herb used for almost 3000 years by Ayurvedic medicinal specialists. It is referred to as medhyarasayana, a medication used to boost memory and intellect (Medhya). Since the sixth century AD, the herb has been listed in many ancient Ayurvedic compositions, including the Charaka Samhita, in which it is prescribed as a diuretic, an energy booster for the nervous system and heart, in formulations for the management of anxiety, low cognition and lack of concentration. The plant has been utilized extensively as a nootropic, digestive aid and to improve learning, memory and respiratory function [5]. The herb helps to repair damaged neurons, neural synthesis, restore synaptic activity and enhances the function of the brain. *B. monnieri* is effectively used in various inflammatory disorders such as asthma, bronchitis, dropsy and rheumatism. These plants are also used for the prevention of dermatitis, anemia, diabetes, heart problems, schizophrenia, and epilepsy. It is also used in boils, as a blood purifier and for complications with cataracts. The leaf juice is given to children for the relief of bronchitis and diarrhea, leaf paste is used as a treatment for rheumatism and leaves with tender stalks are eaten in western Bengal in decoction form to relieve the cough. *B. monnieri* when administered with ginger juice, sugar and *Moringa oleifera* bark extracts, used as a healthy cardiac tonic, offering relief from anxiety neurosis in patients. It has also been marked as a potent bronco-vasodilator and antioxidant [6-9].

PHYTOCHEMICAL CONSTITUENTS:

In view of the importance of this plant in the indigenous medicine system, several groups of researchers have performed systematic chemical analyses of the plant. Bose and Bose reported the isolation of the *B. monneria* alkaloid brahmine in 1931. The alkaloids are nicotinine and herpestine. It contains D-mannitol and a saponin, hersaponin and potassium salts [10,11].

The 3-(alpha-L-arabinopyranosyl)-O-β-D-glucopyranoside-10,20-dihydroxy-16-keto-dammar-24-ene was assigned as Bacosides A, is the key chemical agent shown to be responsible for the memory-facilitating activity of *B. monniera* [12]. Bacopa saponins A, B and C are isolated and identified as 3-O-alpha-L-arabinopyranosyl-20-O-alpha-L-arabinopyrasonyl-jujubogenin,3-O-[alpha-L-arabinofuranosyl-(1→2)-alpha-L-arabinopyranosyl] pseudojujubogenin and 3-O-β-D-

glucopyranosyl-(1→3)-{alpha-L-arabinopyranosyl-(1→2)}-alpha-Larabinopyrasonyl] pseudojujubogenin respectively by spectroscopic and chemical transformation methods [13]. They also reported the new dammarane-type pseudojujubogenin glycoside, bacopasaponin D, defined as 3-O-[α-L-arabinofuranosyl-(1→2)-β-D-glucopiranosyl] pseudojujubogenin by spectroscopic and chemical transformation methods. Two new pseudojujubogenin glycosides reported as bacopasides I and bacopasides II from the methanol extracts [14]. In addition, the glycosidic fraction of *B. monniera* was isolated from three new phenylethnoid glycosides, called monnierasides B [15]. Three new saponin have been isolated from the *B. monniera* designated as bacopasides III, IV, V with structures 3-O-α-L-rabinofuranosyl-(1→2)-β-D-glucopyranosyljujubogenin,3-O-β-D-lucopyranosyl-(1→3)-α-L-arabinopyranosyl jujubogenin, 3-O- β-D-glucopyranosyl-(1→3)-α-L-arabinofuranosyl pseudojujubogenin.

Phenylethanoid glycosides, flavonoids, amino acids such as alpha-alanine, aspartic acid, glutamic acid, betulinic acid, stigmasterol, b-sitosterol and stigmastenol are other significant compounds identified in this plant [16,17].

PHARMACOLOGICAL STUDIES:

B. monnieri has been found to possess significant cognition and neuropharmacological, antidepressant activity, antianxiety, sedative, tranquilizing, anticonvulsant, anticancer, anti-inflammatory, antioxidant, antibacterial, antifungal, antiulcer, antidiarrheal, antihypertensive, analgesic and anti-toxicity activities.

Memory enhancement and Neuropharmacological activity:

Animal behavioral tests have shown that *Bacopa* enhances motor learning, and acquisition and retention, and slows the regression of newly learned behavior [18]. In the forced swimming test (FST) and tail suspension test (TST) in mice, methanol extract and various fractions of *B. monniera* were tested for antidepressant activity [19]. In cognitively intact cohorts, *Bacopa* improved memory processing, with Pycnogenol enhancing working memory [20]. The behavioral study showed that *B. monniera* substantially reversed the amnesia caused by diazepam [21], mitigating cognitive dysfunction triggered by phenytoin [22].

In older persons, *Bacopa* dramatically increased knowledge acquisition and retention [23]. *B. monnieri* reduced the rate of forgetting of newly acquired information [24,25]. Animal model trials indicate the effectiveness of *Bacopa* extracts to enhance memory ability and neuroprotective activity toward Alzheimer's disease [26]. In Parkinson's disease, *B. monnieri* may provide a platform for potential therapeutic discovery and new therapeutic approaches and can act as an antiparkinsonian agent [27,28].

Antidepressant and antianxiety activity:

In an earlier review, the antidepressant potential of *B. monnieri* was tested where it showed a significant antidepressant efficacy in the most widely used behavior paradigms in animal depression models, including forced swim test and learned helplessness tests [29-31]. In a rat model of clinical anxiety, *Bacopa* extract developed a dose-related anxiolytic efficacy, qualitatively comparable to that of lorazepam [32].

Sedative and tranquillizing properties:

Several Studies reported a sedative effect of glycosides named hersaponins [33]. A subsequent research showed that the alcoholic extract and, to a lesser extent, the entire plant extract had tranquillizing effects on albino rats and dogs [34]. On the other hand, the plant alcoholic extract and chlorpromazine have been found to enhance the efficiency of rats in motor learning [35]. A previous study stated that in promoting the acquisition and retention of brightness discrimination reaction, a single dose of glycoside hersaponin is better than pentobarbitone [36].

Antiepileptic activity:

Study trials have confirmed the efficacy of *Bacopa* alcoholic extract in reducing epileptic seizure symptoms [37]. The neuroprotective activity of extract of the *Baccopa* plant in glutamate mediated excitotoxicity during seizures and cognitive damage in pilocarpine induced epilepsy was reported [38]. The influence of *B. monnieri* on the binding and gene expression of Gamma amino butyric acid (GABA) was recorded in the cerebral cortex area of epileptic rats [39,40].

Antioxidant and adaptogenic activity:

The oxidative damage from free radicals is responsible for various human diseases such as atherosclerosis, hypertension, arthritis, gastritis, ischemia, Alzheimer's disease, diabetes mellitus and AIDS. The oxidation can be prevented by antioxidant. The Bacosides have been reported to scavenge free radicals such as peroxides, superoxides, and hydroxyl radicals [41], thus Bacosides have shown an antioxidant and antistress activity as

suggested from animal study which revealed that the release of certain enzymes involved in the formation and scavenging of reactive oxygen species in the brain is modulated by *Bacopa* extracts. [42,43]. The adaptogenic properties of the herb were found to be useful in the treatment of stress-related illnesses, as the capacity to be effective in stress was shown by *Bacopa* extracts in a study on rats [44,45].

Antiasthmatic activity:

In the tracheal muscle of rabbit and guinea pigs, the extract of *B. monnieri* had relaxant properties with a partial contribution of β-adrenoreceptor and prostaglandins.[46] It also induced broncodilation in anaesthetized rats [47] promoting the typical use of this plant for various respiratory diseases [48]. One of the study indicates that the antagonistic action of calcium is present in ethanolic extract of *B. monnieri* [49]. In addition, it has been reported that methanolic extract exhibited a potent mast cell stabilizer, indicating the potential usefulness of *B. monnieri leaves* in allergic conditions [50].

Anticancer activity

Anticancer activity has been observed with stigmasterol, a phytosterol extracted from aerial parts of *B. monnieri* [51]. Cytotoxic activity of *B. monnieri* ethanolic and dichloromethane extract against cancer cell line have been observed [52]. The anti-cancer action of *B. monnieri* ethanolic extract against the human breast cancer cell line may be due to the synergistic effect of the extract's secondary metabolites [53].

B. monnieri may protect against brain injury and enhance brain development [54]. Bacopaside II prevents aquaporin AQP 1 action, thus reducing the movement of endothelial cell and induces apoptosis [55].

Anti-inflammatory activity:

In traditional medicine, *B. monnieri* possesses anti-inflammatory activity as its ethanol extract selectively blocked prostaglandin E (2) [56]. The methanolic and aqueous extract of *B. monnieri* caused a significant reduction in the edema paw volume in carrageenan and histamine-induced edema models in rats [57-59].

Antiulcer activity:

Potential antiulcer and ulcer-healing activities was observed in normal (More pronounced) and non-insulin dependent *Diabetes mellitus* rats with *B. monnieri* extract, which may be due to their effects on the offensive and defensive factors of the mucosa [60,61].

Hepatoprotective activity:

The ethanol, ethyl acetate and n-butanol fraction of *B. monnieri* produces significant hepatoprotective activity in ethanol-induced hepatotoxicity in rats, which might be due to presence of Saponins in the extract [62,63]. In the albino mice model, administration of *B.* ethanolic extract from either source (*in vitro* or natural) substantially prevented CCl_4-induced hepatic damage, as shown by the hepatic damage levels of serum markers (SGPT, SGOT and bilirubin) [64].

Anti-diarrheal activity:

The anti-diarrheal effect of *B. monnieri* ethanolic extract on castor oil-induced diarrheal mice was assessed, which might be due to presence of tannins and phenolics [65].

Antihyperglycemic activity:

The plant methanolic extract of *B. monnieri* showed significant anti-hyperglycemic activity in streptozotocin-induced diabetic rats [66,67]. The extract of *B. monnieri* indicates potential application in diabetics for the treatment of hyperlipidemia [68].

Antifungal activity:

Methanolic extract shows strong antifungal activity against *Candida albicans* and *Aspergillus Niger* and *Malassezia furfuras* [69,70]. *B. monnieri* has significant antifungal activity against the Alternaria *alternate* and *Fusarium fusiformis* fungi [71].

A very strong anti-fungal activity against dermatophyte fungi, including *Aspergillus niger*, *Aspergillus flavus*, *Trichophyton rubrum* and Microsporum, was demonstrated by both aqueous and ethanolic extract of *B. monnieri* [72].

Antihypertensive activity:

B. monnieri decreases blood pressure partially through the release of nitric oxide from the endothelium in addition to acting on vascular smooth muscle Ca^{2+} homeostasis [73], thus treat primary hypertension in human being.

B. monnieri enhances myocardial function following ischemia/ reperfusion injury by improving the coronary blood supply, contractile force and a reduction in infarct rate [74,75].

Endocrine effects:

The thyroid hormone, T4, was raised by 41 % in mice by the extract of *B. monnieri.* T3 was not induced, suggesting that the extract would specifically induce T4 synthesis and release at the glandular level while not influencing T4 to T3 conversion [76].

Hair growth promoting activity:

It was found that, among the other formulations tested, the hair oil formulation produced the best outcome by demonstrating follicular size enlargement and anagen process prolongation [77-79].

Antispasmodic activity:

B. monnieri extract has spasmolytic activity in smooth muscles due to inhibition of calcium influx via both voltage and receptor-operated calcium channels of the cell membrane [80]. However, the lack of any modification of either, nor-adrenaline or caffeine-induced contractions in the presence of *B. monnieri* extract suggests that this natural compound has no observable effect on mobilization of intracellular calcium.

Antinociceptive activity:

B. monnieri aqueous extract exhibits analgesic action through participation in the analgesic function of β1-adrenergic, β2-adrenergic receptors and 5-HT receptors [80]. It was also found that when the extract was administered in combination with naloxone, the latency for analgesic action did not improve, suggesting opioid receptor involvement in analgesic activity [81].

CONCLUSION:

It is concluded by above literature that *B. monniera (L.)* is a highly potential medicinal plant that has been used in Ayurveda since a long time. Lots of experimental and 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 activities. However extensive research are required in the future to validate its effectiveness in various disorders.

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