IJPSR (2023), Volume 14, Issue 7 (Review Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 13 October 2022; received in revised form, 25 November 2022; accepted, 28 November 2022; published 01 July 2023

# ETHNOMEDICINAL AND PHARMACOLOGICAL IMPORTANCE OF *BACOPA MONNIERI*: A REVIEW

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**Keywords:**

*Bacopa monnieri*, Ethnomedicine, Pharmacological, Phytochemical, Medicinal plant

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**ABSTRACT:** Despite the considerable advancement in medical sciences and allopathic medicines, the use of complementary and alternative medicines has dramatically increased worldwide. *Bacopa monnieri* is one of the most important and highly studied medicinal plants that is being used as an ayurvedic or ethnomedicine for thousands of years. It improves intelligence rejuvenation and treats mental illness, fever, a blood disorder, anemia, *etc*. The main phytoconstituents of *B. monnieri* have been reported as alkaloids, saponins, flavonoids, and glycosides, including various sterols and potassium salts. The plant possesses multiple pharmacological properties, such as memory enhancer, anti-depressant, anti-inflammatory, antioxidant, gastroprotective, anxiolytic, hepato-protective, anti-cancer, anti-hyperglycemic, antimicrobial, *etc*. The pharmacological properties of the plant can be attributed to the presence of saponin-bacoside. The formulations of this plant are used for clinical applications by numerous research groups and pharmaceutical companies worldwide, including in Asia, Australia, and the United States of America. Considering the importance of the plant, the present review summarizes the ethnomedicinal and pharmacological activities of *B. monnieri*, which may help in exploring the untapped potential of this natural gift to humankind.

**INTRODUCTION:** Nature has a unique fashion of safeguarding humankind from the atrocities of various health ailments by providing natural ingredients with an array of bioactivities. Traditional knowledge is a distinctive form of custom or set of methods that evolved in antiquity and perpetuated through millennia *via* the passing of information constrained to a particular clan, native communities, and family dynasties.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.14(7).3255-63

This article can be accessed online on www.ijpsr.com

DOI link: http://doi.org/10.13040/IJPSR.0975-8232.14(7).3255-63

Ethnomedicine pertains to the traditional medical approaches that consider cultural perspectives on health, illness, and diseases that involve healthcare strategies and curative modalities [1]. Thus, the ancient storehouse of traditional knowledge serves as the foundation for ethnomedicine. Ayurveda, which has its parentage in India, is among the oldest medicinal practices based on conventional knowledge [2].

*Bacopa monnieri* (L.) Pennell, commonly called Brahmi, is also known as Indian pennywort, water hyssop, thyme-leafed gratiola, and herb of grace **Fig. 1**. It is an annual creeper that predominantly grows in marshy, wet, and humid areas of tropical climates in countries, like India, China Nepal, Vietnam, Sri Lanka, Taiwan, Hawaii, *etc*.

It is a member of the Scrophulariaceae family, which has 200 genera and 4500 species [3]. In Ayurvedic literature, *B. monnieri* is specially mentioned for its rejuvenating and nootropic properties as it aids in various mental problems, such as impaired cognitive function and lack of attention [4].

*B. monnieri* has recently attracted more attention on a global scale because of its wide range of pharmacological properties [5]. The bioactivities of *B. monnieri* are because of the presence of numerous phytoconstituents, like alkaloids, saponin, flavonoids, and glycosides [6]. Saponin and bacosides are important bioactive molecules which gained extensive research attention in recent years [7]. *B. monnieri* formulations are used for clinical applications by numerous research groups and pharmaceutical companies worldwide, in Asian countries, Australia, New Zealand, and the USA. Multiple laboratory animal models have shown to improve behavior under various experimental conditions after the treatment of bacosides-enriched standardized extract of *B. monnieri* [8].

**FIG. 1: BRAHMI OR INDIAN PENNYWORT PLANT [*BACOPA MONNIERI* (L.) PENNELL]**

Recently, both industrialized and developing nations have seen a sharp rise in the use of complementary and alternative medicines. The relentless quest of humankind for efficient and safe medicine has garnered attention towards the traditional system of medicine. The ability of herbal treatments to treat even otherwise incurable refractory conditions is now beyond dispute. Everyone in every community is aware of the advantages plants may provide, particularly for maintaining health and enhancing the quality of life. According to WHO, 3.5 billion people use plant-based medicines in developing nations for primary healthcare. Currently, drugs of natural origin comprise around half of all medications used in clinical settings [9]. In this context, this review summarizes the ethnomedicinal and pharmacological properties of *B. monnieri*.

**Ethnomedicinal Importance of *B. monnieri*:** In the Ayurvedic medicaments, *B. monnieri* has been one of the most sattvic plants since the Vedic era[1]. Early accounts of it can be found in texts from the sixth century AD like the Charaka Samhita, Atharva-Ved, and Susurtu Samhita [10]. The early Ayurvedic sages, who were also excellent physicians, outlined how *B. monnieri* enhanced intelligence, longevity, nervous system rejuvenation, strength, and effectivity in sleep. *B. monnieri* has been used throughout the millennia to treat various ailments, including diabetes, cough, edema, anemia, leprosy, blood disorders, poisoning, fever, and mental illness [10, 1, 11].

The plant has long been an antipyretic, anti-inflammatory, antispasmodic, and antiepileptic drug. Ayurvedic experts in India have revered *B. monnieri* for three thousand years as an herb that promotes rejuvenation [10]. Due to the absence of adequate essential healthcare services, traditional medicines are a necessity in underdeveloped areas as a form of the medical system. *B. monnieri*is widely used in a variety of cultures around the world, highlighting its rich ethnobotany[10]. This plant is crucial to Rajasthani folk medicine in India. Blisters, rheumatism, bronchitis, stomach problems, bone fractures, asthma, urinary duct inflammation, and leg edema are just a few conditions for which this plant is used for treatment. The locals in the Virudhunagar region of Tamil Nadu, India, use *B. monnieri*to to treat dysentery. They also use this herb to sharpen their memories [12].

The villagers of Dakshin Dinajpur in west Bengal, India, use both the leaves and roots of *B. monnieri* for the improvement of memory as well as to alleviate neurological disorders [13]. The leaf of this herb is also traditionally used to treat nasal congestion, cold, and cough in the Indian state of Odisha. They use the leaves to combat asthma and constipation, while the root extract is used as an

eye drop to manage cataracts. For the indigenous people of Madhya Pradesh's East Nimar region, this herb is lauded as an aphrodisiac where problems like throat infection or cough are treated with leaf extract of *B. monnieri*. It is also said to be used as a memory enhancer and to treat worm infestations in children. Additionally, this herb is thought to be beneficial in treating diabetes mellitus [2]. In the Wayanad district of Kerala, India, the plant's powdered form is taken orally to treat epilepsy and asthma. The Malayan tribes in southern Kerala use *B. monnieri* leaves to treat urinary problems and revitalize the abdominal area [14]. In Srilanka, *B. monnieri* is recommended for fevers in under the name Loonooweella. On the other hand, it is used as a diuretic in the Philippines and India because of its aphrodisiac properties [15].

**Pharmacological Importance of *B. monnieri*:** On the priority list of significant Indian medicinal plants, *B. monnieri* is currently listed as number two. The ranking is based on the plant's potential for use in medicine and potential economic value [2]. The estimated market demand for this important medicinal plant is approximately a thousand tonnes per year, per National Medicinal Plants Board [3]. Besides using as folk medicine, *B. monnieri* has also been used in modern pharmacology. The scientific community has demanded experimental proof to emphasize the medical significance of B. monnieri further. Scientific investigations have been planned and carried out to pharmacologically support these assertions, taking inspiration from the long-standing ethnomedical use of this extremely valuable plant.

**Phytochemical Constituents:** Numerous phytochemical studies on *B. monnieri* reported the presence of bioactive substances like alkaloids, saponins, glycosides, and flavonoids, including various sterols and potassium salts. There is a total of 20 phytochemicals reported in the ethanolic extract of *B. monnieri* [11]. The alkaloids include herpestine, apigenin, brahmine, D-mannitol, nicotine, plantainoside B, cucurbitacin, and monniersides I–III. Hersaponin, monnierin, bacoside A ([3-(L-arabinopyranosyl)-O-Dglucopyranoside-10, 20-dihydroxy-16-keto-dammar-24-ene]) and bacoside B are examples of saponins. Bacoside is a triterpenoid saponin belonging to the dammarane class. It has glycone units that are either jujubogenin or pseudo-jujubogenin moieties [3]. Ebelin lactone and bacogenin-A1 are generated when the bacoside A is acid hydrolyzed, whereas jujubogenin and pseudojujubogenin are produced as sapogenins when Smith-de Mayo degrades the bacoside A. There are 12 recognized analogs in the family of bacosides. Bacosides A3, Bacopaside II, Bacopaside I, Bacopaside X, Bacopasaponin C, and Bacopasaponin N2 made up the majority of the bacopasaponins. In contrast, Bacopasaponin F, Bacopasaponin E, Bacopasaponin N1, Bacopasaponin III, Bacopaside IV, and Bacoside V made up the minor components [16]. There have been reports on discovering the biologically significant bacopa saponins E and F; two new dammarane-type jujubogeninb is desmosides. Bacopasaponins A, B, and C are the three novel dammarane-type triterpenoid saponins of biological significance [17]. A thorough review of the dammarane-type triterpenoid saponin's research from *B. monnieri* was also published recently [18]. Betulinic acid, stigmasterol, and beta-sitosterol are other active ingredients found, in addition to a wide variety of bacosides and bacopa saponins [11].

**Pharmacological Activities:** Numerous investigations have been done to study the pharmacological effects of *B. monnieri*. These effects were primarily attributable to distinctive saponins known as "bacosides" [5]. The plant has been reported to have significant activity for the central nervous system. It possesses anti-depressant, anti-inflammatory, antioxidant, cardiovascular, gastroprotective, anxiolytic, hepatoprotective, anti-cancer, anti-hyperglycemic, and antimicrobial activity. The important pharmacological activities of *B. monnieri* are discussed in the following.

**Brain Activities:** Nootropic compounds demonstrate a wide range of brain activities and improve the central nervous system's performance. As a result, cognitive capacities such as memory and the ability to learn are enhanced. According to animal behavioural studies, *B. monnieri* enhances motor learning, acquirement, reservation, and slowdown of disappearance of newly acquired characters [4]. Researchers have cited neuroprotection against dementia, amnesia, Alzheimer's disease, memory impairment,

Parkinson's disease, schizophrenia, and epileptic seizures as one of the most notable therapeutic effects of *B. monnieri* [19]. In comparison to two nutraceuticals, Panax ginseng and modafinil, a synthetic eugeroic medication, *B. monnieri* demonstrated the most consistent and greatest impact[6]. It was found that bacoside A significantly reduced GABA receptors linked to epilepsy, improved memory and cognitive abilities, and inhibited beta-amyloid poisoning and fibrillation [20]. *B. monnieri* reportedly increases protein kinase activity in the hippocampus [4]. The ability of *B. monnieri*-containing products to improve memory was examined using a mouse model of amnesia, which had been reported to have decreased AChE activity. As evidence for this, *B. monnieri* treatment returned epileptic rats with elevated AChE activity to normal [21].

**Anti-depressant Activity:** Affective disorders like depression are characterized by melancholia, psychomotor retardation, mood swings and a lack of interest in one's environment [22]. The herb *B. monneri*is regarded as a brain stabilizer, and the extract of the whole plant has antidepressant qualities. They all demonstrate antidepressant properties: bacosides A and B, bacosides I and II, and bacopa saponin C [17]. According to a recent study, the alcoholic extract of *B. monneri* demonstrated considerably better outcomes than the control group at doses of 40 and 80 mg/kg. Its antidepressant effect is comparable to the common antidepressant medication imipramine [22]. Three new triterpene glycosides, bacosides VI-VIII, and their three known counterparts, Bacopaside I, Bacopaside II, and Bacopa saponin C showed antidepressant effects when tested on forced swimming and mouse tail suspension, respectively [23].

**Anti-inflammatory Activity:** The prevalence of chronic inflammatory illnesses continues to rank among the significant health problems of the world. Inflammation is the result of living tissues responding to injury. A few complex processes include fluid extravasations, mediator release, enzyme activation, tissue degradation, cell migration, and repair [24]. The extract of bacosides and triterpenoids is effective in treating a variety of inflammatory diseases [18]. Through modulation, *B. monneri* can release inflammatory mediators. When *B. monnieri* supplements were used in animal brains, they subsequently reduced the effect of oxidative stress and inflammation [25]. At a 400 mg/kg body weight dose, bacopa leaf extract significantly reduced inflammation in rat test models exposed to carrageenan- and histamine-induced edema [26].

**Antioxidant Activity:** *B. monnieri* contains antioxidant capabilities in the form of alcohol and hexane that mitigate the effects of lipid Peroxidation [27]. Other studies demonstrated the antioxidant activity of *B. monnieri* through different mechanisms, such as the inhibition of the activities of enzymes, such as catalase, superoxide dismutase, and glutathione peroxidise [28]. The antioxidant potential of *B. monnieri* aqueous extracts from liquid-cultured and acclimatized plants was investigated, and the shoot is doubling time was also estimated. Aqueous extracts of acclimated plants showed a 10-fold better overall antioxidant capacity than *in-vitro* liquid cultivated plantlets [29]. A study was reported on streptozotocin-induced diabetic rats to determine the protective effects of *B. monnieri* on tissue antioxidant defense system and lipid peroxidative status [30]. In the kidney and parts of the central nervous system of diabetic rats. *B. monnieri* has been found to reduce the activity of antioxidants, their GSH activity, and lipid peroxidation compared with clinical drug antioxidant enzyme activity Glibenclamide. According to the study, *B. monnieri* extract modulates antioxidant activity and improves the resistance of diabetic rats' damage caused by ROS.

**Cardiovascular Activity:** In treating several malignancies, cardiovascular disease, and induced lipid peroxidation, *B. monnieri* protects against the harmful effects of free radicals [31]. According to a study, an ethanolic extract of the whole *B. monnieri* plant showed cardiac depressive activity on left ventricular contractility, heart rate, and coronary flow in an isolated rabbit heart [32]. *B. monnieri* maintains blood flow by contracting the left ventricle. The effect of bacoside on the structural and functional integrity of the membrane in cigarette-smoking rats prevented the leakage of creatine kinase from the corresponding tissues, which could be attributed to its free radical scavenging and anti-lipid peroxidative effect [33].

**Gastroprotective Activity:** A study reported that *B. monnieri* has gastroprotective activity in humans [33]. It is especially beneficial in intestinal spasms, such as irritable bowel syndrome [2]. The plant's extracts have shown anti-ulcer qualities. However, the study also reported that the juice of *B. monnieri* gives a gastroprotective effect because the mucosal membrane enhances mucin secretion and reduces cell shedding. In a study, *B. monnieri's* methanolic extract showed dose-dependent anti-ulcerogenic action on a range of gastric ulcer models induced by ethanol, aspirin, 2 hours of cold restraint stress, and 4 hours of pylorus ligation. *B. monnieri* extract at a dose of 20 mg/kg, administered twice daily for 10 days, had healing effects against 50% of gastric ulcers brought on by acetic acid [34].

Except for ethanol-induced ulcers, where 100 mg/kg was not found to reduce the ulcer effect significantly, *Bacopa* juice of 100-300 mg/kg produced significant antiulcer activity in all experiments. *Bacopa* extract may have an ulcer-protective effect because it affects mucosal defensive factors rather than offensive factors like pepsin and acid, such as increased mucin secretion, mucosal glycoprotein, and decreased cell shedding [35].

**Anxiolytic Effect:** The *B. monnieri* extract with 25% bacoside A has shown comparable anxiolytic activity to the popular benzodiazepine anxiolytic drug, lorazepam. This plant is significant compared to lorazepam because it does not cause amnesia and has memory-improving properties in addition to its anxiolytic activity [4]. *Bacopa* extract demonstrated anxiolytic action in ethanol withdrawal-induced anxiety in rats at 100, 200, and 400 mg/kg doses with no central nervous system depressant action even at 400 mg/kg [36].

**Hepatoprotective Activity:** In recent years, numerous findings supported the hepatoprotective properties of *B. monnieri* against chemically induced liver toxicity. The hepatoprotective activity is attributed to the phytochemical bacoside A. Carbon tetrachloride ($CCl_4$) is one of the causative chemicals of liver cirrhosis, as demonstrated by various investigations [37]. The liver cells' metabolism is disturbed by $CCl_4$, which alters the behaviours of enzymes. A recent study showed that previously treating methanolic extract of *B. monnieri* against $CCL_4$ protects the liver structure and preserves dilation of liver sinusoids and congestion of the central vein in rats [38]. The activity of *B. monnieri* has been associated with a decrease in serum levels of AST, ALT, and bilirubin when treated with 400 mg/kg of whole plant aqueous and ethanolic extracts [39]. The report also concluded that *B. monnieri* extract might protect against paracetamol-induced hepatotoxicity. Pre-treatment with *B. monnieri* extract had a significant protective role against morphine-induced liver and kidney functions, according to the serum levels of urea, creatinine, and uric acid, as well as the activities of glutamate oxaloacetate transaminase, glutamate pyruvate transaminase, and alkaline phosphatise [40].

**Thyrogenic Activity:** Thyroxine (T4) and triiodothyronine (T3), the thyroid hormones, are critical regulators of many bodily processes, including lipid and carbohydrate metabolism, oxygen uptake, nerve conduction and reproduction. Changes in these hormones' normal levels cause physiological and clinical anomalies, including hypothyroidism and hyperthyroidism. Male mice were given 200 mg/kg of *B. monnieri* leaf extract, which increased T4 concentration by 41% without increasing hepatic lipid peroxidation (LPO). This suggests that *B. monnieri* leaf extract could be employed as a thyroid-stimulating drug [41].

By experimenting with the plasma levels of thyroid hormones (T3, T4 & TSH), lipid profile, and liver antioxidants, another study was conducted to evaluate the effects of *B. monnieri* (200 mg/kg) on experimentally induced hypothyroidism in male Wistar rats [42]. The findings from this study imply that *B. monnieri* improved hypothyroidism as seen by the reversal of several biochemical abnormalities and the histology of the thyroid gland in rats [42].

**Anti-cancer Activity:** Bacosides A and B from the *B. monnieri* plant's ethanolic extract have demonstrated anti-tumour properties. In a study, the saponin-rich ethanolic extract was analyzed and reported bacoside A as the active ingredient responsible for the anti-cancerous effect[43]. Similarly, an examination of ethanolic extract for sarcoma 180-cell culture found that the cell proliferation was reduced as the concentration of

the extract was increased [44]. Another study, using Swiss albino mice, investigated the anti-tumour effect of stigmasterol, extracted from the aerial parts of the *B. monnieri* plant, against Ehrlich ascites carcinoma. Protein phosphatase 2A activation is assumed to be the mechanism by which stigmasterol exerts its anti-tumour effects [45].

A study was performed on *in-vivo* tumour model testing and short-term *in-vitro* chemosensitivity and reported that orally administered extract of the plant impedes the growth of the tumor [46]. Recently, cucurbitacin has garnered attention for its powerful anti-oncogenic and anti-proliferative properties. Cucurbitacin arrests the cell cycle at the G2/M phase and halts the development of multiple cells [47].

**Anti-hyperglycemic Activity:** It was reported that the ethanolic extract of *B. monnieri* significantly lowered the blood glucose levels compared to diabetic control rats [45]. Bacosine raised the amount of glycogen in the liver and was found to increase peripheral glucose uptake in the diaphragm of in-vitro alloxan-induced diabetic rats, according to their findings. Thus, the study concluded that bacosine might have properties like insulin, and an increase in peripheral glucose consumption might explain its anti-hyperglycemic effect. *B. monnieri* was investigated for its potential to treat mice with glucose intolerance for hyperglycaemia.

The extract significantly reduced the rise in serum glucose concentrations when given in four doses of 50, 100, 200, and 400 mg/kg body weight. Glibenclamide, a common antihyperglycemic medication, inhibited the rise in serum glucose when treated at 10 mg/kg of body weight. The findings indicate that the plant's methanolic extract has significant antihyperglycemic potential [48]. In another study, rats given streptozotocin-induced diabetes were administered *B. monnieri* (500 mg/kg) for 30 days, and it was observed that the rats' levels of lipid peroxidation, blood sugar, and glycated haemoglobin were significantly higher, while their activities of catalase and superoxide dismutase were noticeably decreased [49].

**Antimicrobial Activity:** A study on the antimicrobial activity of *B. monnieri* with its aerial parts revealed the potentiality of this herb in curing pathogenic ailments [50]. In another study, ethyl acetate extract showed antibacterial activity against gram-negative organisms, while diethyl ether extract demonstrated antibacterial activity against gram-positive organisms [51].

The ethanolic extract exhibited higher anti-fungal properties than diethyl ether and ethyl acetate. In the investigation, aerial parts of *B. monnieri* were used on organisms *S. aureus*, *P. vulgaris*, *C. albicans* and *A. niger*. Likewise, an ethanolic extract of the plant was reported as a potent anti-fungal agent than diethyl ether and ethyl acetate [50]. This investigation also showed diethyl ether as an antibacterial agent against gram-positive bacteria, while ethyl acetate against gram-negative bacteria. Anti-fungal activity of *B. monnieri* against *Alternaria alternata* and *Fusarium fusiformis* was also reported [50].

In a recent study, the antimicrobial potency of methanolic extract of *B. monnieri* was demonstrated against multi-drug resistant (MDR) clinical isolates. The methanolic extract was prepared from the *in-vitro* cultured and field-grown micro propagated plants against human urinary tract infecting (UTI) and respiratory tract infecting (RTI) pathogens [52].

**CONCLUSION:** The current review shows that *B. monnieri,* used for the last three thousand years as an ethnomedicine, is a highly potent medicinal plant in modern pharmacology. It has been established that the plant contains numerous phytoconstituents like alkaloids, glycosides, flavonoids, and saponins, out of which saponins-bacoside A and B are the most significant ones responsible for diverse pharmacological effects. The plant shows promising results in memory enhancement, neurodegenerative disorders, and other mental ailments. Other pharmacological activities include antioxidant, antimicrobial, anticancer, hepatoprotective, etc. However, *B. monnieri* still has much-untapped potential for treating many illnesses. The clinical evidence supporting the medicinal benefits is few, and there is a paucity of information about human randomized controlled trials. It is necessary to plan and carry out clinical trials that contrast the therapeutic advantages of *B. monnieri* with the currently available standard medications.

**ACKNOWLEDGEMENT:** The authors are thankful to the faculties and staff of the Dept. of Zoology, Gauhati University, Assam, India, for their support and cooperation.

**Funding:** This study did not receive specific financing from the government, commercial, or non-profit organizations.

**CONFLICTS OF INTERESTS:** The authors declared no conflict of interest among them.

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**How to cite this article:**
Das S and Kalita JC: Ethnomedicinal and pharmacological importance of *Bacopa monnieri*: a review. Int J Pharm Sci & Res 2023; 14(7):3255-63. doi: 10.13040/IJPSR.0975-8232.14(7).3255-63.