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THERAPEUTIC POTENTIAL OF NOO-TROPIC *BACOPA MONNIERI* IN PREVENTION & TREATMENT OF DISEASES: AN OVERVIEW

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ABSTRACT

In recent existence, a number of natural compounds have been identified that could potentially help in prevention and treatment of diseases. One plant that has been used in mental conditions and illnesses is *Bacopa monnieri* Wettst. (syn *Herpestis monniera*). It is commonly known as Indian water hyssop or Brahmi and belongs to the family Scrophulariaceae and useful in increasing the sharpness of perception by the sense organs and in the promotion of memory in children. In addition, Brahmi is found to be useful in the prevention and alleviation of convulsions. In adults, it helps to relieve insomnia. Brahmi has a bitter taste. Traditionally, the fleshy leaves and stems are made into a paste or pressed for juice extraction. It has been used in Ayurvedic formulations for conditions ranging from catarrhal complaints, gastrointestinal disturbances due to excessive tobacco use, habitual abortions and high blood sugar due to anxiety disorders and epilepsy. In certain parts of India, Brahmi is believed to be an aphrodisiac. This review is intended to prominence the treatment strategies of Brahmi in terms of various diseases prevention.

Keywords: *Bacopa*, Brahmi, Memory and Nootropic.

INTRODUCTION

In recent times, the interest in the use of herbal products has increased tremendously in the western world as well as in developed countries. The vast majorities of currently available neuro-drugs and herbal remedies today seem to be reflection of such situation. Therefore, several plants have been selected based on their use in traditional systems of medicine. *Bacopa monnieri* (family: Scrophulariaceae) is a reputed drug of Ayurveda [1]. Of all Indian herbal therapies, *Bacopa monnieri* (BM) was, and still is, considered to be the premier herb for treating brain problems and age related mental decline as well as to improve cognitive processes. It is also used as a stomachic, digestive herb and to rejuvenate for promoting memory and intellect. This medicinal herb is also useful for skin disorders, and has been found to act as an antiepileptic, antipyretic, and analgesic.

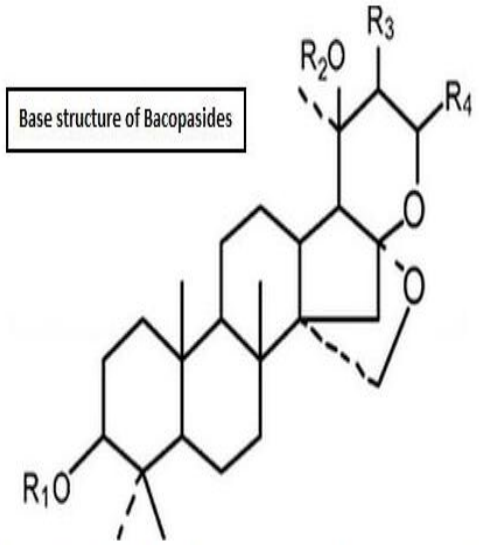
In a sector study by the Export–Import Bank of India, *B. monnieri* was placed second in a priority list of the most important medicinal plants, evaluated on the basis of their medicinal importance, commercial value, and potential for further research and development [2].

The *Bacopa monnieri* (Common name- Bramhi, Water hyssop) is a creeping, glabrous, succulent herb, rooting at nodes whose habitats include wetlands and muddy shores. Stem 10-30 cm long, 1-2 mm thick, soft, glabrous; branches ascending. Leaves 0.6-2.5 cm long and 3-8 mm broad, sessile, obovate-oblong or spathulate, entire, nerves obscure and lower surface dotted, flowers blue or white with purple veins, axillary and solitary on long pedicles and capsule ovoid glabrous, up to 5 mm long, no distinct odor, taste slightly bitter [3, 4]. The plant is propagated through cuttings. It is known as *Brahmi, Nir-brahmi* in Sanskrit, *Brihmi-sak*, *Jalanimba* in Bangali, *Brahmi* in Hindi, *Nirubrahmi* in Kannada, *Nirbrahmi* in Malayalam, Marathi and Tamil, *Sambranichettu* in Telugu [5, 6]. *Bacopa* is sometimes referred to as an a*indri* (a classification), due to its neuro-active properties [7] and may be referred to as *Brahmi* [8, 9]. Additionally, due to its rejuvenative properties and acting on the brain it is commonly referred to as a *Medhya*

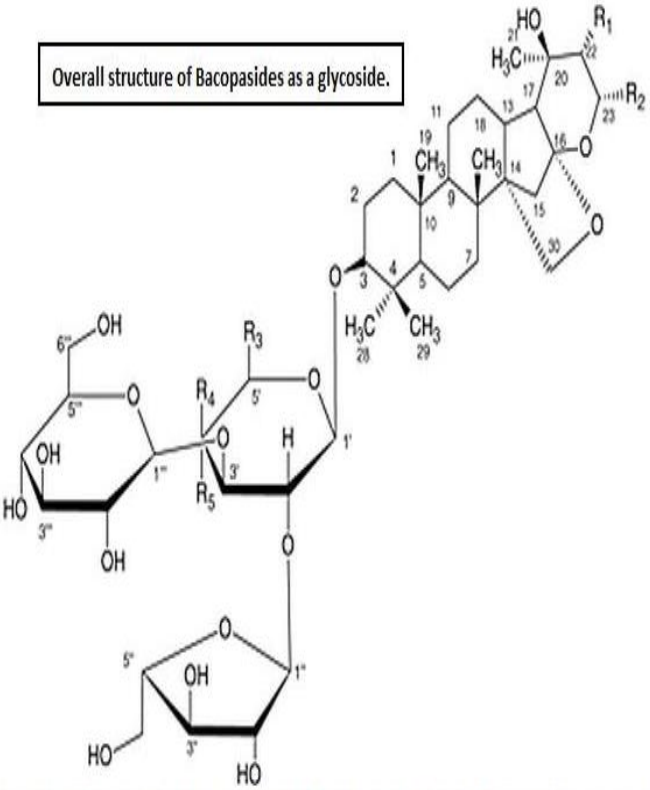
Rasayana (another classification), *Medhya* denoting the rejuvenative properties on the Nervous System [10]. The main traditional usages of *Bacopa Monnieri* are for anxiety, depression, learning, and various neuropharmacological disorders[11], whereas it has also been used for anti-inflammatory, antipyretic, astringent, laxative, cough, poisoning, and blood disorders[12]. It has traditionally been given to children as well

to boost brain power [11]. From recent research, it was focused primarily on its cognitive-enhancing effects, specifically memory, learning and concentration. The plant also possesses antioxidant properties, which finally provide protection from free radical damage in cardiovascular disease and certain types of cancers.Flowers and fruit appear in summer and the entire plant is used medicinally. [13]

Compounds responsible for the pharmacological effects of BM include alkaloids, saponins and sterol. Brahmine an alkaloid was first reported as isolated compound [14] of the plant. Later, other alkaloids like nicotine and herpestine have also been reported. BM contains major constituents such as des-saponin glycosides-



(Modified from: Zhou Y, et al. Triterpene saponins from Bacopa monnieri and their antidepressant effects in two mice models. J Nat Prod. (2007))



(Modified from: Srivastava P, et al. Stability Studies of Crude Plant Material of Bacopa monnieri and Quantitative Determination of Bacopaside I and Bacoside A by HPLC. Phytochem Anal. (2012)

triterpenoid Saponins (Bacosides A & B) [15, 16]. It also includes other minor constituents saponins, bacosides A1 & A3 [17, 18], hersaponin [19], Betulic acid, monnierin[20], alkaloids, Herpestin and Brahmine [21], flavonoids [22], luteolin-7-glucoside,glucoronyl-7-apigenin and gluucoronyl-7-luteonin, common phytosteroids [23]. Of these, the most bioactive components appear to be Bacoside A3, Bacopaside II, and both (jujubogenin and pseudojujubogenin) Bacosasaponin Cs [10, 24]. Temperatures of 40-60°C

(104-140°F) appear to be able to slowly degrade Bacopasides over time, whereas heat exposure up to 80°C (176°F) can rapidly decrease Bacopaside content [25].

Proper storage of *Bacopa Monnieri* is at 30°C (86°F) or less, with a relative humidity of 65% or less [26].

Classification and Chemical constituents:

Classification-

Kingdom : Plantae
Division : Angiospermae
Class : Dicotyledonae
Order : Lamiales
Family : Scrophulariaceae
Genus : *Bacopa*
Species : *monnieri*

Figure 1: *Bacopa monnieri* plant

Table 1: Chemical Compounds, Melting Points & Yield Percentage of *Bacopa monnieri*

Compound	Melting Point, ° C	Yield (%) on dry basis
Bacoside A	250°-251(decomposes)	1.54
Bacoside B	203° (decomposes)	0.65
Betulinic acid	315°	0.11
D-Mannitol	166°	0.02
Stigmastanol	170°	0.0013
b-Sitosterol	137°	0.0014
Stigma sterol	141°	0.005

PHARMACOLOGICAL ACTIVITIES

Anticancer Activity

Different extracts of the plant, bacosides A and B, bacopasides I, II, and X, and bacopasaponin C, showed potent activity in a brine shrimp lethality assay (an assay that is predictive of potential anticancer activity) [27, 28]. In addition, the bacoside a fraction and its individual components were found to be more active than the bacoside B fraction [29,30]. The ethanolic extract of the plant exhibited anticancer activity against Walker carcinosarcoma 256 in rat [31] and sarcoma-180 cell culture [32].

Neuroprotective Acitivity

Bacopa Monnieri (BM) extract may be able to increase memory formation by the enzyme Tryptophan Hydroxylase (TPH2) and increasing the expression of the serotonin transporter (SERT) [33]. Bacopa does appear to have some connections with the serotonin system, and may have downstream effects on the cholinergic system through this [34, 35]. Additionally, dendritic intersections and branching points in neurons have been noted to be proliferated with *Bacopa Monnieri* supplementation after 4 and 6 weeks,

but failed to have any changes at 2 weeks [36]. This neuronal growth effect occurs in adult rats [37] and younger rats undergoing growth spurts, [38] and occur in areas of the brain known to be involved with memory, such as the hippocampus and the basolateral amygdale [36, 38]. These changes coincide with memory enhancement seen in human studies, where usage for less than 2 weeks is not associated with any cognitive enhancement but additional usage is; implicating dendritic enhancement as a probable explanation for memory enhancement.

Ethanolic extract of *B. monnieri* afforded a neuroprotective role against aluminium-induced toxicity and prevented oxidative stress induced by aluminium in the hippocampus of rats [39] and the activity was comparable to that of α-deprenyl (a monoamine oxidase-B inhibitor and neuroprotectant used in Parkinson's disease). The extract used in that study comprised 55–60 % bacosides [40]. The extract was shown to inhibit lipid per oxidation, protein oxidation, and lipofuscin accumulation. Co-administration of the extract with aluminium was shown to reverse the aluminium-induced oxidative stress and ultra structural changes in the hippocampus [41] and prevent the accumulation of lipid and protein damage. Furthermore, the reduced activity of the endogenous antioxidant enzymes due to treatment was restored to normal level.

Antioxidant Activity-

Bacopa Monnieri, at 40mg/kg body weight in rats, has been noted to modulate the stress response rather than merely suppress it. BM reduces superoxide dismutase (SOD) levels by 2.4-fold in the hippocampus at 20mg/kg oral ingestion, without significantly affecting other areas of the brain [12]. *Bacopa Monnieri* supplementation can reduce oxidative damage from aluminium and prevent an increase in cognitive iron stores in cases of overload. These effects are also seen with mercury, in which Bacopa Monnieri appears to reduce oxidative damage from mercury on brain tissue *in vivo* where near pre-testing levels of damage were achieved with 40mg/kg bodyweight, although full protection is not seen [42]. In general, *Bacopa Monnieri* appears to protect the brain from the damage induced by excessive mineral status [43].

The whole plant methanolic extract was investigated for any *in vitro* antioxidant

property and total phenolic content. Further, the antioxidant activity of the plant was studied using three *in vitro* models. The methanolic extract of the plant had free-radical-scavenging activity and provided protection against DNA damage in human non-immortalized fibroblasts [44].

Muscle Relaxant Activity

Ethanolic extract of whole plant of BM has shown cardiac depressive activity on left ventricular contractility, heart rate and coronary flow in isolated rabbit heart and it was found that the activity in all parameters appears similar like quinidine [45]. Animal studies have demonstrated that the *Bacopa* extract has a relaxant effect on chemically-induced broncho-constriction and the effect may be probably via inhibition of calcium influx into cell membranes. Earlier to this, Dar and Channa have demonstrated the broncho-vasodilatory activity of *B. monnieri* on the rabbit and guinea pig trachea by *in vitro* study. They also demonstrated the effect of BM on pulmonary artery and aorta [46].

The anti-ulcer and ulcer-healing activities of the *Bacoppa Monnieri* extract may be due to its effects on various mucosal offensive and defensive factors [47]. *In vitro* studies have demonstrated direct spasmolytic activity on intestinal smooth muscle, *via* inhibition of calcium influx across cell membrane channels. This property of BM may have beneficial role in conditions characterized by intestinal spasm such as irritable bowel syndrome. The results indicated the direct action of the extract on smooth muscles [48].

Anti-inflammatory and Anti-bacterial Activity

The ethanolic extract of *B. monnieri* (100 mg, i.p.) exhibited a very good anti-inflammatory activity against carrageenan induced paw edema in mice and rats, and it selectively inhibited PGE**2**-induced inflammation [49]. Bacosine, isolated from the plant, exhibited a moderate analgesic activity and was found to be opioidergic in nature [50]. The *n*-butanol extract of the plant was shown to have good antibacterial activity against a battery of human pathogens and cattle pathogens tested *in vitro* [51]. Betulinic acid isolated from *B. monnieri* showed good antifungal activity against *Alternaria alternata* and *Fusarium fusiformis*.

Hepatoprotective Activity-

BM possesses protective effect against morphine-induced liver and kidney toxicity in rats. It was found that pretreatment with BM extract has shown to possess a significant protective effect against morphine-induced liver and kidney functions in terms of serum glutamate oxaloacetate transaminase, serum glutamate pyruvate transaminase, alkaline phosphatase, lactate dehydrogenases and gamma-glutamyl transferase activities and urea, creatinine and uric acid level respectively [52]. Even, alcohol extract of BM exerted a hepatoprotective effect against morphine induced liver toxicity [53].

Others

Bacopa monnieri is used for centuries as a memory enhancing, anti-inflammatory, analgesic, antipyretic, sedative and antiepileptic agent. Recent studies concluded that extract of *Bacopa monnieri* may be an alternative direction for ameliorating neurodegenerative disorders like Alzheimer disease and Parkinson's disease. This most popular herb is a well-known memory booster and BM has also shown to have thrombolytic activity in one recent *in vitro* study [54]. In addition to all pharmacological studies mentioned above, herb-drug and herb-herb interactions of BM need to be studied. The diverse studies indicated that interactions between herbal medicines and synthetic drugs exist and can have serious consequences [55, 56]. Therefore, it is necessary to consider the possibility of BM-drug interactions. The anti-fertility potential of BM was recently disclosed in male mice, wherein it was shown to cause reversible suppression of spermatogenesis and fertility, without producing apparent toxic effects [57].

Many studies have been subject to meta-analysis, where it is concluded that *Bacopa* shows preliminary efficacy in improving general memory with little influence on other parameters of cognition [58, 59].

The investigation from the neuroprotective effects of the standardized extract of *Bacopa monnieri* (BM) against paraquat/diquat-induced toxicity (Paraquat exposure as a potential risk factor for the onset of PD) showed that a pretreatment with the BM extract, protected the rat dopaminergic PC12 cell line against paraquat/diquat-induced toxicity in various cell survival assays [60].

DISCUSSION

From the recent researches, it is concluded that further studies are being conducted to find out the impact of the extracts on other mediators of inflammation and its ultimate effect on gene expression. The botanical extracts containing multiple classes of chemical entities with synergic property may hold a better promise for therapeutic benefits and applicability in neuroprotection as compared to single chemical entity. More recently preclinical studies have reported cognitive enhancing effects with various extracts of *Bacopa monnieri* but the exact mechanism of its actions is still uncertain as its multiple active constituents make it pharmacology complex. Brahmi has been used as traditional medicine due to its neurotonic and memory enhancing property. This study demonstrates that Brahmi extract diminishes neuronal death induced by amyloid peptide partly through the suppression of Acetyl Choline Esterase activity (AChE). The dual LOX/COX-2 inhibition by *Bacopa monnieri* explains history as an efficient herbal medicine for the treatment of inflammatory disorders.

Overall outcome from the present study imply the potential of Brahmi extract as a therapy to prevent memory loss in natural aging, other diseases as well as an alternative cure for neurodegenerative disorders associated with oxidative stress and amyloid-induced memory failure. The major clinical activity in disease circumstances might be due to the presence of biologically active compounds. This review is intended to accent the treatment strategies of Brahmi in terms of various diseases prevention.

REFERENCES

1. Bammidi SR, Volluri SS, Chippada SC, Avanigadda S, Vangalapat M. A Review on Pharmacological Studies of *Bacopa Monniera*. Journal of Chemical, Biological and Physical Sciences 2011; 1(2): 250 – 259.
2. Export-Import Bank of India, Indian Medicinal Plants: A Sector Study. Occasional paper No. 54, 2, Quest Publications, Bombay, India; 1997.
3. Chopra RN, Nayar SL, Chopra IC. Glossary of Indian medicinal plants; Calcutta, New Delhi, 1956; 32-40.
4. Aiyer KN, Kolammal M. Pharmacognosy of Ayurvedic drugs; Department of pharmacognosy, University of Kerala, Trivendrum 1964; (1-8): 27.
5. Prasad S, Amer J. Pharmacognostical studies of Brahmi; stem and leaf characteristics of Herpestis monniera H. B. and K. and Hydrocotyle asiatica Linn. J. Am. Pharm. Assoc. 1947; 36(12): 393-401.
6. Data SC and Mukerji B. Pharmacognosy of Indian leaf drugs; Govt. of India press, Ministry of Health, Calcutta, 1952; 62-63.
7. Russo A, Borrelli F. *Bacopa monniera,* a reputed nootropic plant: an overview. Phytomedicine 2005; 12(4): 304-317.
8. Shinomol GK, Muralidhara, Bharath MM. Exploring the role of "Brahmi" (*Bocopa monnieri* and *Centella asiatica*) in brain function and therapy. Recent Pat Endocr Metab Immune Drug Discov. 2011; 5(1): 33-49.
9. Singh RH, Narsimhamurthy K, Singh G. Neuronutrient impact of Ayurvedic Rasayana therapy in brain aging. Biogerontology 2008; 9(6): 369-374.
10. Mukherjee S, *et al*. Evaluation of comparative free-radical quenching potential of Brahmi (*Bacopa monnieri*) and Mandookparni (*Centella asiatica*). Ayu. 2011; 32(2): 258-264.
11. Shinomol GK, Muralidhara. *Bacopa monnieri* modulates endogenous cytoplasmic and mitochondrial oxidative markers in prepubertal mice brain. Phytomedicine 2011; 18(4): 317-326.
12. Chowdhuri DK, Parmar D, Kakkar P. Antistress effects of bacosides of *Bacopa monnieri*: modulation of Hsp70 expression, superoxide dismutase and cytochrome P450 activity in rat brain. Phytother Res. 2002; 16(7): 639-645.
13. Mathew KM. The flora of Tamil Nadu and Carna Rapinat Herbarium St. Joseph's College,Trichirapalli India 1984.
14. Bose KC, Bose NK. Observations on the actions and uses of *Herpestis monniera*. J. Ind. Med. Assoc. 1931; 1: 60-69.
15. Chaterjee N, Rastogi RP, Dhar ML. Chemical examination of *Bacopa monneri*. Indian J. Chem. 1965; 3: 24-29.
16. Basu N, Rastogi RP, Dhar ML. Chemical examination of *Bacopa monniera* westst: Part III- Bacoside B. Indian J. Chem. 1967; 5: 84-86.
17. Jain P, Kulshresta DK. Bacoside A1, a minor saponin from *B. monniera*. Phytochemistry 1993; 33: 449-451.

18. Rastogi S, Pal R, Kulshreshtha K. Bacoside A3—a triterpenoid saponin from *B. monniera*, Phytochemistry, 1994; 36: 133-137.
19. Shashtri MS, Dhalla NS, Malhotra CL. Chemical investigation of *Herpestis monniera* Linn (Brahmi). Indian J. Pharm. 1959; 21: 303-304.
20. Basu UP, Dutta T. The structure of monnierin. Tetrahedron Lett. 1967; 2931-2937.
21. Schulte KE, Rucker G, Etkersch M. Nicotin and 3-formyl-4-hydroxy-2H-pyranaus *Herpestis monniera*. Phytochemistry 1972; 11(8): 2649-2651.
22. Chaterjee N, Rastigi RP, Dhar ML. Chemical examination of *Bacopa monniera* Wettst. Part I: Isolation of chemical constituents. Indian. J. Chem. 1963; 1: 212-215.
23. Singh HK, Dhawan BN. The effect of *Bacopa monniera* Linn. (*Brāhmi)* extract on avoidance responses in rat. J. Ethanopharmaco. 1982; 5 (2): 205 -214.
24. Deepak M, Sangli GK, Arun PC, Amit A. Quantitative determination of the major saponin mixture bacoside A in Bacopa monnieri by HPLC. Phytochem Anal. 2005; 16(1): 24-29.
25. Srivastava P, Raut HN, Puntambekar HM, Desai AC. Stability Studies of Crude Plant Material of Bacopa monnieri and Quantitative Determination of Bacopaside I and Bacoside A by HPLC. Phytochem Anal. 2012; 6(12): 147-153.
26. Phrompittayarat W, Wittaya-areekul S, Jetiyanon K, Putalun W, Tanaka H, Ingkaninan K. Stability studies of saponins in Bacopa monnieri dried ethanolic extracts. Planta Med. 2008; 74(14): 1756-1763.
27. McLaughlin JL, Chang CJ, Smith DL. Simple bench-top bioassay (brine shrimp and potato discs) for the discovery of plant antitumour compounds. In Human Medical Agent from Plants. Kinghorn, A.D and Balandrin, M.F (Eds), ASC Symposium, Washington D.C. American Chemical Society. Am. Chem. Soc. Sympos. Ser 1992; 534:112-137.
28. McLaughlin JL, Rogers LL, Anderson JE. The use of biological assay to evaluate botanicals. Drug Inform J 1998; 32:513-524.
29. Souza PD, Deepak M, Rani P, Kadamboor S, Mathew A, Chandrashekar AP, Agarwal A. Brine shrimp lethality assay of *Bacopa monnieri*. Phytother Res 2002; 16(2): 197-198.
30. Sivaramakrishna C, Rao VC, Trimurtulu G, Vanisree M, Subbaraju GV. Triterpenoid glycosides from *Bacopa monniera*. Phytochemistry 2005; 66: 2719-2728.
31. Bhakuni DS, Dhar ML, Dhar MM, Dhawan BN, Mehrotra BN. Screening of Indian plants for biological activity. Indian J Exp Biol 1969; **7**(4): 250-262.
32. Elangovan V, Govindasamy S, Ramamoorthy N, Balasubramanian K. In vitro
studies on the anticancer activity of *Bacopa monniera*. Fitoterapia 1995; 66: 211-215.

33. Charles PD, Ambigapathy G. *Bacopa monniera* leaf extract up-regulates tryptophan hydroxylase (TPH2) and serotonin transporter (SERT) expression: implications in memory formation. J Ethnopharmacol 2011; 134(1): 55-61.
34. Rajan KE Singh HK, Parkavi A, Charles PD. Attenuation of 1-(m-chlorophenyl)-biguanide induced hippocampus-dependent memory impairment by a standardised extract of *Bacopa monniera* (BESEB CDRI-08). Neurochem Res 2011; 36(11): 2136-2144.
35. Saraf MK Prabhakar S and Anand A. *Bacopa monniera* Attenuates Scopolamine-Induced Impairment of Spatial Memory in Mice. Evid Based Complement Alternat Med 2011; doi:10.1093/ecam/neq038.
36. Vollala VR, Upadhya S, Nayak S. Enhanced dendritic arborization of hippocampal CA3 neurons by *Bacopa monniera* extract treatment in adult rats. Rom J Morphol Embryol 2011; 52(3): 879-886.
37. Vollala VR, Upadhya S, Nayak S. Enhancement of basolateral amygdaloid neuronal dendritic arborization following *Bacopa monniera* extract treatment in adult rats. Clinics (Sao Paulo) 2011; 66: 663-671.
38. Vollala VR, Upadhya S, Nayak S. Enhanced dendritic arborization of amygdala neurons during growth spurt periods in rats orally intubated with *Bacopa monniera* extract. Anat Sci Int. 2011; 86(4): 179-188.
39. Jyoti A, Sharma D. Neuroprotective role of *Bacopa monniera* extract against aluminium-induced oxidative stress in the hippocampus of rat brain. NeuroToxicology 2006; 27(4): 451-457.
40. Pal R, Sarin JP. Quantitative determination of Bacosides by UV spectrophotometry. Indian J. Pharm Sci 1992; 54:17-18.
41. Jyoti A, Sethi P, Sharma D. *Bacopa monniera* prevents from aluminium neurotoxicity in the cerebral cortex of rat brain. J. Ethnopharmcol 2007; 111(1): 56-62.
42. Sumathi T Shobana C, Christina j, Anusha C. Protective Effect of *Bacopa monniera* on Methyl Mercury-Induced Oxidative Stress in Cerebellum of Rats. Cell Mol Neurobiol 2012; 32: 979-987.
43. Tripathi YB Chaurasia S. Tripathi E. *Bacopa monniera* Linn. as an antioxidant: mechanism of action. Indian J Exp Biol 1996; 34: 523-526.
44. Sharan SV, Chaitanya S, Srinivasa RB, Meena V. In Vitro Anti-oxidant Activity and Estimation of Total Phenolic Content in the Methanolic Extract of *Bacopa monniera*. Rasayan J. Chem 2011; 4(2): 381-386.
45. Rashid S, Lodhi F, Ahmad M, Usmanghani K. Cardiovascular effects of *Bacopa monnieri* (L.) pennel extract in rabbits. Pak. J. Pharm. Sci 1990; 3(2): 57-62.
46. Dar A, Channa S. Relaxant effect of ethanol extract of *Bacopa monniera* on trachea, pulmonary artery and aorta from rabbit and guinea-pig. Phytother. Res 1999; 11: 323-325.
47. Dorababu M, Prabha T, Priyambada S, Agrawal VK. Effect of *Bacopa*

monniera and *Azadirachta indica* on gastric ulceration and healing in experimental NIDDM rats. Indian J. Exp. Biol 2004; 42(4): 389-397.

48. Dar A, Channa S. Calcium antagonistic activity of *Bacopa monniera* on vascular and intestinal smooth muscles of rabbit and guinea-pig. J. Ethnopharmacol 1999; 66: 167-174.
49. Channa S, Dar A, Anjum S, Atta-ur-Rahman YM. Anti-inflammatory activity of *Bacopa monniera* in rodents. J. Ethnopharmacol 2006; 104(1-2): 286-289.
50. Vohora SB, Khanna T, Athar M, Ahmad B. Anagelesic activity of bacosine, a new tritepene isolated from *Bacopa monniera*. Fitoterapia 1997; 68(4): 361-365.
51. Ravikumar S, Nazar S, Nuralshiefa A, Abideen S. Antibacterial activity of traditional therapeutic coastal medicinal plants against some pathogens. Journal Environmental Biology J. Environ. Biol 2005; 26(2): 383-386.
52. Sumathi T, Niranjali, Devaraj S. Effect of *Bacopa monniera* on liver and kidney toxicity in chronic use of opioids. Phytomed 2009; 16(10): 897-903.
53. Sumathy T, Subramanian S, Govindasamy S and Balakrishna K. Protective role *of Bacopa monniera* on morphine induced hepatotoxicity in rats. Phytother. Res 2001; 15(7): 643-645.
54. Prasad S, Kashyap RS, Deopujari JY, Purohit HJ. Effect of *Fagonia Arabica* (Dhamasa) on in vitro thrombolysis. BMC Compl. Alt. Med 2007; 7: 36.
55. Izzo AA, Ernst E. Interactions between herbal medicines and prescribed Drugs; A systematic review. Drugs 2001; 61: 2163-2175.
56. Gohil KJ, Patel JA. Herb-drug interactions: A review and study based on assessment of clinical case reports in literature. Ind. J. Pharmacol 2007; 39: 129 -139.
57. Singh A, Singh SK. Evaluation of antifertality potential of brahmi in male Mouse. Contraception 2009; 79: 71-79.
58. Pase MP, Kean J, Sarris J, Neale C, Scholey AB, Stough C. The cognitive-enhancing effects of *Bacopa monnieri:* a systematic review of randomized, controlled human clinical trials. J Altern Complement Med 2012; 18(7): 647-652.
59. Neale C, Camfield D, Reay J, Stough C, Scholey A. Cognitive effects of two nutraceuticals Ginseng and Bacopa benchmarked against modafinil: a review and comparison of effect sizes. Br J Clin Pharmacol 2013; 75: 728-737.
60. Singh M, Murthy V, Ramassamy C. Neuroprotective mechanisms of the standardized extract of *Bacopa monniera* in a paraquat/diquat-mediated acute toxicity. Neurochemistry International 2013; 62: 530–539.