

Mini Review

Bacopa Monnieri: A Wonder Drug Changing Fortune of People

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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 Ayurvedic 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 BM 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. BM is conventionally used for diverse ailments, but is best known as memory enhancer. A vast range of studies using methanolic and ethanolic extracts of BM have shown its effect in treatment of wide range of diseases like diabetes, depression, cancer, inflammation etc. BM 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 anti-depression, anti-inflammatory, anti-oxidative amongst many others which can surely help in betterment of markind.

Keywords: Bacopa monnieri; Phytochemical; Alkaloids; Flavonoids; Glycosides; Triterpenoids

Abbreviation: BM – Bacopa monnieri

Introduction

Bacopa monnieri Linn. Known as 'Brahmi' in Hindi and water hyssop in English is a perennial, creeping herb with small leaves, white or purple flowers belonging to family Schrophulariaceae. It is found in warm wetlands and native to India and Australia and also found growing in United States and East Asia (Barrett and Strother, 1978). It has been used as medicinal herb in Ayurveda since time immemorial. It is used for treatment of epilepsy, asthma, ulcers and tumours (Ramawat and Gopal, 2004). It was originally described around 6th century A.D. in texts like Charaka Samhita, Atharva- ved and Susurtu Samhita. Bacopa monnieri has been used in various constitutions as medhya rasayana, a class of drugs used for promoting mental health and amelioration of memory(Singh and Dhawan, 1997). Natural products have been precious as biologically validated rostrum for drug development. Natural products have been used for thousands of years in the treatment of several diseases. According to the World Health Organization (WHO) about 80 % of the world's population depends on traditional medicines to meet at least some of their primary healthcare (WHO fact sheet, 2003).Many herbs contain dozens of active constituents that combine to give the plant its therapeutic value. The medicinal value of plants lies in some chemical substances that produce a distinct physiological action on the human body. The most important of these bioactive compounds of plants are alkaloids, flavonoids, tannin and phenolic compounds (Rajan *et al.*, 2015).

This review will elucidate the therapeutic use of *Bacopa monnieri* focusing on neuro-pharmacological mechanisms unveiling the nootropic effect of herb while taking into account its impact on other properties as well.

Taxonomic Classification

Kingdom: *Plantae* Division: *Tracheophyta* Class: *Magnoliopsida* Order: *Lamiales* Family: *Schrophulariaceae* Genus: *Bacopa* Species: *monnieri* (L.)



Fig. 1: Bacopa monnieri – creeping herb

Geographical Distribution

Bacopa monnieri is found growing in Nepal, Sri Lanka, China, Taiwan and Vietnam, 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. Warm (30-40 °C) and humid (65-80 %) climatic conditions with plenty of sunshine and abundant rainfall are ideal for growth of Bacopa monnieri (Barrett and Strother, 1978).

Therapeutic Importance

It is used in traditional Indian medicine, the Ayurveda, for the treatment of anxiety, memory boosting activity, it is also claimed to be useful in the treatment of cardiac, respiratory and neuropharmacological disorders like insomnia. It was reported to possess anti-inflammatory, analgesic, antipyretic, sedative, free radical scavenging and anti-lipid peroxidative activities also (Kishore and Singh, 2005).

Neuro-Pharmacological Activity

The use of Bacopa monnieri has been reported to improve behaviour of many laboratory animal models under broad range of experimental conditions, e.g. mice (Prabhakar et al., 2008). Bacopa monnieri has been reported for its therapeutic potential in treatment of neurological diseases, improving memory (Russo and Borrelli, 2005; Vohora et al., 1997). The principal constituents are dammarane types of triterpenes saponins known as bacosides. They are responsible for cognitive function (Singh and Dhawan, 1997). Two types of saponins jujubogenin and pseudojujubogenin differing in only nature of sugar units in glycosidic chain are found (Russo et al., 2003). The major chemical entity responsible for neuropharmacological effects of BM is bacoside A (Rajan et al., 2015). It is milieu of bacoside A3, bacopaside II, bacopasaponin C and a jujubogenin isomer of bacosaponin C (Deepak et al., 2005). A study has confirmed that orally treated BM extract taken by the system shows behavioural improvements. HPLC

analysis shows the presence of bioactive compounds bacoside A in serum of *Bacopa monnieri* extract treated rats (Charles *et al.*, 2011).

Hepatoprotective Activity

Ethanolic extract of *Bacopa monnieri* is rich in saponins and it possess hepatoprotective property too which is attributed to bacoside-A. Extensive research work has been carried out using rat, mice and human model systems (Gudipati *et al.*, 2012). Many studies have shown that carbon tetrachloride (CCl₄) induces liver cirrhosis (Lal *et al.*,2007). CCl₄ disturbs metabolism of liver cells leading to changes in activities of enzymes (Gudipati *et al.*, 2012). Pre-treatment with methanolic extract against CCl₄ has shown protective effect. It has preserved the liver structure besides congestion of central vein, dilation of sinusoids etc in rats (Muhammad and Fazal, 2014). Chemically induced hepatotoxicity in animals have been widely used for the screening of hepatoprotective herbal compounds.

Antioxidant Activity

Antioxidants help in preventing oxidative damage by free radicals. Oxidative stress happens when free radicals subjugate the homeostatic defence mechanism of cells (Aguiar and Borowski, 2013). (Anbarasi *et al*, 2006) evaluated the anti-oxidant role of bacoside-A against chronic cigarette smoking induced oxidative damage in brain of rat. An adult albino rat was exposed to cigarette smoking for 12 weeks and administration of bacoside-A (10mg) was done simultaneously. The measurements of concentration of both enzymatic and non-enzymatic antioxidants as well as trace elements were done. The researchers found that bacoside-A improved anti-oxidant level. Thereby suggesting that smoking exposure enhances oxidative stress and bacoside-A protects the brain through its anti-oxidant capacity.

Antioxidant activity of alcoholic and hexane extract of *Bacopa monnieri* on lipid peroxidation by ferrous sulphate and cumene hydroperoxide in rat liver homogenate has been documented by (Tripathi *et al*, 1996).

Another study was done by (Bhattacharya *et al.*, 2000) which assessed the role of *Bacopa monnieri* extract on rat brain-frontal cortex, striatal and hippocampus regions.

Anti-Depressant

Depression is a common life threatening condition. Patients with depression generally reflect decrease in brain neurotransmitters like dopamine, serotonin and norepinephrine (Singh and Dhawan,1997). (Sairam *et al*, 2002) performed an experiment using methanolic extract of *Bacopa monnieri* in the dose of 20 and 40 mg/Kg orally once daily for 5 days and compared with anti-depressant drug imipramine (15mg/Kg) on rodents which reflected significant anti-depressant activity.

(Hazra *et al.*, 2012) evaluated the anti-depressant activity in rat. The extract was administered in dose of 80 and 120 mg/Kg and compared with anti-depressant drug fluoxetine hydrochloride. The *Bacopa monnieri* extracts reduced escape latency and plasma corticosterone level in rats greatly and showed anti-depressant activity.

Anti-Epileptic

Khan *et al.* (2008) 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 *et al.*, 2007) reported the effectiveness of alcoholic extract of *Bacopa monnieri* in decreasing symptoms of epileptic seizures.

Mathew *et al.* (2012) 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.

Anti-Diabetic Activity

Diabetes mellitus is a metabolic disorder affecting carbohydrate, fat and protein metabolism. Approximately 1% of the population suffers from this disease. Diabetes mellitus poses a serious problem (Sabina *et al.*,2014).

Ghosh *et al.* (2011) worked on ethanolic extract of *Bacopa monnieri* and they reported that bacosine, a triterpene is responsible for increase in glycogen content in diabetic rats. The extract also resulted an increase in peripheral glucose utilisation *in vitro* in the diaphragm of diabetic rats. There by showing insulin like activity in alloxan-induced diabetic rats.

Anti-Ulcerative

The fresh juice from whole plant of *Bacopa monnieri* was examined by (Rao *et al*, 2000) using gastric ulcer models induced by ethanol, aspirin. *Bacopa monnieri* juice were given orally twice daily for 5 days at dose of 100 and 300 mg/Kg and sucralfate at 250mg/Kg. The juice showed antiulcer activity in gastric ulcer models except for ethanolinduced ulcers. The effect is attributed to mucosal defensive factors like enhanced mucin secretion, mucosal glycoprotein and decreased in mucosal cell exfoliation.

Dorababu *et al.* (2004) performed an experiment using methanolic extract of *Bacopa monnieri* on susceptibility of NIDDM/ normal rats and found that 50mg/kg body weight extract dose to be effective in healing penetrating ulcers induced by acetic acid and HCl after 5-10 days of treatment.

(Goel *et al*, 2003) showed anti-helicobacter pylori activity at 1000μ g/ml of *Bacopa monnieri* extract while at the dose of 10μ g/ml it showed an increase in prostanoids. This

contributed to anti-ulcerogenic activity of *Bacopa monnieri* extract.

Anti-Cancer Activity

Ghosh *et al.* (2011) examined the anti-tumour activity of stigmasterol which is isolated from aerial parts of *Bacopa monnieri* against Ehrlich ascites carcinoma in Swiss albino mice. The anti-tumour activity of stigmasterol is thought to be mediated through activation of protein phosphatase 2A.

Another study by (Kumar *et al*, 1998) also examined the anti-tumor activity of ethanolic extract of *Bacopa monnieri*. Oral administration of extract delayed the development of solid tumor. The study was carried out on *in vitro* short term chemosensitivity and *in vivo* tumor model test systems.

D'Souza *et al.* (2002) evaluated that ethanolic extracts and saponon rich fraction showed anti-tumour potentiality. Bacoside-A was reported as active constituent responsible for anti-cancerous activity. The extract was tested for brine shrimp lethality also.

Elangovan *et al.* (1995) reported alcoholic extract of *Bacopa monnieri* as anti-cancerous drug. The Ethanolic extract was tested for sarcoma-180 cell culture. The cell growth was inhibited with increasing concentration of the extract.

Anti-Inflammatory

Inflammation is a type of biological response to stimuli, like pathogens, damaged cells or irritants. It is characterized by redness, swollen joints, joint pain, its stiffness and loss of joint function (Kumar *et al.*, 2013). (Hossain *et al.*, 2014) evaluated that methanolic extract of *Bacopa monnieri* possess anti-inflammatory activity. The study was carried out through carrageenan and histamine-induced oedema test on rats. 200 and 400 mg/Kg body weight of extract was administered and the dose of 400mg/Kg extract showed significant anti-inflammatory activity compared to drug indomethacin.

Channa *et al.* (2006) reported that ethanolic extract of *Bacopa monnieri* showed anti-inflammatory effect against carrageenan-induced paw edema in mice and rats. The extract was treated with chemical mediators like serotonin, histamine and the extract selectively inhibited prostaglandin E_2 induced inflammation. There by showing anti-inflammatory property.

Anti-Microbial

(Sampathkumar *et al*, 2008) evaluated the anti-microbial activity of ethanolic, diethyl acetate, ethyl acetate and aqueous extracts of aerial parts of *Bacopa monnieri*. Diethyl ether extract showed anti-bacterial activity against gram positive while ethyl acetate extract showed activity against gram negative organism. The test was carried out on bacteria like *Staphylococcus aureus*, *Proteus vulgaris*, etc. Ethanolic extract exhibited anti-fungal activity against *Aspergillus niger*, *Candida albicans*.

(Khan *et al*, 2010) reported the anti-bacterial activity of ethyl acetate and methanol extracts of *Bacopa monnieri* against 7 gram negative and 11 gram positive bacteria by disk diffusion method.

The antifungal activity against *Alternaria alternata* and *Fusarium fusiformis* by phytochemicals isolated from aerial parts of *Bacopa monnieri* like betulinic acid and oroxindin is also reported (Chaudhuri *et al.*, 2004).

Cardiovascular

Kamkaew *et al.* (2011) studied the effect of intravenous *Bacopa monnieri* extract administered in the dose of 20-60 mg/Kg on arterial blood pressure and heart rate of anaesthetized rats. The extract decreased systolic and diastolic pressures without disturbing heart rate. It was concluded that blood pressure reduced partly via releasing nitric oxide from endothelium and partly by actions on vascular smooth muscle Ca^{2+} homeostasis.

Channa *et al.* (2003) reported the broncho-vasodilatory activity of *Bacopa monnieri* extract in anaesthetized rats. The work was done on various fractions derived from *Bacopa monnieri* and the activity was observed because of inhibition of calcium ions.

Analgesic

Vohra *et al.* (1997) isolated bacosine from aerial parts of *Bacopa monnieri* and found that it possess analgesic effect. The effect was opioidergic in nature. It was also reported that bacosine didn't show any effect on barbiturate narcosis, haloperidol-induced catalepsy, conditioned avoidance response.

Siraj *et al.* (2012) investigated the analgesic effect of ethanol extract of BM. The extract yielded noteworthy writhing inhibition in acetic acid induced writhing in mice at the oral dose (250 and 500 mg/kg) compared to standard drug diclofenac sodium (25mg/Kg).

Conclusion

It is now becoming exceptionally apparent that available therapeutics does not properly meet demands of a vast majority of patients with health problems, and thus traditional medicines are enjoying an upsurge because of less toxicity. Bacopa is one amongst the traditional plant which is used in Ayurveda and herbal medicines. BM demonstrates massive potential in the amelioration of various neuro-pharmacological, depressions, inflammation and other disorders. The methanolic and ethanolic extract of BM plays a pivotal role in treatment of human disorders in varying concentrations. The chief chemical entity responsible for therapeutic effect identified through various research models is bacoside A. However, further studies are required in order to determine the targeted activity of the bioactive compounds present in the bacoside fraction isolated from BM. The antioxidant activity of BM may be useful in the treatment of human pathologies in which free

radical production plays a key role which requires further study. The ethanolic extract of BM proved significant effect in treatment of Diabetes which poses a serious threat in world today; further studies on this extract can prove to be beneficial for humans. Biomedical research on BM is still in its formative years, but preliminary results such as those depicted in this review will surely open the research floodgates.

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