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Review

Bacopa monniera

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SUMMARY

The plant is used in India as well as several countries since several centuries for treating different types of ailments. The plant is an important constituent of the Ayurvedic Materia Medica and finds mention in several ancient texts including Caraka Sanhita (6th century A.D.) and the Bhavprakasa (16th century A.D.). The scientific studies on this plant have reported several activities of this plant. Though the plant has cardiotonic, vasoconstrictor, sedative, neuro-muscular blocking, and anticancer activities, it is more popular as memory enhancer. Traditionally, a poultice made of the boiled plant is placed on the chest in acute bronchitis and coughs of children. The plant contains saponins: bacosides A and B, hersaponin, sapogenins: bacogenin A_1, A_2, and A_3, stigmasterol, and flavonoids: luteolin and luteolin-7 glucoside, nicotine, brahmine, and herpestine. This review focuses on the scientific data published since 1931.

Key words: Ayurvedic Materia Medica; Caraka Sanhita; Bhavprakasa

INTRODUCTION

The plant *Bacopa monniera* (L) Pennell, [Syn: *Bacopa monniera* Wettst; *Gratiola monniera* (Linn); *Herpestis monniera,* H.B.K. or *Monniera cuncifolia* Mich (Scrophulariaceae) is a small creeping plant found in moist or wet places, such as on the borders of water channels, wells, irrigated fields, etc. in all parts of India. In India it is known as Brahmi. The leaves are fleshy and roots arise on the nodes of the stem, also. Flowers arise in the axils of the leaves and are borne on short pedicels. One of the five petals is longer than others. The corolla is bluish-white in color and 1 cm across (Kapur, 1990). The plant is reported to have multiple uses in the traditional system of medicine and is extensively used in the Ayurvedic proprietary medicine, particularly as a memory enhancing herb. In the Ayurvedic system of medicine it is being extensively used for treatment of various nervine disorders, such as insanity, epilepsy, and hysteria. The total extract of *Bacopa monniera* has cardiotonic, vasoconstrictor, sedative and neuro-muscular blocking actions. It has a spasmodic action on rabbit's and guinea pig's ilea and uteri. The alcoholic extract has an anticancer activity against Walker carcinosarcoma. Leaves and stalks are very useful in the stoppage of urine. Traditionally, a poultice made of the boiled plant is placed on the chest in acute bronchitis and coughs of children.

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Constituents

The plant contains saponins: bacosides A and B (Chatterjee *et al*., 1963; Chatterjee *et al*., 1965), hersaponin, sapogenins: bacogenin A_1, A_2, and A_3

(Basu *et al.*, 1967; Rastogi *et al.*, 1994), stigmasterol (Banerjee and Chakravarti, 1963), and flavonoids: luteolin and luteolin-7 glucoside (Schulete *et al.*, 1972), nicotine, brahmine, and herpestine (Chopra *et al.*, 1956; Schulete *et al.*, 1972), and Dammarane type triterpenoid saponins (Garai *et al.*, 1996). Both the bacosides A and B are identical as regards their carbohydrate and aglycone moieties and, therefore bacoside B has the same gross structure as Bacoside A (Fig. 1). Other constituents identified are betulic acid and β-sitosterol, bacopaside HI, bacopasaponin G, bacopaside C, and bacopasaponin E and F (Mahato *et al.*, 2000; Hou *et al.*, 2002). Um *et al.* (2002) have identified 3-βO-[βD-glc(1-3) βD glc]-pseudojujubogenine (Fig. 2) and 3β-O-[β-D-glc(1-3)-αL-ara] pseudojujubogenine (Fig. 3). Recently Chakravarti *et al.* (2003) have isolated bacopasides III and IV.

Traditional uses

Bacopa has a long history of use in the Ayurvedic system of medicine. The whole plant- roots stalk and leaves are used. According to the indigenous system of medicine Bacopa is claimed to be a potent nervine tonic, enhancing memory (that has been impaired by some ailment), and improving mental function. It is used in treatment of epilepsy, insanity, hysteria, asthenia, nervous breakdown and other mental disorders. It is also diuretic, cardiotonic, and is also useful in asthma, constipation, bronchitis, diarrhea and skin diseases (Chopra *et al.*, 1956; Anonymous, 1988; Nadkarni, 1993; Yoganarsimhan and Chelladurai, 2000). Juice mixed with petrolatum is a good application in rheumatism. A powder composed of *Acorus calamus*, *Chebulic myrobalan*, a root of *Justica adhatoda*, and long pepper is given with honey in treatment of hoarseness. Medicated ghee is useful in cases of hysteria and epilepsy (Nadkarni, 1993).

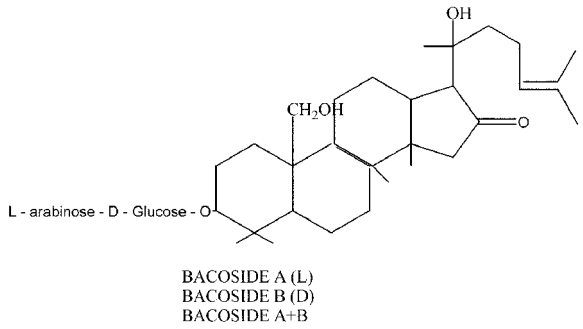

Fig. 1. Gross Structure of the bacosides.

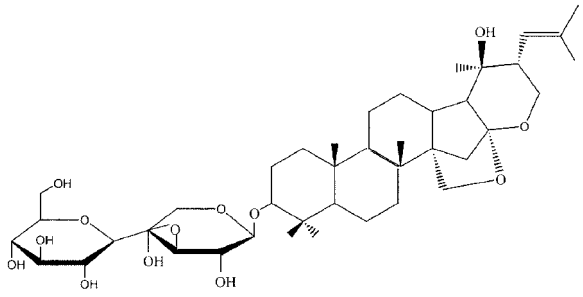

Fig. 2. 3-βO-[βD-glc(1-3) βD glc]-pseudojujubogenine.

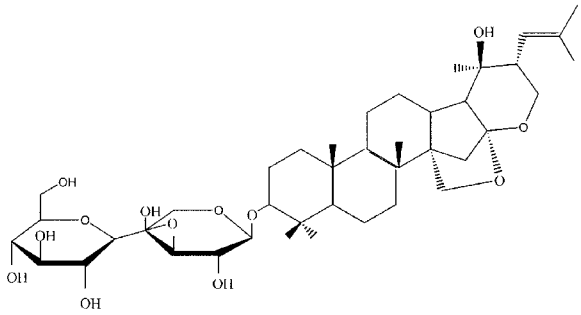

Fig. 3. 3β-O-[β-D-glc(1-3)-αL-ara] pseudojujubogenine.

Clinical studies

The *Bacopa monniera* has been in use in Ayurvedic medicine since many years. Many clinical studies have confirmed the veracity of claims made about Bacopa in the Ayurveda. The leaves are useful in weakness and nervous breakdown (Bose and Bose, 1931). A medicated ghee preparation known as Brahmighrita is useful in treatment of epilepsy and hysteria (Nadkarni, 1954). Bacopa is used for memory enhancing, epilepsy, insomnia and as a mild sedative (Chunekar, 1960; Satyavati *et al.*, 1976). Several studies have been carried out to investigate nootropic activity of *Bacopa monniera.* Though *B. monniera* is reported to exert cognitive

enhancing effects in animals, the effects on human cognition are inconclusive. The Central drug Research Institute of Lucknow (India) has developed a product, which contains Bacosides A & B as active components for improving learning and memory (Darshan and Doreswamy, 1998).

Some studies suggest that the memory enhancing effect of *B. monniera* may be mediated by modulation of cholinergic system and/or its antioxidant activity (Agrawal, 1993). Since increased cholinergic transmission has a well-established role in cognitive function (Drachman and Leavitt, 1974), several workers have studied the effect of Bacopa on learning and memory. Nathan *et al.* (2001) in thirty eight normal healthy subjects studied the effect of acute administration of hydro-alcoholic extract of *B. monniera* using Rey Auditory Verbal Learning Test, Digit Span Memory Task and Digit Symbol Substitution Test, and found that the treatment was without any significant changes on the cognitive functions. Stough *et al.* (2001) showed that on chronic treatment (12 weeks) the *B. monniera* extract improved speed of visual information processing, learning rate and memory consolidation suggesting that *B. monniera* may improve higher order cognitive processes that are critically dependent on the input of information. Roodenrys *et al.* (2002) have investigated the effect of *B. monniera* extract on seventy-six adults aged between 40 and 65 years in a double blind randomized, placebo control study employing various memory functions. The results showed a significant effect on a test for retention of new information without any effect on short term memory, working memory and the rate of acquisition of the information. Brahmi decreased the rate of forgetting of newly acquired information.

In a study conducted by Nathan *et al*. (2004), cognitive testing was done in three sessions; at pretreatment and following 2 and 4 weeks post treatment. Following the baseline testing, subjects were asked to take two tablets (either placebo or tablet containing extract of G. biloba and Bacopa) once a day for 4 weeks. Testing was repeated at 2 and 4 weeks post treatment. A wide range of cognitive variables including attention, short term and working memory, verbal learning, memory consolidation, executive processes, planning and problem solving, information processing speed, motor responsiveness, and decision making were assessed. They found that the extract containing *Ginkgo biloba* and *Bacopa monniera* was devoid of any cognitive enhancing effect in healthy subjects.

***In-vitro* studies**

Pharmacological studies also showed adrenergic activity of saponins of Bacopa (Khanna and Ahmed, 1992). The ethanolic extract of *B. monniera* significantly inhibits Sarcoma-180 cell growth in a concentration dependent way possibly by acting on the DNA replication stage (Elangovan *et al*., 1995). A mixture of two bacosides A and B which are known to be the active principles of Bacopa are without any effect on the chromosome aberration, sister chromatid formation and micronuclei formation indicating that bacosides A and B are not genotoxic (Giri and Khan, 1996). Dar and Channa (1997a) have studied relaxant effect of the ethanolic extract of Bacopa on trachea, pulmonary artery and aorta from rabbit and guinea pig and observed that relaxation involves prostacyclin compounds in all tissues and β-adrenergic receptors in trachea. This relaxation was independent of endothelium and muscarinic receptor activation. The ethanolic extract of *B. monniera* also produced bronchodilation in anaesthetized rats, which substantiates the traditional use of Bacopa in treatment of respiratory diseases (Dar and Channa, 1997b). Dar and Channa (1999) have also demonstrated calcium antagonistic activity of alcoholic extract of *Bacopa monniera*. The ethanolic extract of whole plant inhibited the spontaneous movements of both guinea pig ileum and rabbit jejunum. The extract also inhibited acetylcholine, histamine, and calcium chloride-induced responses.

The pet ether, methanolic and aqueous extract of *B. monniera* leaves possess mast cell stabilizing activity and the activity of methanolic extract was comparable to that of disodium chromoglycate (Samiulla *et al*., 2001). The *in-vitro* studies using guinea pig ileum showed that addition of various concentrations of the alcoholic extract of *B. monniera*, 15 min before exposure to morphine reduced the naloxone-induced contractions in a dose dependent manner suggesting that *B. monniera* may be useful in reducing the withdrawal symptoms induced by morphine (Sumathi *et al*., 2002). They observed that ethanolic extract of Bacopa (whole plant) reduced morphine-induced withdrawal contraction precipitated by naloxone in the isolated guinea pig ileum.

Tripathi *et al*. (1996) and Bhattacharya *et al*. (2000) have demonstrated an antioxidant property of Bacopa. Tripathi *et al.* (1996) found that 100 µg of the alcoholic extract of Bacopa is equivalent to 58 µg of vitamin E. Interestingly, higher concentrations (more than 100 µg/ml) enhanced the rate of oxidation and the extract was less effective in protecting the auto-oxidation and ferrous sulphate-induced oxidation of reduced glutathione. Tripathi *et al*. (1999) compared anti-oxidant activities of identical doses of ethanolic extracts of *Hypericum perforatum, Nardostachys jatamansi*, and *Bacopa monniera* and found Bacopa extract more effective against free radicals generated after lipid peroxidation, salicylate hydroxylation, and iron chelation. Russo *et al*. (2003) investigated free radical scavenging activity of methanolic extract of *B. monniera* and found a protective effect on hydrogen peroxide-induced cytotoxicity demonstrating the free radical scavenging activity. They also noted protective effect of the extract on DNA cleavage in human non-immunized fibroblasts.

The antioxidant capacity of the methanolic extract may explain, at least in part, the antistress, immunomodulatory, cognition enhancing, anti-inflammatory and anti-aging effects produced by it. The anticancer activity of saponin rich fraction and bacoside A has been reported using brine shrimp lethality assay (D'Souza *et al*., 2002). The methanolic extract of Bacopa in the concentration of 1mg/ml inhibited growth of *Helicobacter pylori* and the effect was comparable with that of bismuth subcitrate, a known *H. pylori* growth inhibitor (Goel *et al*., 2003). The ethanolic extract of Bacopa showed a concentration dependent anticholinesterase inhibition in mice (Das *et al*., 2002).

In-vivo studies

Central effects

Prakash and Sirsi (1960) have reported psychotropic action of *Herpestis monniera*. Aithal and Sirsi (1961) have shown that the alcoholic extract of the drug exhibited tranquilizing effect on rats and dogs. Malhotra *et al*. (1960) have established hypnotic action of hersaponin in mice. The hersaponin reduced amphetamine toxicity in aggregated mice. Dhalla *et al*. (1961) studied the effect of alcoholic extract, its alkaloidal fraction and hersaponin on respiration of rat brain and reported varying degrees of inhibitory actions of the total extract and its alkaloidal fraction on the oxidative process. Hersaponin had no depressing action on the brain respiration. It is now well established that increase in brain oxidative stress is responsible for mild cognitive impairment (Pratico *et al*., 2002). The oral administration of bacosides dissolved in distilled water exhibited antistress activity and modulated the activities of heat shock polypeptide 70 (Hsp 70), cytochrome P450 and superoxide dismutase thereby possibly allowing the brain to be prepared to act under adverse conditions such as stress (Chowdhuri *et al*., 2002). They showed that oral administration of bacosides in doses of 20 and 40 mg/kg administered for 7 days significantly decreased Hsp70 expression in the hippocampus of the stressed rats. The superoxide dismutase activity was decreased by 2.4 folds in the hippocampus and by 35% in the cerebral cortex by the 20 mg/kg dose of bacosides. The cytochrome P450 activity was restored by the bacosides in the

stressed rats. Rai *et al.* (2003) have reported adaptogenic (anti-stress) activity of a standardized extract of Bacopa in rats. They found that rats pretreated with Bacopa extract reversed stress-induced changes in ulcer index, adrenal gland weight, creatine kinase, and aspartate aminotransferase.

The ethanolic extract of *B. monniera* increases gamma-aminobutyric acid (GABA) level profoundly 15 min after administration and suggest a correlation between the sedative property of Brahmi and the increased GABA level of cerebral tissue (Dey and Dutta, 1966). Ganguly and Malhotra (1967) carried out neuropharmacological and behavioral studies using an active fraction from *Herpestis monniera* (*B. monniera*) and reported tranquilizing activity which was much weaker than chlorpromazine. Dey and Chatterjee (1968) showed that alcoholic extract of *B. monniera* leads to a depression, minimal motor activity, eye-lid closure, potentiated pentobarbitone-induced sleep and suppressed mescaline induced central action. The ethanolic extract of *B. monniera* initially reduced acetylcholinesterase activity of mouse *in vivo* and later increased the enzyme activity (Datta, 1969). The aqueous as well as ethanolic extract of *B. monniera* increased the duration of pentobarbitone-induced sleep and delayed the onset of pentylenetetrazol-induced seizures and aqueous extract was more potent than the ethanolic extract (Martis *et al.*, 1992). Brahmighritam, an herbal formula for the control of epilepsy was given orally to male albino rats and was compared with benzdiazepam in controlling pentylenetetrazol-induced seizures. Thirty day pretreatment with the Brahmighritam made rats less sensitive to epileptogenic events (Shanmugsundaram *et al.*, 1991). Vohora *et al.* (1997) have reported analgesic activity of Bacosine (Fig. 4), a triterpene isolated from aerial parts of the plant. Bacosine exhibited moderate antinociceptive action, which was partially blocked by naloxone.

Using elevated plus maze, open field, social interaction and novelty-suppressed feeding latency

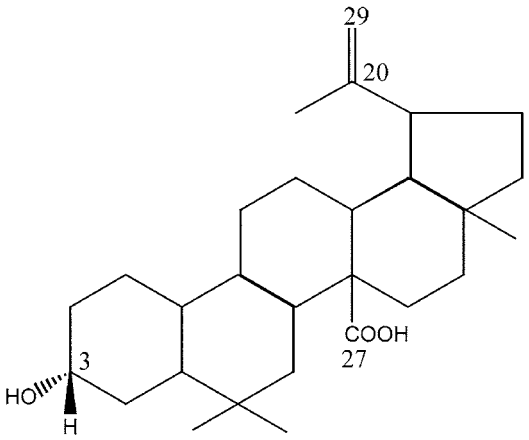

Fig. 4. Bacosine.

tests in rats, Bhattacharya and Ghosal (1998) compared anxiolytic activity of a standardized extract of Bacopa (Bacoside A content - 25.5 ± 0.8%) administered orally in doses 5, 10, and 20 mg/kg with lorazepam (0.5 mg/kg i.p.) and found the extract effective in alleviating anxiety in doses of 10 and 20 mg/kg. The Bacopa extract did not produce any motor deficit as evidenced by using Rota-rod test. Sairam *et al.* (2002) have reported antidepressant activity of standardized extract of Bacopa (containing 38.0 ± 0.9% bacoside A and B) administered in doses of 20 and 40 mg/kg for 5 days. The extract was found to have significant antidepressant activity in forced swim and learned helplessness models of depression and was comparable to imipramine (15 mg/kg i.p.).

Learning and memory

Many workers have attempted the scientific evaluation of Brahmi on the learning process. Since loss of memory has been mentioned in the Ayurveda, it is reasonable to believe that the medicinal plants can be a good source of drugs useful in improving memory. Prakash and Sirsi (1962) carried out a comparative study of the effects of Brahmi and chlorpromazine on motor learning in rats. Administration of both the drugs to animals, still in the process of learning, improved

their performance. Dey *et al*. (1976) reported that 24 days treatment with aqueous decoction of Brahmi showed the maximum improvement in the maze learning of albino rats. Singh and Dhawan (1982) administered alcoholic extract of Brahmi to albino rats and observed better acquisition, improved retention and delayed extinction in shock motivated brightness discrimination reaction. Further, in an active conditioned flight reaction, the drug treated animals showed shorter reaction time than the controls. The aqueous suspension containing Bacosides enhanced the relearning index in the shock motivated brightness discrimination reaction in a single oral dose of 10 mg/kg (Singh *et al*., 1988).

Maharishi Amrit Kalash, an Ayurvedic medicinal preparation administered orally in a dose of 500 mg/kg for 2 months to guinea pigs significantly increased the activity of choline acetyltransferase and acetylcholinesterase in the older animals. The study indicated that this food supplement can be helpful in alleviating the cholinergic deficits in the old age (Vohora *et al*., 2001). Many epileptic patients suffer from cognitive impairments: both the underlying pathology and antiepileptic drug therapy can cause such deficits. Vohora *et al*. (2000) have studied the protective activity of *Bacopa monniera* against the phenytoin-induced cognitive deficit. Phenytoin adversely affected cognitive function in the passive avoidance task. Ethanolic extract of *Bacopa monniera* given for 7 days significantly reversed the phenytoin-induced cognitive impairment. Both acquisition and retention of memory improved without affecting the anticonvulsant activity.

Das *et al*. (2002) in their comparative study in rodents of standardized extracts of *Bacopa monniera* and *Ginkgo biloba* noticed a dose dependent inhibitory effect on acetylcholinesterase activity and *Bacopa monniera* was less potent than *G. biloba* in this inhibition. Both the drugs attenuated effect of scopolamine in the passive avoidance test. Singh and Dhawan (1997) have shown that a mixture of two saponins identified as bacoside A and B significantly attenuated electro-convulsive shock-induced amnesia as well as scopolamine-induced amnesia. They also showed that healthy volunteers well tolerated bacosides in single dose (20 - 300 mg) and multiple doses (100 and 200 mg) administered for 4 weeks in double blind placebo controlled and non-crossover regulatory phase - I clinical study. Bhattacharya *et al*. (2001) administered the standardized extract of *B. monniera* (82.0 ± 0.5% Bacoside A content) in doses of 5 and 10 mg/kg orally to groups of rats. They used two animal models of Alzheimer's disease, by injecting colchicine intra-cerebro ventricularly (i.c.v.) and by lesioning of nucleus basalis magnocellularis with ibotenic acid. Apart form noting the effect of *B. monniera* on memory deficits they also studied its effect on i.c.v. colchicine -induced depletion of acetylcholine concentration, reduction in choline acetyltransferase activity and decrease in muscarinic receptor binding, in the frontal cortex and hippocampus of rats. The extract reduced the magnitude of memory deficit and reversed colchicine-induced reduction in frontal cortex and hippocampus acetylcholine, choline acetyltransferase activity and muscarinic receptor binding. The findings indicate that *B. monniera* facilitates memory as well as cholinergic transmission.

Mentat, an herbal preparation which contains *B. monniera* was investigated in short term memory paradigms in mice. The preparation improved short term memory and reversed amnesia induced by scopolamine and electroconvulsive shocks (Kulkarni and Verma, 1993). In another study Mentat was given for 5 weeks and 4 weeks after withdrawal, avoidance learning during endurance performance was assessed by Bhardwaj and Srivastav (1995). They observed improvement in avoidance learning during endurance performance due to intake of Mentat. Recently, Um *et al*. (2002) have isolated and identified two new compounds *viz*. 3β-O-[β-D-glc(1-3)β-D-glc]-pseudojujubogenine and 3β-O-[β-D-glc(1-3)-α-L-ara]-pseudojujubogenine

from butanolic extract of Bacopa having nootropic activity in the object recognition test in rats.

Endocrine

The hydro-alcoholic extract of leaves of *B. monniera* increased T_4 concentration in the thyroid glands in male mice suggesting its thyroid-stimulating role. The extract increased T_4 concentration by 41% without enhancing hepatic lipid peroxidation suggesting that it can be used as a thyroid stimulating drug (Kar *et al*., 2002). The aqueous extract of *B. monniera*, in diabetics, increased IgG and decreased IgA levels (Arora *et al*., 2002). The methanolic extract of *B. monniera* was without any effect on the blood glucose level in non-insulin dependent diabetes mellitus in rats (Dorababu *et al*., 2004).

Gastrointestinal tract

The juice (Rao *et al*., 2000) and standardized extract (Sairam *et al*., 2001) of fresh whole plant of *B. monniera* exhibited ulcer protective and healing activity in different animal models. The methanolic extract containing 38% bacoside – A when given in dose of 10-50 mg/kg, twice daily for 5 days showed dose-dependent anti-ulcerogenic action on gastric ulcers induced by ethanol, aspirin, 2 h cold restraint stress and 4 h pyloric ligation. The effect was attributed to enhancement of defensive mucosal factors like mucin secretion, life span of mucosal cells and anti-oxidant effects rather than on the offensive mucosal factors like acid and pepsin secretion (Sairam *et al*., 2001). In further studies Goel *et al*. (2003) found that the extract of *B. monniera* inhibited *Helicobacter pylori* and increased colonic concentration of prostaglandin E and Prostaglandin I_2. Dorababu *et al*. (2004) have reported protective effect of methanolic extract of Bacopa against ulcers induced by aspirin, pylorus ligation, acetic acid, hydrochloric acid, and cysteamine.

Anti-inflammatory activity

Brahmi Rasayan, an Ayurvedic preparation, was studied for its anti-inflammatory activity in rats. The drug suppressed carrageenan-induced inflammation, sponge pellet-induced granuloma, and nystatin-induced rat paw edema and did not show ant gastric irritation in anti-inflammatory doses (Jain *et al*., 1994). Its anti-inflammatory activity was comparable to that of indomethacin.

Cardiovascular effects

The total extract of *Bacopa monniera* has cardiotonic, vasoconstrictor, sedative and neuro-muscular blocking actions (Malhotra and Das, 1959).

Protective activity

Morphine causes increase in lipid peroxidation and decrease in liver antioxidant enzymes such as superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase, and glutathione levels. Oral administration of alcoholic extract of Bacopa induced a significant hepatoprotective effect by preventing these alterations (Sumathy *et al*., 2001). Jagetia and Baliga (2003) studied the effect of Mentat, an herbal preparation containing Bacopa against radiation-induced mortality in mice. Mice were treated with ethanolic extract of Mentat (5 - 160 mg/kg i.p.) for five days before exposure to 10 Gy of γ-radiation. The onset of main symptoms of γ-radiation i.e. reduction in food and water intake, irritability, epilation, weight loss, lethargy, diarrhoea, facial edema was delayed by Mentat. The lowest mortality (25%) occurred after administration of 40 and 80 mg/kg. The exact mechanism of action of Mentat is not known, however, it may scavenge free radicals produced by radiation. Alternatively it may increase the level of endogenous glutathione providing protection against radiation-induced damage.

The review has attempted to provide the results of several studies carried out so far in different laboratories. Although lot of research has been carried out on *Bacopa monniera*, the US FDA needs more conclusive evidence on efficacy of Bacopa. More sophisticated studies are therefore necessary

to confirm the veracity of claims made about *Bacopa monniera*.

REFERENCES

Abhang R. (1993) Studies to evaluate the effect of micro medicine derived from Brahmi (*Herpestis monniera*) on students of average intelligence. *J. Res. Ayur. Siddha.* **14**, 10-24.

Agrawal A. (1993) A comparative study of psychotropic drugs and bio-feedback therapy in the prevention and management of psychosomatic disorder (thesis). Institute of Medical Sciences, Banaras Hindu University, Varanasi, India.

Aithal HN, Sirsi M. (1961) Pharmacological Investigations on *Herpestis monniera* H.B. & K. *Indian J. Pharmacol.* **23**, 2-5.

Anonymous. (1988) Wealth of India, Raw Materials, National Institute of Science Communication, New Delhi, India. 2B, pp. 2-3.

Arora D, Kumar M, Dubey SD. (2002) Singh U. Immunomodulating effects of Rasayana drugs in diabetics – A clinical study. Ancient Science of Life. XXII, p. 42-48.

Banerjee SK, Chakravarti RN. (1963) Stigmasterol from *Herpestis monniera*. *Bull. Calcutta Sch. Trop. Med.* **11**, 57-58.

Basu N, Rastogi RP, Dhar ML. (1967) Chemical examination of *Bacopa monniera* Wettest Part III. Bacoside B. *Indian J. Chem.* **5**, 84-86.

Bhardwaj SK, Srivastav KK. (1995) Effect of composite Indian herbal preparation, CIHP(III) on avoidance learning during endurance performance in rats. *Indian J. Exp. Biol.* **33**, 580-584.

Bhattacharya SK, Bhattacharya A, Kumar A, Ghosal S. (2000) Antioxidant activity of *Bacopa monniera* in rat frontal cortex, striatum, and hippocampus. *Phytother. Res.* **14**, 174-179.

Bhattacharya SK, Ghosal S. (1998) Anxiolytic activity of a standardized extract of *Bacopa monniera*: an experimental study. *Phytoedicine* **5**, 77-82.

Bhattacharya SK, Kumar A, Ghosal S. (2001) Effect of *Bacopa monniera* on animal models of Alzheimer's disease and perturbed central cholinergic markers of cognition in rats. Emerging Drugs, Wesbury, NY, USA, pp 21-32.

Bose KC, Bose NK. (1931) Observations on the actions and uses of *Herpestis monniera*. *J. Indian Med. Asso.* **1**, 60.

Chakravarti AK, Garai S, Masuda K. (2003) Bacopasides III-IV: the new triterpenoid glycosides from *Bacopa monniera.* **51**, 215-217.

Chatterji N, Rastogi RP, Dhar ML. (1963) Chemical examination of *Bacopa monniera* Wettest. Part I. Isolation of chemical constituents. *Indian J. Chem.* **1**, 212.

Chatterji N, Rastogi RP, Dhar ML. (1965) Chemical examination of *Bacopa monniera* Part II. The constitution of Bacoside A. *Indian J. Chem.* **3**, 24.

Chopra RN, Nayar SL, Chopra IC. (1956) Glossary of Indian Medicinal Plants. Council of Scientific and Industrial Research. New Delhi, p. 32.

Chowdhuri DK, Parmar D, Kakkar P, Shukla R, Seth PK, Srimal RC. (2002) Antistress effects of Bacosides of *Bacopa monniera*: Modulation of Hsp70, superoxide dismutase and cytochrome P450 activity in rat brain. *Phytother. Res.* **16**, 639-645.

Chunekar KC. (1960) Bhav Prakash Nighantu, Chaukhamba Bharati Publication, Varanasi, p. 56.

D'Souza P, Deepak M, Rani P, Kadamboor S, Mathew A, Chandrashekhar AP, Agarwal A. (2002) Brine shrimp lethality assay of *Bacopa monniera*. *Phytother. Res.* **16**, 197-198.

Dar A, Channa S. (1997a) Relaxant effect of ethanol extract of *Bacopa monniera* on trachea, pulmonary artery and aorta from rabbit and guinea pig. *Phytother. Res.* **11**, 323-325.

Dar A, Channa S. (1997b) Bronchodilatory and cardiovascular effects of ethanol extract of *Bacopa monniera* in anaesthetized rats. *Phytomedicine* **4**, 319-323.

Dar A, Channa S. (1999) Calcium antagonistic activity of *Bacopa monniera* on vascular and intestinal smooth muscles of rabbit and guinea pig. *J. Ethnopharmacol.* **66**, 167-174.

Darshan S, Doreswamy R. (1998) Medicinal Plant patents scenario in the new era of drug development. *Indian Drugs* **35**, 55-66.

Das A, Shanker G, Nath C, Pal R, Singh S, Singh HK. (2002) A comparative study in rodents of standardized extracts of *Bacopa monniera* and *Ginkgo biloba*: Anticholinesterase and cognitive enhancing activity. *Pharmacol. Biochem. Behav.* **73**, 893-900.

Datta C. (1969) Effects of psychotropic drugs on

acetylcholinesterase activity of mouse brain. *Indian J. Exp. Biol.* **7**, 225-228.

Dey CD, Bose S, Mitra S. (1976) Effect of some centrally active phytoproducts on maze learning of albino rats. *Indian J. Phys. Allied Sci.* **30**, 88-97.

Dey PK, Chatterjee BK. (1968) Studies on the neuropharmacolical properties of several Indian medicinal plants. *J. Res. Indian Med.* **3**, 9-17.

Dey PK, Datta C. (1996) Effect of psychotropic phytochemicals on cerebral aino acid level in mice. *Indian J. Exp. Biol.* **4**, 216-218.

Dhalla NS, Sastry MS, Malhotra CL. (1961) Some in-vitro effects of *Herpestis monniera* Linn on the respiration of rat brain. *Indian J. Med. Res.* **49**, 781-787.

Dorababu M, Prabha T, Priyambada S, Agrawal VK, Aryya NC, Goel RK. (2004) Effect of *Bacopa monniera* and *Azadirachta indica* on gastric ulceration and healing in experimental NIDDM rats. *Indian J. Exp. Biol.* **42**, 389-397.

Drachman DA, Leavitt J. (1974) Human memory and the cholinergic system. *Arch. Neurol.* **30**, 113-121.

Elangovan V, Govindswamy S, Ramamoorthy N, Balasubramanian K. (1995) *In-vitro* studies on the anticancer activity of *Bacopa monnieri*. *Fitoterapia* **66**, 210-215.

Ganguly DK, Malhotra CL. (1967) Some behavioral effects of an active fraction from *Herpestis monniera*, Linn. (Brahmi). *Indian J. Med. Res.* **55**, 473-482.

Garai S, Mohato SB, Ohtani K, Yamasaki K. (1996) Dammarane type triterpenoid saponin from *Bacopa monniera*. *Phytochemistry* **42**, 825-820.

Giri AK, Khan KA. (1996) Chromosome aberrations, sister chromatid exchange and micronuclei formation analysis in mice after in vitro exposure to bacoside A and B. *Cytology* **61**, 99-103.

Goel RK, Sairam K, Dora Babu M, Tavares A, Raman A. (2003) In vitro evaluation of *Bacopa monniera* on anti-Helicobacter pylori activity and accumulation of prostaglandins. *Phytomedicine* **10**, 523-527.

Hou CC, Lin SJ, Cheng JT, Hsu FL. (2002) Bacopaside HI, bacopasaponin G, and bacopaside A, B, and C from *Bacopa monniera*. *J. Nat. Prod.* **65**, 1759-1763.

Jagetia GC, Baliga MS. (2003) Treatment of mice with a herbal preparation (Mentat) protects against radiation-induced mortality. *Phytother. Res.* **17**, 876-881.

Jain P, Khanna NK, Trehan N, Pendse VK, Godhwani JL. (1994) Anti-inflammatory effects of an Ayurvedic preparation, Brahmi Rasayan in rodents. *Indian J. Exp. Biol.* **32**, 633-636.

Kapur LD. (1990) *Bacopa monniera*. CRC Handbook of Ayurvedic Medicinal Plants. CRC press Inc. Boca Raton, Florida, p. 61.

Kar A, Panda S, Bharti S. (2002) Relative efficacy of three medicinal plant extracts in the alteration of thyroid hormone concentrations in male mice. *J. Ethnopharmacol.* **81**, 281-285.

Khanna T, Ahemd B. (1992) Beta adrenergic activity of saponins from *Bacopa monniera*. In Proceedings of the conference on trends in molecular and cellular cardiology, Lucknow, India 4-5 May, p. 20

Kulkarni SK, Verma A. (1993) Br-16A (Mentat®), a herbal preparation, improves learning and memory performance in mice. *Indian Drugs* **30**, 97-107

Malhotra CL and Das PK. (1959) Pharmacological studies of *Herpestis monniera*, Linn (Brahmi). *Indian J. Med. Res.* **47**, 294-305.

Malhotra CL, Das PK, Dhalla NS. (1960) Some neuropharmacological actions hersaponin – An active principle from *Herpestis monniera* Linn. *Arch. Int. Pharmacodyn.* **129**, 290-302

Martis G, Rao A, Karanth KS. (1992) Neuropharmacological activity of *Herpestis monniera*. *Fitoterapia* **62**, 399-406

Mohato SB, Garai S, Chakravarti AK. (2000) Bacopasaponins E and F: two jujubogenin bisdesmosides from *Bacopa monniera*. *Phytochemistry* **53**, 711-714.

Nadkarni KM. (1993) Indian Materia Medica, Bombay, Popular Prakashan, p. 624.

Nadkarni KM. (1954) Indian Materia Medica. Popular Prakashan Pvt. Ltd. Mumbai, India, pp. 624-625.

Nathan PJ, Clark J, Lloyd J, Hutchison CW, Downey L, Stough C. (2001) The acute effects of an extract of *Bacopa monniera* (Brahmi) on cognitive function in healthy normal subjects. *Human Psychopharmacol. Clin. Exp.* **16**, 345-351.

Nathan PJ, Tanner S, Lloyd J, Harrison B, Curran L, Oliver C, Stough C. (2004) Effecvts of combined extract of *Ginkgo biloba* and *Bacopa monniera* on cognitive function in healthy humans. *Human Psychopharmacol. Clin. Exp.* **19**, 91-96.

Prakash JC and Sirsi M. (1961) Proc, XXVII Mysore state Med. Conf. Manipal, India.

Prakash JC and Sirsi M. (1962) Comparative study of

the effects of Brahmi (*Bacopa monniem*) & Chlorpromazine on motor learning in rats. *J. Sci. Ind. Res.* **21C**, 93-96 .

Pratico D, Clark CM, Liun F, Lee YM, Trojanowski JQ. (2002) Increase in brain oxidative stress in mild cognitive impairment. *Arch. Neurol.* **59**, 972-976.

Rai D, Bhatia G, Palit G, Pal R, Singh S, Singh HK. (2003) Adaptogenic effect of *Bacopa monniera* (Brahmi). Pharmacol. Biochem. Behav. **75**, 823-830.

Rao Ch V, Sairam K, Goel RK. (2000) Experimental evaluation of *Bacopa monniera* on rat gastric ulceration and secretion. *Indian J. Physiol. Pharmacol.* **44**, 435-441.

Rastogi S, Pal R, Kulshreshtha DK. (1994) Bacoside A3 – a triterpenoid saponin from Bacopa monniera. *Phytochemistry* **36**, 133-137.

Roodenrys S, Booth D, Bulzomi S, Phipps A, Micallef C, Smoker J. (2002) Chronic effects of Brahmi (*Bacopa monniem*) on human memory. *Neuropsychopharmacol.* **27**, 279-281.

Russo A, Izzo AA, Borelli F, Renis M, Vanella A. (2003) Free radical scavenging capacity and protective effect of *Bacopa monniera* L. on DNA damage. *Phytother. Res.* **17**, 870- 875.

Sairam K, Dorababu M, Goel RK, Bhattacharya SK. (2002) Antidepressant activity of Standardized extract of *Bacopa monniera* in experimental models of depression in rats. *Phytomedicine* **9**, 207-211.

Sairam K, Rao Ch V, Dora BM, Goel RK. (2001) Prophylactic and curative effects of *Bacopa monniera* in gastric ulcer models. *Phytomedicine* **8**, 423-430.

Sairam K, Rao CV, Babu MD, Goel RK. (2001) Prophylactic and curative effects of *Bacopa monniera* in gastric ulcer models. *Phytomedicine* **8**, 423-430.

Samiulla DS, Prashanth D, Amit A. (2001) Mast cell stabilizing activity of *Bacopa monniera*. *Fitoterapia* **72**, 284-285.

Satyavati GV, Raina MK, Sharma M. (1976) Medicinal plants of India, Vol. 1, ICMR, New Delhi. 118-122.

Schulte KE, Ruecker G, El-Kersch M. (1972) Components of Medicinal Plants. *Phytochemistry* **11**, 2649-2651.

Shanmugsundaram ERB, Mohammed Akbar GK, Shanmugsundaram KR. (1991) Brahmighritam, an Ayurvedic herbal formula for the control of epilepsy. *J. Ethnopharmacol.* **33**, 269-276.

Singh HK, Dhavan BN. (1997) Neuropsychopharmacological effects of the ayurvedic nootropic *Bacopa monniera* Linn. (Brahmi). *Indian J. Pharmacol.* **29**, 359-365.

Singh HK, Dhawan BN. (1982) Effect of *Bacopa monniera* Linn (Brahmi) extract on avoidance responses in rat. *J. Ethnopharmacol.* **5**, 205-214.

Singh HK, Dhawan BN. (1997) Neuropsychopharmacological effects of the Ayurvedic nootropic *Bacopa monniera* Linn. (Brahmi) *Indian J. Pharmacol.* **29**, S359-S365.

Singh HK, Rastogi RP, Srimal RC, Dhawan BN. (1988) Effect of Bacoside A and B on avoidance response in rats. *Phytother. Res.* **2**, 70-75.

Stough C, Lloyd J, Clark J, Dawney LA. (2001) Hutchison CW, Rodgers T, Nathan PJ. *Psycho. Pharmacol.* **156**, 481-484.

Stough C, Lloyd J, Clarke J, Downey LA, Hutchison CW, Rodgers T, Nathan PJ. (2001) The chronic effects of an extract of *Bacopa monniera* (Brahmi) on cognitive function in healthy human subjects. *Psychopharmacogy* **156,** 481-484.

Sumathi Thangrajan, Nayeem M, Balakrishna K, Veluchamy G. Devraj SN. (2002) Alcoholic extract of *Bacopa monniera* reduces the in vitro effects of morphine withdrawal in guinea pig ileum. *J. Ethnopharmacol.* **82**, 75-81.

Sumathy T, Subramanian S, Govindaswamy S, Balkrishna K, Veluchamy G. (2001) Protective role of *Bacopa monniera* on morphine induced hepatotoxicity in rats. *Phytother. Res.* **15**, 643-645.

Tripathi YB, Chaurasia S, Tripathi E, Upadhyaya A, Dubey GP. (1996) *Bacopa monniera* Linn as an antioxidant: mechanism of action. *Indian J. Exp. Biol.* **34**, 523-526.

Tripathi YB, Pande E, Dubey GP. (1999) Antioxidant property of *Hypericum perforatum* (L) of Indian origin and its comparison with established Medhya rasayanas of Ayurvedic medicine. *Curr. Sci.* **76**, 27-29.

Um BH, Bouchet MJ, Lobstein A, Callizot N, Maciuk A, Mazars G, Poindron P, Anton R. (2002) Bioguided research of nootropic substance from Bacopa monnieri. Revista de Fitoterapia 50th Annual Congress of Society for Medicinal Plant Research S1, 155.

Um BH, Bouchet MJ, Lobstein A, Callizot N, Maciuk A, Mazars G, Poindron P, Anton R. (2002) Bioguided research of nootropic substances from *Bacopa monnieri. Rev. Fitoterapia* **2**, S1.

Vohora D, Pal SN, Pillai KK. (2000) Protection from phenytoin-induced cognitive deficit by *Bacopa monniera*, a reputed Indian nootropic plant. *J. Ethnopharmacol.* **71**, 383-390.

Vohora SB, Khanna T, Athar M, Ahmad B. (1997) Analgesic activity of bacosine, a new triterpene isolated from *Bacopa monniera.* Fitoterapia. **68**, 361-365.

Vohra BPS, Sharma SP, Kansal VK. (2001) Maharishi Amrit Kalash, an Ayurvedic medicinal preparation, enhances cholinergic enzymes in aged guinea pig brain. *Indian J. Exp. Biol.* **39**, 1258-1262.

Yoganarsimhan SN, Chelladurai V. (2000) Meidicinal Plants of India, Vol. 2. Government Siddha Medical College, Palayamkottai, Tamil Nadu, India, p. 67.