BACOPA

Bacopa monnieri (L.) Wettst.

Family

Plantaginaceae, the plantain family. Formerly the Scrophulariaceae family, the figwort family.

Parts Used

Herb.

Description

Bacopa is also known as water hyssop (a popular aquarium plant) and brahmi (after the Hindu creator god Brahma) and is not to be confused with other species also known as brahmi such as gotu kola *(Centella asiatica)*. Native to Australia and India, bacopa is a creeping, succulent perennial that grows naturally in moist or wet places such as the borders of irrigated fields, streams, water channels and wells. It has small oblong leaves and light purple or white flowers[1]

Traditional Use

Bacopa is a very important plant in Ayurvedic medicine where it has been used for almost 3000 years. Throughout this time it has been associated with a variety of health benefits including heightened learning capacity, promoting memory and concentration, as a nerve tonic, for psychological disorders, for treating skin diseases, fever, oedema, anaemia, increased frequency and cloudiness of urine and to support cardiovascular health. Bacopa is recommended in various Ayurvedic texts to be taken during each decade of life after the first decade. It was described around the 6th century A.D. in texts such as the Charaka Samhita, Athar Ved and Susrutu Samhita as a nootropic (medhya rasayana) herb taken to sharpen the intellect and improve mental deficits. It was also said to be used by ancient Vedic scholars to memorise lengthy sacred hymns and scriptures. As mentioned

above the common name brahmi is derived from the word "brahma", the creator of the universe in the Hindu pantheon. Because the brain is the centre for creative activity any compound that improves brain health in Ayurveda is called brahmi, which also means "bringing knowledge of the supreme reality". In Siddha (Tamil) medicine it is used for constipation, painful urination, oedema, nervous debility and poor memory and in Unani (Islamic) medicine for treatment of brain and nervous weaknesses. It is currently being marketed in Western countries as a memory enhancing agent.[2,3,4,5]

Constituents

Triterpenoid saponins (bacoside A, bacoside B), flavonoids (apigenin), alkaloids, glycosides, D-mannitol, stigmasterol.[6]

Actions

Nootropic, anxiolytic, sedative, nervine tonic, adaptogen, neuroprotective, antioxidant, antidepressant, anti-inflammatory, vasodilator, antinociceptive, mild anticonvulsant.

Pharmacological Activity

Neuroprotective, Nootropic and Antioxidant Activity

The scientific significance of bacopa in improving memory and learning skills was first published in 1982 and since then it has been studied extensively in various *in vitro* and animal models, and humans, to determine the numerous properties it exhibits.[8] This monograph will focus on the human studies.

Recent clinical studies on bacopa (see below) have reported significant improvements on various aspects of memory and learning when bacopa extract is taken long term including in healthy older adults, as well as in a population of older adults with age-associated memory impairment. The postulated mechanisms of action on the central nervous system are varied and include the modulation of cholinergic densities and acetylcholine levels, beta amyloid scavenging properties, scavenging of free radicals, increasing cerebral blood flow as well as anxiolytic processes.[9,10]

A 2019 research paper on bacopa found that, overall, studies have concluded that bacopa can be used for treatment of Alzheimer's disease and other neurological disorders.[11]

A randomised double-blind, placebo-controlled noncrossover, parallel trial evaluated the effect of bacopa on the memory of medical students for six weeks. This was a unique study because it was done on a group of individuals with already high cognitive abilities. Sixty medical students of either gender from second year of medical school received either 150mg of standardised bacopa, or matching placebo, twice daily for six weeks. Statistically significant improvement was seen in the tests relating to the cognitive functions with use of bacopa. Blood biochemistry also showed a significant increase in serum calcium levels (still within normal range). To make a standardised product the plant material was washed with water. After discarding the water the material was dried at 50 degrees Celsius for 12 hours. The dry material was extracted with four volumes of methanol twice at 60 degrees Celsius. The methanol extract was concentrated and the material was spray dried to get a powder. The extract contained 45% bacopa saponins.[12]

The acute effects of standardised bacopa (320 and 640mg doses) on stress and mood swings generated by multitasking were demonstrated in a double-blind, placebo-controlled clinical trial involving 17 healthy volunteers. Bacopa supplementation reduced stress as observed by reduction in cortisol levels and alleviated mood in these participants. It was concluded that acute bacopa supplementation produced some adaptogenic and nootropic effects.[13]

An open label study showed that standardised bacopa (225mg per day for six months) produced significant improvement in attention deficit hyperactivity disorder (ADHD) symptoms of participants (31 children, ages six to 12). In this study the symptom scores for restlessness were reduced in 93% of children, while self-control was improved in 89% of ADHD participants. The attention deficit symptoms were also reduced in 85% of children. Learning problems, impulsivity and psychiatric problems symptom scores were also reduced. The efficacy of bacopa in this context has been attributed to its neuroprotective and antioxidant effects, as well as regulation of dopamine, and inhibition of cholinesterase.[14]

A meta-analysis compared the nootropic effects of bacopa to *Panax ginseng* and modafinil (a wakefulness promoting drug used to treat excessive daytime sleepiness, such as narcolepsy or for shift workers, but also used as a cognitive enhancer). Bacopa administration appears to predominantly enhance learning and memory with effects restricted to chronic administration. Chronic bacopa use produced the most consistent and largest effect sizes of the three. Bacopa showed small to medium effect sizes for attention and information processing tasks. Larger effect sizes were evident for auditory verbal learning tasks. These findings substantiate the potency of bacopa, particularly in measures of verbal recall. Remarkably these contemporary findings appear to support the above alleged use of bacopa by scholars in Vedic antiquity memorising lengthy hymns.[15,16]

A systematic review concluded that three months' bacopa supplementation improves learning and free recall of information in healthy people. Six studies met the final inclusion criteria and were included in the review. Trials were all conducted over 12 weeks. Across the trials three different standardised bacopa extracts were used at dosages of 300 to 450mg per day.[17]

In older adults without dementia, compared with the placebo group, daily administration of standardised bacopa improved power and speed of attention, continuity of attention and quality and speed of memory (150mg twice daily for three months). The randomised double-blind, placebo-controlled study was performed on 60 people. To standardise the herb the aerial part of bacopa was collected, cut into small pieces and dried in a hot air oven at 50 degrees Celsius and then crushed. This dried powder was percolated for eight hours with 95% ethanol (1g in 6mL) three times and then filtered. The filtrate was evaporated under reduced pressure. The percent yield obtained was 10 per cent. The total saponin content was determined using HPLC five per cent (w/w) of the crude ethanol extract and was comprised of a mixture of bacoside A3, bacopaside II, bacopasaponin X, bacopasaponin C, and bacopaside I. The researchers postulated that the mechanism for the results might be that bacopa suppresses the function of acetylcholinesterase in the cerebral cortex, especially in the parietal cortex and hippocampus, leading to increased available acetylcholine in that area, giving rise to enhanced attention and memory operation capability or cognitive processing and finally resulting in enhanced working memory.[18]

Acute neurocognitive effects were identified for bacopa in a double-blind, placebo-controlled, crossover study involving 24 healthy participants who took standardised bacopa extract. Two doses of bacopa (320mg and 640mg) were compared to each other and placebo for effects on participants' performance on six repetitions of a cognitively demanding series of tests. The treatment dose of 320mg improved performance on the first, second and fourth repetition of the tests.[19]

A systemic review of clinical trials to assess the current evidence of herbal and nutritional interventions for ADHD found bacopa is a promising candidate for future research. Bacopa could provide potential efficacy in improving attentional and hyperkinetic disorders via a combination of cognitive enhancing and sedative effects.[20]

An open label, prospective, uncontrolled, non randomised trial reported that in 39 Alzheimer's disease patients bacopa (standardised to 300mg taken twice a day) improved attention, language, writing and comprehension following six months' intervention. The patients involved in this trial also reported improvement in their quality of life and a decrease in irritability and insomnia. To standardise the plant material it was washed with water. After discarding the water the material was dried at 50 degrees Celsius for 12 hours. The dry material was extracted with four volumes of methanol twice at 60 degrees Celsius. The methanol extract was concentrated and the material was spray dried to get powder.[21]

Bacopa significantly improved memory acquisition and retention in healthy older Australians in a randomised, double-blind, placebo-controlled study. Ninety-eight healthy participants aged over 55 years of age were randomised to receive 300mg per day of a 20:1 alcohol extract standardised to contain 40 to 50% bacosides or placebo for 12 weeks. The bacopa group showed significantly improved memory acquisition and retention.[22]

Bacopa showed potential for safely enhancing cognitive performance in aging people in a randomised, double-blind, placebo-controlled

clinical trial. The extract was manufactured from the dried aerial parts of bacopa from India. It was extracted with methanol:water (70:30) to produce a 50:1 dry extract with a minimum of 50% bacosides A and B. This extract was combined with pharmaceutical grade excipients, calcium hydrogen phosphate, cellulose, sodium starch glycolate, magnesium stearate and hypromellose to produce an oval tablet that was given a final brown film coat. Each tablet contained the equivalent of approximately 15g bacopa and 150mg of bacosides A and B. Each of the 48 healthy participants, 65 years or older, who completed the study were given either 300mg once a day of the bacopa extract or placebo for 12 weeks. Over the course of the study the bacopa group had improved delayed recall memory and reaction times assessing the ability to ignore irrelevant information, while the placebo group experienced no change. The bacopa group also experienced decreased depression and anxiety while the placebo recipients increased in both.[23]

In another study 62 healthy volunteers were given either 300mg of bacopa, standardised to at least 55% bacosides, or placebo, daily for 90 days. Participants underwent a cognitive assessment at baseline and at the end of the study. The bacopa group experienced significantly improved performance in spatial working memory accuracy.[24]

An earlier double-blind, placebo-controlled trial by the same Australian author, using the same product on 46 healthy volunteers aged 18 to 60 years old, evaluated their performance on a battery of cognitive tests after five weeks and after 12 weeks of 300mg of bacopa extract daily. The investigators reported significant improvements in neuropsychological testing measures including statistically significant changes in learning rate, information processing speed and reduced anxiety at 12 weeks but not at five.[25]

Another three month randomised, double-blind, placebo-controlled clinical trial to test the effect of bacopa on anxiety and various memory functions in 37 healthy adults, aged 40 to 65 years old, showed a significant effect of bacopa (300mg for persons under 90kg, and 450mg for persons over 90kg, equivalent to 6g and 9g dried rhizome, respectively) on the retention of new information in delayed recall of word pairs.[26]

A third trial in 20 people over 55 with age associated memory impairment, again with three months of treatment, produced significant improvement on mental control, logical memory and paired associated learning with no loss of the cognitive gains four weeks after ending active treatment. The subjects received either 125mg of standardised bacopa, or placebo, twice a day for 12 weeks. Each subject was evaluated for cognition with a battery of tests comprising mental control, logical memory, digit forward, digit backward, visual reproduction and paired associate learning.[27]

In a nondouble-blinded study conducted in 40 children aged six to eight years from rural India those receiving bacopa syrup (350mg) three times daily for three months showed increased exploratory drive, improved perceptual images of patterns and increased perceptual organization and reasoning ability compared with children who received placebo.[28]

Bacopa is an antioxidant with *in vivo* and *in vitro* studies indicating several modes of action that may protect the brain against oxidative damage including the binding and detoxification of metal ions, free radical scavenging and increasing antioxidant activity.[29]

An *in vivo* study found that the neuroprotective and antioxidant activity of bacopa may alleviate ischemia induced brain injury.[30]

An *in vivo* study on rats concluded that a standardised extract of bacopa possesses potent adaptogenic activity.[31]

Mechanisms involved in the neuroprotective and memory enhancing effects of bacopa may include the binding and detoxification of metal ions and metal ion chelating effects. Metal chelation has been suggested as a potential therapy to reduce oxidative stress. Hydrogen peroxide is generated during the beta-amyloid aggregation process that leads to fibril formation. Interactions of divalent metals such as iron and copper with hydrogen peroxide can produce hydroxyl radicals and highly toxic reactive oxygen species. Both of these metal ions may contribute to membrane associated oxidative stress. Reduction of hydrogen peroxide formation, or blocking the effects of hydrogen peroxide on DNA, proteins and lipids, is a potentially important mechanism of action to be explored in developing

effective Alzheimer's disease therapeutic agents. The results of an *in vitro* study demonstrated that bacopa reduced divalent iron suggesting that the antioxidant properties of bacopa include chelation of divalent iron which can decrease the formation of reactive oxygen species. An earlier study on the *in vitro* antioxidant properties of bacopa found it to be a potent antioxidant and suspected it to work dose dependently as a metal chelator and perhaps also a free-radical chain reaction-breaker.[32,33]

The findings of an *in vivo* study suggest that bacopa has the potential to protect rat brains from oxidative damage resulting from methyl mercury induced neurotoxicity. After 21 days treatment the researchers found that the methyl mercury exposure in rats' cerebellums significantly inhibited the activities of important enzymes that protect the cells from oxidative damage by reactive oxygen species. These alterations were prevented by the administration of bacopa. Bacopa also positively influenced behavioural interferences in the methyl mercury exposed animals.[34]

An *in vivo* study has shown that bacopa can possibly lessen lead induced oxidative stress in tissues, in different regions of rat brains, by chelation and antioxidant actions. Results indicated a significant increase in oxidative stress markers in the lead treated brains but the markers were lowered after treatment with bacopa.[35]

Vasodilator Activity

In a study on the *in vitro* vasodilator properties of bacopa it was found that it decreased systolic and diastolic blood pressure without significantly affecting heart rate.[36]

Thyroid Activity

Preliminary animal research suggests that bacopa boosts T4 but not T3. Results from animal experiments have found that bacopa increases thyroxine concentrations by 41% without enhancing hepatic lipid peroxidation suggesting that it could be used as a thyroid stimulating herb.[37]

Antiepileptic Activity

Some preclinical and traditional evidence indicates that bacopa can be anti-epileptic, or anticonvulsive, and additionally that it could help attenuate some of the negative effects of anti-convulsant medications such as cognitive impairment. The results of an *in vivo* study on rats indicated bacopa is effective in promoting restorative and neuroprotective action in convulsions.[38,39]

Pain relieving Activity

In animal models bacopa has been shown to exhibit significant analgesic and antinociceptive effects comparable to morphine, which is particularly applicable in cases of neuropathic pain. Bacopa may strengthen the analgesic effects of morphine treatment while improving some of the negative effects of opioids such as depression, opioid tolerance and increased sensitivity to pain related to morphine withdrawal, while also protecting major organs against toxicity. Its pain-relieving properties are possibly mediated via COX-2 inhibitory anti-inflammatory pathways.[40]

Gastrointestinal Activity

Some *in vitro*, animal and human studies have investigated the effects of bacopa 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 bacopa may be of benefit in conditions characterised by intestinal spasm such as irritable bowel syndrome. Animal and *in vitro* studies suggested that bacopa may have a protective and curative effect on gastric ulcers and studies were reported for its antiulcerogenic activity.[41]

Indications

- Improving cognitive function, learning, memory, intelligence, mental health; and assist with exam performance and studying
- Prevention and treatment of age-related cognitive decline, menopausal cloudy thinking
- Dementia, Alzheimer's disease, Parkinson's disease and other neurodegenerative disorders
- Chronic fatigue syndrome, fibromyalgia syndrome
- Memory problems and mood disorders associated with epilepsy and migraine
- Ischaemic stroke rehabilitation
- Anxiety, depression, stress, insomnia, nervous exhaustion, debility, mental overwork

- Prophylactic reduction of oxidative damage (oxidative stress is one of the most important factors in aging and age-related illnesses)
- Cerebral atherosclerosis
- Hypothyroidism
- Chronic pain
- To speed up recovery from head trauma
- Gastric ulcer treatment, irritable bowel syndrome
- Possible use in attention deficit hyperactivity disorder (ADHD)

Energetics

Cooling, bitter.[42]

Use in Pregnancy

Bacopa is recommended as a tonic for anxiety in pregnancy according to traditional Ayurvedic medicine however insufficient information is available to confirm safety during pregnancy.[43]

Contraindications

Bacopa is well tolerated however in trials using standardised bacopa the most common side effects are minor gastrointestinal disturbances, nausea, abdominal cramps, increased stool frequency and diarrhoea.[43] Caution is advised in hyperthyroidism as bacopa has been shown to significantly elevate thyroxine levels *in vivo*. The clinical significance of this finding is unknown.[44]

Drug Interactions

Bacopa appears to affect acetylcholine levels so theoretical and speculative interactions include acetylcholinesterase (AChE) inhibitors (used in Alzheimer's disease), anticholinergic drugs (used for conditions such as urinary incontinence, asthma and Parkinson's disease. Benadryl has this effect.) and serotonergic drugs for depression such as selective serotonin reuptake inhibitors (SSRIs), antidepressants such as citalopram (Celexa), fluoxetine (Prozac), fluvoxamine, paroxetine (Paxil) and sertraline (Zoloft).

Administration and Dosage

Liquid Extract:	1:1
Alcohol:	50%
Weekly Dosage:[45]	15 to 40mL

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