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Review Article

PHARMACOGNOSTIC AND PHARMACOLOGICAL ASPECT OF *BACOPA MONNIERI:* A REVIEW

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ABSTRACT

It is said that the use of *Bacopa monnieri* (BM) for memory enhancement goes back 3000 years or more in India, when it was cited for its medicinal properties, especially the memory enhancing capacity, in the vedic texts "Athar-Ved Samhila" (3:1) of 800 BC and in Ayurveda. In the folklore of Indian medicine, several herbs have been used traditionally as brain or nerve tonics. One of the most popular of these neurotonics is BM, a well-known memory booster. Brahmi has been administered at religious institutions to help students to enhance their memory for learning ancient, religious hymns. It is also used as cardio-tonic, tranquilizer and sedative, improves the process of learning, restores memory, and enhances power of speech and imagination, diuretic and nervine tonic, antistress, for nervous and mental strain, use in insanity, epilepsy, hysteria, esthenia, nervous breakdown. It is a small, creeping succulent herb. The leaf and flower bearing stems are 10-30 cm long and arise from creeping stems that form roots at the nodes with pale blue or pinkish white flowers belonging to family *Scrophulariaceae* grown nearly banks of freshwater streams and ponds, paddy fields, and other damp places. The chief phytoconstituents present are brahmine, herpestine, alkaloids, and saponins.

Keywords: Ayurveda, Brahmi, Memory booster, Herb, Neurotonics, Tranquilizer.

INTRODUCTION

Herbal drugs constitute only those traditional medicines which primarily use medicinal plant preparations for therapy. The earliest recorded evidence of their use in Indian, Chinese, Egyptian, Greek, Roman, and Syrian texts dates back to about 5000 years. The classical Indian texts include Rigveda, Atharvaveda, Charak Samhita, and Sushruta Samhita. The herbal medicines/traditional medicaments have, therefore, been derived from rich traditions of ancient civilizations and scientific heritage.

Description of the herb

Bacopa monnieri (BM) is a small, creeping, somewhat succulent herb. The leaf and flower bearing stems are 10-30 cm long and arise from creeping stems that form roots at the nodes. The growth habit of *Bacopa*, therefore, resembles that of peppermint. The leaves are simple, obovate-oblong, opposite, approximately 2 cm × 1 cm, with entire margins, flowers are blue or white with purple veins, solitarily 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 persistent calyx (Fig. 1). *Bacopa* is a member of the family *Scrophulariaceae* [1,2].

Macroscopic

The plant is succulent when fresh but becomes shriveled on drying; slightly bitter in taste, without any characteristic odor and composed of crumpled, matted broken pieces of roots, branching stems, leaves, flowers, and few tender fruits [3,4].

Root

Fragments of dried main roots are cylindrical, about 5 mm in diameter, longitudinally wrinkled and off-white in color.

Stem

Pieces of the stem are cylindrical, glabrous, nodes prominent, at places attached with vertically growing branches and ventrally to cluster of tortuous, brittle roots, internodes about 1-1.5 cm in length and 3-4 mm in diameter, pale yellowish green and with purplish tinge.

Leaf

Simple, opposite and decussate, somewhat sessile, glabrous, obovate-oblong to spatulate in shape, 0.6-2.5 cm in length and 3-8 mm in width, entire, lower surface dotted with minute specks, obscurely 1-3 nerved, color faint green [5].

Flower

Pale blue or pinkish white, nearly regular, solitary, axillary. 0.6-3 cm in length, usually longer than the leaves with two linear bracteoles, pedicel slender, calyx glabrous, deeply 5 partite Corolla gamopetalous, stamens 4, didynamous, anthers 2 celled, pistil carpel, syncarpous ovary two chambered with many ovules, style dilated toward the top, stigma-bilobed [6,7].

Fruit

Globose to ovoid, glabrous capsule, 5 mm in length, enclosed within persistent calyx, ped 1-3 cm long purplish when fresh.

Seed

Numerous, very minute, <1 cm wide, oblong or irregular.

Microscopic

Root

The root is irregularly circular to angular in shape and show an outermost piliferous layer, parenchymatous cortex with intervening air spaces and a centrally located solid core, of xylem encircled by narrow phloem. The piliferous layer is replaced by formation of cork cells, cortex is wide, parenchymatous, traversed with simple and compound starch grain intervened with air spaces, endodermis is distinct, a narrow band of phloem surrounding the located solid core of xylem composed of radially arranged isolated vessels, fibers, and medullary rays (Fig. 2) [8,9].

Stem

The stem is almost circular in outline, shows outer epidermis, broad aerenchymatous cortex occupying the major area of the

section, a distinct endodermis encircling the ring of stellar tissue and central parenchymatous pith with a layer of thick-walled celled epidermis covered with thin cuticle, cortex is very wide, consisting of chlorenchymatous aerenchyma embedded with starch grains, endodermis is distinct, encircling the narrow band of parenchymatous phloem and xylem, the central region being occupied by narrow parenchymatous pith embedded with simple and compound starch grains.

Leaf

The leaf passing through the midrib is almost cylindrical in outline with a very narrow elevation on the upper side of the midrib. Upper and lower epidermis, the cells of the upper being bigger in size and at places show striated cuticle, both the epidermis are embedded with stomata and bear sessile-glandular trichomes with multi cellular head. A narrow collenchymatous band is located underneath both the epidermis of the midrib and shows a centrally located conjoint collateral meristele encircled by a parenchymatous sheath. The mesophyll tissue of the lamina is composed of spongy parenchyma, traversed with vascular strands; prismatic and few cluster crystals of calcium oxalate are embedded throughout the parenchymatous cells of the leaf [7,10].

Powder

Shows fragments of upper and lower epidermis of leaf in surface view embedded with sessile-glandular trichomes with 4-8 celled head and diacytic to anomocytic stomata, they being more on the lower side, with sinuous anticlinical walls and at places shows striated cuticle; prismatic, cluster crystals of calcium oxalate, starch grains and oil globules scattered as such throughout or embedded in the parenchymatous cells, fragments of longitudinally cut annular and spiral vessels, transversely cut fragments of stem showing aerenchymatous cortical cells, papillose marginal cells of the petal, testa of the seed in surface view and transversely cut fragments of cotyledon [11].

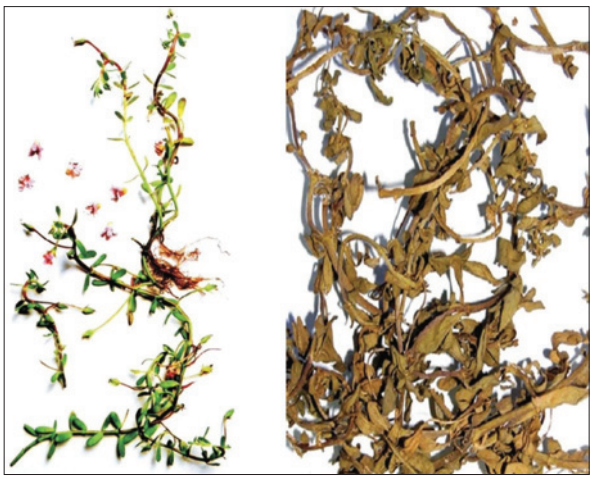

Fig. 1: Fresh and dried herb of *Bacopa monnieri*

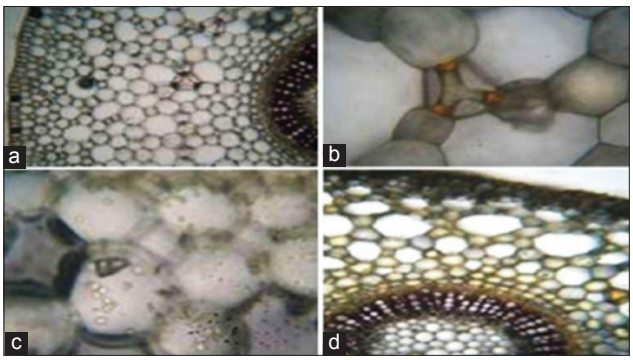

Fig. 2: (a) Vascular bundles, (b) parenchymatous cells, (c) calcium oxalate crystals, (d) xylem and phloem

Chemical constituents

Major

Bacoside A: The chief constituents are brahmine, herpestine, alkaloids, and saponins. The saponins designated as bacoside A, bacoside B, and betulic acid (Figs. 3 and 4). D-mannitol, stigmastanol, β-sitosterol, and stigma sterol have been isolated, bacoside A, on acid hydrolysis gave three sugars, two of which have been identified as glucose and arabinose bacoside B also gave on hydrolysis glucose and arabinose [12].

Others

Bacoside B, bacoside A_1, bacoside A_3, bacogenin A_1, bacogenin A_2, bacogenin A_3, bacogenin A_4, bacopa saponin-C, bacopasides I and II, bacopasides III-V, bacopasides VI-VIII, bacobitacins A-D, monnieraside I, monnieraside III, monnieri, plantioside B; jujubogenin, pseudojujubogenin, 3-O-β-D-glucopyranosyl-(l—»3)-[β-D-glucopyranosyl] jujubogenin, 3-O-[β-D--glucopyranosyl-(l—»3)-[β-D-glucopyranosyl] pseudojujubogenin, betulinic acid, wogonin, oroxidin, luteolin, luteolin-7-glucoside, luteolin-7-glucuronide, apigenin-7-glucuronide; nicotine, 3-formyl-4-hydroxy-2H-pyran, bacosine, bacostcrol, bacosterol-3-O-β-D-glucopyranoside, stigmasterol, stigmastanol, β-sitosterol, D-mannitol, and an uncharacterized glycoside [11].

Quantitative standards [13]

Foreign matter: Not more than 2.0%.
Total ash: Not more than 7.0%.
Acid-insoluble ash: Not more than 2.0%.
Ethanol-soluble extractive: Not <40.0%.
Water-soluble extractive: Not <50.0%.
Moisture content: Not <80.0%.

PRELIMINARY PHYTOCHEMICAL SCREENING

The aqueous and ethanolic extract of BM (BME) was subjected to preliminary phytochemical investigation for the detection of the following metabolites (Table 1):

- Alkaloids
- Carbohydrates
- Glycosides

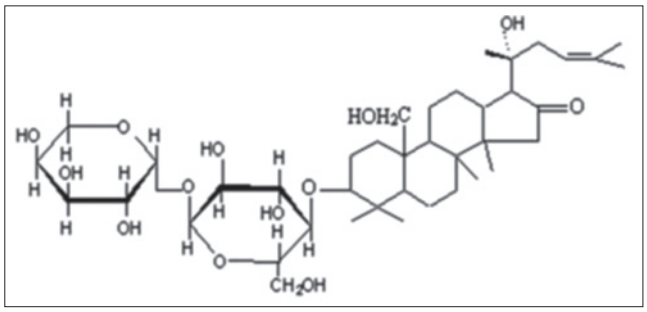

Fig. 3: Bacoside A

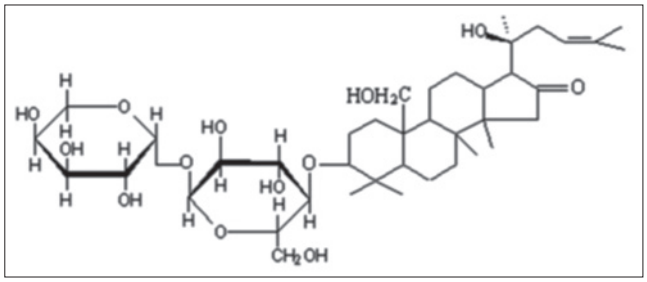

Fig. 4: Bacoside B

Table 1: Phytoconstituents present in aqueous extract of BM [11,14]

S. No.	Phytoconstitutent	Presence/absence
1	Tannins	−ve
2	Saponins	+ve
3	Alkaloids	−ve
4	Carbohydrates	+ve
5	Protein	+ve
6	Sterols	−ve
7	Volatile oil	−ve
8	Flavonoids	+ve
9	Triterpenoids	+ve
10	Glycoside	+ve
11	Fixed Oil	−ve

+ve: Presence, −ve: Absence, BM: *Bacopa monnieri*

- Phenolic compounds
- Flavonoids
- Protein and free amino acids
- Saponins
- Sterols.

Pharmacology

Ethanol extract (10 mg/kg) brahmi improved motor learning in rats. Both ethanol extract as well as the active principle hersaponin exhibited tranquilizing activity. The active principle also reduced the concentration of noradrenaline and 5-hydroxytryptamine in brain. Antianxiety effect was reported in ethanol extract and saponin in rat. Antidepressant activity has also been reported. Ethanol extract (50 mg/kg) was found to have antigastric ulcer activity in normal and diabetic rats and also had anti-*Helicobacter pylori* activity *in vitro.* Other pharmacological activities reported were antioxidant, anticonvulsant, analgesic, antiallergic, antifungal, cardiac depressant, and cardio-tonic either by crude extract or pure principle.

Major therapeutic claims

Antileprotic, antiepileptic, antipyretic, antidiabetic, anti-inflammatory, and anxiolytic [15].

Antiepileptic

A clinical study was undertaken with the crude aqueous and defatted alcoholic extracts of the plant in 24 patients with varied mental disorders. The study revealed improvement in learning process and correction in the abnormal behavior of epileptic patients treated with defatted-alcoholic extract (2-4 mg/kg b.w.) and crude aqueous extract of "brahmi" two dose daily for 5 months. Defatted alcoholic extract of "brahmi" was found to be more potent than the aqueous form in alleviating the epileptic fits [16]. A controlled clinical trial was carried out with crude BMEs (4 patients), *Marsilea minuta* (2 patients), and *Acorus calamus* (6 patients) in epileptic patients with special reference to electroencephalography (EEG) changes to substantiate their sedative and tranquilizing properties. The defatted alcoholic extract of "brahmi" showed improvement in one case each of temporal lobe epilepsy and petit mal epilepsy. There was a close parallelism between the clinical improvement and EEG changes in these two cases [17].

Antianxiety and antidepressant activity

Research using a rat model of clinical anxiety demonstrated that a BME containing 25% bacoside A exerted anxiolytic activity comparable to lorazepam, a common benzodiazepine anxiolytic drug, and it was attentively noted that the BME did not induce amnesia, side effects associated with *lorazepam*, but instead had a memory-enhancing effect [18]. The antidepressant potential of BM has been evaluated in an earlier study, wherein it showed a significant antidepressant activity in the most commonly used behavior paradigms in animal models of depression, namely, forced swim test and learned helplessness tests. In the study, the BME in the dose range of 20-40 mg/kg was given once daily for 5 days, and it was found comparable to standard antidepressant drug imipramine in antidepressant activity in rodent animals. The same study has postulated the role of serotonin and gamma amino butyric acid (GABA) in the mechanism of action attributed for its antidepressant action along with its anxiolytic potential, based on the compelling evidence that the symptoms of anxiety and depression overlap each other [19].

Memory enhancer

Efficacy of plant was studied in revitalizing intellectual functions in 40 school going children from rural area in Varanasi. One group was given "brahmi" syrup one teaspoon full (350 mg), thrice daily for 3 months, and the other group was given syrup "simplex" used as placebo in the same dose. There were renovation and improvement of the perceptual-motor functions during the development phase in the group receiving "brahmi." A double-blind controlled study was carried out to evaluate the effect of a micro ("suksma") medicine derived from the plant by 1 month treatment on 110 boy students in the age of 10-13 years and having average IQ 100. The study showed encouraging results in enhancing some factors of intelligence, *viz*., memory (direct), arithmetic skill, and some verbal factors. Need for long-term study was felt [20].

Sedative and tranquilizing properties

Earlier studies reported a sedative effect of glycosides named hersaponins. A subsequent study has found that the alcoholic extract, and to a lesser extent the aqueous extract of the whole plant exhibited tranquilizing effects on albino rats and dogs. On the other hand, it has been found that the alcoholic extract of the plant and chlorpromazine improved the performance of rats in motor learning. A previous study has reported that a single dose of the glycoside hersaponin is better than pentobarbitone in facilitating acquisition and retention of brightness discrimination reaction [21].

Central nervous system effects

Brahmi Rasayan, an ayurvedic preparation, was studied in mice and rats for its effects on the central nervous system at oral doses ranging between 1 and 30 g/kg. Observational screening in mice was carried out following a multiparametric check list. The test material was studied for its effect on pentobarbitone hypnosis, motor coordination, tail-withdraws reaction time, electroshock, chemoconvulsions, haloperidol-induced catalepsy and conditioned avoidance response. The test material exhibited a sedative effect and significantly prolonged the hypnotic action of pentobarbitone. It produced a variable blockade of conditioned avoidance response. The presence of a significant antinoclceptive effect, coupled with the ability of the test substance to offer protection against electroshock seizures and chemoconvulsions plus the ability to antagonize the haloperidol-induced catalepsy, suggests an involvement of the GABAergic system in the mediation of the central nervous system effects of Brahmi Rasayan [22].

Antioxidant and adaptogenic properties

BME or bacosides have shown an antioxidant activity and antistress [21]. A previous study suggests an involvement of the GABAergic system in the mediation of these central nervous system effects of BM [22]. Based on animal study results, bacosides were shown to have antioxidant activity in the hippocampus, frontal cortex, and striatum [23]. Animal research has shown that the BMEs modulate the expression of certain enzymes involved in generation and scavenging of reactive oxygen species in the brain. It was suggested that the adaptogenic properties of the herb would be beneficial in the management of stress related conditions as BM showed the potential to be effective in stress in a study on rats [24]. In the study, BME was found not only to induce the constitute expression of heat-shock protein 70 (Hsp70) but also induce the cytochrome P450 (CYP 450) enzymes in all regions of the brain. The level of Hsp70 was found to be increased in the brain as a response to stress. On the other hand, the group that was pre-treated for 1 week with 20-40 mg/kg/daily, before giving stress, the Hsp70 was found to be in lower concentration. An increase in the activity of CYP 450-dependent enzymes 7-pentoxyresorufin-odealkkylase and 7-ethoxyresorufin-o-

deethylase was observed in all the brain regions after exposure to stress alone and with both doses of BME although the magnitude of induction observed was less with a higher dose of the same. Thus, it was suggested that the BM primed the brain for stress by stockpiling these useful enzymes even before stressful conditions and that our susceptibility to stress could be lowered by using this medicinal herb. It was speculated that this induction may be an adaptive response to the stress which needs further investigation. The level of superoxide dismutase (SOD) was also increased in the brain in the groups pre-treated with BME. The data indicated that BME has a potential to modulate the activities of Hsp70, CYP 450, and SOD and thereby possibly allowing the brain to be prepared to act under adverse condition-like stress [25].

Endocrine effects

BME (200 mg/kg orally) increased the thyroid hormone, T4, by 41% in mice. T3 was not stimulated, suggesting that the extract may directly stimulate synthesis and/or release of T4 at the glandular level while not affecting conversion of T4 to T3 [26].

BMEs caused reversible suppression of spermatogenesis and fertility. The treatment caused reduction in motility and viability of the sperms and reduced the number of spermatozoa in cauda epididymis and testis, and caused alterations in the somniferous tubules in mice [26].

Morphine withdrawal effects

The effect of the alcoholic extract of the whole plant of BM (*Scrophulariaceae*) on morphine withdrawal was evaluated *in vitro* in guinea-pig ileum. After a 4 minutes, *in vitro* exposure to morphine, addition of naloxone-induced a strong contraction, addition of various concentrations of the alcoholic extract of BM (100-1000 µg/ml) 15 minutes before exposure to morphine reduced the naloxone-induced contraction in a dose-dependent manner The results suggest that BM extract may be useful in reducing the withdrawal symptoms induced by morphine [27].

Free radical scavenging effects

BM is an ayurvedic medicine, clinically used for memory enhancing, epilepsy, insomnia, and as a mild sedative. In this work, the free radical scavenging capacity of a methanol extract of BM and the effect on DNA cleavage induced by H202 ultraviolet-photolysis was investigated. In addition, it is examined whether this plant extract is capable of reducing the hydrogen peroxide-induced cytotoxicity and DNA damage in human non-immobilized fibroblasts. It showed a dose-dependent free radical scavenging capacity and a protective effect on DNA cleavage. These results were confirmed by a significant protective effect on H_2O_2-induced cytotoxicity and DNA damage in human non-immortalized fibroblasts. The antioxidant capacity of BM may explain, at least in part, the reported antistress, immune modulatory, cognition n-facilitating, anti-inflammatory, and antiaging effects produced by it in experimental animals and in clinical situations and may justify further investigation of its other beneficial properties. Moreover, this experimental evidence suggests that because of its antioxidant activity, this ayurvedic drug may be useful in the treatment of human pathologies, in which free radical production play's role [28].

Cigarette smoking is implicated as a major risk factor in the development of cardiovascular and cerebrovascular diseases creatine kinase (CK), and its isoforms have beer advocated as sensitive markers in the assessment of cardiac and cerebral damage. Therefore, in the present study, it reports the isoenzyme patterns of CK in rats on exposure to cigarette smoke and the protective effect of bacoside against chronic smoking-induced toxicity. Adult male albino rats were exposed to cigarette smoke and simultaneously administered with bacoside A, the active constituent from the plant BM, for a period of 12-week the activity of CK was assayed in serum, heart, and brain, and its isoenzymes in serum were separated electrophoretically. Rats exposed to cigarette smoke showed a significant increase in serum CK activity with concomitant decrease in heart and brain also cigarette smoke exposure resulted in a marked increase in all the three isoforms in serum. Administration of bacoside a prevented these alterations induced by cigarette smoking, cigarette smoking is known to cause free radical mediated lipid peroxidation (LPO) leading to increased membrane permeability and cellular damage in the heart and brain resulting in the release of CK into the circulation the protective effect of bacoside on the structural and functional integrity of the membrane prevented the leakage of CK from the respective tissues, which could he attributed to its free radical scavenging and antilipid peroxidative effect [29].

Hair growth promoting activity

Herbal hair oil formulated from *Emblica officinalis,* BM, and *Cyperus rotundus* alcoholic extract or as a whole drug. The hair oil was prepared individually and in a varying concentration of all three herbs and a mixture of all the three herbs in fixed proportion using coconut oil as base. The formulated oil in varying concentration was evaluated physical, chemical, and hair growth properties of formulated oil by applying it topically on shaved skin of albino rats. Primary skin irritation test and hair length test were performed, and the hair growth was compared with standard minoxidil 2% ethanolic solution using healthy albino rats. It was observed that hair oil formulation showed the best result among the other formulation evaluated by showing an enlargement of follicular size and prolongation of the anagen phase [30-32].

Antimicrobial effect

The antibacterial activity of BM was screened for different bacterial strains using methanol, ethanol, chloroform, and petroleum ether. The phytochemical screening was carried out to know the compounds responsible for these activities. Methanol, ethanol, and chloroform extracts were tested against *Bacillus amyloliquefaciens* (MTCC 1270), *Streptococcus pyogens* (MTCC 1923), *Vulgarica*, *Bacillus megaterium* (MTCC 3353), *Aspergillus niger* (MTCC 281), *Bacillus pumilus*, *Salmonella typhi*, *Bacillus subtilis*, and *Micrococcus luteus*. The susceptibility of the bacteria to the crude extracts on the basis of zones of growth inhibition varied according to microorganism and extracting solvent. In most of the above-mentioned plants, the methanol extract produced the highest activity. On the basis of the results obtained, it could be concluded that methanol could be used for extracting antimicrobial compounds from leaves [33].

Gastrointestinal effects

Some *in vitro*, animal and human studies have investigated the effects of BME on the gastrointestinal tract. *In vitro* studies have demonstrated direct spasmolytic activity on intestinal smooth muscle, via inhibition of calcium influx across cell membrane channels. This property suggests that BME may be of benefit in conditions characterized by intestinal spasm such as irritable bowel syndrome [30,34]. The results indicated the direct action of the extract on smooth muscles. Furthermore, calcium chloride-induced responses observed in the rabbits' blood vessels and jejunum were reduced in the presence of the BME (10-700 mcg/mL), suggesting direct interference with the influx of calcium ions. However, since the extract did not affect contractions induced by noradrenalin or caffeine, the authors concluded that the extract had no appreciable effect on the mobilization of intracellular calcium. Based on the results of the experiment, it is postulated that the spasmolytic effect of BME on smooth muscles is predominantly due to the inhibition of calcium influx, applicable to both electrical impulse-mediated and receptor-mediated calcium channels in the cell membrane. Animal and *in vitro* studies suggested that BM may have a protective and curative effect on gastric ulcers, and studies were reported for its antiulcerogenic activity [35,36]. In rats, a BME standardized for bacoside A was evaluated for its prophylactic and healing effects in five models of gastric ulcers [37]. At a dose of 20 mg/kg for 10 days, BME significantly healed penetrating ulcers induced by acetic acid, significantly strengthened the mucosal barrier and decreased mucosal exfoliation. The extract also alleviated stress-induced ulcers as observed by a significant reduction in LPO in rat gastric mucosa. BM's antioxidant properties and its ability to balance SOD and catalase levels were postulated to account for this effect. A recent *in vitro* study also

demonstrated its specific antimicrobial activity against *H. pylori*, a bacterium associated with chronic gastric ulcers. When the extract was incubated with human colonic mucosal cells and *H. pylori*, it resulted in the accumulation of prostaglandin E and prostacyclin, prostaglandins known to be protective for gastric mucosa.

Anticonvulsant

Crude plant extract of BM or bacosides has also shown anticonvulsive action.It possessed neuroprotective effects in glutamate-mediated excitotoxicity during seizures and cognitive damage occurring in association with pilocarpine-induced epilepsy. The ethanolic extract of BM was tested for anticonvulsant activity using different convulsive models (pentylenetetrazol, maximal electroshock, and strychnine-induced convulsion in rats, as well as hypoxic stress-induced convulsions in mice and lithium-pilocarpine-induced status epilepticus). The ethanolic extract of BM was administered as 50-55 mg/kg orally for rats and mice, respectively, 2 and 4 hrs before the respective convulsive stimuli. The ethanolic extract of leaves produced significant anticonvulsant activity for all the different models studied with a mechanism of action similar to that of benzodiazepines (GABA agonist) [16,18].

Safety aspects

The drug used in traditionally prescribed doses may be considered safe.

Dose

Powder: 1-3 g.

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